acatech DISCUSSION

Materials Research: Inspired by Nature

Innovation Potential of Biologically Inspired Materials

Peter Fratzl, Karin Jacobs, Martin Möller, Thomas Scheibel, Katrin Sternberg (Eds.)

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Foreword

Nature has always been a source of and inspiration for inventions and innovations. This is as true of the manufacture of sustainable products based on biogenic starting materials as it is of the development of bio-inspired materials, for example for lightweight construction in the building and transport sector, novel surfaces and even health care. Many bio-inspired products have been in use for some time: hook and loop fasteners or water-repellent coating materials and surfaces inspired by the lotus leaf are well-known examples of engineering imitating Nature, or biomimetics in the narrowest sense.

In recent years, both science and engineering have benefited greatly from dynamic developments in the "Enabling Technologies". A good example is biotechnology: since the nineteen nineties massive progress has been made, including in Germany, by bringing together life science findings and processes from the field of molecular biology with tools from completely different fields such as process engineering, automation and in particular digitalization.

The use of biotech methods, new manufacturing options such as 3D printing and increasing digitalization, in particular, continue to open up ever broader prospects for bio-inspired materials science. There is consequently a need for modern, highly efficient analytical methods, semi-automated systems and the evaluation of significant volumes of data.

If biological materials and processes are being ever better researched and understood and in some cases modified and further developed by engineers, then new applications are also possible: for example "smart materials" capable of interacting with their environment may be obtained. The innovation potential of "Bits meet Bio" is particularly relevant, and not just to medical applications.

Biologically inspired materials research can also play an important role in achieving the United Nations' Sustainable Development Goals and in implementing the German government's sustainable development strategy. No new products should be developed without careful attention being given to future repair mechanisms, reusability or biodegradability. Materials are therefore key to the development of sustainable products and can make a significant contribution to the current "Circular Economy Initiative Deutschland" established by the German Federal Ministry of Education and Research.

This discussion paper presents a wide range of examples from various disciplines – from chemistry and energy through medicine and robotics to art and design. The range of examples is impressive and underlines the interdisciplinarity and the major innovation potential of this field of research. We need to translate Germany's excellent research status into sustainable value creation.

At this juncture, we should like to offer our sincere thanks to everyone who has contributed to this DISCUSSION, the authors, other experts from the worlds of science, associations and business who have made themselves available for interview, and to the project team.

Prof. Dr. Dieter Spath
President acatech

Prof. Dr. Martina Schraudner
Member Executive Board acatech

Synopsis and Areas of Research

Innovation Potential of Biologically Inspired Materials

Peter Fratzl, Karin Jacobs, Martin Möller, Thomas Scheibel, Katrin Sternberg

Materials already play a crucial part in virtually all products and areas of technology. Their significance to our daily lives is set to increase still further: demographic changes, greater shortages of resources and climate change require a more sustainable economy, which is where materials research is expected to make an even greater contribution. Key concepts, such as more efficient materials synthesis and less wasteful materials production, recyclable or biodegradable products, smart, i.e. self-repairing or self-adapting materials or indeed increasing customization, for example in medical applications make one thing clear: changing requirements lead to increased complexity in materials research.

Researchers are well aware that composition and structure of materials interrelate with their properties and functions. Despite recent progress with synthesis and manufacturing processes over a wide range of scales, they are nowhere near reaching Nature's levels of performance. Using small numbers of building blocks, Nature efficiently synthesizes a multiplicity of extremely complex structures with different functions as well as adaptation capabilities. The resultant materials are naturally recycled and combine efficiency and functionality into one system, sometimes in a quite astonishing way.

That is why the "biologicalization" of materials research – that is to say taking inspiration from Nature as to how biological resources, principles and methods can be used – holds major innovation potential for Germany as a location for research and business.

The first successful examples, such as the increasing role played by bio-inspired synthesis building blocks and polymers, are making it clear that the reorientation of materials research has already started and involves all-important future fields, such as lightweight construction, medicine, robotics or energy.

In conjunction with increased digitalization and progress in Artificial Intelligence, it will for example be possible to develop materials, which have information about their subsequent use incorporated into their structure from the outset. This holds the promise of progress in additive manufacturing such as 3D printing of tissue, for example. Self-assembly processes and novel self-healing materials with an extended service life do not only play a part in medicine and pharmaceutics, but will increasingly be used in all fields of technology. More efficient cross-scale processing methods for targeted nano- and micropatterning of surfaces can be used not only in the development of adhesives and bonding agents but also for the surface treatment of ships' hulls. Soft robotics enables mechanically rigid robotics to evolve towards more seamless interaction with the natural environment.

It is clear from these selected examples that bio-inspired materials have the potential to make a decisive impact in the next few years on Germany as a location for research and technology. They will make a major contribution to achieving the targets set by Germany's Hightech Strategie 2025 and to the interdisciplinary "From Biology to Innovation" agenda, which is currently being put together, and to Germany's yet to be developed "Circular Economy" roadmap. With its excellent research landscape and as a prime location for business and innovation, Germany is in a very favourable position to make a significant contribution to this important field in terms of academic institutions, start-ups, SMEs and industry. High skill levels in process engineering, biotechnology and Industry 4.0 will allow Germany to benefit from competitive advantages associated with innovative materials in the medium term and, in a longer perspective, of an improved resource conservation.

To ensure that the innovation potential of materials science will be reflected in patents, in entrepreneurial activities and products, as well as in customer demand and jobs, overarching processes are needed which encompass the various disciplines and procedures across the entire value chain in an interdisciplinary and integrated manner. A striking aspect of the contributions to this DISCUSSION is just how important interdisciplinary approaches are in this particular area of research. Knowledge transfer requires the development of new formats for interdisciplinary cooperation in research and teaching. In addition to process engineering, digitalization and Artificial Intelligence provide an interface with bio-inspired materials science and need to be included in the necessary basic skills.

There is a need for a wider interdisciplinary framework, if multidisciplinary approaches to research are to be promoted. For instance, talented young scientists working across disciplines need to have the same career opportunities as are available to those engaged in single-discipline research, where specific measures of success have already been established, such as monographs, publications in peer-reviewed specialist journals, conferences or exhibitions, which have to be adapted to the needs of multidisciplinary research.

Technology transfer starts off with technology evangelism and requires cooperation between multiple stakeholders. In particular with materials inspired by Nature, which are produced by individual growth and often result in tailor-made materials and products, upscaling of production processes is a particular challenge which needs to be separately researched and tested. Given suitable support and funding, start-ups could be particularly helpful in this regard.

Sustainability and resource conservation need to be considered from the outset and Life-Cycle Assessments (LCA) should be incorporated as early as possible into the process of material and product development.

Regulatory developments and approval standards have not so far been keeping up with the unusual requirements of responsive, adaptive or self-healing materials, and an early discussion on these aspects has to accompany the development of such materials.

The same is true when it comes to presenting the innovation potential of bio-inspired materials research to the general public. As with other fields of research, transparent communication and a social dialogue are required.

This acatech DISCUSSION use examples to demonstrate the multiplicity of structural, functional and synthesis principles with which Nature is already inspiring and advancing materials research. For various fields of application, examples of material-based innovations at the interface of biology and technology show how they may benefit society and economy. In addition, a brief overview is provided on the status of national and international research.

Based on the contributions to the DISCUSSION by various authors and on the interviews conducted with associations, businesses and scientists, the project group has identified the following important research areas:

1. **Biologically Inspired Synthesis**
   When synthetic materials are compared with naturally grown matter, it becomes obvious how much more varied and complex the structures of the latter are. This is primarily due to the growth process, in which building blocks are assembled step by step into ever larger units. Growth takes place under ambient conditions, i.e. under temperatures, pressures, and solution conditions that correspond to the immediate environment. In such processes, raw materials and energy are taken directly from the environment.

2. **Multifunctionality by the Combination of Material Properties**
   A wide range of examples from Nature show that one material can combine apparently incompatible properties such as being hard and tough, light and strong or refractory. Following such examples will open the possibility of developing new materials with previously unknown combinations of properties, while production needs to remain as efficient as possible in terms of resources and energy.

3. **Novel Active Properties of Materials**
   Natural growth processes are dynamic and generally allow continuous adaptation to requirements. This adaptability is displayed by plants during growth and by animal organisms throughout their lives, which is exemplified by the amount of muscle and bone that can be enhanced by physical training. Studying such processes should provide concepts and allow the development of new types of responsive and adaptive material systems.

4. **Complex Materials as Technical Systems**
   In Nature, the terms material and system tend to become blurred: for instance, plant stems and muscles are simultaneously material and organ, whereby the complexity of the material structure anticipates the function of the organ. On the basis of this concept, one should explore ways of combining the fields of materials development and systems design in many areas of technology. The field of microelectronics may serve as a model, because this is one area where materials development and systems integration already go hand in hand.

5. **Information Storage in Materials Structures**
   The internal structure of biological materials, for example porosity, fibre arrangements, lamellar structures etc., determines their functional properties and thus also those of the overall system. If these structures are adapted during growth (or in industrial systems during production) to their subsequent function, for example as a sensor, actuator, signal generator etc., the information about this function is stored in the structure of material. Systematic research into this analogue information storage holds great promise, in particular in the following technological field.

6. **Smart Materials as Essential Building Blocks of Digitalization**
   The rapidly increasing digitalization of all technical operations is making "smart" materials ever more important. The previously assumed paradigm of a separation between "passive" material and "active" information systems cannot be maintained due to finite (energy) resources and computing capacities. The structure of materials will have to be considered in such a way that they become highly efficient analogue machines on a micro- and nanometre scale and thus complement the flexibility of digital intelligence.

Project

Project title

Research into the Innovation Potential of Biologicalization in Materials Science

Project leader

- Prof. Dr. Peter Fratzl, Max Planck Institute of Colloids and Interfaces

Project group

- Prof. Dr. Peter Fratzl, Max Planck Institute of Colloids and Interfaces
- Prof. Dr. Karin Jacobs, Saarland University
- Prof. Dr. Martin Möller, Leibniz Institute for Interactive Materials
- Prof. Dr. Thomas Scheibel, University of Bayreuth
- Prof. Dr. Katrin Sternberg, Aesculap AG

Authors

- Prof. Dr. Markus Antonietti, Max Planck Institute of Colloids and Interfaces
- Prof. Dr. Eduard Arzt, INM – Leibniz Institute for New Materials
- Prof. Dr. Paul W. M. Blom, Max Planck Institute for Polymer Research
- Prof. Dr. Aldo R. Boccaccini, Friedrich-Alexander University Erlangen-Nürnberg
- Prof. Dr. Markus J. Buehler, Massachusetts Institute of Technology MIT
- Prof. Dr. Ingo Burgert, ETH Zurich
- Prof. Dr. Chokri Cherif, Technische Universität Dresden
- Prof. Dr. Helmut Cölfen, University of Konstanz
- Prof. Dr. Hendrik Dietz, Technical University of Munich
- Prof. Dr. Claudia Doblinger, Technical University of Munich
- Prof. Dr. Christoph Eberl, Fraunhofer Institute for Mechanics of Materials IWM
- Prof. Dr. Claudia Fischbach-Teschl, Cornell University
- Prof. Dr. Peter Fratzl, Max Planck Institute of Colloids and Interfaces
- Dr. Michael Friedman, Humboldt-Universität zu Berlin
- Prof. Dr. Magnus Fröhling, Technical University of Munich
- Dr. Paschalis Gkoupidenis, Max Planck Institute for Polymer Research
- Prof. Dr. Sebastian J. Goerg, Technical University of Munich
- Prof. Dr. Stanislav Gorb, Kiel University
- Prof. Dr. Jürgen Groll, University of Würzburg
- Prof. Dr. Matthew Harrington, McGill University
- Dr. René Hensel, INM – Leibniz Institute for New Materials
- Prof. Dr. Karin Jacobs, Saarland University
- Dr. Tobias Keplinger, ETH Zurich
- Prof. Dr. Jan Knippers, University of Stuttgart
- Dr. Karin Krauthausen, Humboldt-Universität zu Berlin
- Prof. Dr. Cecilia Laschi, Sant'Anna School of Advanced Studies
- Prof. Dr. Thomas Lenarz, Hannover Medical School
- Prof. Dr. Karl Leo, Technische Universität Dresden
- Prof. Dr. Markus Linder, Aalto University
- Dr. Liliana Liverani, Friedrich-Alexander University Erlangen-Nürnberg
- Dr. Barbara Mazzolai, Istituto Italiano di Tecnologia
- Prof. Dr. E. W. Meijer, Eindhoven University of Technology
- Prof. Achim Menges, University of Stuttgart
- Prof. Dr. Martin Möller, Leibniz Institute for Interactive Materials
- Dr. Karsten Moh, INM – Leibniz Institute for New Materials
- Andreas Nettsträter, Fraunhofer Institute for Material Flow and Logistics IML
- Dr. Richard M. Parker, University of Cambridge
- Christian Prasse, Fraunhofer Institute for Material Flow and Logistics IML
- Prof. Christiane Sauer, weißensee kunsthochschule berlin
- Prof. Dr. Wolfgang Schäffner, Humboldt-Universität zu Berlin
- Prof. Dr. Thomas Scheibel, University of Bayreuth
- Prof. Dr. Thomas Schimmel, Karlsruhe Institute of Technology
- Dr. Detlef Schumann, Aesculap AG
- Prof. Dr. Metin Sitti, Max Planck Institute for Intelligent Systems
- Dr. Olga Speck, University of Freiburg
- Prof. Dr. Thomas Speck, University of Freiburg
- Prof. Dr. Katrin Sternberg, Aesculap AG
- Dr. Markus Storr, Gambro Dialysatoren GmbH, Baxter International Inc.
- Prof. Dr. Michael ten Hompel, Fraunhofer Institute for Material Flow and Logistics IML
- Dr. Silvia Vignolini, University of Cambridge

- Prof. Dr. Carsten Werner, Leibniz Institute for Polymer Research
- Dr. Marc-Denis Weitze, acatech Office
- Dr. Birgit Wiltschi, ACIB – Austrian Centre of Industrial Biotechnology
- Prof. Dr. Cordt Zollfrank, Technical University of Munich

Interviewees and further experts

- Dr. Horst Beck, Henkel AG & Co. KGaA
- Prof. Dr. Alexander Böker, Fraunhofer IAP
- Dr. Viola Bronsema, BIO Deutschland e.V.
- Prof. Dr. Stefan Buchholz, Evonik Creavis GmbH
- Prof. Dr. Xiaodong Chen, Nanyang Technological University
- Dr. Frank O. R. Fischer, Deutsche Gesellschaft für Materialkunde e.V. (DGM)
- Prof. Dr. Robert Full, University of California, Berkeley
- Prof. Dr. Santiago J. Garcia Espallargas, TU Delft
- Karoline von Häfen, Festo AG & Co. KG
- Alex Horisberger, BASF SE
- Prof. Dr. Olli Ikkala, Aalto University
- Prof. Dr. Don Ingber, Wyss Institute at Harvard University
- Prof. Dr. Lei Jiang, Beihang University
- Prof. Dr. Henk Jonkers, TU Delft & Green Basilisk
- Dr. Lutz Kloke, Cellbricks GmbH
- Andreas Mägerlein, BASF SE
- Prof. Dr. João Mano, CICECO - Aveiro Institute of Materials
- Dr. Héctor Martínez, CELLINK
- Dr. Carsten Momma, CORTRONIK GmbH
- Dr. Heinz Müller, CORTRONIK GmbH
- Dr. Jens Rieger, BASF SE
- Dr. Lin Römer, AMSilk GmbH
- Dr. Oliver Schauerte, Volkswagen Aktiengesellschaft
- Prof. Dr. Stefan Schlichter, Institut für Textiltechnik Augsburg gemeinnützige GmbH
- Prof. Dr. Sybrand van der Zwaag, TU Delft
- Prof. Dr. Kurt Wagemann, DECHEMA
- Dr. Ljuba Woppowa, VDI-Gesellschaft Technologies of Life Sciences
- Andreas Wüst, BASF SE
- Prof. Dr. Hisashi Yamamoto, Chubu University

Project coordination

- Dr. Lena Simon, Max Planck Institute of Colloids and Interfaces
- Dr. Christine Metz-Schmid, acatech Office

Editorial assistance, interviews and translations

- Dr. Lena Simon, Max Planck Institute of Colloids and Interfaces

Further assistance

- Johannes Simböck, acatech Office
- Dr. Martina Kohlhuber, acatech Office
- Farras Fathi, acatech Office
- Dr. Khashayar Razghandi, Max Planck Institute of Colloids and Interfaces

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1 Introduction

Materials are used in almost all areas and are the basis of most technical system solutions surrounding us in our daily life. Our modern urban infrastructure and architecture would be inconceivable without steel, for example. Plastics have made many products affordable to large parts of the population. Semiconductor transistors have opened up the era of information technology and digitalization. Studies show that around seventy per cent of all innovations are attributable to material developments.

Germany sells around one billion euro of materials every year and around five million jobs are dependent on them.[1] In the processing industry, which is of huge importance to Germany, materials accounted for approximately 45 per cent of total costs in 2011.[2] This social and economic significance is also the reason why a correspondingly high proportion of funding for academic research is allocated to this field: around twenty per cent of the total resources awarded to engineering sciences by DFG, the German Research Foundation, between 2014 and 2016 went to materials science and technology.[3]

While in the past, the development of new materials was crucial to the development of society and the building of our industrial civilization, today socioeconomic and environmental demands define the direction of new-materials-based innovation. This is not least the result of finite resources, growing demands for climate protection and corresponding national and international goals for sustainable development, all of which also cover the production and consumption of goods. Key concepts are circular economy, recycling and degradability of materials, leading to ever more requirements in terms of modern materials, which can only be met by increasing the structural complexity of the materials themselves. To achieve this, we will need new manufacturing technologies, and a new mindset to develop them. This is where the inspiration from Nature comes in: structural complexity and diversity, constantly adapting structures and the resulting functional characteristics show new ways to design, synthesize and process materials, which have ultimately to encompass all structural levels from the molecule to the component.

Nature fascinates and inspires in equal measure, with the many specialized biological individual and system solutions, which have adapted to the surrounding environment over millions of years of evolution. During development, living organisms have succeeded in adapting their energy and resource requirements, in gaining intelligent strategies for information processing and in recycling and running optimal, time-coordinated metabolic reactions in the highly confined spaces. The basis for these efficient biological systems is synthesis and resorption processes running both accurately and to a significant degree concurrently, self-learning and generally (energy-)efficient systems, purposefully switchable mechanisms for example for regulation and information transfer and a high degree of interaction between independent modules within a damage-tolerant overall system. This constitutes a repertoire of ideas from which materials research can learn and benefit.

It is now possible to make use of our increasing understanding of biological structures and growth processes to develop new materials. This discussion paper sheds light on the current and future potential inherent in the biologicalization of materials research, that is to say, the use of biological resources, principles and methods in the development, use and recycling of materials. The paper looks not only at progress in the analysis of biological systems and the initial implementation of biomimetic applications but also the targeted transfer of biological processes and principles. Core aspects of this application of Nature's principles to modern materials development are:

- the multicomponent structure across hierarchical levels, which is characteristic of Nature and results in materials with a high information content and makes it possible to encode new and specific functions in the material structure,
- the selection of "intelligent" (functional) structures by computer simulation and modelling,
- the integration of synthesis and manufacturing technologies, to enable the production of complex materials of this type, and
- compatibility with Nature and linkage with natural structures and functions.

1 | See Deutsche Gesellschaft für Materialkunde e.V. 2015.

2 | See Weber/Oberender 2014.

3 | See Deutsche Forschungsgemeinschaft 2018 as basis for own calculation.

To shed light on the current status of these developments, this publication provides an overview in the form of contributions which underline the importance of biologicalization in materials research. This is done by specialist contributions in selected technological areas and the approach can be divided into three basic topics:

1. inspiration from natural structures, syntheses and processes: biomimetic and bio-inspired materials for industrial applications ("materials *through* Nature")
2. use of renewable resources: natural and bio-based materials ("materials *from* Nature")
3. application as biomedical and implant materials ("materials *for* Nature").

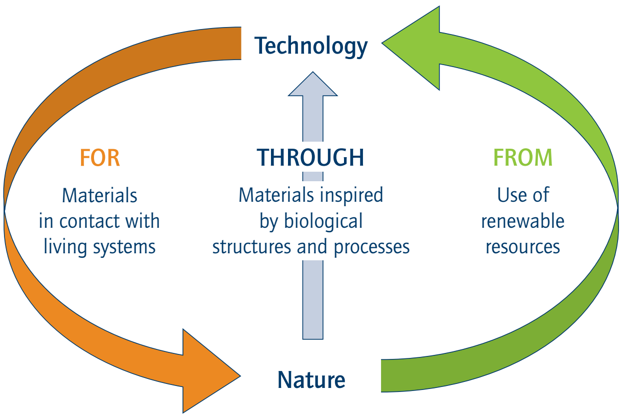

Figure 1: Alongside the use of renewable resources or the biotechnological production of materials (materials FROM Nature), and the development of materials for biomedical or agricultural applications (materials FOR Nature), biologically inspired materials science is a particularly promising area of innovation (materials THROUGH Nature) (source: Peter Fratzl, Max Planck Institute of Colloids and Interfaces).

In future, the transfer of natural basic principles to the manufacture and processing of modern materials will open up many new prospective applications. One example is the industrial application of evolution strategies, which is expected to enable mutation-induced optimization of material and component properties. This would significantly reduce time-consuming and cost-intensive development work. A deeper understanding of fundamental biological material properties, such as self-organization, repairability, adaptability and energy-efficient processes, is opening up new opportunities in terms of manufacturing methods, information processing, logistics and resource efficiency, thus improving the global competitiveness of Germany as a location for research and industry.

The rapidly increasing digitalization of all technical operations, and in particular production processes, is making "smart" materials ever more important. The previously assumed paradigm of a separation between "passive" material and "active" information systems cannot continue to be maintained due to finite resources and computing capacities. The proportion of global final energy consumption (which is growing by approx. 1.5 per cent year on year) attributable to digital technology will have grown by almost seventy per cent over the period from 2013 to 2020.[4] This is not something which can readily be reconciled with the German government's climate targets. Just as joints define movement sequences, the increasing structural complexity of material structures will encapsulate and process information relating to technical operations. In this way, materials become analogue machines on the micro- and nanometre scale, which, though reducing the flexibility of technical operations because the material structure cannot so easily be modified, increases efficiency by saving computing power and the associated energy consumption. This interface between digital and analogue information needs much more research to be defined and optimized und underpins the future of digitalization in the technical/industrial field.

Bio-inspired Materials Research – Some Examples Showing the Current State of Knowledge

If synthetic materials are compared with matter which has grown naturally, it is conspicuous how much more varied and complex natural structures are.[5] A major reason for this is in particular the growth process, in which building blocks are assembled step by step into ever larger functional units. Can inspiration from natural materials and their life cycles be used to develop innovative approaches in materials science and materials technology? What contribution could this "biologicalization" of materials science make to new technical solutions?

4 | See The Shift Project 2019.
5 | See Eder et al. 2018.

Comparison of the growth process with synthetic production methods[6] quickly leads to the following observations:

- Hierarchical structures are characteristic of natural material,[7] i.e. molecules form functional assemblies, which are in turn combined into larger units.
- The growth process is dynamic and allows continuous adaptation to the respective requirements.[8] This capacity is displayed by plants during growth and by animal organisms throughout their entire lives, for example muscle and bone mass can be adapted to more stringent requirements by physical training.
- Growth results in a particularly complex material structure, which to a significant extent already anticipates the expected function of the organ. For instance in a plant stem the distinction between material and functional organ is not possible as they constitute a unity. Muscle and liver behave similarly: they are simultaneously both organ and material. Moreover, in Nature, multifunctional properties are the rule rather than the exception.
- Growth proceeds under conditions which are adapted to the surrounding environment in terms of pressure and temperature. The primary materials and energy required are taken directly from the surrounding environment.

This makes it obvious that in general materials cannot simply be classified as metals, ceramics or polymers. The possibility of combining primary materials with one another and producing structures on different scales rapidly increases the number of hybrid material and composite variations: even paper has long been a composite of cellulose fibres and plastics-based binders. This development came about due to massive progress in synthesis and manufacturing methods and an ever improving understanding of the interrelationships between multi-scale structure (extending over many orders of magnitude) and properties.

The following synopsis provides a selective overview of current trends in this area.[9]

Multifunctionality

Modern materials have not only to fulfil individual functions such as mechanical strength or electrical, optical or magnetic properties. Rather, they are increasingly required to combine multifunctional, adaptive, interactive and stimulus-responsive material properties.[10]

In Nature, materials often meet many of these requirements, since they exhibit excellent primary material properties, such as high strength or toughness, which, combined with secondary properties, yield complex multifunctional biological systems. As a result, a range of major system features are brought together, such as high performance, damage-tolerance, adaptability, modularity and multifunctionality.[11] A number of bio-inspired materials have already found their way into everyday life, including hook and loop fasteners, self-cleaning surfaces which make use of the lotus effect, self-repairing polymer membranes, gecko tape for glue-less reversible adhesion, Sharklet AF™ (antifouling surfaces based on shark skin) and the artificial spider silk known as BioSteel®.

Hierarchical Structure

A fundamental inherent property of natural materials is their multi-scale hierarchical structure extending from the molecular to the macroscopic scale. This design enables functions to be integrated, with specific functions being established either at a single hierarchical level or over several such levels.[12] Examples of hierarchically structured systems in Nature are plant-based cell walls (including wood), chitin carapaces in crustaceans and insects, bioceramics such as diatoms and bone, and also reversible adhesion systems as in the gecko, or self-cleaning surfaces with the lotus effect.

6 | See Fratzl 2007.
7 | See Fratzl/Weinkamer 2007.
8 | See Weinkamer/Fratzl 2011.
9 | Partially published in Bargel/Scheibel 2018.
10 | See Speck et al. 2012.
11 | See Zollfrank et al. 2014.
12 | See Speck/Speck 2009.

One example of a "bio-inspired" fibre composite material is the now well-established vibration-damped technical plant stem, which is a technical textile developed by the Plant Biomechanics Group of the University of Freiburg together with DITF Denkendorf. The plant-based models used in developing the technical plant stem were the giant reed, the horsetail and bamboo and the basic principles deduced and transferred were the arrangement of the fibres in the composite, a gradual change in structural size and a lightweight construction in the form of a sandwich structure. Like reinforced concrete, also a biomimetic material, patented in 1867 by Joseph Monier, the technical plant stem is characterised by high strength and rigidity and high dynamic loading capacity combined with a very high level of vibration damping.[13]

Biotemplating and Biomineralization

Biotemplating is another possible approach, which takes biopolymer structures and converts them into inorganic functional and structural materials.[14] It is difficult, using current methods, to produce industrial materials with cross-scale multifunctionality and a complex structure. A general approach to the industrial production of such materials is the locally defined deposition of strong, durable inorganic materials on predefined biological architectures.[15] This enables the production, for instance, of biogenic (polymer) structures and their conversion into composite materials for a range of industrial or biomedical applications. One example of biotemplating is the hierarchical structuring of porous ceramic materials and composites. This structuring proceeds by nano-impression of plant cell walls, the model used being the pine cone. Even the active directional movement through asymmetric layering as found in the natural model is retained, albeit on a distinctly smaller scale.[16] One bio-inspired approach which has increasingly been capturing the attention of materials scientists in recent years is the coating of regularly shaped, readily available templates with inorganic compounds, ranging from the nanometre to the micrometre scale. Biopolymers such as polysaccharides or proteins are used for this purpose, as well as colloids,[17] and nanostructures such as rod-shaped viruses to enable controlled construction of nanomaterials.[18] The objective is effective, bio-inspired manufacture of hierarchically structured, fibre-reinforced composite materials and robust, miniaturized industrial application in devices. The main challenges when synthesizing such mineralized nanostructures are the selectivity and adjustability of the inorganic materials deposited on the biological templates. The thickness and surface profile of the resultant coating are important as is preventing aggregation into undesirably enlarged supramolecular structures. Templates such as the nanotubular tobacco mosaic virus (TMV) have proven particularly useful: its multiply charged protein coating can be specifically functionalized by high surface density conjugation with specific peptides, enzymes, colourants and active ingredients or inorganic components. A number of industrial applications are the result, ranging from biomedical imaging and therapeutic approaches through large-surface batteries to biosensors.[19]

In addition to biotemplating, very small structures in the nanometre range can also be obtained by using molecules for the nucleation and controlled growth of biominerals, the molecules then being known as molecular templates.[20] When it comes to the bio-inspired synthesis of semiconductors, nanowires or nanoparticles, the model is radiolaria (unicellular algae), whose microskeleton consist of silicon dioxide and is formed by the interplay of lipid vesicles and phosphate- and amine-rich proteins (silaffins, long-chain polyamines and silacidins). To produce synthetic materials, specific functional peptides are therefore used, which bind selectively to inorganic materials and control both nucleation and mineral growth.

13 | See Speck et al. 2012.
14 | See Zollfrank 2014.
15 | See Zollfrank et al. 2014.
16 | See Van Opdenbosch et al. 2016.
17 | See Preiss et al. 2014.
18 | See Bittner et al. 2013.
19 | See Koch et al. 2016.
20 | See Nudelman/Sommerdijk 2012.

Interactive and Adaptive Materials

The interaction of materials with a changing environment is another current area of research and development. Interactive materials are materials which respond to a change in the environment (stimulus) with a non-specific, non-directional response or passive interactive response. Adaptive materials, on the other hand, respond with an active response, which matches the changed situation; they are therefore often also known as smart materials. Interactive and adaptive materials are in particular those which exhibit intrinsic properties in response to a stimulus, these including self-healing, self-assembly, self-replication, self-cleaning or self-renewal. They are therefore also known as self-X materials and have high innovation and application potential, for example in the development of self-repairing industrial materials. For example, the search is on for biomimetic self-repair concepts modelled on wound-sealing plant-based latex and resin systems which can be used with polymer materials in vibration-damping or sealing systems. The principle here is the release of two (or more) chemical components, which are stored in microcapsules or microtubes embedded in the material and are released locally and polymerize in the event of damage (e.g. microcracks), so preventing further crack propagation and repairing the crack.[21]

Biotechnological Methods

Modern biotechnology is also gaining rapidly in significance in terms of the development of new materials. The focus of materials research is to analyze and understand the properties and intra- and intermolecular interactions of the basic building blocks of natural materials. Of significance are not only basic biopolymer building blocks, such as polysaccharides, nucleic acids and proteins, but also inorganic biominerals, which occur for example in composite materials such as bone, teeth or shells. An essential natural principle when combining these modular constituents into larger functional units is self-organization, which also includes self-assembly. Auxiliary structures and intermolecular interactions assist these processes, which take place in Nature generally under mild reaction conditions, such as low temperatures (around 25 degrees Celsius) and atmospheric pressures (around 1,010 millibars).[22] In other words, the formation of larger functional units (from modular building blocks along an energy gradient from smaller to larger units) takes place in aqueous systems "as though by itself".[23] By exploiting these naturally occurring mechanisms, new combinations of materials and properties can be developed (and thus wider industrial applications for functional materials). However, these self-assembly processes are essentially based on the fact that the primary structure of the biomacromolecules defines the supramolecular structure as it forms, i.e. "programmes it in". Biomacromolecules and the production of biopolymers using biotechnology remain unsurpassed for high-precision structures. The desired molecular building blocks or "raw materials" may however be produced in a fermenter using the biotechnological processes of host organisms, such as bacteria or yeast cells, and then processed to yield materials. Modern biotechnology not only enables wild-type synthesis, but also access to modified structures, in individual cases even without natural basic building blocks. One class of substances that is of particular interest for materials science is proteins, since they take on a wide variety of biological tasks and may for example form high-strength fibres.[24] One very interesting protein fibre is insect silk and above all spider silk, as used in cocoons or webs. Spiders, for instance, produce different types of silk for specific functions, with the dragline silk formed by the major ampullate (MA) exhibiting extraordinary mechanical properties – its toughness (a combination of tensile strength and elongation) is greater than that of high-performance engineering materials, such as Kevlar or carbon fibre.[25]

Other Technological Fields

This acatech DISCUSSION also considers industrial applications which have not been mentioned above, such as new concepts in robotics (soft and resilient actuators, coupled systems) and in bonding and adhesive technology or innovative approaches to production, storage and energy saving. The latter includes research into and development of dye-sensitized solar cells ("Grätzel cells") and artificial photosynthesis. Although it is the case either that development is still in the initial stages, as with artificial photosynthesis, or that efficiency has not yet reached competitive levels, bio-inspired materials in general have great potential to make a major contribution to the development of sustainable technology. However, this "biomimetic promise" does not necessarily apply *per se* to all bio-inspired innovations,[26] but rather in particular to those innovations which are capable of delivering economically useful, environmentally friendly alternatives to petroleum-based systems and conventional materials and their (often energy-intensive) production methods.

21 | See Speck et al. 2013.
22 | See Volkmer 1999.
23 | See Speck et al. 2012.
24 | See Römer/Scheibel 2007
25 | See Grunwald et al. 2009.
26 | See Speck et al. 2012.

2 Chemical Synthesis[27]

Prof. Dr. Martin Möller
Leibniz Institute for Interactive Materials, Aachen, Germany

Structural complexity is characteristic of living Nature. The structural and functional diversity of Nature is here too the fundamental challenge facing bio-inspired materials science. The structural variety of biological materials and the associated information content of the material configurations show the way forward for the transition from a material with a uniform composition to functionally determined systems. We are only just beginning to learn from Nature how new properties can be brought about via the synthesis of complex material structures. Nature offers an unsurpassed model in this respect while simultaneously presenting us with the "synthetic" challenge of finding out which functional properties we can program into the structure of a material.

Future developments thus depend on rapid further development of our capabilities to synthesize ever more complex structures. This entails widening our understanding of synthesis to encompass substantially more than "merely" the production of chemical bonds and molecules. Synthesis will increasingly require complete mastery of structure and the creation of properties across all length scales. This includes the entire chain from atom to molecule to nanoscopic building blocks to their combination on the micrometre scale right up to macroscopic structural elements. Today, the pathway from molecule to device is broken down into very clear individual development stages, with experts for each length scale who develop their methods and specialist knowledge in dedicated disciplines before passing on their products for use in the next stage. In contrast, Nature's growth processes offer a fully integrated synthesis technology which permits the construction of complex hierarchical structures with particular and active properties from comparatively few basic building blocks.

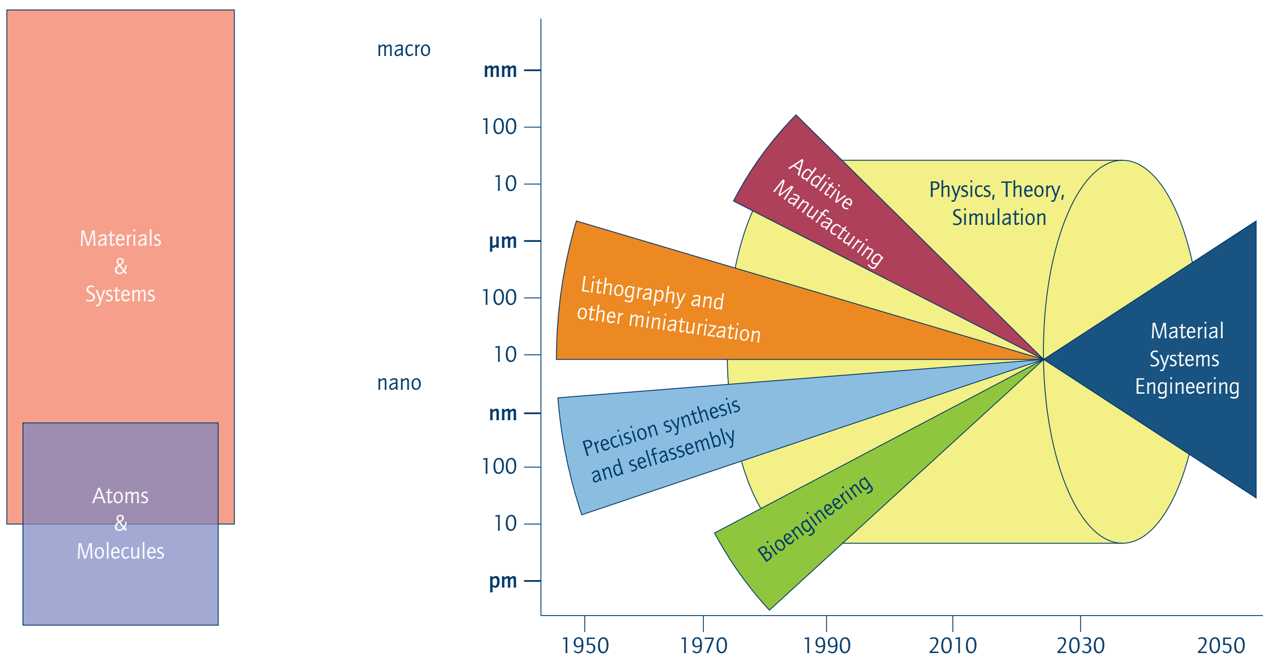

Figure 2: Drivers and interdisciplinary links for the development of complex molecular materials. In addition to mastering ever smaller length scales in lithographic and additive processes (top-down), progress is determined by an increasing ability to synthesize and perform molecular simulations of ever larger units (bottom-up) (source: Martin Möller, Leibniz Institute for Interactive Materials).

27 | This contribution was translated from German into English.

The development of integrated synthesis and manufacturing technologies which span length scales is thus a fundamental challenge facing the "biologicalization of materials science". New forward integrated synthesis technologies are a fundamental requirement for mastering the formation of structure and function in multicomponent materials.

However, the complexity and diversity of structures also gives rise to another aspect of the "biologicalization of materials science", namely the necessity of identifying the particular "smart" structures which encode new and highly developed functions.[28] This firstly involves a need for new, efficient selection methods. While increasing use may indeed be made of evolutionary selection principles, associated with high-throughput methods for keeping their time requirements within bounds, accelerated technical development can only succeed if we have a good understanding of the complex interactions. On the one hand, developing our understanding requires many and varied characterization methods which permit detailed, time-resolved structural and morphological elucidation of such structures. On the other hand, complex mathematical models and simulations are increasingly the only way to interpret and evaluate the profusion of data. Non-destructive and, in particular, real-time characterization, in conjunction with real-time data evaluation throughout a product's production process and service life, are thus becoming ever more significant for materials technology and processing. Hence, the synthesis and production of ever more complex material structures, making use of specific interactions, can only succeed with the assistance of new theoretical models and numerical simulations which make it possible to capture all the interrelationships at different scales of length and time. Developments in high-performance computing in particular will open up new pathways to making predictions *in silico*. Close cooperation between macromolecular chemistry, polymer technology, polymer physics and mathematical simulation will make it possible to expect new and progressive responses for stabilization, predictability, self-healing and also controlled ageing.

In addition to these three aspects of the "biologicalization of materials science" outlined above, which present a challenge far beyond the use of biological components, there is also an increasing need to give primacy to natural components. This fourth aspect follows from the urgent necessity for new synthesis and use technologies which are compatible with or can be integrated into natural cycles. The requirements which apply to a material are accordingly increasingly extending from an exclusive focus on use to the environmental consequences which are associated with the production and use of the materials and with the technologies applied during production and use. This relates to availability, energy input and a sustainable balance between technological benefits and impact on the functioning of natural cycles. These give rise to additional challenges for a new materials technology which is complemented by natural concepts and building blocks. One particular opportunity here lies in the use of relatively complex natural building blocks, materials and processes and the supramolecular structures predetermined in them (see the example of nanocellulose in section 6.3).

Moving away from fossil resources and reducing environmental impact entail a reorientation towards material streams which are based either on the utilization of biomass with its very heterogeneous composition or on power-to-X technologies which are still in their infancy.[29] At the same time, new requirements are arising with regard to materials being biocompatible and for the purposes of an efficient circular economy. Interest is accordingly growing in new monomers and polymers to compete with established polymers with their excellent performance. Examples are not only furandicarboxylic acid and 1,3-propanediol, but also CO_2 and CO for bio-based and bioresorbable polyesters. As for established bio-based and biodegradable products such as polyhydroxyalkanoic acids (PHAs) and polylactic acid, the need remains for a marked extension of their range of properties. Another aspect is that many bio-based resources originate from extensive farming and even compete with the food supply. Due to the many and varied effects of monocultures on local biological communities and living conditions, there is a great need no longer predominantly to obtain these resources from plantations but instead to an ever greater extent to produce them in biological and chemical synthesis plants. This leads, furthermore, to an increasing requirement for water-based, non-toxic chemical processes and mastery of physical transformations and self-assembly processes. Established examples are water-based coating materials and coatings, adhesives and also applications in the construction and cosmetics sectors. Getting a grip on ageing and failure behaviour is another fundamental challenge for a resource-efficient technology.

If the above four criteria for the "biologicalization of materials science", (i) cross-scale synthesis technologies as a prerequisite for (ii) a high information content of the material structure and extended functionality, (iii) the possibility of selecting smart structures which have the "right" properties and (iv) the use of complex natural building blocks, materials and processes, are summed up, it

28 | The term „smart materials" is widely used to refer to adaptive materials. Such smart or adaptive properties often depend on very complex structural variations.

29 | See Power to X Allianz 2019.

becomes clear that we are today "at a tipping point in science and engineering", i.e. at the start of a challenging new development which contains elements of a paradigm shift.[30]

Taking molecular materials by way of example, Figure 2 addresses the technological and scientific prerequisites with which these challenges can be successfully met in future so that the "biologicalization of materials science" as an emerging field of research can take on great practical significance.

Progress in the chemical synthesis of ever larger and also very uniform molecules has opened up the way to preparing varied and defined superstructures via self-assembly processes. Examples are artificial vesicles, supramolecular gels and the dimensionally restricted growth of inorganic solids (see also section 2.1). At the same time, numerous switchable functional molecules are now available, including the first molecular motors, as were synthesized by Ben Feringa (Nobel Prize 2016). The molecular machines made from DNA molecules described by Hendrik Dietz are one particularly impressive example of how, using self-assembly processes, i.e. by a build-up method, building blocks and complete functional elements can be constructed on a nanometre scale (see section 2.2). The first synthetic examples of dissipative structure formation (dynamic self-assembly) which are defined structures, the formation of which is dependent on constant energy input and which break down when the energy input necessary for producing them is interrupted, are an addition to this toolkit.[31]

The meteoric development of the life sciences is not only providing a profound molecular understanding of biological processes but has also led to synthetic biology. At variance with the core purpose of the life sciences, namely contributing to an understanding of biological processes, synthetic biology is increasingly also directed towards using biological mechanisms for new synthesis systems and new products. The synthetic approaches of materials science are here complemented by those of biology. While chemical synthesis can indeed provide increasingly more complex and functional molecules, it is still a very long way from matching the capabilities of Nature in synthesizing functional biomacromolecules. In Nature, these molecules' superstructures, complexation and switchability between different states are the highly precise result of the information which is encoded in the primary structure of the molecules. For new material systems and hybrid constructs in which artificial functional building blocks are combined with biological components, biotechnological methods mean we can draw not only on molecules in wild-type form, but also on targeted modifications and neosyntheses. Examples of these developments are the phage display and directed evolution methods which were awarded the Nobel Prize in chemistry in 2018. In this context we must also consider the DNA origami approaches using PCR synthesis, as highlighted by Hendrik Dietz's contribution already mentioned above.

The possibilities offered by the hybridization of artificial and natural building blocks present new challenges to chemistry. At the level of the smallest building blocks, there are molecules which are similar to natural but modified and can be incorporated into biological synthesis mechanisms. One example is Birgit Wiltschi's contribution, which sets out the non-canonical amino acids which can be incorporated as protein building blocks in biosynthesis (see section 2.3).

The major potential for the synthesis of new materials using modern biotechnology is described in the interview with Lin Römer (see section 2.6). His company AMSilk uses Nature's synthesis technology to produce new spider silks which have custom properties for entirely different applications in cosmetics and for high-performance fibres and are completely integrated into natural cycles from the necessary raw materials to regeneration (see section 2.6).

Hybridization is a concept which is not solely limited to the molecular building blocks, but is also, by the combination of larger microscopic components, suitable for materials with novel, unprecedented property profiles. This is illustrated by Markus Antonietti's contribution, which takes shells and their perfectly layered platelet structures by way of example (see section 2.4). The combined "brick and mortar" construction here enables levels of strength and toughness which the base material alone cannot achieve. The contribution by Helmut Cölfen then impressively demonstrates how this principle can be transferred to a material such as cement in order to impart elastic properties which have hitherto been thought impossible (see section 2.5).

At a length scale of greater than a few micrometres, connecting metallic and ceramic building blocks on the one hand with organic materials on the other always presents a particular challenge. Today, inorganic and organic materials are largely separately produced due to the huge differences in processing and decomposition temperatures and we are now just on the threshold of being able to integrate such components. There are also no universal ways of tackling this task. At the same time, there are already many technologically highly pertinent examples,

30 | As was stated when the Wyss Institute at Harvard University was founded in 2009: „...we are now at a tipping point in the history of science and engineering – we are beginning to understand enough about how Nature builds, controls and manufactures that entirely new engineering principles are already beginning to be discovered".

31 | See Timonen et al. 2013.

such as the electrodeposition of metal layers, the use of precursor compounds from which the metal can be generated in the gas phase, sputtering processes, laser-based additive manufacturing processes in which only very small volumes are locally heated, as well as the use of amorphous metals which can be welded under pressure or using ultrasound.

These points once again indicate that developments from different disciplines will in future have to be brought together to a greater extent. This not only relates to approaches in which chemical synthesis will increasingly make use of building blocks from biotechnology or will provide new building blocks and reactions for lithography and additive manufacturing processes but there will also be a requirement for it to be possible to combine the various processes with one another. One example which has as yet received little attention is the combination of additive manufacturing processes with a self-assembly process, for example to produce a high-strength material, the structure of which is adapted to the loading directions.[32] In comparison with established dispersion systems, such as high-impact polystyrene or carbon black- and silica-reinforced elastomers, models from Nature, such as the nacre mentioned above,[33] or wood or bone structures show major development potential for constructed and anisotropic hybrid structures. Simpler examples have long been established on a large industrial scale, such as the deposition of a metal-effect coating, during which the aluminium flakes orient themselves parallel to the surface and so produce the desired glitter effect.[34]

The possibility of producing nanocomposites with a well-defined superstructure also opens up the way to new materials with particular electronic, optical and mechanical properties. One example are the heterostructures (bulk heterojunctions, BHJ) for organic photovoltaic cells (OPV).[35] Such very small structures, which go right down to molecular dimensions, can increasingly be produced by lithographic methods. Multiphoton lithography processes are one example which shows that top-down methods have already reached the boundary of molecular dimensions even for 3D structures. This example thus shows that rapidly developing additive manufacturing processes are advancing into the molecular dimension range.[36] Other examples of additive processes which follow on from chemical synthesis are layer-by-layer processes which were initially developed for the deposition of polyelectrolytes and have for some time also been used for other build-up reactions, for example "atomic layer deposition" for producing nanolayers in microsystems engineering.

Complex highly functional hybrid structures can furthermore be obtained by the integration of biological processes and synthetic structures. Hydrogels serving as a synthetic scaffold for fabricating living tissue are one example. One particular, cross-sectoral field which holds much promise for the future is personalized healthcare technology with research into biomedical hybrid systems and the development of "advanced therapy medicinal products" (ATMPs).[37] This involves, for example, providing synthetic scaffolds with living cells or vectors with gene therapy agents.

Another specific feature with regard to the "biologicalization of materials science" which is becoming apparent in particular for such biohybrid developments is that new properties are becoming possible which can no longer be directly derived from a knowledge of the subunits. Material synthesis will here itself move towards the transition to living matter. The associated emergent behaviour builds on impressive advances which have been made in recent years:[38] (i) capabilities enabling cross-scale "building" of structures by means of equilibrium driven self-assembly of molecules and advanced lithography methods, (ii) increasing availability of molecular switches, (iii) mastery of bistable structures and hysteresis effects and (iv) controlled energy absorption enabling dissipative structure formation processes and (v) integration of active feedback mechanisms.

While the focus of Figure 2 is on molecular materials, it must be borne in mind that the diversity of molecular structures also permits a huge diversity in material structures and that it is precisely for this reason that Nature developed living matter on the basis of organic molecules. However, this does not mean that the smart structure of biological material presents no challenges for the further development of metals and other inorganic materials. If biologicalization is defined as the challenge to synthesize ever more complex hierarchical structures and to master the resultant functions, then it is precisely for these materials that synthesis extends from chemical bonding to structure formation during processing. Accordingly, given the great significance of grain structure, it is the combination of chemical composition and

32 | See Gantenbein et al. 2018.
33 | See Wegst et al. 2015.
34 | See Wißling 2006.
35 | See Dennler et al. 2009.
36 | See El-Tamer et al. 2017.
37 | See Paul-Ehrlich-Institut 2006.
38 | See Merindol/Walther 2017.

processing which define properties of metals and ceramics. Stress states and internal interfaces determine not only functional properties but also ageing and failure behaviour.

This point also leads to the issue of the boundaries which arise for the development of the scheme shown in Figure 2 or the underlying roadmap. Figure 2 only encompasses structure formation on small length scales. In many cases, we do not have the manufacturing processes to fabricate complex material structures on a length scale greater than the micrometre range. Nature causes structures to grow, in most cases layer-by-layer. These growth processes are slow and frequently associated with chemical changes such as lignification, keratinization and calcification, and they are adaptive. Industrial manufacturing processes have to give rise to the component or product quickly and efficiently. This is why additive and derived adaptive manufacturing processes will be of great significance to future developments.

Adaptive formation of structure and function becomes possible where synthesis and production occur at the same time as, i.e. during application. The resultant possibilities for optimizing structures are shaping a new requirement for such products, for example for biohybrid implants in which a scaffold structure is colonized with living cells which are intended to form new tissue or even an organ there. Another area requiring adaptive properties is arising around the increasing demand for materials and products which are integrated into natural cycles and thus know when they need to provide a particular function. For example, materials could initially start their life cycle as a solid structural material, then be easily broken down into components which can be reassembled for another use and finally, after a decomposition process, become available as a raw material or fertilizer for the next cycle.

2.1 The Challenge of Fabricating Lifelike Materials

Prof. Dr. E.W. Meijer
Eindhoven University of Technology, Eindhoven, The Netherlands

Nature sustains life by dynamically controlling highly selective, specific, efficient, but complex molecular assemblies and networks. Inspiration from these systems has led chemists over the last 150 years to synthesize a wide range of sophisticated molecules via covalent synthesis to serve societal needs. And, beyond the molecule, in the field of supramolecular chemistry, some higher-order synthetic building blocks or superstructures can be assembled from several or many molecules by intermolecular non-covalent interactions directed by the self-recognition programmed into their covalent framework.

However, constructing hierarchical multicomponent materials and systems is challenging, in particular because it requires a subtle balance of interactions and geometries between the complementary recognizing motifs in order to connect the different molecular entities. Major and significant steps have been made in the understanding of self-organization, self-assembly and self-recognition. However, the word "self" reveals the limits of our methods for constructing multicomponent systems as assembly relies primarily on serendipity, i.e. on a chance observation and discovery of a complex assembly step, rather than on reproducible procedures and predictive rules. This strategy cannot truly advance our ambition to make more complex and lifelike molecular materials and so create unprecedented functions. Stochastic exploration of the available structure/energy combinations of the system under consideration thus needs to be replaced by a systematic approach. Assembly processes accordingly require very rigorous protocols of procedures to ensure that the non-covalent synthesis is reproducible and functions in multiple laboratories.

We must endeavour to achieve a major paradigm shift in materials science and engineering which translates the successful concepts of covalent synthesis into the realm of non-covalent synthesis. Multicomponent systems should be built following a multi-step pathway which is not only directed by the information stored in the covalent framework of the components but is also controlled by the kinetics and thermodynamics of the pathways selected. The future of building functional molecular materials by protocols in multiple non-covalent steps modelled on Nature is just beginning and it will also give us some idea about how "life" started out of a collection of millions of "dead" molecules. Important applications for such novel materials are foreseen in tissue engineering, drug delivery, adaptive materials for soft robotics, and molecular information, but the development of lightweight, biocompatible materials that might contribute to a sustainable society without plastic waste may perhaps be even more important.

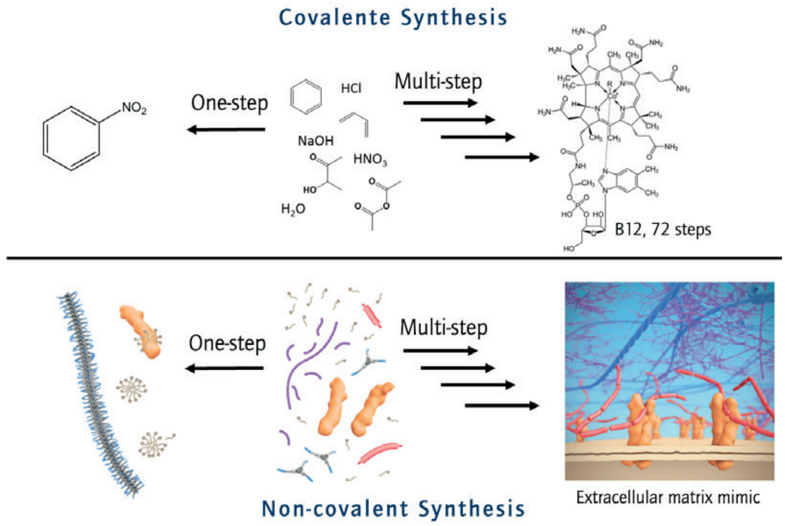

Figure 3: Proposed paradigm shift for the fabrication of bio-inspired lifelike materials by multi-step non-covalent synthesis following the same development as covalent synthesis did over the past 150 years[39] (source: E.W. Meijer, Eindhoven University of Technology)

2.2 Construction with DNA[40]

Prof. Dr. Hendrik Dietz,
Department of Biomolecular Nanotechnology, Technical University of Munich, Garching, Germany

Building artificial molecular structures with thousands of atoms at controlled coordinates is at present an insuperable challenge for traditional methods of chemical synthesis. Nature, however, does provide a way of tackling this challenge, by making use of biopolymers composed of amino acid and nucleic acid chains in each case containing a defined alphabet of chemical building blocks. The structures of natural molecular machines are encoded in the sequences of the chemical building blocks and the structures form by self-assembly. One possible approach to creating complex artificial molecular structures with new functions determined by the designer involves adopting both the materials and the principles which are used by Nature to build up synthetic molecular structures. This is the strategy that is pursued by biomolecular designers in the fields of *de novo* protein design, RNA nanotechnology and DNA nanotechnology. All of these approaches are driven by the idea of encoding structures in sequences.

Why specifically should DNA be considered as the basis for constructing molecular structures or machines given that DNA occupies a somewhat passive role as an information storage medium in Nature? DNA has physical and chemical properties which also make this type of molecule suitable for building structures. User-defined DNA sequences are readily available via solid-phase chemical synthesis or gene synthesis and via biotechnological methods. Moreover, in comparison with RNA and proteins, DNA molecules exhibit remarkable chemical stability. Single strands of DNA are flexible polymers, whereas double-helical DNA domains are comparatively rigid with persistence lengths of the order of around fifty nanometres. A wide range of local rigidity may therefore be achieved by combining flexible and rigid elements. The thermodynamics of the formation of double-helical DNA domains is well understood and the domains' stability can be relatively accurately predicted from their sequence. The same also applies to the tendency of single-stranded DNA to form secondary structures. Watson-Crick base pairing between DNA strands with complementary sequences provides a strong and readily controllable physical interaction for planning secondary structures which may in turn be hierarchically arranged in tertiary and quaternary structures. The limited chemical diversity of naturally occurring DNA could potentially limit the range of functionalities achievable with objects which are built up from canonical DNA bases. Fortunately, an abundance of chemical modifications and non-canonical bases are also available which can be

39 | See Vantomme/Meijer 2019.
40 | This contribution was translated from German into English.

site-selectively introduced into DNA objects in order, where necessary, to achieve a substantial expansion of chemical diversity. Furthermore, even DNA molecules of standard chemical composition may also be catalytically active ("DNAzymes"). DNA has thus ultimately taken on the nature of an unusual and versatile material. These properties are also already being put to practical use: there are a number of applications in which specially shaped DNA-based carrier structures are used for transporting plasmonic or photonic effects or as a liquid crystalline matrix. Furthermore, a series of structures are currently being investigated in model studies in order to obtain an understanding of the potential of DNA carrier structures for applications as active substance transporters or for other diagnostic and therapeutic purposes.

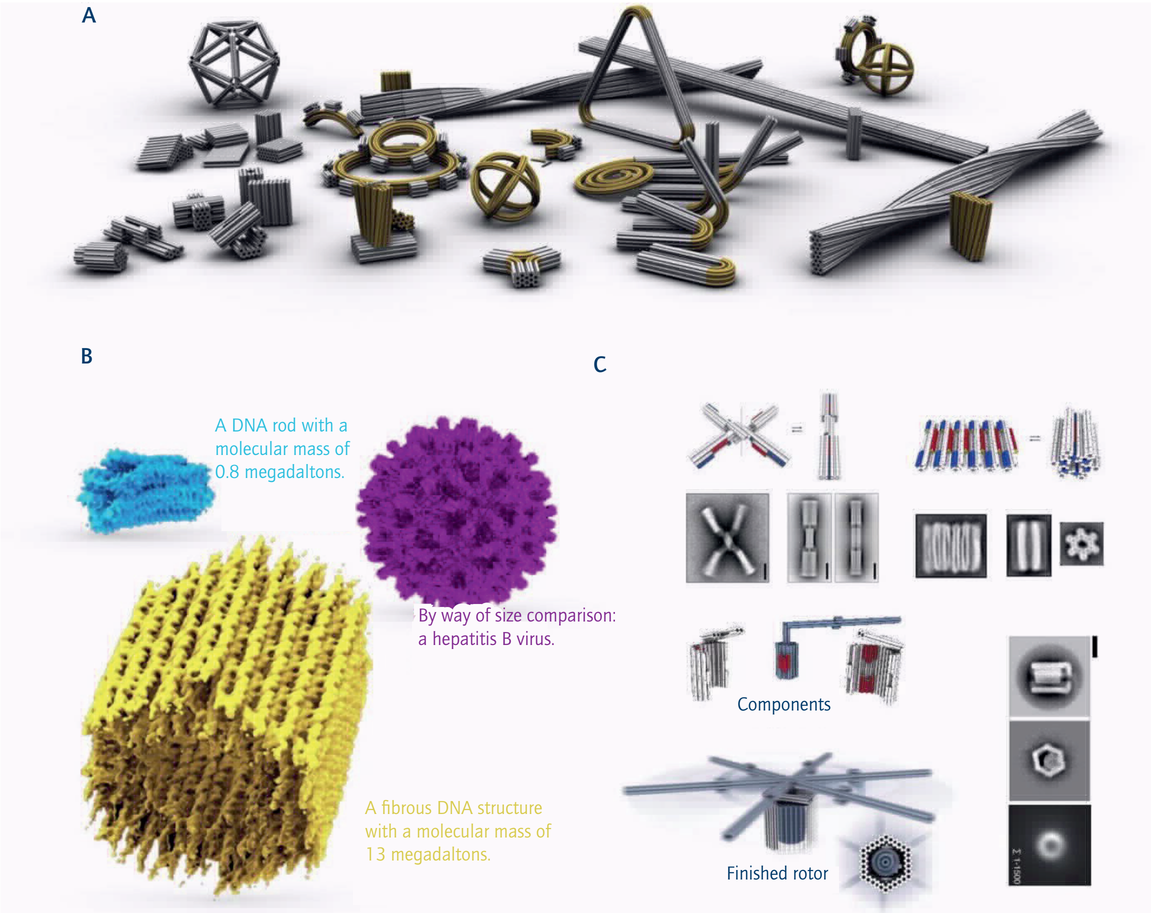

Figure 4: A: Range of shapes of conceivable DNA-based molecular structures, some already commercially available.[41] The figure shows a three-dimensional model of DNA-based molecular structures. The cylinders represent individual DNA double helices while the yellow coloured regions are deliberately curved or twisted. Designers typically make use of such representations at the design stage. B: Structural validation is an important part of practical implementation. By way of example, the figure shows two electron densities of DNA nanostructures (yellow and blue) and, for size comparison, an electron density of a hepatitis B virus. All micrographs (unpublished) obtained by cryotransmission electron microscopy (TEM). C: Examples of DNA nanostructures with internal degrees of freedom for producing switches and rotor modules, in each case with TEM images. A fluorescence trace directly demonstrating the rotation of a rotor particle is shown bottom right (source: Hendrik Dietz, Technical University of Munich).

41 | For example from tilibit.com

One of the key aims of biomolecular designers is to create autonomously operating molecular machines. Machines are typically characterized by a directed process which is driven against external forces via a motor unit. Such motors as well as the machines coupled to them could possibly be produced with the assistance of DNA nanotechnology. Motor units entail the construction of mechanisms which exhibit precisely defined degrees of rotational or translational freedom and furthermore have structural features which result in asymmetric periodic energy landscapes. By applying various kinds of deterministic or stochastic thermal, chemical or mechanical disturbance, the systems could then be moved away from thermal equilibrium towards directed Brownian motion, which would give rise to motors. A number of variants of such mechanisms are currently under investigation internationally.[42]

Obtaining efficient artificial molecular motors would be a huge step forward. Such motors could for example assist in investigating out-of-equilibrium transport phenomena. Both the process of constructing such functional motor units and the resultant units could assist in uncovering the principles of construction which underlie the functioning of natural macromolecular machines. Artificial molecular motors could moreover help to clarify how classical mechanical motion can actually be coupled to quantum-mechanical chemical reactions. Finally, robustly functioning artificial motors will also be of great practical benefit. Provided that they are sufficiently modular and integrable, they could drive a range of processes in which work has to be done, for example for pumping and separating molecules via barriers, for packaging molecules, in enzymatic chemical synthesis and for actively driving active substance transporters.

It is therefore of interest to obtain answers to these questions and to understand the part DNA will play in providing the corresponding technical solutions. DNA has so far proved to be an extremely versatile material for the production of ever more complex structures which could in turn provide the basis for building the machines in question. For a more in-depth discussion, please see the recent review article by Ramezani and Dietz.[43]

2.3 Non-canonical Amino Acids[44]

Dr. Birgit Wiltschi

ACIB – Austrian Centre of Industrial Biotechnology, Graz, Austria

Proteins perform an extraordinary diversity of functions in all living organisms, from microorganisms via plants and animals to humans. They provide hair with strength and make spider silk elastic. In the form of enzymes, they convert e.g. sugar to alcohol or as antibodies, they protect us from diseases. To generate these various functional properties, Nature uses amino acids as small protein building blocks and joins them together to form chains of differing composition and length. Surprisingly, a set of just twenty "canonical" amino acids is sufficient to biosynthesize the proteins that generate the amazing biodiversity in the world.

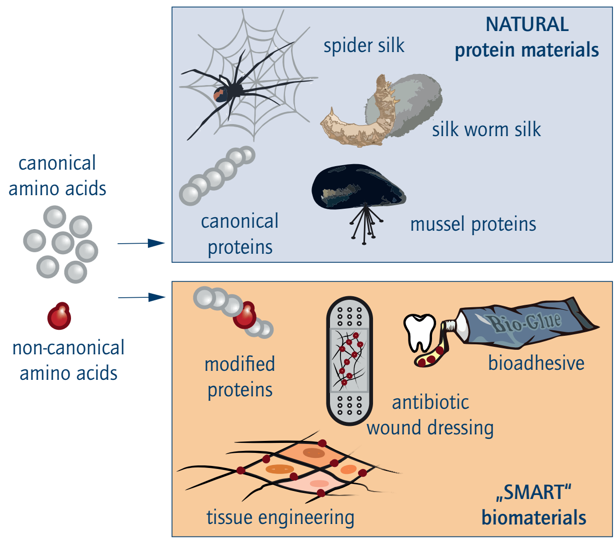

Figure 5: Non-canonical amino acids transform natural protein materials into smart biomaterials. Natural protein materials such as spider silk, silk worm silk or mussel silk consist of canonical amino acids. New functionalities can be introduced into these materials by incorporating non-canonical amino acids. The modified proteins are the basis for smart biomaterials with highly promising applications in the future (source: Birgit Wiltschi, Austrian Centre of Industrial Biotechnology).

42 | See Ketterer et al. 2016.
43 | See Ramezani/Dietz 2019.
44 | This contribution was translated from German into English.

Industry is increasingly making use of chemically modified proteins which are customized for particular applications in modern medicines, diagnostics and biomaterials. Current methods for the chemical modification of proteins are, however, either not selective or cannot be applied at every desired position in the protein. Site-selective introduction of non-canonical amino acids with unique chemical properties is one solution to this problem. As their name would suggest, non-canonical amino acids are not provided by Nature for protein biosynthesis. However, a recombinant host organism for protein production can be engineered to incorporate the non-canonical amino acid, and thus the desired property, at a selected position in the target protein.

Protein modifications can be precisely controlled using this technique, which has been successfully used to make targeted chemical modifications in protein materials such as silk. The research group around Neil Thomas, Professor of Medicinal and Biological Chemistry at the University of Nottingham (UK) incorporated a reactive non-canonical amino acid into spider silk protein for this purpose.[45] The reactive side chain of this non-canonical protein building block was then selectively linked with an antibiotic. Thanks to the natural fibre-forming characteristic of spider silk protein, an antibiotically active material was obtained which could be applied for example as 'smart' dressing in wound treatment. By feeding silkworms with a reactive non-canonical amino acid, it was possible to dye the silk selectively and stably with a fluorescent dye.[46] In future, such chemical modifications of protein materials such as silk, collagen or mussel proteins are conceivable which could find industrial application, for instance by coupling with antibiotics as a wound dressing, by modification with growth factors in tissue engineering or, in the case of mussel protein, as a bioadhesive[47] (see Figure 5). Relatively low protein yields together with considerable costs for the non-canonical amino acids are still limiting factors at present. Biosynthesizing the compounds from inexpensive precursors is one route to dramatically reduce future costs for the biotechnological production of site-selectively modified protein materials. The biosynthesis approach can supply the industry with non-canonical amino acids as new building blocks for 'smart' biomaterials.

2.4 Biologically Inspired Hybrid Materials[48]

Prof. Dr. Markus Antonietti
Max Planck Institute of Colloids and Interfaces, Potsdam, Germany

Nature's achievements are quite incredible particularly in the area of hybrid materials, i.e. composites of organic polymers and inorganic crystalline nanostructures. One such example is provided by shells or nacre (produced from chitin, proteins and calcium carbonate) in which the grown composite is 5,000 times tougher than the crystalline $CaCO_3$ from which it is made.

Shells, like teeth, arose in the "Cambrian revolution" as the result of an arms race between hunter and prey, with calcium carbonate, or chalk, actually being a waste product formed from "hard water" and metabolically produced CO_2 and thus not in any way a substance from which materials would usually be made: Nature, however, makes use of what is available.

Biomimetic materials, which are constructed using the same principles, are however not subject to the same biological limitations

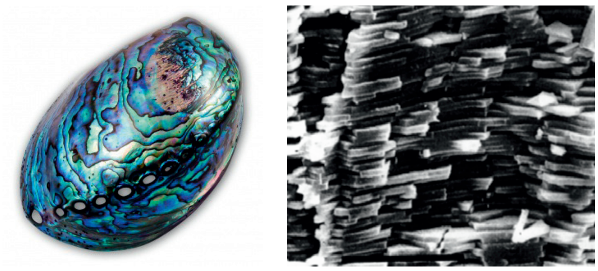

Figure 6: Abalone shell nacre and scanning electron micrograph of its constituent nanostructure. The colours are caused by the thickness of the platelets being in the region of half the wavelength of light, as a result of which they act as Bragg reflectors. Nacre is not only highly resistant to breakage, but is also anti-adhesive, anti-soiling and enables conformal coatings (source: Markus Antonietti, Max Planck Institute of Colloids and Interfaces MPIKG).

45 | See Harvey et al. 2017.
46 | See Teramoto et al. 2018.
47 | See Budisa/Schneider 2019.
48 | This contribution was translated from German into English.

(synthesis in water at room temperature, neutral pH range, etc.). They are simply "mimetic" and merely make use of the structural principles. For instance, platelets of super-hard tungsten carbide or super-strong graphenes can be combined with highly stable modern resins to give rise to new composite materials from which a new generation of aircraft or the safety cell of future Formula 1 racing cars could be made.

The next generation of research is biologically inspired to such an extent that it is hoped that it might prove possible for such composite materials to be broken back down at the end of their life as a material so that the primary materials can be returned to the materials cycle. Degradation is no problem for shells or bone. Similar "switchable chemical weak points" can also be taken into account during material selection. "Nanocellulose" has the potential to replace carbon fibre in many areas. The situation is similar for lignin-like adhesives which could render epoxy resins obsolete, with wood here obviously serving as the inspiration and source of "bio-inspired" molecules. Accordingly, the generation after next of aircraft, ships or houses could possibly in part be "wooden", but without the biologically determined weaknesses of this conventional material.

2.5 Bio-inspired Elastic Cement[49]

Prof. Dr. Helmut Cölfen

Physical Chemistry, University of Konstanz, Germany

Biominerals produced by living organisms exhibit unsurpassed properties. Mussels, for example, can accordingly create nacre, a material which is up to 5,000 times more resistant to fracture than the chalk which makes up 95 per cent of it. Such outstanding material properties are explained inter alia by the hierarchical structure of these materials with their brick and mortar architecture ranging from the nano- to micrometre scale. Another factor is the contrast of properties between a hard but brittle inorganic material and a soft but elastic material. Various materials such as bone or a sea urchin spine have a similar structure. Anyone who has inadvertently trodden on a sea urchin knows that its spine is in no way as brittle as the chalk of which it consists but is instead resistant to breakage and can so act as a defence mechanism against predators.

This brick and mortar structure at the nanometre scale can also be applied to synthetic materials. We have therefore attempted to transfer this construction principle to calcium silicate hydrate (CSH), the binder in cement. The best and most selective binding motifs for molecules were firstly identified from a biological library and then a search for a synthetic analogue was conducted. When this additive was used in CSH synthesis, a brick and mortar structure of the cement particles with soft polymers at the interfaces was actually found at the nanometre scale. In other words, the biological structure of the sea urchin spine could be successfully replicated by self-assembly of the CSH platelets in the presence of a macromolecular additive.

Mechanical testing (see Figure 7) revealed elastic deformation of the test beam without breakage. Calculations of the bending strength from the flexure revealed a bending strength of nacre, the gold standard for all bio-inspired material syntheses in this field, which is approximately one hundred times higher than that of cement and concrete.

This means that outstanding material properties can be achieved even with humanity's most widely used and highly heterogeneous building material, namely cement, and these properties will make it possible, given appropriate nanostructuring, to achieve identical strength using substantially thinner structural elements or, in future, perhaps to build without steel frameworks. It must nevertheless be emphasized that, while these investigations show what might theoretically be possible with conventional construction materials, scaling up to the volumes currently used in construction is not at present possible and is moreover economically unattractive.

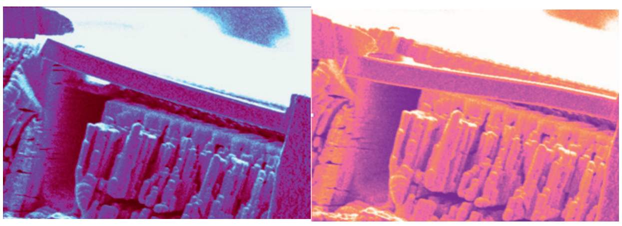

Figure 7: Micromanipulator experiment with a 3×3 μm^2 beam of mesocrystalline cement. On the left, before the experiment; on the right, marked flexure of the beam under pressure without breakage. After deformation, the beam returns to its original position (left), revealing advantageous elastic deformation; all the energy is reversibly returned (source: Helmut Cölfen, University of Konstanz).

49 | This contribution is based on the original publication Picker et al. 2017 and was translated from German into English.

2.6 Interview with Lin Römer, AMSilk[50]

Dr. Lin Römer is Managing Director and co-founder of AMSilk. He is a biochemist and responsible for the company's research and development activities.

Dr. Römer, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

For me it is the special combination: high-performance materials from biological primary materials. Great new products should perform well but also be sustainable. Achieving this combination is difficult with petroleum-based materials and simply going back to jute bags and cotton products is probably also not the right way forward for us all. As a first step, we can combine new materials with existing ones. If we manage to replace just a few percent of current products with more sustainable materials, this is a very good step forward and one we ought to take.

What role do models from Nature play in materials development in your company?

We are guided by the spider silk which spiders spin in Nature to build their webs. This silk consists entirely of proteins. Interestingly, our initial materials development efforts were indeed guided by spider webs, but our current commercial products no longer have much to do with a web. The focus thus initially tends to be on copying a naturally occurring material using biotechnology and then in a subsequent step on investigating areas in which it might be used best. We do produce fibres which are very similar to natural spider fibres, but that is just one aspect. For example, our proteins are used as a gel or powder in cosmetics or as a coating for implants in medical engineering. We thus copy Nature, improve, optimize processes and put the development result to the broadest possible use and not just where Nature had originally intended it to be used.

So your cosmetic products are thus ultimately less directly based on Nature than your textiles?

A spider web is not the role model for the development of cosmetic products and the corresponding function of the biologically inspired materials. Instead, we established that our silk is capable of coating and thus protecting the skin. A second skin, of pure protein, is formed which protects our own skin from external influences. We thus don't have some acrylate, a plastic, or a layer of fat on the skin. The silk has advantages over existing materials and numerous good properties, which are in great demand in cosmetics. The advantages are so convincing that we were recently able to sell AMSilk's cosmetics business to the international specialty chemicals company

Figure 8: Prototype high-performance adidas sports shoe made from Biosteel® fibre (source: adidas)

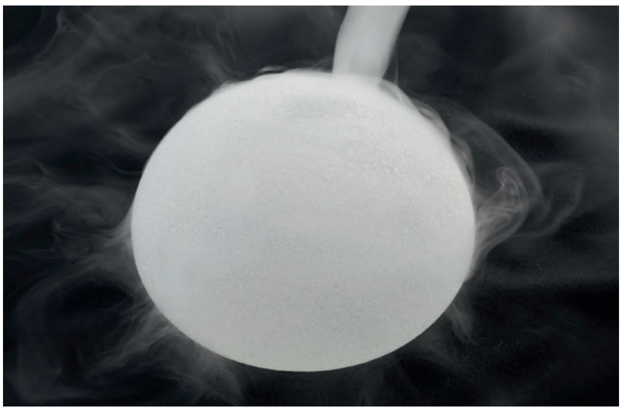

Figure 9: Textured silicone implants from POLYTECH are improved by a thin homogeneous coating of silk protein (source: AMSilk).

50 | The interview was originally conducted in German.

Givaudan S.A. from Switzerland. Givaudan plans to further develop this silk technology so it will be able to offer many new products.

What are the major hurdles and challenges for you?

"Scaling up", i.e. producing large, industrially significant volumes has been, and remains, a challenge because it is time-consuming and capital-intensive. Producing significant volumes requires very large plants which take a long time to set up. These new materials are then initially all more costly than an oil-based material which has been optimized for 60 years and is already produced in million tonne volumes. The respective market acceptance first has to be created for a product which is perhaps somewhat costlier at the outset. On the other hand, it should be a matter of demonstrating more sustainable alternatives that are not necessarily accompanied by renunciation.

What progress do you expect to see in the coming years in bio-inspired materials development?

I'm firmly convinced that in the next 10 to 15 years we will be coming across biotechnological and in particular protein-based materials everywhere in department stores, whether it's the trainer we have recently jointly developed with partners or other products. New materials are gradually coming onto the market and are being accepted and we will see many new developments in the coming years. As I already mentioned, combining new performance, new properties and, at the same time, sustainable thinking is vital. We don't all want to do without good products – but also protect the environment. We have to find new ways, which are more acceptable for our planet. Innovation itself is only the beginning, but new products must ultimately find their way onto the market:
I expect to see some successful examples in the short-term.

3 Additive Manufacturing[51]

Prof. Dr. Jürgen Groll
Department for Functional Materials in Medicine and Dentistry, University of Würzburg, Germany

Prof. Dr. Thomas Scheibel
Department of Biomaterials, University of Bayreuth, Germany

One definition of Additive Manufacturing (AM), often also known colloquially as 3D printing, drawn from ISO and ASTM standards, is "a process of joining materials to make parts from three-dimensional (3D) model data, usually layer-by-layer".[52, 53] Additive manufacturing technologies open up interesting possibilities, specifically for producing functional materials and parts with a complex, heterogeneous structure.[54] The origins of 3D printing probably date back to Charles Hull[55] being granted a patent for stereolithography in 1986. Various technologies have subsequently been developed such as "Powder Bed Fusion", "Fused Deposition Moulding", "Inkjet Printing" or "Contour Crafting".

Applications for additive manufacturing have since been found in many fields, for example in the construction industry, in prototyping or in biomedicine.[56] Examples from industry in which additive manufacturing is already used for the mass production of parts include 3D-printed elements for the Boeing Dreamliner, 3D-printed General Electric engine components and more than one million 3D-printed BMW vehicle components, all of which indicates the significance of additive manufacturing in Industry 4.0. The advantage of this manufacturing technology is the possibility to manufacture materials and components which are capable of exhibiting locally defined chemical and mechanical properties in combination with a specified 3D micro- and macrostructure, something which cannot be achieved by conventional processing methods.

Inspiration is often drawn directly from Nature or from biological systems in which anisotropic building blocks with an optimized size and aspect ratio are organized over many length scales. A combination of strong and weak bonds between these building blocks is used to produce dynamic functions (with interesting possibilities for adaptation, remodelling, self-healing, etc.).[57] The potential of additive manufacturing resides in the fabrication and evolutionary further development of material and component properties.[58] This is particularly the case in personalized medicine, especially in tissue regeneration. Processing biomaterials by means of additive manufacturing and subsequently bringing the construct into contact with biological components, whether by cell colonization or by use as an implant, are becoming increasingly significant for various clinical applications (see also sections 3.1 and 3.2). Bioactive functionalization of polymers which permits a specific interaction with cells, in combination with suitable fabrication techniques, paves the way for the development of tissue-mimetic cell-material constructs as *in vitro* models and for regenerative medicine. Simultaneous processing of cells and materials to form three-dimensional cell-material hybrid structures is known as biofabrication.[59] In contrast with the previously conventional 3D printing of biomaterials, this young and very active field of research thus involves direct processing of materials formulations containing cells, so-called "bioinks".[60] This new set-up demands new materials and printing processes since processing must proceed in its entirety under cell-compatible conditions (aqueous environment, physiological temperatures, salt concentrations, etc.), considerably restricting the selection of fabrication methods, materials and the chemical reactions usable for solidifying the structures after printing.

Currently, the potential of additive manufacturing is far from being exhausted. So far, single component systems are being processed and they are frequently obtained from a small range of commercially obtainable materials. This limits not only physico-chemical properties but also the to-be-obtained

51 | This contribution was translated from German into English.
52 | See ASTM/ISO 2013.
53 | See acatech et al. 2016.
54 | See Studart 2016.
55 | See Hull 1986.
56 | See Ngo et al. 2018.
57 | See Studart 2016.
58 | See Ibid.
59 | See Groll et al. 2016.
60 | See Groll et al. 2018.

structures of the 3D-printed components. In addition, many 3D printers are currently limited to use just a few inks and materials and are not compatible with other materials. The resolution of the printers is also in many cases far from the range in which biological models can generate (micro)structures. It is also important to note that biofabrication research is still at its infancy. The core hypothesis that an intrinsic hierarchy in cell-material constructs is advantageous for developing replacement tissue with functional characteristics remains to be confirmed for various applications (see also sections 3.1 and 3.2). One central challenge facing this field of research remains the lack of materials which are suitable for biofabrication and can thus form the basis of bioinks.[61, 62] High print resolutions can often only be achieved under conditions which are not ideal for cells, while, due to the low material contents in formulations, high cell compatibility is achieved at the expense of dimensional accuracy of the constructs. A central theme of biofabrication research is therefore currently the enlargement of this biofabrication "window": customized (bio)polymers provide the material basis; supramolecular principles of interaction are attracting research interest with the aim of influencing rheology and cell compatibility. In addition, future bioinks must not only be printable but should also be capable of precisely controlling post-printing cell behaviour and tissue maturation. If (multi) functional tissue is to be successfully produced, it is furthermore essential to have not only a detailed knowledge of the tissue-specific structures and combinations of materials and cells and their interaction but also an understanding of how tissue is formed in terms of developmental biology. In biomedical applications, issues such as regulation of approval and quality assurance are further hurdles.

Additive manufacturing in principle makes it possible to produce a material or component modelled on principles as seen in Nature: it permits the creation of multifunctional and dynamic structures (i.e. which vary over time or in response to external triggers) with spatially resolved chemistry, mechanical properties and functionality. As a consequence, this is a developmental process based on multiple criteria rather than a single criterion as is still typical in engineering. Three-dimensional replication in biomedicine, for example tissue-specific hierarchical structures in combination of different cells and materials, enables progress for instance in relation to the formation of new blood vessels and functional characteristics and the speed of maturation in comparison to conventional 3D tissue engineering. As yet unexploited possibilities arise for the rational design of 3D *in vitro* tissue models which have great potential in various fields of application: for drug testing instead of animal experimentation, as standardized models for research and, in the long-term, as a therapeutic option in regenerative clinical medicine. The latest research has shown that one very promising strategy for many tissues may be to use the intrinsic "programmes" present in stem cells, for example including the endochondral process of osteogenesis from cartilage.

Additive manufacturing sets new standards and enables a paradigm shift in material design in a way that was previously the sole preserve of Nature. In the future, functions will no longer be determined solely by chemistry and composition of the material, but instead graduated and textured heterogeneous architectures of the 3D-printed components will revolutionize the development of new applications based on multiple criteria. The emphasis is here both on identifying and overcoming the existing print-related technical limitations and on developing strategies for dynamically modifying hierarchical structures in printed components (e.g. 4D print strategies for time-dependent adaptation of structures and functions to a changing task) and designing heterogeneous composites which can be locally adapted in such a way that they remain functional in changing environments. Research should moreover focus on the development of sustainable, biocompatible and biodegradable materials which can nevertheless be used in durable and defect-tolerant components and on the influence of materials and fabrication conditions on the behaviour of cells during and after the fabrication process. Finally, the development of quality assurance methods, non-destructive in-process control and the combination of various additive manufacturing methods will also be of central significance not only with one another but also with conventional methods.

The following two interviews throw some light on the additive manufacturing of cell-based living materials (see sections 3.1 and 3.2).

61 | See Malda et al. 2013.
62 | See Jungst et al. 2016.

3.1 Interview with Héctor Martínez, CELLINK

Dr. Héctor Martínez is the Chief Technology Officer at Cellink, a biotechnology start-up that designs bioinks and bioprinters for culturing various cell types.

Dr. Martinez, what do you consider to have been the most important development in biologicalization in materials science?

Materials are extremely important for taking biology to the next level, but equally important have been the developments in affordable hardware and software technology: equipment that used to cost hundreds of thousands of dollars is now available for tens of thousands. Ease of use is also important: in the past, this equipment was designed for engineers while today it's designed for a multidisciplinary group with a particular focus on biologists. Ease of use applies to the software too. The systems are getting ever easier to understand, so simplifying the scientists' work.

How would you rate the innovation potential of knowledge derived from Nature – for your company and in general?

In the bioengineering sector you are 100 per cent looking at models from Nature: what is the composition of the natural material and what is the potential application? In mechanics and robotics too, there is well-established software based on natural processes and Artificial Intelligence in particular draws a lot of inspiration from the brain. It very much depends on the innovation at hand.

To return to innovation potential, can you see any?

Absolutely, yes. We have institutions being set up all around the world, we work in more than 50 countries and we see more and more research departments of bio-inspired or biomimetic engineering popping up. It's thrilling to see researchers from all these different disciplines working on a common issue!

You mentioned that you work in many countries. Who are the frontrunners in this field and how do they compare to one another?

In my opinion, the US are in the lead given their numerous publications and innovative results. US universities have a mixture of very heterogeneous researchers with students, postdocs and faculty from all over the world and they bring their brains together and create something amazing. We have a lot of access to what our customers are doing around the world and can see that the US is in pole position. But it's difficult to say which country might be in second place. I can see Japan has made major progress and of course there's Germany, the UK, Singapore and China too.

But how do you create space for innovation? We think that fundamental science is pretty strong in Germany, but how can this be transferred to innovation?

There are different cultures in Europe but you can still see a common mindset. In the US, the question from researchers is, "What's the latest? Has it been done before? No? Then I'll do it!" You don't have to be an expert, just do it! In Sweden and Germany, people are more like, "OK, there's something new. It sounds interesting. But has it been done before? No? What are the risks? What are other fields doing, can we combine it?" So from my standpoint, I have to sell it a lot more and have to do more convincing, Europeans are usually more sceptical.

Let's go one step back. What exactly does your company sell and how is this bio-inspired?

Our company sells various bioinks, bioprinters and software. For example, if you are replicating a human tissue, one of the most important steps is to incorporate the vascular bed. We use plants as role models and integrate their type of vascularity into the tissue. We have developed technologies with which the vascularity of, for example, a leaf can be mimicked and printed. This is how we make the printed tissue more tissue-like.

What are the major challenges right now and how do you assess the developments in the coming years?

It is all about looking at what my customers are doing: how can they create innovation with what we provide them and which applications are solvable by bioprinting? Then the question is: what could be the one application closest to market? And then we start working with the customers on how to advance the application, establishing partnerships with different institutions and working closely with transfer offices. With the technology and resources we have today, it's a matter of sounding out the limits of the feasible while also ensuring we create the right expectations.

3.2 Interview with Lutz Kloke, Cellbricks GmbH[63]

Dr. Lutz Kloke is the founder and CEO of Cellbricks GmbH, a company which specializes in bioprinting – printing with biological material.

Dr. Kloke, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

My initial response is of course "additive manufacturing", which will bring about huge changes in industrial production. This is clear from examples such as printing an entire aircraft wing and of course what they'd really like to do is produce an entire car in a 3D printer. But additive manufacturing is also moving into biology as well or has already well and truly arrived there and from our point of view it's an exciting process. I would say in general that technical methods which are used at interfaces and originally had nothing whatsoever to do with one another are becoming ever more relevant, as is precisely the case with the combination of additive manufacturing with biotechnology.

So what can we copy from Nature here?

Nature had to learn how to be economical with energy and materials and to build efficiently and there's plenty to inspire us and teach us valuable lessons.

What role do models from Nature play in materials development in your company?

We are attempting for example to replicate the barrier function of individual body parts, for example the placenta. Pregnant women have little certainty about whether drugs can or cannot be taken because it is not known whether they are capable of passing through the placenta. This is why we are attempting to replicate the placenta's barrier function in a Petri dish in order to carry out corresponding tests with the medicines. Printing cartilage is also of interest to us, not only would it be incredibly exciting but there is also a large market. It's actually a simple structure but we're finding it really difficult to replicate perfectly. These are the issues we're puzzling out and researching at the moment.

And where does additive manufacturing come into play?

We are trying to print these structures. Micrometre scale accuracy is required because reproducing the desired functionality entails locating the cells precisely where they can carry out their action. Of course, three-dimensional architectures are involved here and they can only be handled by additive manufacturing.

Do you have a product on the market?

We will probably have a barrier model on the market by late summer 2019.

What, in your opinion, are the major hurdles to future development and implementation in this field?

Customer acceptance. If Germany wants to be a technological pioneer in this field, we will have to focus tightly on deep-tech breakthrough innovations. It will be important to prepare our key industries for upcoming innovations.

Does the biologicalization of materials science have a part to play here, do you think?

It is making its arrival at various levels and the biology/technology interface in particular will be of interest, for example in the health sector. Biologicalization is happening right now and we must make sure we don't miss out!

63 | The interview was originally conducted in German.

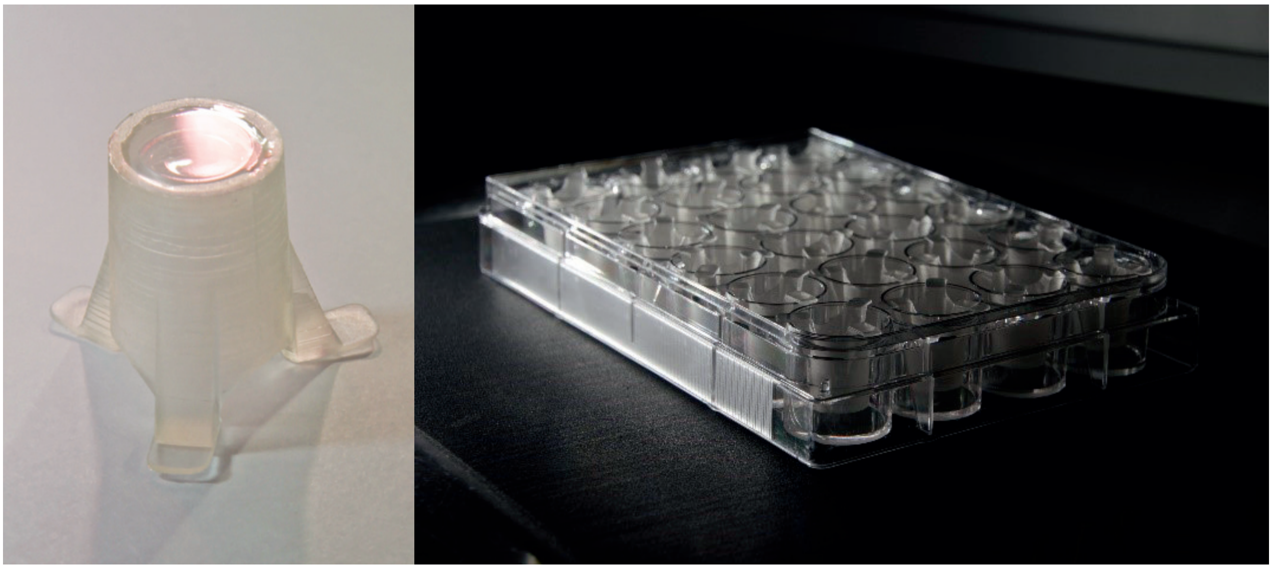

Figure 10: Cellbricks' "Membrick" acts as a standardized base for constructing three-dimensional in vitro barrier models such as placenta, intestine and lung (source: Cellbricks GmbH).

What kind of regulatory framework would you like to see here?

I would like policymakers to become aware of what biologicalization might become. There ought to be better support for small and medium-sized companies working in this high-risk area. I would also like large companies to cooperate more with start-ups and for incentives to be created, for example using tax-saving schemes.

What, in your opinion, are Germany's particular strengths and weaknesses in this area?

We are good at deep-tech, i.e. technologically demanding projects for which there is as yet no product and which relate more to basic research. On the other hand, we're not so good at translation. If there is a good product idea, we must let it actually turn into a product. We need to work on this translation bottleneck.

How do you think Germany is doing compared to other countries?

I think we have already been overtaken for example by China. The pressure to innovate and rate of innovation there are utterly different. Only time will tell whether the effects of this are good or bad.

But do you think that Germany can play a role or is already doing so?

It certainly can and indeed already is. There is great potential but we are sometimes rather too grey and bureaucratic, which holds us back. We need to be more courageous in investing at every level. Perhaps we need a generation which has more entrepreneurial courage and a "Let's just give it a go!" mindset.

4 Bio-inspired Lightweight Construction[64]

Prof. Dr. Thomas Speck
Faculty of Biology, University of Freiburg, Germany

Industrial lightweight construction, materials systems and structures and how to optimize them have been central themes in the aerospace industry for many decades. In recent years, however, lightweight construction has also grown in significance in other economically significant areas. Examples are the automotive industry, driven in particular by the switch to electromobility (range issues), civil and structural engineering, in particular due to the anticipated raw materials shortages (suitable sand for concrete production -> lightweight concrete) and increased use of alternative materials systems in building construction, and mechanical engineering, where it is becoming ever more important to achieve materials savings and the associated savings in transport costs.

Looking at the general context, political and societal pressure for sustainable development is constantly increasing, and this applies to all areas of technology. Lightweight construction can contribute significantly to sustainable development. Bio-inspired lightweight construction will be of central importance for the future development of sustainable technologies, by "borrowing" and incorporating resource-efficient approaches from biology. These approaches have still to be developed in many areas of technology and need to enable full recycling and feedback of the used raw materials (as far as possible without loss) into the resource loop once a technical structure has reached the end of its useful life. It should be emphasized at this point that although bio-inspired (lightweight construction) products have a high sustainability potential (the reasons for this will be explained below in detail), they are not sustainable *per se*, which means that each of these (lightweight construction) products needs its own sustainability analysis. It would moreover be desirable for these analyses to run alongside the development of novel lightweight construction systems and structures, rather than merely being performed "a posteriori", i.e. after completion of the development, as has so far been the case. Bio-inspired lightweight construction has the potential to contribute not only to the environmental and economic aspects but also to the social aspects of sustainability, as drawing inspiration from living Nature often leads to not only particularly functional but also markedly aesthetic results.[65] In addition, this "bio-inspiration" could help to connect the fields of Nature and technology, which are currently often miles apart.

Nature provides wide-ranging inspiration, which may contribute directly (biomimetic) or indirectly (bio-inspired) to the development and improvement of lightweight construction, materials systems and structures. From an evolutionary standpoint, material and energy savings, i.e. resource efficiency, are very important and are a selection advantage which should not be underestimated. This was summarized pithily by Julian Vincent in his rewording of Charles Darwin's most famous phrase "survival of the fittest" as "survival of the cheapest".[66]

An essential basic principle of biological lightweight construction is the pronounced hierarchical structuring of biological materials systems, which generally makes it impossible, and simultaneously unnecessary, to distinguish between material and structure. In biological lightweight materials systems, such as tree trunks, fruit skins and seed coats, bones, sea urchin spines or tortoise carapaces, it is typically possible to distinguish between five and nine hierarchical levels: these levels extend from molecular structure (sub-nanometre range) through cell wall ultrastructure (nano- to micrometre range), cell and tissue structure (micro- to centimetre range) to the structure of the overall organism (in the case of trees up to a maximum of a hundred metres) and thus span twelve orders of magnitude. Biological lightweight materials systems typically consist of a cellular (porous) matrix, in which fibres or fibre bundles are embedded in a load-optimized direction and distribution. This gives rise to materials systems which are simultaneously rigid and tough, and which also display characteristic, benign failure behaviour. The fibres are generally connected to the matrix by gradual transitions, involving multiple hierarchical levels, which not only reduces the risk of delamination but also improves damping properties.

After analysis and abstraction of the structure/function relationship of biological model systems, the targeted transfer of individual or multiple structural parameters can result in the development of particularly resource-efficient novel lightweight materials systems specifically for application in the most varied fields of technology. It is moreover possible to make these materials systems "smarter" in a bio-inspired way, for example so that they respond self-adaptively to environmental influences or other disturbances. These adaptations are stored in their molecular structure, making the materials systems "trainable". In addition,

64 | This contribution was translated from German into English.
65 | See Knippers et al. 2019.
66 | See Vincent 2002.

(low-level) damage may be repaired autonomously, resulting in highly robust and resilient bio-inspired materials systems. Using bio-inspired approaches in materials science opens up the way to major innovation potential; paradigm shifts in materials system functionalization and functional integration are anticipated.

Germany is in a very good position to develop such novel, smart, bio-inspired materials systems due to its very active, innovative materials research, which covers all areas, from basic research to application-focused and industrial research, and its long and successful tradition of developing bio-inspired materials. The "Living, Adaptive and Energy-autonomous Materials Systems (*liv*MatS)" Cluster of Excellence is a good example of this. The cluster was launched in January 2019 at the University of Freiburg with the aim of developing bio-inspired interactive and energy self-sufficient materials systems without involving living cells.

In industry and research, lightweight materials systems and structures are an increasingly important focus of research and development worldwide. However, although the idea of "bio-inspiration" is often discussed in terms of optimizing and functionalizing lightweight materials systems and indeed used in basic materials research, conversion to market mature commercial products is still in its infancy. This widely debated "Valley of Death" can be bypassed or bridged most effectively if it is not (only) R&D departments of the companies involved that participate in research- and development projects but also predevelopment and ideally also pre-series and series development departments.

One challenge is that many innovative, bio-inspired lightweight materials systems and structures are based on composite materials, with various technical fibres (sometimes with bio-inspired arrangement and distribution) embedded in a porous or foamed, sometimes graduated matrix. This results in extremely lightweight, functionalizable materials systems with a high mechanical loading bearing capacity. However, due to their composite structure, such systems represent a major challenge when it comes to separating them into their individual constituents, a necessary step if they are to be reused in the context of a sustainable recycling policy. One option, of which many examples are to be found in biology (e.g. leaf fall), is therefore to develop methods for separating the individual material constituents once the lightweight materials system has reached the end of its useful life. Another option is to produce single-material lightweight structures, in which individual areas of the same material are made to be more rigid or resilient during the production process. Nature provides many different models for this too, such as highly rigid and extremely resilient zones of the exoskeletons of insects and crustaceans.

4.1 Bio-inspired Modification of Wood[67]

Prof. Dr. Ingo Burgert and Dr. Tobias Keplinger
Institute for Building Materials, ETH Zurich, Switzerland

Future biologicalization of materials development is closely linked with more differentiated, more demanding use of the renewable resource wood. Wood is characterized by a porous structure which is capable of withstanding high mechanical loads. The reason for this is the evolutionary optimization of the structure of wood to fulfil two material requirements and functions which, though contradictory, are both essential to the living tree: on the one hand, efficient water transport from the roots to the crown, which requires a porous structure oriented along the length of the tree, and on the other hand high stiffness and strength, which is guaranteed by compact wood fibres, to allow growth upwards while resisting the force of the wind. If the age of several thousand years which trees can reach is also introduced into the equation, wood from trees may be regarded as a long-life, extremely energy-efficient, mechanically stable lightweight structure.

Therefore, when working on the innovative development of wood-based materials, not only the natural structure of this CO_2-storing resource but also the tree's physiological processes can be taken as bio-inspiration for the design of an optimized material. To lend wood improved or new properties and so open up additional possibilities for its use, technically mature, scalable modification and functionalization approaches are needed. As a result, it will in future be possible to replace materials with finite availability or with energy-intense production processes with an at least roughly equivalent renewable resource. In the past, various methods have been developed to make wood more durable, more dimensionally stable or less combustible for common applications, but also electrically conductive, magnetizable or transparent for new fields of application.

67 | This contribution was translated from German into English.

One example from the more recent past, which demonstrates the highly promising synthesis of bio-inspiration with use of the renewable resource wood, is high-strength cellulose composites, which are produced by removing lignin from the cell wall and middle lamella of the wood, in a process derived from papermaking. However, separation of the wood fibres is avoided and the hierarchical structure of the wood and thus the parallel fibre arrangement is retained (see Figure 11). The large interior surface area of the exposed cellulose skeleton opens up the way to a wide range of functionalization approaches and new property profiles. In addition, in the wet state, multiple shaping options become available which may be exploited for complex component geometry. An optimized grain, inspired by the way branches connect to the trunk, is one example of what can be achieved. A compaction step produces high-strength cellulose composites, with a uniform or gradual density profile depending on intended use.

These new cellulose composites can be used as the basis for new material concepts, which may result in optimized utilization of wood as a renewable resource for bio-based high-performance materials. Intensive research needs to be carried out, however, to transfer the basic methodology to industrial manufacturing processes and so convert the new concepts into actual products.

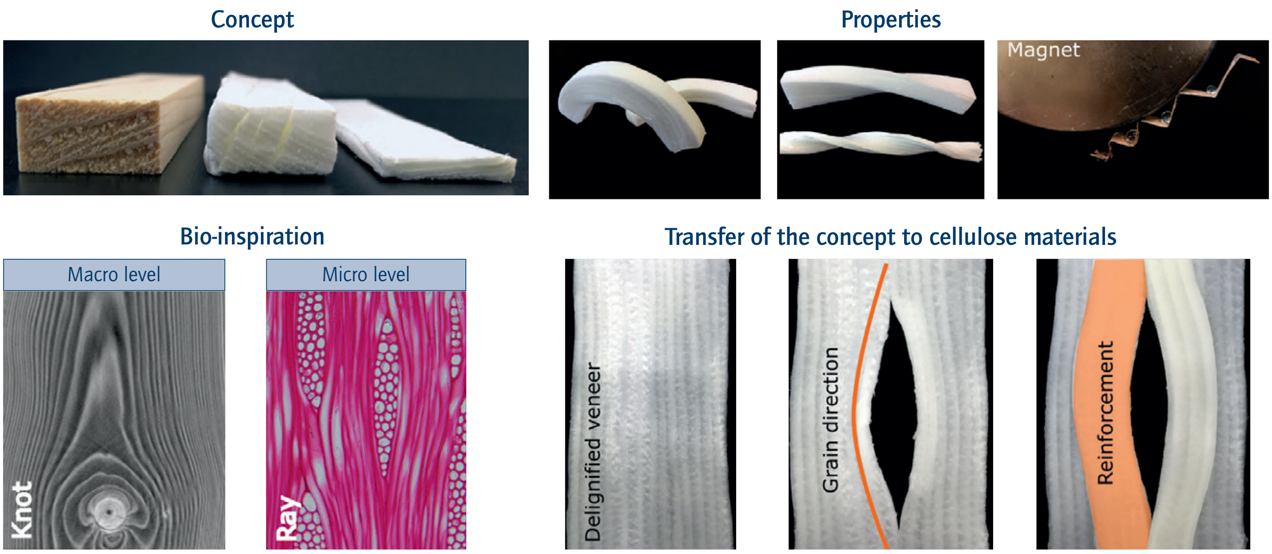

Figure 11: Cellulose composites based on a synthesis of bio-inspiration with use of the renewable resource which is wood in modified form (source: in part from Frey et al. 2018 and Frey et al. 2019)

4.2 Example: Fibre Pavilion at the Bundesgartenschau, Heilbronn, 2019[68]

Prof. Achim Menges
Institute for Computational Design and Construction, University of Stuttgart, Germany

Prof. Dr. Jan Knippers
Institute of Building Structures and Structural Design, University of Stuttgart, Germany

Embedded in the undulating landscape of the Bundesgartenschau (BUGA) grounds in Heilbronn in 2019, the BUGA Fibre Pavilion offers visitors an astounding architectural experience and a glimpse of future construction. The pavilion builds on many years of biomimetic research at the Institute for Computational Design and Construction (ICD) and the Institute of Building Structures and Structural Design (ITKE) at the University of Stuttgart.[69]

In biology, most load-bearing structures are fibre composites. These are made from fibres, such as cellulose, chitin or collagen, and a matrix material that supports them and maintains their relative position. Both the astounding performance and unrivalled resource efficiency of biological structures stem from these fibrous systems. Their organization, directionality and density are finely tuned and locally varied in order to ensure that material is only placed where it is actually needed.

The BUGA Fibre Pavilion aims to transfer this biological principle of load-adapted, highly differentiated fibre composite systems into architecture. The composites of glass and carbon fibre that were used for this building are ideally suited for such an approach because they share fundamental characteristics with natural composites.

The pavilion's load-bearing structure is robotically produced solely from fibre composites. The pavilion covers a floor area of around 400 square metres and its largest free span is more than 23 metres. The primary load-bearing structure is made wholly from sixty bespoke fibre composite components. At 7.6 kilograms per square metre, it is exceptionally lightweight, approximately five times lighter than a more conventional steel structure.

This globally unique structure is not only highly efficient and exceptionally lightweight, but also provides a distinctive yet authentic architectural expression and an extraordinary spatial experience.

It shows how an interdisciplinary exploration of biological principles together with the latest digital technologies can lead to a novel, digital fibre composite building system. Only a few years ago, a pavilion of this type would have been impossible to design or build.

Figure 12: Fibre Pavilion at the Bundesgartenschau (BUGA) 2019 (source: Institute for Computational Design and Construction ICD/Institute of Building Structures and Structural Design ITKE, University of Stuttgart)

68 | This contribution was translated from German into English.

69 | Project partners: Institute for Computational Design and Construction (ICD), University of Stuttgart: Prof. Achim Menges, Serban Bodea, Niccolo Dambrosio, Monika Göbel, Christoph Zechmeister; Institute of Building Structures and Structural Design (ITKE), University of Stuttgart: Prof. Jan Knippers, Valentin Koslowski, Marta Gil Pérez, Bas Rongen; FibR GmbH, Stuttgart: Moritz Dörstelmann, Ondrej Kyjanek, Philipp Essers, Philipp Gülke; Bundesgartenschau Heilbronn 2019 GmbH: Hanspeter Faas, Oliver Toellner.

4.3 Interview with Stefan Schlichter, Institut für Textiltechnik Augsburg gGmbH[70]

Prof. Dr. Schlichter is managing director of the Institut für Textiltechnik Augsburg gGmbH, which is affiliated to Material Resource Management at Augsburg University. He is also a Division Manager at the Institut für Textiltechnik at RWTH Aachen University.

Prof. Schlichter, how much involvement do you have with bio-inspired materials?

Our activities fall within the "from Nature" heading, and we are mostly working on materials research into bio-based raw materials. However, the aspect of recycling as a resource and materials source is also of major importance, so we have just run a major project.

What, in your opinion, has been one of the most significant developments in bio-inspired materials science in recent years?

The use of natural raw materials to produce industrial products. It has to be said that, worldwide, the majority of natural fibres in general, and in particular cotton, are still used in the clothing sector, at least if we're talking by weight. However, high-performance materials can also be produced on the basis of renewable resources, for example natural-fibre-reinforced plastics. Natural fibres bring many advantages, especially in the clothing sector, for instance their water-absorption properties are ideal from the standpoint of clothing psychology. It is unlikely that we will be able to wholly replicate this with man-made fibres, but overall big steps forward are being made in research, all that's missing is implementation.

What does this depend on or rather what are the hurdles and challenges to implementation?

One of the main problems with natural raw materials is the greater variation in properties compared with man-made fibres which is the natural result of harvest and growth conditions. Still, much as already been achieved in the past few years: in the automotive industry Mercedes-Benz has moved over to flax-based composites in some areas, for instance. However, the disadvantage is that the composites still contain polypropylene, i.e. synthetic materials, on the plastics side. No breakthrough has as yet been made which enables the use of fully bio-based composites. In textiles, in recent years much has also been achieved with milk, i.e. lactate-based fibres, these are growing in significance as a possible replacement for conventional man-made fibres and display very good properties.

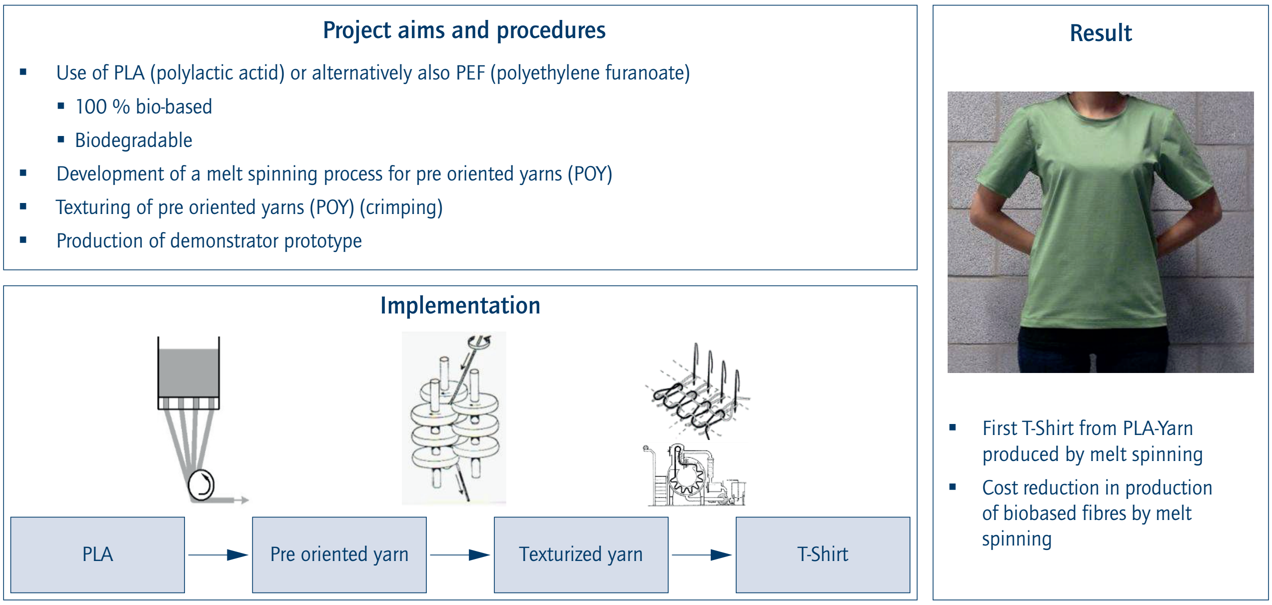

Figure 13: Second generation biopolymers – development of the process chain for a T-shirt made from polylactic acid PLA (source: Institut für Textiltechnik Augsburg gGmbH/RWTH Aachen University)

70 | The interview was originally conducted in German.

Industrially, however, it is economics which ultimately count and that is preventing a breakthrough. Many people persist with conservative approaches and prejudices, for example that flax releases odours, making a car smell of hay.

What structural changes would be necessary for headway to be made?

On the one hand, legislation can be helpful: for example a decision was taken that the EU's Waste Management Directive also has to be fully implemented in the textile sector by 2025. This would mean all clothing must be recycled, and the statutory provisions are sure to provide motivation to reduce the cost difference too. On the other hand, however, there are of course still some technical aspects which need work, for instance the database for bio-based raw materials is not yet complete. And new raw materials will need to be created in future. In this respect, I should like to talk about CO_2 capture, by way of an example. If I were to filter out CO_2 from the air and use it to make a hydrocarbon, I would then have the basis for making high-performance materials, in other words I would have Green Carbon. At present, carbon is produced from oil using complex, energy-intensive methods. There are new approaches, which produce it using lignin, but the properties of these carbons aren't up to scratch yet. There are other approaches, which use glycerol from biogas production (which is available in enormous quantities), or indeed actually from CO_2 capture. In terms of composite materials, it will also be important to produce the matrix materials from natural materials, since only then is a raw material obtained which is actually fully biodegradable. What we have at the moment is a misleading compromise, because polypropylene and glass fibre are often included. Nonetheless there is considerable potential for innovation. It must always be borne in mind that textiles are one of the biggest sources of raw materials which are processed worldwide. By weight, steel is obviously in first place, but by volume there is no raw material in the world which is processed as much as textiles.

So what has to happen to make full use of this considerable innovation potential?

Well, clearly we need more research programmes. Also we still have the cost problem, which in many aspects is just a problem of scale. However, a life-cycle assessment will reveal that whether something is worthwhile is just a question of the observation time frame. For example, it is obviously initially cheaper to use polypropylene, but the only recycling option for that is thermal energy recovery, so costs are ultimately incurred again. Another aspect of materials development which I consider important is that we have to build a database to enable designers to work with these materials. Industrially, it is often the case that product designers don't have the data to hand that they need about the characteristics of textile products or naturally based fibres. We need a database if we're to come up with designs, and "design for recycling" is where we need to be, i.e. my raw material has not only to be bio-based, but I also need to produce a product which allows raw material recovery once it reaches the end of its useful life.

How is Germany doing compared to other countries?

In the textile sector, our level of know-how is still relatively high. The general assumption is that the textiles industry has moved abroad, and that is true to a considerable extent of the clothing industry, because we don't grow the essential raw materials and we have virtually no weaving and spinning mills left which process natural materials. The knowledge is still there though. Germany is still a leading country in textile machine industry, in particular with regard to processes and industrial methods. We have the development culture and right industrial base. Not many people know that Germany is a leader in engineering textiles. So where are the engineering textile products? It's a good question and I always tell my students, look around your car, it's full of textiles: the roof liner, the carpet, the door trim, the luggage compartment, the sound insulation, the whole of the seat, the seat belt, and so on. The hygiene sector or road construction are equally good examples, which use lots of engineering textiles and continue to be highly active, innovative branches of industry of relevance to Germany. We also still have a large number of textile research institutes in Germany, the world's leading textile mechanical engineering sector, leading processors and a great deal of know-how in fibrous materials. The Faserinstitut Bremen e.V. (associated with the Bremen cotton exchange) continues to lead the world in materials research into natural textiles, and our Institute is the world leader in producing fibres from biopolymers.

5 Soft Robotics

Prof. Dr. Metin Sitti
Max Planck Institute for Intelligent Systems, Stuttgart, Germany

Two of the major scientific challenges of robotics are robust and efficient operation of robots in complex natural environments and robust and safe interaction of robots with human beings. One of the recent approaches to solving these challenges is the creation of fully or partially soft-bodied robots, similar to animals in Nature that make smart use of soft materials and structures. Soft robotics, which combines robotics with materials science and biology, has thus emerged as a new field of robotics within the last decade.

Many new capabilities could be offered to robots at different length scales if they had soft-bodied designs inspired by soft-bodied animals, such as octopuses, squid, jellyfish, caterpillars and worms or also fungi, moulds, many cells, and microorganisms (amoeba, algae, bacteria, spermatozoids, *C. elegans,*[71] etc.) or animal organs (e.g. the elephant's trunk). This is firstly because soft-bodied robots can dramatically change their shapes passively or actively to adapt to their dynamically changing, constrained and complex environments. Secondly, large, nonlinear and programmable deformations of body shape enable many diverse forms of locomotion and functions, such as camouflage or manipulation, that are not possible with rigid robots. Soft robot designs may thus potentially have reduced mechanical and algorithmic complexity. Finally, such designs provide safe and robust human-robot interaction, since soft robot mechanisms can be designed to have inherently limited force output capabilities, which would prevent any possible damage to the human body even in a worst-case scenario.

There are currently two main approaches to designing soft robots. Firstly, synthetic soft materials, mechanisms, and forms of locomotion inspired from animals have been discussed for creating soft robots. For soft robotic locomotion systems, the main focus has been on octopus-inspired soft arms and swimming, jellyfish-inspired swimming, and caterpillar-inspired surface crawling robots. These robots are actuated by stimuli-responsive hydrogels or elastomers. Such soft actuators are driven by light, heat, electrical fields, magnetic fields, pH, or air/fluid pressure. Actuators of this kind set a soft mechanism, such as a soft arm, in motion to achieve a gentle robotic swimming or surface crawling movement, feedback control being possible by integrating (capacitive or resistive) soft sensors.

Currently the most advanced soft robotic locomotion system, magnetically driven "millirobots" have magnetic particles embedded in them in such a way that a well-defined magnetic profile is obtained, so that they can be driven by an external magnetic field which varies in direction and strength and simultaneously perform seven types of locomotion. This millirobot study is a good example of how a minimalist soft robot can achieve complex dynamic shape programming, so opening up a wide range of dramatically different behaviours for various complex natural environments.

In the second approach, biologically active cells such as muscle cells (e.g. cardiomyocytes) or microorganisms (e.g. bacteria or algae) are integrated with synthetic soft materials to create soft biohybrid (biological + synthetic) robots. A squid-like biohybrid swimming robot has recently been produced which has electrically driven micropatterned cardiomyocytes or skeletal muscle cells attached directionally to elastomer structures. So far, it has only proved possible to demonstrate actuation and locomotion of such biohybrid robots.

Soft robots are intended for use in the most varied applications. Mobile soft robots are set to be used in medical applications (e.g. soft medical devices have already been tested inside the gastrointestinal tract and other regions of the human body), as service robots made of inflatable fabrics to interact with people safely, and as field robots to monitor, explore and remediate the natural environment. So far, such robots are just prototypes and no commercial application has yet been demonstrated. On the other hand, soft robotic grippers can be used to manipulate complex objects. Jamming-based soft grippers which operate by compacting granular media inside an elastomeric skin under internal vacuum control have recently been presented, as have soft grippers which are capable of robust 3D manipulation of complex objects and are inspired by both the elephant's trunk and the gecko's feet. Several start-ups in the USA and Festo GmbH (see section 5.3) in Germany are currently commercializing both inflatable and jamming-based grippers.

In current bio-inspired synthetic soft mobile robot designs, it has so far only been possible to provide simple (e.g. no stiffness tuning and directionality) and inefficient soft actuators. Moreover, the focus has previously been solely on actuators and locomotion mechanisms. There is a significant need for new bio-inspired active soft actuator materials with high efficiency and programmable, directional and variable stiffness. Furthermore, no computational modelling and simulation tools are yet available to provide rigorous and universal design methods for creating soft robots with nonlinear active and passive material and motion

71 | A nematode of the order Rhabditida.

behaviour. Another challenge is that of integrating soft sensors into such soft robot mechanisms to enable advanced feedback control. Moreover, current simple soft robot control methods are not yet robust and adaptive because the complex dynamics of soft robots, environmental disturbances, and uncertainties cannot yet be modelled. Finally, fully soft robots also require a soft power source, computing and electronics. A group at Harvard has recently demonstrated preliminary microfluidic circuits for soft electronic devices. In developing biohybrid soft robot designs, there are many scientific and engineering challenges in relation to interfacing biological cells and synthetic soft materials (e.g. adhesion and biocompatibility issues), achieving more complex functions other than just actuation and locomotion, and demonstrating them in realistic applications. So far, there has been no killer application or demonstration of the commercialization of soft robots in the real world. In medical applications, soft robots need to be biocompatible and even biodegradable. In addition to the locomotion capabilities that have already been demonstrated, they need to have medical functions, such as drug delivery, remote heating, tissue biopsy, and closing or opening up of vessels. Moreover, shape change and position need to be visualized in real time using medical imaging methods for feedback control. Achieving such diverse medical functions which can be tracked using medical imaging methods is a major challenge for the field of soft robotics.

New bio-inspired and biohybrid active soft actuator materials with high efficiency and programmable directional and variable stiffness are vital. Liquid crystal elastomer (LCE)-based hybrid soft actuators (e.g. magnetic + LCEs, pneumatic + LCEs) are highly promising for such new actuator materials. Next, new computational modelling and simulation tools need to be developed for universal design methods for creating soft robots. Moreover, new hybrid (soft + rigid) designs need to be explored since fully soft robots have limited capabilities and applications, in particular at large scales, where most large animals combine rigid and soft-bodied materials in their mechanisms and bodies. Given the nonlinear, uncertain and as yet unmodelled dynamics of soft robots, there is a need for advanced, reinforcement learning-based control methods. These will enable learning and control of soft robot dynamics and so create the foundations for autonomous robot navigation and functional control. Finally, high-impact real-world applications of soft robots need to be demonstrated in medicine, robotic manipulation, mobile robotics, and service robotics.

Germany has the potential to be a world leader in soft robotics. A new Priority Programme from DFG,[72] the German Research Foundation, for soft robotics is already in place which began in 2019 and is intended to intensify the research activities in Germany in this new field. However, it would be more relevant to boost scientific activity, collaborative projects, and visibility in this field by larger scale centres, e.g. funded by DFG and BMBF, the German Federal Ministry of Education and Research, for high-risk and high-impact research activities. Moreover, it is essential to support the formation of new start-ups in this field in Germany in order to translate some of the new scientific discoveries into commercial applications to demonstrate the real-world use of soft robots and increase their social and industrial impact. Finally, it is to be anticipated that medical applications of soft robots will have the greatest scientific and social impact, so supporting such scientific research and the formation of start-ups using various bio-inspired and biohybrid material approaches would be a highly promising direction to follow.

Two examples of soft robots inspired by natural organisms are described below. Barbara Mazzolai presents plant-inspired robots (see section 5.1) while Cecilia Laschi (see section 5.2) describes a soft robot developed on the basis of the octopus. The interview with a representative of Festo, one of Germany's leading robotics companies, highlights the potential of bio-inspiration and the need for broad collaboration between different branches of industry and academia both in Germany and internationally (see section 5.3).

5.1 Robots Based on Plants

Dr. Barbara Mazzolai
Center for Micro-BioRobotics, Istituto Italiano di Tecnologia (IIT), Pisa, Italy

Plants show amazing capabilities for growth and endurance, with smart, effective, and efficient adaptation strategies. Across sea and land, they are able to sense their surroundings and to respond by growing their body and by adapting their shape to limiting and stressing conditions. Plants can anchor themselves and resist unpredictable external forces, such as wind, waves, or falling debris, across a variety of scenarios, and can survive in constantly changing environments by using highly energy-efficient strategies. Because of these unique features, plants have recently been regarded as inspirational models for the design of innovative technologies and systems in robotics, specifically for the development of self-morphing, growing robotic machines capable of better challenging unstructured and extreme environments thanks to their ability to continuously adapt their bodies.

72 | SPP 2100: Soft Material Robotic Systems.

For over ten years, the Center for Micro-BioRobotics of the Istituto Italiano di Tecnologia (IIT) has been investigating plants to propose robotic solutions inspired by these living organisms. At the outset, we focused on the investigation of plant roots with the aim of developing autonomous robots or "plantoids" capable of moving in soil both on Earth and on other planets and carrying out monitoring tasks. These robots are endowed with distributed sensors, actuators and intelligence. Roots, in fact, are the plant organs responsible for seeking out nutrients and for anchoring. In performing these tasks, roots, which have tips equipped with numerous sensors and explore the environment in an efficient way, constantly adapt to their environment, avoid obstacles, penetrate soil and selectively collect the minerals and water which are essential to plant life. To reduce friction and high pressures in soil as they move, roots grow by adding new cells at the apical region of the root tips and then absorbing water from the environment. In this way, only the tip is pushed further into the soil while the rest of the root body does not move, so reducing soil resistance. Analogously, the PLANTOID robot (see Figure 14) grows its roots apically by using an additive manufacturing process embedded in the apical part, i.e., the tip, of the robotic root. Using a miniaturized 3D printer, the system is able to deposit a filament of new material and, layer-by-layer, advance the tip of the robotic root, so penetrating the soil as it "grows", the direction of growth being determined on the basis of external stimuli perceived by the sensors integrated in the tip.

More recently, the group has also started to consider climbing plants as a new model to propose a disruptively new paradigm of movement in robotics inspired by their moving-by-growing abilities. Many climbing plants do not form a sufficiently strong stem to support their growth and, without an external support, they flop and creep along the ground. These plants accordingly have structures to enable them to actively seek out and use physical supports. Most of these species use exaggerated circumnutation (CN) movements to come into contact with and climb neighbouring objects. The new generation of climbing plant-inspired robots, named GrowBots, will be low-mass and low-volume artefacts, endowed with multifunctional materials to sense and interact with the environment and capable of anchoring themselves, negotiating voids, and climbing, where current climbing robots based on wheels, legs, or rails would get stuck or fall.

Soft robotics has the potential to create systems with improved movement and adaptability performance in unknown, challenging, environments. Beyond the concept of pre-formed soft robots, the new class of plant-inspired growing machines, able to self-create their own body, is expected to open up new operations in unstructured scenarios under unpredictable external conditions. By mimicking the ability of biological systems to be energy-efficient, change their morphology and adapt and grow their body and functionality over their lifetimes, these new robots promise to introduce entirely new capabilities in exploration, agriculture, analysis or emergency scenarios.

From a scientific perspective, these bio-inspired soft robots will also have an impact by improving our understanding of plant science. Since these robotic solutions are designed on the basis of specific plant features, a new generation of robots for biology can be envisaged which are intended to provide insights into the biology of organisms and elucidate the basis of complex biological behaviours. The robot in fact offers the advantage of being programmable and reconfigurable so that different hypotheses can be tested. While in many cases the models can be implemented and tested in software simulations, a robot can help explain the behaviour of biological systems by evaluating their capabilities in the real world. Bridging the gap between robotics and biology in this way will help to consolidate the fundamental and emerging role of robotics over the coming decades and open up exciting new opportunities in both science and engineering.

Figure 14: The PLANTOID robot is an artificial replica of an organic plant (source: Barbara Mazzolai, Istituto Italiano di Tecnologia, Pisa, Italy).

5.2 How an Octopus Inspired Soft Robotics

Prof. Dr. Cecilia Laschi
BioRobotics Institute of the Sant'Anna School of Advanced Studies, Pisa, Italy

Look at an octopus with a roboticist's eyes: it has a soft body, its arms are soft and deformable and they can bend in any direction at any point along the arm, but they can also stiffen when needed and grasp and pull objects with considerable force. This huge range of movement is elegantly controlled by the animal without any apparent effort.

Despite the rapid growth of robotics technologies and the huge potential for a massive introduction of robots into our daily lives that is widely discussed today, the materials robots are built of have not previously been the focus of robotics research. Most robotics theories and techniques are based on rigid-link robots which provide the exceptional accuracy, speed, robustness and reliability of today's robots, which are mainly used in manufacturing. "Service" robots which are capable of negotiating the natural environments of our daily lives still struggle to achieve the same levels of effectiveness and a comparable market share.

An octopus can demonstrate a different approach, in which the focus is on investigating materials and in particular their variable rigidity. By understanding the secrets of the octopus' soft dexterity and copying a few key principles, a soft-bodied eight-arm robot that can crawl in water and pick up objects with a firm grasp has been built and tested. This octopus-like robot is a good demonstration of the feasibility of soft robots and related technologies, but its particular contribution is that it has put the spotlight on robot materials and drawn attention to the role of soft materials in improving robot capabilities in real-world applications.

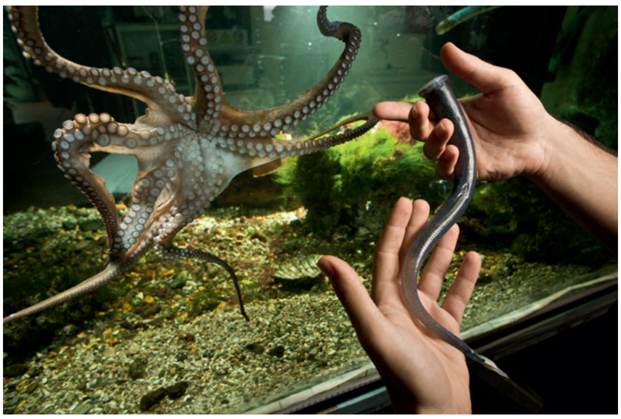

Figure 15: Octopus-like robot arm prototype together with its real-world inspiration, an octopus (source: Massimo Brega)

Today, there is a significant community of scientists studying soft robotics, who are not only picking up the many interdisciplinary challenges of building soft robot components and systems, but are also focusing on suitable applications in biomedicine, in exploration, and even in manufacturing.

5.3 Interview with Karoline von Häfen, Festo AG & Co. KG[73]

Karoline von Häfen is designer and Head of Corporate Bionic Projects at Festo AG & Co. KG and her work primarily focuses on conceptual design and on project management in the Bionic Learning Network. The Bionic Learning Network, which creates a link between Festo and renowned universities, institutes and development companies, provides new ideas for technical applications and industrial practice which are inspired by Nature.

Ms. von Häfen, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

Even though it doesn't have a great deal to do with my own work, I find the 3D printing of organs fascinating. It is incredible that something as complex as a human organ can simply be printed. It's a perfect example of combining what we can learn from Nature with what technology can offer in order to provide a huge benefit to humanity.

What's your opinion in general of the innovation potential offered by knowledge inspired by Nature?

It's impossible to overstate its value. In our field of bionics, the key questions are: what can we learn from Nature? What vital principles can we find that we want to put into practice? Nature is able to draw on a huge variety of ideas and solutions for the most varied tasks and issues which we haven't even addressed yet. But we have already had some successes, for example in decoding bird

73 | The interview was originally conducted in German.

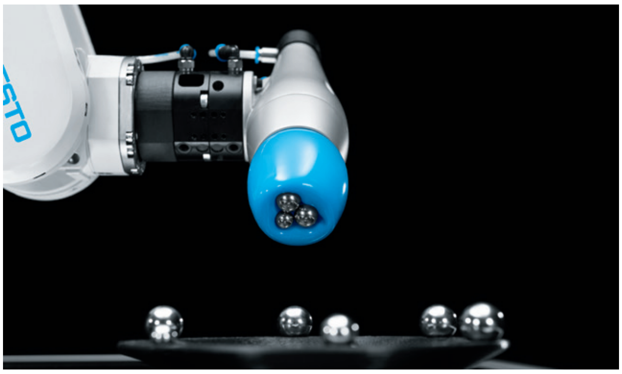

Figure 16: Inspired by the chameleon's tongue, the FlexShape-Gripper is capable of grasping a huge range of objects by moulding itself around them (source and copyright: Festo AG & Co. KG, all rights reserved).

flight. Humans will, of course, never come close to the original as Nature has a huge lead on us. Nature provides an endless repertoire of new ideas. It's much simpler to copy something from Nature than to think something up from scratch. Everything has been put to the test by evolutionary processes, and the defects have been eliminated over a vast period of development.

Could you describe a specific field of application where your company is carrying out materials development?

Over the past year, we have been taking a close look at the flying fox, specifically its skin. Its skin has to be as stretchy as a sheet of rubber while simultaneously being extremely light - any additional weight would stop it taking off. We've managed to find a great combination which has exactly these properties. And this arose from the requirement: if the material is not elastic, the flying fox can't fly and if it's not light, it can't either. However, this material is not yet commercially mature.

Do you also have an example of something which you've seen in Nature and have subsequently found an application for?

Yes, the chameleon's tongue: firstly, it's sticky and, secondly, it has a tip which can curl back around its prey to hold it tight. That caught our attention because in automation we also have to grip things and hold them tight. We exhibited the gripper as a prototype four years ago at the Hannover Messe trade fair and it has been commercially available as a series product since earlier this year (see Figure 16). In addition to the tongue's gripping function, it was also of interest from the point of view of material: taking the tongue as basis, we created a tulip-shaped silicone rubber gripper tip capable of gripping a wide range of non-specific objects, even several at once, without requiring a sensor system.

So what do you think are the major hurdles or challenges for the development and implementation of bio-inspired materials?

My thinking is heading off in a somewhat different direction at the moment, towards Artificial Intelligence. "Reinforcement learning", i.e. learning by confirmation and reward, is another idea copied from nature. But how can a machine be rewarded? By an algorithm is the answer, but the principle is the same. And there is already anxiety about whether machines will take over our jobs and whether humans have outlived their usefulness. It would be advisable to make technology usable in a supportive role for humans and to communicate this clearly to them.

What would you like to see happen so bio-inspired materials can move forward?

Good ideas and innovation cannot be shared often enough. This is a principle we apply in our Bionic Learning Network, in which we collaborate with numerous partners, including internationally. We have many ideas and, when it comes to materials or principles of design amongst other things, we are counting on cooperative projects with universities and other companies to see them put into practice. This way, we have the opportunity always to be working on something new and to make major strides forward, so that we don't stagnate. Many ideas come from outside, so business, universities and students all benefit.

Do you think that a product from the area we've been discussing takes longer to get to market or are the challenges different?

That's not quite how things work. As a rule, products or demand for them comes from the market. How can customer needs be met? Where are there applications for which there is not yet any solution? If, however, we are learning from Nature, the focus is not on what a customer need might be, but on what is there that's interesting for us to learn here? And when we've learned something interesting, the question then arises of how it might fit with the needs? So we start from the solution and then look for the problem - which is a completely different approach.

Do you have any idea how it might be possible to create a better environment for bringing about such a paradigm shift or new mindset?

Mindset is the right word here. After all, there is no shortage of ideas and approaches. Perhaps there's a need for more latitude so that we're not just mechanistically managing tasks, but companies do have to keep an eye on the economics of what they're doing. We have a good university and research landscape, which is a very good starting point.

6 Bio-inspired Energy Materials[74]

Prof. Dr. Martin Möller
Leibniz Institute for Interactive Materials, Aachen, Germany

The question of energy conversion and energy storage is possibly the most challenging future issue in terms of the biologicalization of materials science. There is certainly no doubt that this is the area where there is the greatest gap between environmental requirements and current practice. Whatever we do to develop technology which is in harmony with Nature, it will be dependent on our having sufficient quantities of renewable energy available both to meet growing human needs and to enable clean or green technology. A perfectly functioning circular economy of the future cannot be achieved without sufficient energy input, either. In other words, energy-saving measures and the development of energy-efficient processes cannot replace future efforts to find new renewable energy sources.

Basically, we are aware of only three sources: chemical energy, light and heat and stored electrical energy, all of which have their origin in solar radiation. While around eighty per cent of the world's current energy requirements are met by fossil sources, these are in fact solar energy stored over the course of the Earth's history as chemical energy in the form of coal, oil and gas. Sunlight and the resultant heating are the drivers of wind and hydroelectric power. We generate electrical energy from these sources either indirectly, or directly via photovoltaics.

Given that sunlight is the Earth's primary energy source, there are questions to be answered as to whether this source is sufficient and why we do not make greater use of it. The first question is easily answered. The radiant energy which reaches the ground can, under a clear sky, reach a power of 1,000 watts per square metre and, on dull winter days, fall to 50 watts per square metre. This results in an annual energy input for Germany of 1,000 kilowatt-hours per square metre, and for the Sahara of 2,200 kilowatt-hours per square metre. The figures indicate that solar energy irradiation exceeds humanity's energy requirements by more than four orders of magnitude even when all "green" technology requirements are included. So the emphasis has to be on the second question, which is why we do not make direct, and above all much more, use of sunlight as an energy source. If we disregard today's dominant factors, such as lack of infrastructure, which means not only high levels of capital investment but also long development times are required, political uncertainty in the particularly sun-rich regions of the Earth and competitiveness with fossil energy sources, then two technical arguments remain, which will be examined in this study. These are firstly the comparatively low efficiency with which light is collected and converted into technically usable energy, such as heat or electricity, and secondly the limited options for storing the harvested energy so it can be provided at the right place at the right time.

Plants, bacteria and algae make direct use of light for life via photosynthesis, but this process is also not very efficient, with less than four per cent of the light energy being converted into chemical energy. Synthetic biology, however, is already able, using artificial but fully biological metabolic pathways, to chemically bind carbon dioxide from the air with twenty per cent greater efficiency than plant photosynthesis, and combining photovoltaics with power-to-X methods is opening the way to even greater improvements. Power-to-X research is focusing on the development of efficient plants and rapid introduction to the market. In his interview (see section 6.5), Stefan Buchholz points to the Evonik project, in which electricity from renewable sources is used for an electrolysis process in combination with microbiological fermentation to produce butanol and hexanol as important basic chemicals via biohybrid photosynthesis.

The outlook is completely different if the materials used as system components themselves become energy collectors. Here, Nature provides the model of integration and decentralization. Energy is supplied externally in the form of light and no longer necessarily via electrical connections or as mechanical energy. One example is provided by the "artificial leaves" presented by Marc-Denis Weitze, which integrate light absorption and hydrolysis (see section 6.2). Other examples have already been presented by Metin Sitti under the Soft Robotics heading (see section 5). Against the background of sunlight being the most readily available natural energy source, Karl Leo's and Marc-Denis Weitze's contributions discuss the major potential and the challenges of artificial photosynthesis (see sections 6.1 and 6.2). Organic photovoltaic elements play a particular role here, not only because they enable molecule-based transparent, flexible solar cells but also because they can be connected to other plastics as system components. A particular challenge for the direct use of light as an energy source is light guidance and injection over a wide or indeed limited wavelength range. The contributions

74 | This contribution was translated from German into English.

from Cordt Zollfrank and Richard M. Parker with Silvia Vignolini show the potential of the natural renewable raw material cellulose for photonic pigments and multimodal photonic crystals (see sections 6.3 and 6.4).

6.1 Light as an Energy Source in Materials Development[75]

Prof. Dr. Karl Leo
Dresden Integrated Center for Applied Physics and Photonic Materials, Technische Universität Dresden, Germany

The capture of solar energy and its conversion into fuels and raw materials is a global challenge. To recover, store and transport energy, materials and component concepts are needed which fulfil specific functions, such as light absorption, production and transport of charge carriers in solar cells or storage and transport of ions in storage batteries. Over hundreds of millions of years, biology and evolutionary processes have combined to develop a wealth of strategies for problems of this type, which fulfil sometimes complex functions often in a very elegant manner.

An example of one such solution found in Nature is photosynthesis. In this process, a chemical combustion fuel is generated directly by the absorption of light, without further conversion steps being necessary. The processes used by these photosynthetic systems are extremely complex, but have been increasingly well understood over the past decades. Figure 17 shows by way of example a diagram of one such photosynthesis reaction, in which multiple photons are absorbed extremely elegantly and energy is transported via a number of molecular complexes in order to produce an energy-rich molecule. In addition to this example, the principle behind which is an inspiration for artificial photosynthesis, there are many biological processes which might prompt the development of technically relevant materials and systems, such as energy harvesting living materials, piezo effects, cellulose-based optical waveguide systems, photocatalytic reactions, bio-inspired optical crystals and photosynthetic films.

However, major hurdles often have to be overcome to transfer biological solutions into real applications, and this has so far prevented bio-inspired strategies from being put to broad practical use. One issue here is that Nature often takes completely different routes from technology, having evolved to enable optimum survival of a system rather than efficiency. For instance, energy recovery through photosynthesis lags significantly behind photovoltaics in terms of energy generated per unit area.

A further important difference between Nature and technology is that the natural processes all almost take place in aqueous solution, which in many cases is impossible in engineering environments. Furthermore, Nature has established ingenious repair mechanisms, which allow damage to the system to be tolerated as it is constantly repaired or regularly renewed, an example being leaves on trees. Such approaches are unknown in conventional energy technology, and implementing them requires openness to new ideas.

To be able to exploit the potential of bio-inspired energy technologies, first of all wide-ranging further research work is needed to understand as fully as possible the microscopic mechanisms found in Nature. Moreover, extensive interdisciplinary efforts are needed to achieve concrete applications for bio-inspired systems for selected problems.

One example which would be comparatively easy to implement is the rational design of molecules and materials, for example for catalysis: enzymes catalyse multielectron reactions and simplify chemical transformations which artificially produced catalysts are still unable to implement efficiently. Another possible example is organic photovoltaics: concepts known from photosynthetic antenna complexes could provide indications as to how excitonic excitation can be optimally transported over long distances to the photovoltaically active interface.

The long-term vision must surely be to achieve complex bio-inspired systems, one outstanding example of which would be an artificial photosynthesis module with a long service life which

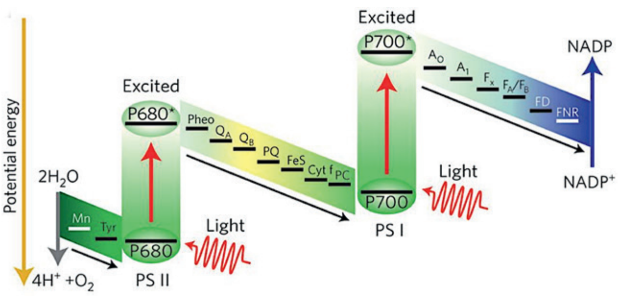

Figure 17: Reaction scheme of photosystem II for conversion of nicotinamide adenine dinucleotide phosphate+ ($NADP^+$) to NADP by absorption of multiple photons in the P680 and P700 pigments (source: Tachibana et al. 2012)

75 | This contribution was translated from German into English.

continuously and very efficiently generates a readily storable, transportable energy carrier.

6.2 Catalysts for Artificial Photosynthesis[76]

Dr. Marc-Denis Weitze
acatech Office, Germany

The German Academies of Science define Artificial Photosynthesis as follows: "Artificial Photosynthesis serves to produce chemical energy carriers and valuable products using sunlight as the sole energy source in integrated apparatuses and systems. The particular strength of this approach lies in the provision of renewable energy stored in material form which can be stockpiled and transported. This is achieved by mimicking a central principle of the biological model: combining light-induced charge separation with catalytic processes for the production of energy-rich compounds".[77]

Though the potential offered by the use of solar energy is huge, the associated scientific and technical challenges are currently of equal size. Current research is more concerned with seeking inspiration from biology,[78] to be implemented by catalytic systems, than with optimizing the biological system.

As Figure 18 shows, the fundamental processes involved in photosynthesis are light absorption and charge separation. In artificial systems, these can take place either via light-absorbing pigment molecules or in the solid state (in photovoltaics use is normally made of semiconductors). However, many pigment molecules are not yet sufficiently stable to be used in catalytic systems. This applies in particular to aqueous solutions.[79]

A strong effort has to be made, especially in terms of proton reduction, to make already known noble-metal-free compounds more efficient, durable and reactive.[80] A typical system for electrocatalytic CO_2 reduction contains an electrode for the oxidation of water and an electrode for CO_2 reduction. Which products arise, is entirely dependent on the catalyst material used for the electrodes.

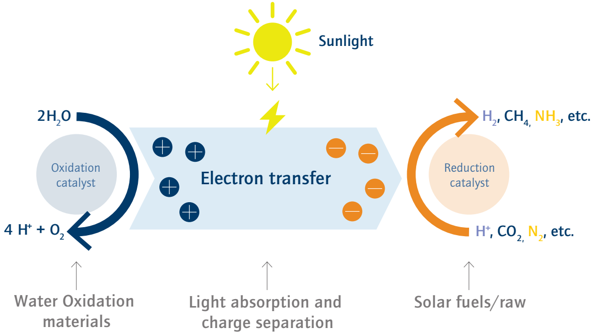

Figure 18: Overview of sub-processes of Artificial Photosynthesis (source: acatech et al. 2018)

Light absorption and electrochemistry can also be combined by carrying out the electrochemical reaction directly on the surface of the light-absorbing semiconductor (Figure 19).[81] Although some highly promising materials for such photoelectric cells have been known for many years, none of them have as yet met all the requirements for industrial use. Two research routes are currently being pursued in order to overcome the limitations of known semiconductor materials for photoelectrodes. On the one hand, a search is being conducted for completely new materials with suitable band gaps and good chemical stability. Alternatively, various materials which are already known could be combined in order to obtain the desired characteristics.

Significant discoveries have been made in recent years concerning the processes taking place at the surface of semiconductor materials which have been coated with protective or catalyst layers. This has become apparent, for example, in the recently developed concept of "adaptive interfaces". These are contacts which differ fundamentally both from conventional semiconductor-electrolyte interfaces and from "packaged" photovoltaic contacts in that their characteristics are influenced by the redox state of the catalyst layer applied onto them. Further thorough investigations are, however, required in order to get a detailed understanding and facilitate production of such adaptive interfaces. This will also require the development of new methods of analysis, such as X-ray spectroscopy or electron microscope measurement during photoelectrocatalysis.[82]

76 | This contribution was translated from German into English.
77 | See acatech et al. 2018, p. 9.
78 | See Dau et al. 2019.
79 | See acatech et al. 2018.
80 | See Ibid.
81 | See Ibid.
82 | See Ibid.

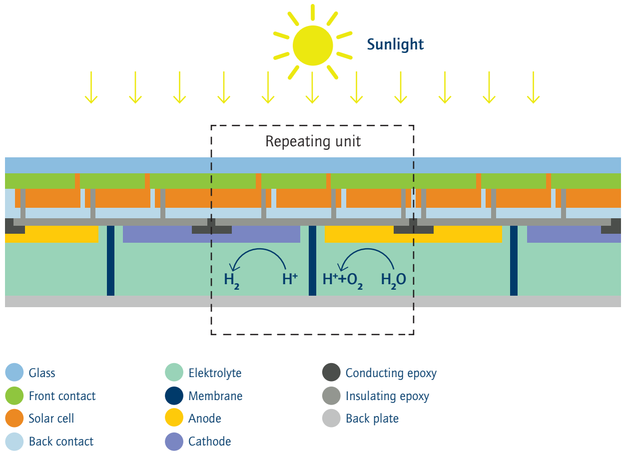

Figure 19: Integrated system for photoelectrochemical water splitting (source: acatech et al. 2018, illustration after Forschungszentrum Jülich)

Currently, the most highly-integrated systems of Artificial Photosynthesis are "artificial leaves". These combine all the light-absorbing materials and catalytic centres in a single, sometimes paper-thin component without external wires being needed to connect subsystems. Prototypes based on ion-permeable membranes, in which light absorbers and catalytic centres are directly integrated, have already been presented by the American Consortium of the Joint Center for Artificial Photosynthesis (JCAP).[83]

Finally, hybrid photosynthetic systems, which are a combination of biological and non-biological components. Siemens and Evonik are currently implementing a combination of electrolysis and fermentation in a pilot plant which initially produces hydrogen and carbon monoxide by electrolysis (using CO_2 electrolysis as described above). In a second step, these gases are fermented to yield acetic acid and ethanol before being converted into butanol and hexanol in further fermentation steps.[84]

The vision of Artificial Photosynthesis is being pursued in many countries throughout the world. It is like the moon shot project half a century ago. The current focus lies on the development and discovery of suitable catalyst materials.

6.3 Cellulose-based Optical Materials

Prof. Dr. Cordt Zollfrank
TUM Campus Straubing for Biotechnology and Sustainability (TUMCS), Technical University of Munich, Germany

Cellulose is the most abundant biopolymer in the world. It is the main structural component in the cell wall of higher plants and algae. Production from sustainable resources (lignocellulosics, algae, bacteria) yields a low-cost, environmentally benign biopolymer, which can be obtained in large quantities and with excellent tuneable and tailored qualities. Cellulose is a homo-polysaccharide in which anhydroglucose units are linked via β(1→4) glycosidic bonds. The cellulose chains are assembled via extensive and variable inter- and intramolecular hydrogen bonding into fibrous structures leading to a variety of crystal structures and self-assembled supramolecular architectures. In nature, colouring is usually achieved with biopolymer-based structures (proteins and/or polysaccharides). The unique optical (generally functional)

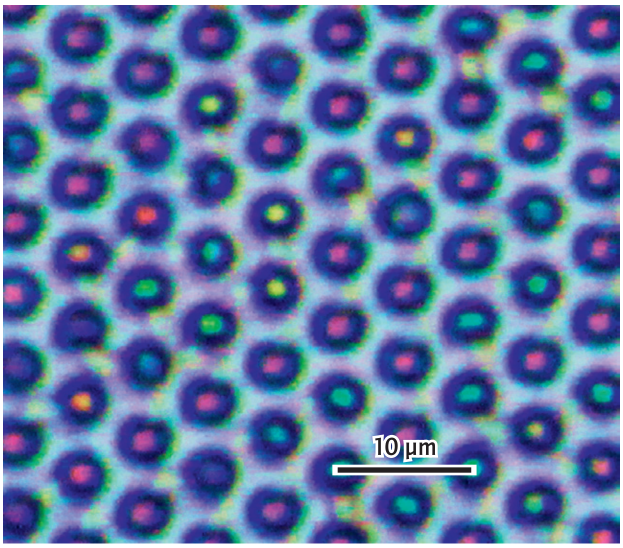

Figure 20: Transparent, surface-patterned films of cellulose with individual colouring in each cellulose ring (full-surface backlighting). These types of patterned materials can be used as multichannel analytical optical sensors or imaging devices (source: Daniel Van Opdenbosch, TUM).

83 | See acatech et. al. 2018.
84 | See Haas et al. 2018.

characteristics in natural systems are achieved by choosing a distinct, often complex structure. The constituent biopolymers typically have low refractive indices. One critical parameter in optical and photonic applications is the refractive index contrast between the materials and structures used. The refractive index for cellulose lies between 1.48 and 1.55, which will provide enough contrast, for example relative to the surrounding air, to generate a variety of vivid structural colours through ordered and disordered structuring. Currently, artificial engineering of biopolymer-based photonic architectures offers only very few options, because of the low refractive indices. The structural arrangement of the cellulose can, however, be used for the design of artificial bio-inspired devices through self-assembly. Dissolution of cellulose in various non-derivatizing solvents can also be useful for the fabrication of a very wide range of structures (fibres, gels and membranes). These cellulose solutions can be subjected to surface structuring techniques (e.g. imprint soft lithography). Transparent surface-structured cellulose films with distinct optical properties are also accessible. Cellulose-based material systems are thus very promising for advanced optical and photonic applications. Optical fibres and waveguides solely made from cellulose do not yet exist, but will be important for photon management and optical information transfer. Cellulose is a high-potential material in optical engineering with sustainable availability and favourable environmentally benign characteristics.

6.4 Natural Colourants from Cellulose

Dr. Richard M. Parker and Dr. Silvia Vignolini
Department of Chemistry, University of Cambridge, Cambridge, UK

Colourants are used throughout industry, from food and cosmetics to textiles and paints, where they not only enhance aesthetics, but also act as a gauge for quality, attractiveness, freshness or taste. While the pigment industry has long relied on the use of complex synthetic dyes or inorganic particles to produce colours and visual effects, there is a growing demand for more natural or sustainable alternatives that avoid the growing concerns over potential long-term health impacts.

To address this challenge, inspiration can be drawn from Nature, both in terms of identifying sustainable biomaterials and the strategies used. Of particular interest is "structural colouration", which is responsible for many of the most vibrant colours in Nature, from the metallic wings of butterflies and the vibrant feathers of birds to the iridescent epidermis of plants. In these natural examples, intense colouration is produced by precise nanoscale architectures of discrete biological building blocks, typically biopolymers (e.g. proteins and polysaccharides) or nanoscale mineral deposits. For example, within certain fruits and leaves, birefringent cellulose fibres are

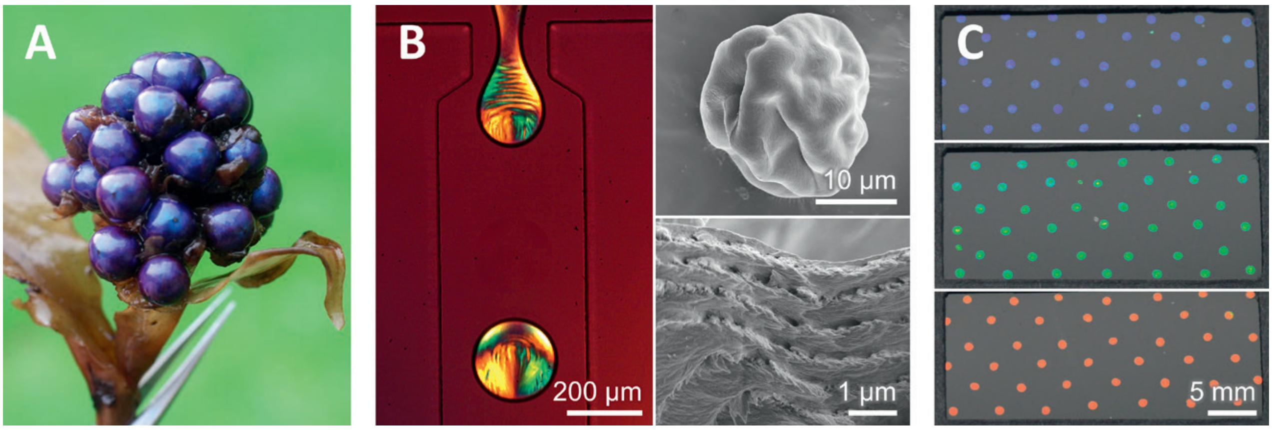

Figure 21: (A) Fruits of *Pollia condensata* collected in Ethiopia in 1974 and preserved in alcohol-based fixative. The specimen was conserved in the Herbarium collection at Royal Botanic Gardens, Kew, United Kingdom (source: Paula Rudall, Royal Botanic Gardens, UK); (B) Photonic microparticles made from cellulose nanocrystals (source: Parker et al. 2016, [CC BY 4.0]); (C) Red, green and blue printed cellulose nanocrystal microfilms (source: Zhao et al. 2019, [CC BY 4.0])

assembled into a periodic helicoidal nanostructure, such that blue light is intensely reflected.[85] By exploiting the most abundant biopolymer on the planet, cellulose, and replicating the natural assembly processes found within the plant cell, researchers are developing a new generation of sustainable "photonic" pigments.

Cellulose nanocrystals (CNCs),[86] industrially extracted from naturally-abundant cellulose fibres, are a highly promising material due to their inherent biocompatibility, biodegradability and scalable production. When dispersed into water, CNCs have been shown to spontaneously assemble on the nanoscale to mimic the natural helicoidal architecture. Upon drying, this structure is retained, enabling the intense reflection of visible light. Using this approach, colours from across the entire visible spectrum can be produced with an optical appearance tailored from matte to glossy or metallic.[87] Now the key challenge is how to develop large-scale fabrication of cellulose-based photonic pigments.

To move beyond small-scale batch production, several strategies can be envisaged. While continuous film fabrication (cf. synthetic glitters) offers many advantages, it has been challenging to realise due to the complexities and timescales required by the evaporation-induced self-assembly process. A more disruptive strategy is to produce CNC pigments directly through the confinement of the self-assembly process within discrete micro-scale water droplets.[88] Upon drying, each droplet produces a discrete, coloured CNC microparticle that can be used as a photonic pigment. Depending upon the confined geometry employed, it is possible by this method to produce a range of microparticles, from iridescent glitters to uniformly coloured pigments in a single step. The advantage of this approach is that it can readily build upon existing industrial emulsion technologies to produce a powder that can be directly incorporated into existing formulations.

The successful scale-up of the fabrication of cellulose-based photonic pigments will allow for the manufacture of a truly sustainable, biocompatible and potentially edible alternative to conventional synthetic dyes for mass-market applications. Cellulose-based pigments are suitable for use in printing ink (market-size: US $20.4 billion by 2022), colouration of food (US $3.75 billion by 2022), cosmetics (US $429.8 billion by 2022) and even sun-creams (US $11.1 billion by 2020).

6.5 Interview with Stefan Buchholz, Evonik Creavis GmbH[89]

Prof. Stefan Buchholz, a chemist by training, is head of Evonik Industries AG's strategic innovation unit Creavis.

Prof. Buchholz, how would you rate the innovation potential of knowledge derived from Nature?

In principle I rate it highly, but I would also warn against idealism. Examples such as biotechnology show that not as much has happened as was imagined at the start of this decade. The use of renewable resources and the application of biotechnological methods have not made anything like as much as progress as was expected at that point. This development is to a considerable extent (though not solely) the result of the current low oil price, which was not expected at the time, and this makes clear the risks taken by companies which are early developers of new technologies.

What role do models from Nature play in materials development in your company, i.e. models for the materials themselves or for the production process?

In our company, biotechnology plays a big role in the development both of new materials and new active ingredients. I'll mention three examples, if I may: last year we brought the biosurfactant Rheance® One to market. The model for that was one we found in Nature and we developed the production strain using molecular biological methods. We use fermentation to produce the surfactant, which is biodegradable, highly biocompatible and kind to skin. We are also addressing the topic of tissue engineering: from human cells, suitable nutrient media and scaffold materials it is possible, for example, to produce substitute cartilage, i.e. a human-identical tissue as an alternative to an implant. Evonik is concentrating its efforts on production of the scaffold materials and the nutrient media.

In the "Rheticus" project, which is funded by the Federal Ministry of Education and Research (BMBF), we are working with Siemens to investigate, in a pilot plant, how speciality chemicals can be produced using electricity from renewable sources and bacteria. Siemens is providing the electrolysis technology. Firstly,

85 | See Vignolini et al. 2012.
86 | See Parker et al. 2018.
87 | See Zhao et al. 2019.
88 | See Parker et al. 2016.
89 | The interview was originally conducted in German.

carbon dioxide and water are converted into carbon monoxide and hydrogen and in the ensuing fermentation we produce the chemicals butanol and hexanol using microorganisms at our site in Marl. This is a sort of hybrid artificial photosynthesis, if you like: a bringing together of biological and non-biological components, with valuable products being synthesized from the raw materials water and carbon dioxide in the fermentation stage.

In your opinion, what major hurdles will development and implementation face in this area in the future, irrespective of the issue of biologicalization?

Cost is definitely one of the main obstacles. There is also the matter of the purpose of biologicalization, and what contribution bio-inspired materials can make to products. It's not a good idea to gloss over things. For example, not every bio-inspired material is in itself biodegradable or sustainable – a life-cycle assessment is needed in each case to get a better overview.

What, in your opinion, are Germany's particular strengths and weaknesses in this area?

I think Germany is well positioned and a leader in Europe. Globally, the USA is definitely out in front. Asia is very much up and coming in the field. We have already established a tissue engineering project house in Singapore, where we can find excellent cooperation partners at very close quarters, of a quality and in a density otherwise only found in the Boston area in the USA. This is helping to enhance the international nature of Evonik's R&D activities.

7 Adhesion and Bonding[90]

Prof. Dr. Karin Jacobs
Saarland University, Saarbrücken, Germany

Nature offers innumerable ways to join two objects together, for example burrs snag in animals' coats, so widely dispersing the seeds and helping to ensure the survival of the plant species. Hook and loop fastenings are based on this mechanical principle of increased friction due to entanglement. Once discovered and described, many such similar adhesion phenomena have quickly become part of our daily lives. It is therefore well worth seeking out more models in Nature for industrial applications. "Non-stick" phenomena, i.e. those cases in which Nature prevents adhesion, can also be usefully investigated for potential in applications relating to antifouling, antibacterial surfaces, non-wetting etc.. Systems which permit controlled adhesion and detachment, as found for example in motor proteins (responsible for example for muscle contraction) or, on a more macroscopic level, in gecko locomotion on vertical or even overhanging surfaces, are of particular interest.

Adhesion and bonding are two terms which describe that a force is holding two things together, but without specifying this force in any greater detail. The term "bonding" is generally used instead of adhesion when a fluid bonding agent is used; the adhesive then adheres to the objects to be joined, such as the pollenkitt which sticks pollen to a bee's legs.[91] Many bonding agents even initiate chemical bonds and so create a particularly strong connection. It is rare for an individual phenomenon to be responsible for object adhesion, as is for example the case with the above-mentioned burrs or octopus suction cups which are capable of grasping prey. In the latter case, adhesion is caused merely by the pressure difference between the suction cup holding the prey and, in this case, the hydrostatic pressure of the surrounding water, so gravity is the origin of the force here. In most cases, adhesion is caused by the interplay between many forces, which are mainly of an electrostatic or electrodynamic origin,[92] for example ionic interactions due to static charges or van der Waals interactions due to interacting (permanent or induced) dipoles.[93] It is therefore often necessary to be aware of the polarization properties of the natural materials involved so that the situation can be optimized in the corresponding industrial application.[94] Despite applying only over a very short range, quantum-mechanical forces (e.g. Born repulsion) also play an important role, for example ensuring that two protein chains cannot interpenetrate. The interplay of electrodynamic and quantum-mechanical forces then for instance determines the contact angle of a liquid on a surface, whether patterned or unpatterned, the adsorption of molecules or the adhesive force of flies, geckos or bacteria on surfaces (see sections 7.1 and 7.2).[95, 96] Adhesion due to capillary forces, or to steric or hydrophobic interactions is thus also attributable to this interplay. Hydrogen and sulfur bridges also provide adhesion; for example, assisted by electrodynamic forces, hydrogen bridges largely stabilize the cohesion of the two strands of DNA. Adhesion and detachment also occurs in motor proteins, where purposeful making and breaking of chemical bonds, permitting muscle contraction, have been optimized over the course of evolution. Light, which can initiate the formation of a specific chemical bond in a molecule, may also be used in this connection, for example in UV-curing adhesives which have now demonstrated their broad potential in applications from the automotive industry to dentistry.

In Nature, evolutionary processes have optimized this interplay of forces for particular situations. One example is the adhesive which fastens mussels to rocks in salty seawater, and another are the gecko's feet which allow it to flit across overhangs thanks to a trillion minuscule adhesive pads which optimize the contact area and so ensure strong, reversible adhesion. The former can for instance be used as a model for novel adhesives (see section 7.3) and the latter for novel robot gripper systems (see section 7.2). When developing an industrial application, the approach is thus either to seek out a system in Nature which solves a very similar problem or to transfer a principle which has been discovered in Nature to a situation of an entirely different kind and adapt it accordingly. Further examples inspired by Nature are described below in greater detail: the hydrophobicity of the

90 | This contribution was translated from German into English.

91 | See Lin et al. 2013.

92 | Electrodynamic interactions are below taken to include electrostatic interactions.

93 | See Israelachvili 2011.

94 | For example, an explanation of gecko adhesion led to an application in reusable adhesive tape ("gecko tape"), while a description of the lotus effect fed into the development of wall paints, roof tiles, ceramic sanitary ware etc. which make good use of the self-cleaning effect of rough, hydrophobic surfaces.

95 | See Huber et al. 2005.

96 | See Bäumchen et al. 2015.

water fern inspires an antifouling coating for ships (see section 7.4) while the Colorado potato beetle points to optimized small adhesive pads (see section 7.1).

Particular attention is currently being paid to biomacromolecules (proteins, peptides, etc.) which have been identified in connection with specific situations, for example in the already mentioned durable and strong adhesion of mussels, in cell-cell adhesion (e.g. in wound healing) or cell-surface adhesion (e.g. bacterial adhesion or its prevention or the adhesion of bone cells to implants). One specific class of small, globular proteins, the hydrophobins, is currently creating quite a stir, for example in food processing. Thanks to their strong interfacially active properties, hydrophobins can stabilize emulsions particularly effectively. Depending on the ingredients of the emulsion and the nature of the preparation, hydrophobins form a mono- or bilayer between the droplets and prevent them from coalescing. Markus Linder describes further properties of these proteins (see section 7.5). Silk proteins are also of huge interest to materials science, in particular due to their mechanical properties and biocompatibility. Biomacromolecules are currently the focus of much attention in industry as raw materials. Applications of such macromolecules, which may be produced from natural substances by fermentation and so avoid the use of petroleum derivatives, include for example as a renewable starting material for synthesizing an adhesive.

As is apparent from these examples, new findings in bio-inspired adhesion can often be put to direct use in industrial or medical applications, which explains why patents are often filed before the underlying principles are published.

This field of bioadhesion is being researched by many groups from different disciplines, so the results are also published in different specialist journals. Advances in one discipline (e.g. in the physical sciences, insights into the role of contact angle in adhesion) make their way only very slowly into neighbouring disciplines. Many published articles thus appear which, while presenting good results for their specific discipline, partially miss the mark in terms of interpretation because they lack insights from other disciplines. Research groups and consortia which take an interdisciplinary approach to a system are much more successful in this respect. It is particularly advantageous if bachelor's and master's degree students, doctoral candidates and postdocs have themselves benefited from interdisciplinary training, for example in biophysics, biomimetics or biophysical engineering. Interdisciplinary research results are, however, often more difficult to get published as the referees themselves frequently lack the interdisciplinary knowledge. New insights from another discipline other than the referee's can therefore be under- or overestimated. Typical points of friction between referees and authors or between speakers and a questioning audience are for example experiments which, because they permit better control of system parameters, are carried out *in vitro* or *in silico* but are nevertheless intended to permit conclusions to be drawn about the *in vivo* situation. Views will always differ about the role of simulations in this field: on the one hand, there are communities for which a simulation in itself has the importance of an experiment and which do not acknowledge the limitations or artefacts of a simulation, while on the other hand the groups publishing simulations do not always clearly describe the limitations possibly associated with simulations. Moreover, the great improvements in new, user-friendly software packages mean that ever more researchers are making use of them but without (any longer) being aware of the details of the simulation. For example, a simulation package which takes no account of temperature fluctuations is nevertheless capable of accurately describing some situations but not others, such as the temperature dependency of the modulus of elasticity of a vesicle membrane.[97]

If, in future, major progress is to continue to be made in this highly dynamic field with its great application potential, there is a need to foster research consortia both large and small which are set up on an interdisciplinary basis and are experienced in working in this way and in which, in addition to research, the emphasis is also on mutual learning. It would additionally be desirable to provide further training for doctoral students working in such consortia in a field which is not taught in their own department. University departments should for example prepare modern research topics in required elective courses in such a way that they can be followed by students from other departments. It would make good sense to establish a new peer-reviewed journal to bring this idea of a research community closer to being a global reality. This journal should focus on high-level research results which can only be achieved by interdisciplinary collaboration and the "supplementary material" to a publication should include specialist knowledge from the discipline which other disciplines would need to understand the article.

97 | See Paulose et al. 2012.

7.1 Hairs with Unlimited Adhesion[98]

Prof. Dr. Stanislav Gorb
Zoological Institute, Kiel University, Germany

Previous findings have shown that many insects rely solely on their microhairs for locomotion on smooth vertical walls and on ceilings and that the shape of these hairs is optimized for different substrates,[99] with particularly strong adhesion being achieved by hairs with spatula- or mushroom-shaped ends[100] (see Figure 22). But while the principles of the glue and micro hooks have long been implemented technically in adhesive tapes and hook-and-loop fasteners, films with microhairs, for example, are not yet part of our everyday lives.

Interestingly, there is no simple explanation for this biological mechanism of attachment. It is a combination of micro- and nanostructured surfaces, viscoelastic materials, biphasic liquids with their transport systems and the nature of the movement itself. Viewed from a physical standpoint, some of these properties are trivial while others are highly complex and require further experimental investigations and theoretical considerations. In addition to adhesion systems for locomotory purposes, there is a huge variety of adhesive systems which perform other functions.

Enabled by the use of the latest experimental techniques, high-speed video, force measurements and complex microscopic methods, there has been a blossoming interest in biological adhesion systems over the last decade. Based on experimental and theoretical investigations, it has been found that biological adhesive structures have some key properties with regard to their functioning, animal evolution and ecology. In addition, detailed information about adhesion structures and their working mechanisms has great potential for biomimetic applications.

Working together with industrial partners, our research group has for the first time successfully mimicked a number of functional principles of microhairs in an artificial adhesion material which was produced by micromoulding technique. The adhesive force of the biomimetic structure is based on microstructures which are shaped like tiny mushrooms[101, 102] (see Figure 23). After investigating more than 300 different biological adhesive systems, we opted for the design of a microstructure which commonly occurs on the sole of the foot of the male of various species of beetles. A few square centimetres of the artificial microstructured material can hold objects weighing several kilograms on smooth glass walls, while their holding capacity on ceilings may be perhaps just one tenth of that. Smooth structures, such as glass or polished wood, are well suited as a substrate for such adhesive strips

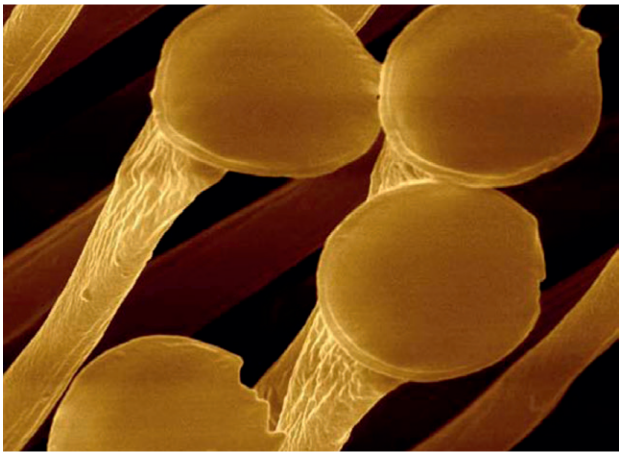

Figure 22: Adhesive hairs on a male Colorado potato beetle *Leptinotarsa decemlineata* (source: Stanislav Gorb, Kiel University)

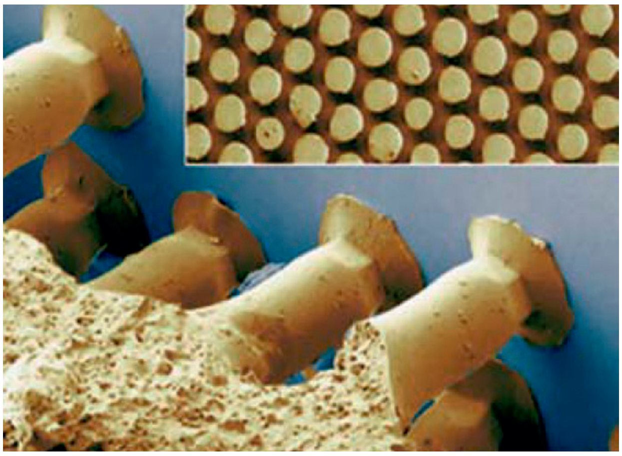

Figure 23: Micrograph of the biomimetic surface structure of the synthetic adhesive material (tips of the adhesive discs 30 µm in diameter). Insect foot-inspired material (ochre) adheres to glass (blue) (source: Stanislav Gorb, Kiel University).

98 | This contribution was translated from German into English and is an excerpt from a publication (see Gorb 2009), which was originally published in the journal Lab & More in issue 1/2009.
99 | See Gorb 2006.
100 | See Gorb et al. 2006.
101 | See Gorb/Varenberg 2007.
102 | See Varenberg/Gorb 2007.

whereas woodchip wallpaper is almost completely unsuitable. Even insects have problems walking on surfaces with fine roughness. This is a fundamental problem of this adhesion mechanism. However, once detached from the surface, the material leaves no visible traces and also still adheres after it has been applied and peeled back off again hundreds of times. Unlike adhesive tape, if it gets dirty, it can even be washed without suffering any loss of adhesive force. Applications of the hairy adhesive material include as a protective film for sensitive glasses or simply as a reusable adhesive tape: farewell fridge magnets, here come the microhairs which also stick to mirrors, cupboards and windows. The material has also demonstrated its abilities in dynamic processes: a robot weighing 120 grams with artificial adhesive fibres on the sole of its feet has been able to climb a vertical glass wall.[103]

The mushroom-headed adhesive microhairs are the technical implementation of just one mechanism which gives insects a hold. And the insects' adhesive technology is still clearly superior to its artificial counterpart: insects, spiders and geckos can change between adhesive and interlocking mechanisms at will depending on the particular surface they are walking on.

These results, which were obtained from investigations on biological specimens, make it clear to materials scientists how necessary it is to associate inherent material properties with contact geometry. The efficiency of natural systems cannot be transposed on a one-to-one basis. Some of the concepts, however, can be transferred to the world of materials, in order to design surfaces with specific properties and functions which have been observed in biological systems (see Figure 24). The huge diversity of biological adhesion mechanisms will accordingly provide materials scientists and engineers with constant inspiration for the development of new materials and systems. Broad-based, comparative functional investigations into biological surfaces should therefore be intensified so as to understand the essential structural, chemical and mechanical principles underlying the functions. Drawing on living Nature as an endless source of inspiration may be considered another reason for maintaining biodiversity.

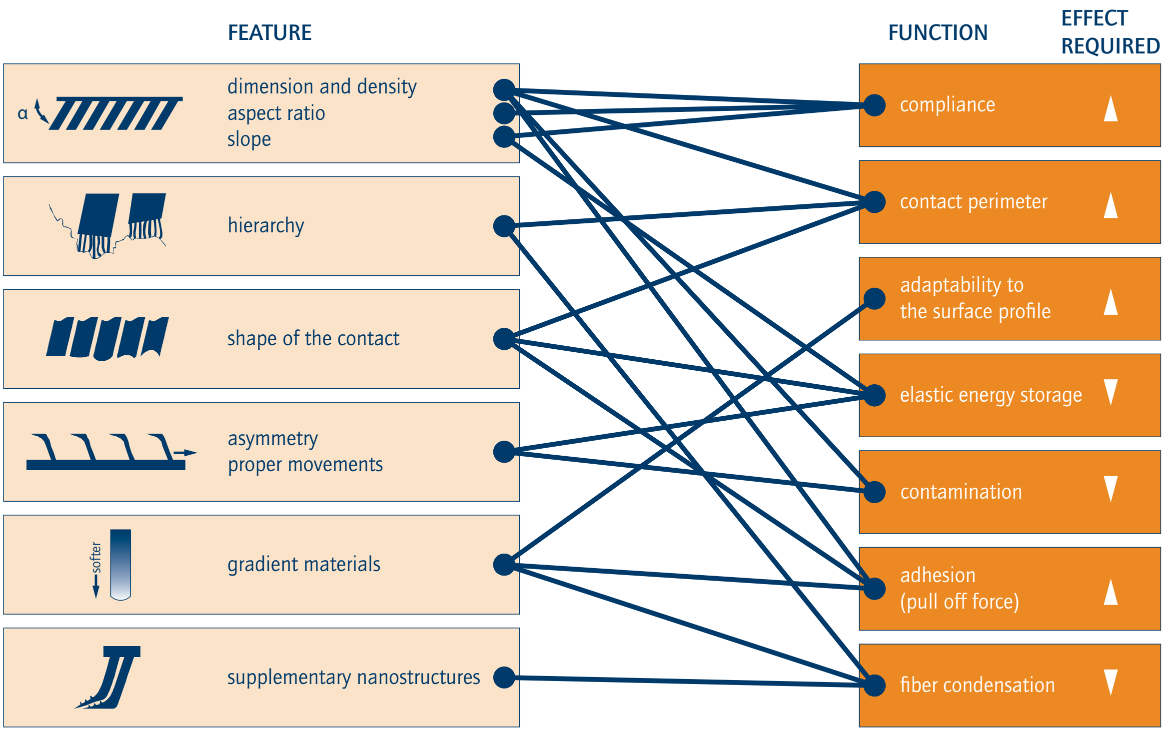

Figure 24: Some principles (properties) by which biological reversible adhesive systems operate and their relationship to specific functions. The resultant effect which is required to produce strong adhesion is shown on the right-hand side. The arrows indicate whether the function is improved or impaired by a specific structural feature. Simultaneous implementation of all these features in a single artificial system is desirable, but virtually impossible. However, depending on the requirements placed on a specific bio-inspired material or system, it is possible to implement one principle or a combination of several of these biological findings (source: Stanislav Gorb, Kiel University).

103 | See Gorb et al. 2007.

7.2 Bio-inspired Adhesive Structures for Robotics and Industry 4.0[104]

Dr. Karsten Moh, Dr. René Hensel, Prof. Dr. Eduard Arzt
INM – Leibniz Institute for New Materials, Saarbrücken, Germany

As digitalization in industrial production advances, new robotic systems need new materials for reliably gripping components and objects. The Gecomer® technology presented here is based on the "gecko" effect. Synthetic adhesive systems are being developed which mimic the finely patterned, hairy adhesive surfaces of a gecko's foot and which, like the gecko's foot, can temporarily and reversibly adhere to the most varied surfaces. The adhesive and thus "sticky" interaction is based on purely physically acting van der Waals forces.[105] This residue-free adhesion without adhesive is thus of interest for numerous applications. Today, 80 to 90 per cent of gripper systems are mechanical or vacuum systems. Our market studies have shown that these established gripper systems will come up against insuperable limits within the foreseeable future: handling of microsystem components with precise positioning and handling under a vacuum will no longer function using conventional technologies. These limits are overcome with Gecomer® technology and offer unique selling points which open up considerable commercial potential for the new technology as an "enabling technology". In addition to miniaturizability and vacuum capability, Gecomer® systems also make it possible to move even highly sensitive objects such as films gently and without residues. The detachment process, which is currently causing problems for many users, can be reliably implemented. Energy and resource efficiency as well as noise emissions are dramatically improved over conventional systems since complex ancillary equipment (e.g. magnet and suction systems) can be entirely dispensed with.

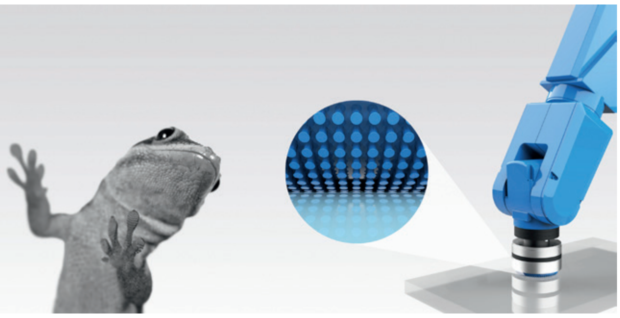

Figure 25: From Nature to technology – bio-inspired adhesive structures for automated handling tasks (source: INM – Leibniz Institute for New Materials)

The scientific and anticipated commercial success of this patented Gecomer® technology illustrates how a concept developed over the course of millions of years of evolution can provide a solution to new technological requirements and so lay the foundation for new applications and products.

7.3 Mussel-inspired Adhesion

Prof. Dr. Matthew Harrington
McGill University, Montreal, Canada

Adhesives play a crucial role in many technological and biomedical applications; yet in hydrated and humid environments modern synthetic adhesives often struggle to hold surfaces together. This is because water, as well as associated ions and biofilms, compete for space on most material surfaces. Thus, an effective underwater adhesive must outcompete these other molecules to create a strong physical or chemical interaction between surfaces, which is especially challenging and relevant for surgical and dental adhesives. In an effort to understand the chemistry of wet adhesion, scientists have turned to the oceans and have asked how organisms are able to adhere to surfaces in the rocky seashore, where the high salinity and pH resemble that of body fluids.

Mussels, in particular, are able to adhere to almost any surface (rocks, wood, Teflon) under seawater conditions despite the exceedingly high salt content and excessive biofouling by algae. Researchers have spent over forty years elucidating the chemistry underlying this ability, and have identified a handful of proteins that are responsible. The mussel adhesive proteins (MAPs) are enriched in a post-translational modification of the amino acid tyrosine, known as 3,4-dihydroxyphenylalanine or more commonly as DOPA.[106] Based on its chemical structure, DOPA is capable of participating in numerous interactions with different surface chemistries via metal coordination, hydrogen bonding, pi-cation[107] and hydrophobic interactions. Furthermore, DOPA can be oxidized under seawater conditions, allowing it to form covalent bonds with biofilms.

104 | This contribution was translated from German into English.
105 | See Huber et al. 2005.
106 | See Waite 2017.
107 | A pi cation interaction is understood as a non-covalent molecular bond.

Polymer chemists have borrowed this chemistry, developing a number of DOPA-enriched mussel-inspired materials and adhesives. Indeed, the last ten years has seen a surge in new materials with dynamic properties including self-healing and even DOPA-based synthetic adhesives used for prenatal surgery where sutures are not possible and ruptured incisions often lead to premature birth. While mussel-inspired adhesives based on catechol chemistry have shown great promise, they have several drawbacks, most notably the tendency of DOPA to oxidize. Thus, recent biological investigations have focused on how mussels process the glue, revealing a complex pH and redox control of microenvironment.

Indeed, MAPs are stored as a liquid-liquid phase separation (LLPS), which is a dense fluid phase with low surface tension that facilitates spreading of the adhesive molecules over the surface in wet environments.[108] Furthermore, positively charged bulky amino acids (lysine, arginine), which are always found near DOPA in MAP sequences, play a role in displacing positively charged counterions on negatively charged surfaces, enhancing underwater adhesion.[109] Researchers are already integrating these newly discovered design principles into the next generation of mussel-inspired adhesives and hydrogels, providing improved performance. It seems likely there are further tricks to be learned as the fascinating chemistry of this and other biological adhesives is elucidated.

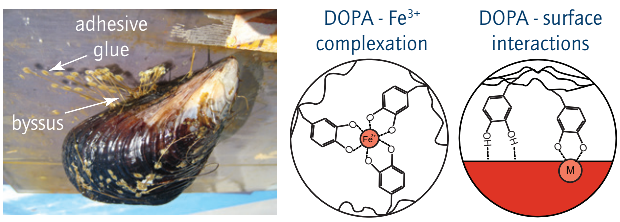

Figure 26: Mussels attach to hard surfaces on rocky seashores using the adhesive plaques of their byssus.[110] Adhesion and mechanical properties of byssal threads are mediated by the various interactions of DOPA residues in byssus proteins (source: Matthew Harrington, McGill University).

7.4 Friction Reduction and Antifouling with Bionic Coating[111]

Prof. Dr. Thomas Schimmel
Institute of Applied Physics and Institute of Nanotechnology and Material Research Center for Energy Systems (MZE), Karlsruhe Institute of Technology (KIT), Germany

Ships carry around ninety per cent of global international trade and cause major environmental impact: it has been estimated that the world's fifteen largest ships produce a volume of sulfur dioxide (SO_2) comparable to that emitted by all the world's cars. Ships also release large quantities of highly toxic substances (biocides) which are applied to their surfaces to counter biofouling or algal growth which increases the friction of the ship's hull in water, so causing large energy losses.

Three of the major problems specific to ships arise from contact of their hulls with water:

- Friction: a large proportion of fuel consumption is due to friction between the ship's hull and the surrounding water.
- Corrosion: this phenomenon is likewise largely caused by the ship being in direct contact with the surrounding strongly saline seawater.
- Fouling: marine organisms would not grow if the ship were surrounded by air rather than water.

Figure 27: Natural surface of the floating fern *Salvinia molesta* with a water drop which is resting on the tips of special hairs and does not touch the surface of the leaf. The image at the right clearly shows the whisk shape of the hairs (source: Thomas Schimmel working group, Karlsruhe Institute of Technology (KIT)).

108 | See Waite 2017.
109 | See Ibid.
110 | Byssus is the name for the secretion from the foot glands of various species of mussel.
111 | This contribution was translated from German into English.

Our approach,[112] inspired by the floating fern (*Salvinia molesta*, see Figure 27), is to "have ships glide in an envelope of air". We are thus pursuing a highly promising way of solving the stated problems: an air layer has a substantially lower viscosity than water and acts as an "anti-friction layer". Furthermore, enveloping the hull with a permanent air layer under water prevents the ship from coming into direct contact with the water and so averts corrosion and fouling.

The prototypes of our artificial surfaces at KIT (see Figure 28) are now capable of maintaining air layers under water for as long as several years. Surfaces which remain dry under water have huge potential for application, for example for ships and oil platforms as well as water pipes and tanks without fouling.

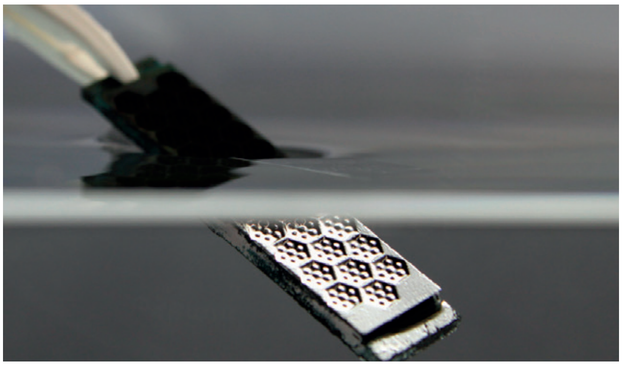

Figure 28: Artificially produced polymer sample with patterned surface which retains air under water. Reflection of light at the air layer makes the black polymer surface look silver under water (source: Thomas Schimmel working group, Karlsruhe Institute of Technology (KIT)).

7.5 Bio-inspired Interface Molecules

Prof. Dr. Markus Linder
Department of Bioproducts and Biosystems, Aalto University, Finland

Interfaces play an essential role in many aspects of materials technology, ranging from adhesives, coatings and cosmetics to foods etc.. Similarly, living organisms also need to control interfaces and have a wide range of solutions for doing so. One system which is of particular interest has been found in filamentous fungi, i.e. the fungi that form long mycelia and often grow fruiting bodies such as the common edible mushroom. Their peculiarity is that variants of one type of protein, known as hydrophobin, have evolved to control the interfaces that these fungi encounter, the different variants for example controlling adhesiveness to surfaces, the wetting properties of spores, or aerial growth of the fungi.

These hydrophobins are of interest in many respects as biomaterials. One practical aspect is that they function as pure proteins that are secreted into the surroundings. We can therefore use them the same way as any chemical ingredient would be used. Research has provided a good understanding of how and why hydrophobins have an interfacial action. Some hydrophobins form a strongly interconnected 2D network at interfaces (see Figure 29).

Atomic force microscopy shows how hydrophobin molecules self-assemble into sheet-like structures that are connected to each other, and more detailed combinations of structural data allow us to model precisely how hydrophobin molecules pack together. The hydrophobins are amphiphilic, i.e. one side of the protein turns away from water, and the other turns towards water. Because all the molecules turn the same way, the entire sheets of interconnected molecules are amphiphilic. The combined properties lead to molecular surface layers that are very elastic, in fact more elastic than any other known system, and form a sort of molecular "cling film". This permits applications such as very strong and stable foams, efficient dispersions of

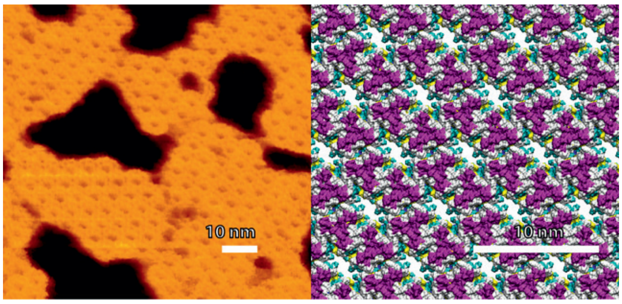

Figure 29: Remarkably strong films are formed by hydrophobin proteins when they interconnect spontaneously at interfaces (sources: Arja Paananen, VTT Technical Research Centre of Finland (AFM image left) and Dmitrii Fedorov, Department of Bioproducts and Biosystems, Aalto University (modelled structure, right)).

112 | The approach was validated as a cooperative project between the universities of Karlsruhe (KIT), Bonn and Rostock in the context of the Federal Ministry of Education and Research (BMBF) ARES project and is now being implemented in the EU AIRCOAT project as part of the Horizon 2020 Programme. The ARES (Air Retaining Surfaces) project was funded by the BMBF VIP+ programme. Another project is being funded by the Baden-Württemberg Stiftung.

insoluble compounds, and self-assembling interfaces in biosensors. The hydrophobin proteins can be used as such and can be made in large volumes in bioreactors. As hydrophobins from edible fungi can be used, their safety for human exposure can be assured. Genetic engineering allows combinations with for example antibodies for sensor interface applications.

Another aspect is that synthetic biomimetic versions could be made, using small particles to imitate size, amphiphilicity, and symmetrical side-by-side packing to achieve similar molecular self-assembling systems to make coatings, to control interfaces, and to achieve adhesiveness.

8 Bio-inspired Biomaterials for Medical Applications[113]

Prof. Dr. Carsten Werner
Leibniz Institute for Polymer Research, Dresden, Germany

Biomaterials research, a still relatively young discipline at the interface between materials science, biology and medical technology, is in a position to draw particular benefit from the meteoric rise in life sciences knowledge. Biomaterials are non-living materials which, when used in medical devices such as implants, organ replacement systems and the vast numbers of disposable items used in medicine, interact directly with a living organism.[114]

The range of materials used in this sector encompasses high-performance materials such as titanium, ceramics and fluoropolymers, commodity plastics such as polyvinyl chloride and polypropylene and also biopolymers isolated from natural sources, such as cellulose and collagen.[115] Many medical devices are based on a combination of different biomaterials. Basic selection criteria for biomaterials are their fundamental suitability for safe use in medical devices and guaranteed device function even after sterilization and storage. The functions of such devices include mechanical support for the locomotor system and membrane separation efficiency in extracorporeal organ replacement systems. At the same time, undesired side-effects of the material used must be avoided: in this respect, it is not only toxic or carcinogenic effects that have to be ruled out but also material-related infections and foreign body responses by the organism need as far as possible to be prevented. The concept of device- or application-specific material biocompatibility is a central requirement in this respect. To ensure biocompatibility, the interface properties of biomaterials are particularly important. According to medical devices legislation, all medical devices must be tested before they are placed on the market, one of the tests being to confirm biocompatibility of the materials for each specific application. Key parameters of the required tests for material biocompatibility are laid down in the standards of the EN ISO 10993 series.

Most recently, biomaterials research has moved beyond the adaptation of available materials primarily into the exploration of regenerative therapies, which has been made possible by progress in molecular cellular biology.[116] Therapies using stem and precursor cells are particularly full of potential, especially for diseases for which no or only unsatisfactory treatments have thus far been available, such as neurodegenerative diseases, diabetes, wound healing disorders and diseases of heart and circulatory system. In the development of materials for regenerative therapies, attention is increasingly being paid to biological communications processes and structural principles of living matter: to be able to activate regeneration processes in a targeted manner using biomaterials, cellular processes have to be controlled by specific molecular interactions and material properties have to be dynamically adapted to tissue formation. This is achieved by using biopolymer-based matrix systems (e.g. decellularized tissue, reconstituted collagen preparations and multicomponent gels such as Matrigel™),[117, 118] biohybrid materials (e.g. proteins modified chemically with synthetic polymers, and glycosaminoglycan-polyethylene glycol hydrogels)[119] or bioactive peptide-functionalized synthetic materials (e.g. polyethylene glycol-based hydrogels).[120, 121] Generally speaking, researchers are seeking to develop adaptable, multifunctional and also multiphasic biomaterial platforms, and are making increasing use of combinatorial methods to achieve this goal, building on the availability of additive manufacturing methods (see also section 3). This enables the identification of polymer-based materials which are suitable for the effective control of human stem cell fate decisions or for providing surfaces with antimicrobial properties.[122, 123, 124, 125] Purposeful modulation of the

113 | This contribution was translated from German into English.
114 | See European Society for Biomaterials 1987.
115 | See Murphy et al. 2016.
116 | See Green/Elisseeff 2016.
117 | See Singelyn/Christman 2010.
118 | See Prewitz et al. 2013.
119 | See Freudenberg et al. 2016.
120 | See Lutolf/Hubbell 2005.
121 | See Place et al. 2009.
122 | See Mei et al. 2010.
123 | See Beachley et al. 2015.
124 | See Ranga et al. 2014.
125 | See Hook et al. 2012.

immune system using biomaterials[126, 127, 128] – often in the form of particles – constitutes a highly promising approach to new cancer treatments and to the treatment of diseases associated with chronic inflammation.

Shaping of biomaterials for regenerative therapies often involves the development or adaptation of new methodologies, resulting in tailoring options for medical devices, that is to say devices can be adapted to patient-specific requirements: in addition to injectable materials in the form of *in situ* assembly systems, macroporous and multiphasic materials are likewise used, as are structures which are produced using additive manufacturing methods. When selecting materials, it is therefore of critical importance whether the materials are suitable for the corresponding shaping processes.[129, 130]

While there are so far very few cell-instructive biomaterials available for therapeutic application, implementation in diagnostic technologies, which is less problematic from a regulatory standpoint, has been relatively quick, with examples including in particular human cell-based tissue and organ models. The aim here is more realistic replication of physiological and pathological structures *in vitro*, in particular for the development of novel active ingredients and for toxicity testing, but also for mechanistic biological investigations into disease processes. The technologies being developed in this area could make valuable contributions to individualizing therapy. The focus at present is on three-dimensional organoid cultures, which are controlled by multifunctional biomaterials. These cultures are often based on human, induced pluripotent stem cells. Important factors in their development are control of scalability, integration, connectivity and reproducibility. Combining biomaterials with established high-throughput methods and microfluidic systems promises valuable new options.

However, clinically well-established medical devices may also benefit considerably from the new biomaterials, which are more in line with the principles of living Nature and which are being developed according to the principles of tissue engineering for regenerative therapies. Examples are already widely used combination devices such as vessel supports (stents), which are provided with coatings which release active ingredients, and also biologically functionalized vessel catheters or electrode systems for use in the nervous system.[131] New developments in materials are needed, moreover, for the digitalization of medical technology, in particular for the implementation of sensors and actuators. Here too, crucial factors for the success of a technology are controlling interface phenomena and ensuring biocompatibility.

Given the wide variety of functional elements and biological interaction processes that can be combined, data-based materials research methods would seem perfectly cut out for biomaterials design, and this field, together with preparative and analytical high-throughput methods,[132, 133, 134] is expected to be of central importance in future.

8.1 Concepts Behind Tissue Engineering and Regenerative Medicine[135]

Prof. Dr. Katrin Sternberg and Dr. Detlef Schumann
Aesculap AG, Tuttlingen, Germany

As far back as the early nineteen seventies, W.T. Green (Boston Children's Hospital, Boston, MA, USA) laid the initial groundwork for innovative approaches to cartilage reconstruction (tissue engineering). Green's method was to colonize bone fragments with cartilage cells and implant these in nude mice. A few years later, this advance was followed by isolated investigations into growing skin and other tissue. In general, however, the work carried out by J.P. Vacanti and R. Langer in the nineteen eighties is thought of as the start of tissue engineering as we understand it today.[136] These days, the terms tissue engineering and regenerative medicine are often used synonymously, but there are crucial differences between the two fields of application. While tissue engineering focuses primarily on the growth of replacement tissue outside the body through a combination of living cells, suitable matrix materials and

126 | See Hubbell et al. 2009.
127 | See Hotaling et al. 2015.
128 | See Sadtler et al. 2016.
129 | See Murphy/Atala 2014.
130 | See Kang et al. 2016.
131 | See Minev et al. 2015.
132 | See Vasilevich et al. 2017.
133 | See Cranford/Buehler 2012.
134 | See Vegas et al. 2016.
135 | This contribution was translated from German into English.
136 | See Vacanti 2006.

growth factors, regenerative medicine centres on the body's ability to heal itself and uses suitable influencing factors to stimulate this process. These may be autologous growth factors such as platelet-rich plasma or bone marrow concentrate and synthetic growth factors such as bone morphogenetic proteins, as well as targeted tissue ingrowth through modified surface structures and/or structurally optimized matrix materials.

In addition to autologous cells obtained by biopsy, blood and bone marrow concentrates and allogeneic cell sources, such as embryonic, umbilical or placental, other methods are also the focus of significant attention. Methods which are looking highly promising but are not yet ready for clinical application include those for reprogramming cell material with the aim of increasing differentiation potential, induced pluripotent stem cells being key here.[137]

The matrix materials used are no longer necessarily conventional collagen-based products but may be xenogeneic or indeed allogeneic materials, such as extracellular matrices and demineralized bone matrices and combinations of natural and synthetic polymers. Complete acellular donor matrices, which were subsequently recolonized *in vivo* with the patient's own cells, also represent a promising approach.[138] In addition, "*in vivo* bioreactors" have been developed for biomaterials and specific tissue explants. These explants may be "precultured" at one site in the patient and subsequently "replanted" at the correct site, i.e. implanted in the wound area. This improves subsequent vascularization.

Another branch of regenerative medicine is increasingly investigating the influence of biomaterial surfaces and interfaces on controlled tissue healing/ingrowth and tissue (re)differentiation. Here too, surface finish, which is determined by cell type, and differentiation potential have been shown to be directly dependent on one another. In particular, a combination of topography (e.g. surface roughness or surface structure) and targeted, localized substitution of growth factors or other stimuli could constitute a useful approach to the regeneration of particularly large-area tissue defects in need of rapid and profound tissue connection. New methods such as additive manufacture for producing complex structures could also work extremely well in the latter case.

Despite major scientific successes over the past decades, neither regenerative medicine nor tissue engineering has as yet proven as useful in clinical practice as originally hoped. In particular, large synthetic polymer-based structures have proven to be associated with disadvantages such as apoptosis and necrosis due to an inadequate nutrient supply and inadequate removal of bioincompatible, acidic breakdown products (e.g. as a result of bulk degradation or low porosity and interconnectivity). Moreover, the influence of mechanobiology (stress shielding, static pressure, no pressure, cyclic pressure or tension which is too low or too high) has been underestimated. It has also proven challenging, in the fields of tissue engineering and regenerative medicine, to transfer preclinical results from animals to humans. The development of multidisciplinary approaches, which involve doctors, pharmacologists, engineers, chemists and biologists, has become an increasingly important factor over the years in moving towards optimally practice-oriented methods. Furthermore, the licensing authorities have had to and must continue to develop new expertise, so that they can adequately evaluate such biological therapeutic approaches. Legislation has also been and continues to be adapted. In light of the novelty, complexity and particular technical features of medicaments for novel therapies (advanced therapy medicinal products, ATMPs), there has been a need for harmonized regulations specifically tailored to ATMPs, to ensure free transportation of ATMPs within the European Union and effective functioning of internal markets in the biotechnology sector. The situation regarding reimbursement by health insurance providers has so far proven problematic.

So far, there has been growing success in everyday clinical practice above all in cartilage regeneration and skin replacement. Cartilaginous tissue is particularly suitable, because human cartilage consists of just one cell type and is nourished only by synovial fluid and its scaffold is itself made up of collagen fibres and proteoglycans. Co-cultures of different cell types are a much greater challenge. Automated production processes, like those described in section 3, will make these fields more attractive in the future. A 3D printer can already produce a hundred square centimetres of very human-like skin in under 35 minutes, and there are plans to make this technology commercially available.[139] Other tissue, such as small arteries right up to a complete trachea, has been cultured and implanted in patients, but for a range of reasons these cases have so far been exceptions. One reason is that the cost of complex tissue growth is still considerable, while on the other hand it has not yet been possible satisfactorily to demonstrate and guarantee positive long-term clinical outcomes. The biggest challenges here are integration and ingrowth of the regenerated tissue into the native wound and the viability and differentiation stability of that tissue over an extended period. For these reasons, an

137 | See Loskill/Huebsch 2019.
138 | See Russell 2014.
139 | See Cubo et al. 2016.

appropriate approach would be to enable rapid connection of the regenerated tissue to the native vascular network. Modern bio-printing methods or other additive manufacturing methods combined with innovative biomaterial solutions should also be considered (see also section 3). Manufacturing costs, which remain excessively high, could be markedly reduced by further process automation, which would also simplify the transfer of biological product solutions to hospitals.

New molecules, for example traction force-activated payloads, stimulate tissue regeneration by enabling specific endogenous cells to release necessary autologous growth factors in the wound as regeneration proceeds.[140]

2018 an Israeli medical team reported for the first time on their ground-breaking clinical successes in growing and implanting tissue for reconstructing shin bones. The stem cells for this were taken beforehand from the patient's adipose tissue.[141]

A further important application of tissue engineering is the production of three-dimensional tissue-like cell constructs, which can be used to test the effect of pollutants such as pesticides, and also the effect of pharmaceuticals and cosmetics, the advantage being a reduction in animal experimentation. It is possible that in future a further major application will be found in form of the biotechnological production of cultured meat, to avoid the disadvantages of intensive farming and the associated issues.

8.2 Bone Material Properties and Their Role in Breast Cancer Bone Metastasis

Prof. Dr. Claudia Fischbach-Teschl
Meinig School of Biomedical Engineering, Cornell University, USA

Breast cancer frequently metastasizes to bone, where it leads to osteolytic bone degradation and a poor clinical prognosis. Nevertheless, therapeutic options to interfere with this process are scarce as the underlying mechanisms remain unclear. Most current research focuses on the cellular and molecular signalling underlying bone metastasis, but changes in bone materials properties may be equally important.

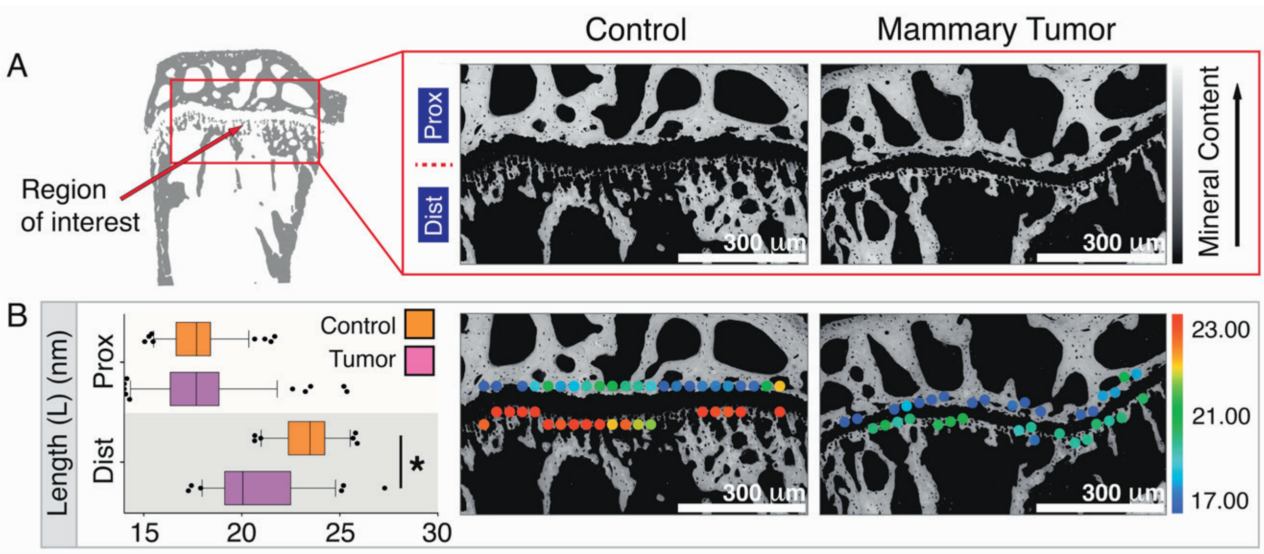

Figure 30: Synchrotron-based small-angle and wide-angle X-ray scattering methods can be used to map the size and orientation of mineral particles in bone with a resolution of several microns. These techniques have identified that, in comparison to mice without a tumour (here labelled "Control"), the presence of a tumour in mice (here labelled "Mammary Tumor") leads to reduced HA nanocrystal maturity (e.g. by reducing HA nanoparticle length below ("Dist") but not above ("Prox") the growth plate, as shown in B). While of functional importance, such changes cannot be detected with conventional clinical imaging techniques (source: He et al. 2017).

140 | See Stejskalová et al. 2019.
141 | See Bonus BioGroup 2018.

Bone is a hierarchically structured nanocomposite of collagen fibrils and co-aligned carbonated hydroxyapatite nanocrystals. The physicochemical properties of HA (i.e. crystallinity, composition, size, aspect ratio, orientation) can vary as a function of skeletal disease, diet and age, but also in response to cancer. Indeed, the presence of a tumour - even in the absence of overt clinical metastasis - reduces bone collagen content and inhibits the maturation of HA nanocrystals via circulating systemic factors (see Figure 30). These findings are of critical functional importance as cancer-mediated changes of collagen and HA not only impair the unique mechanical properties of bone, but can also affect breast cancer cell seeding and progression and thus, ultimately the pathogenesis of bone metastasis.

Nevertheless, there is still an ubiquitous lack of understanding of how bone materials properties regulate breast cancer bone metastasis due in part (i) to a lack of high-resolution analysis techniques to characterize cancer-mediated changes of bone hierarchical structure and (ii) to the lack of *in vitro* and *in vivo* model systems to evaluate the functional consequences of these alterations in relation to cell behaviour. Integrating cancer biology and tissue engineering, high-resolution structural analysis of bone, and bio-inspired materials synthesis promises to generate an improved understanding of the functional contribution of bone materials properties to breast cancer metastasis. This will broadly impact our understanding of breast cancer bone metastasis and challenge the conventional paradigm of this disease as solely initiated by cellular and molecular mechanisms. Insights gained from such studies may yield novel therapeutic targets to treat or possibly even prevent bone metastasis in the future. Given that many other cancers including prostate cancer target bone, such studies are particularly important. Finally, gaining a thorough understanding of how aberrant mineralization affects cell behaviour will also be critical to ensuring the safety of materials designed for bone regeneration approaches.

8.3 Electrospinning Technique for Incorporating Biomimicry in Biomaterials

Dr. Liliana Liverani and Prof. Dr. Aldo R. Boccaccini
Institute of Biomaterials, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany

A biomimetic approach based on an in-depth observation and knowledge of the structure and characteristics of the target tissue to be regenerated, is at the centre of the successful design of scaffolds for tissue engineering applications. In particular, each native tissue is constituted by morphological (in terms of porosity, pore size, interconnectivity, local architecture and (nano)topography), chemical (tissue composition and presence of biomolecule signals) and mechanical (stiffness, gradients) cues. During the process of scaffold fabrication, it is necessary to pursue a bio-inspired approach which starts with proper selection of the biomaterials and fabrication techniques.[142]

Electrospinning, a processing method based on the application of a high electric potential between two electrodes of opposite polarity between which a material in liquid (low viscosity) state, usually a polymer solution, is accelerated, allows the fabrication of fibres on the nano- and micrometre scale, able to reproduce the fibrillar morphology of the extra cellular matrix (ECM) of native tissues. The capability of electrospinning to serve as a powerful and versatile processing method to obtain biomimetic scaffolds has been well-known for more than 20 years.[143]

Besides the intrinsic capability of electrospinning to biomimetically replicate the native tissue ECM, leading to fibrous scaffolds of relevance to applications in soft and hard tissue engineering, the results of recent research have shown that non-toxic (benign) solvents can be used without compromising the range of applications. Several advantages can be obtained by electrospinning from benign solvents in terms of avoiding protein denaturation, elimination of toxic solvent traces from the obtained scaffolds and positive impact on lab worker safety and waste management, without limiting scaffold performance and applications in comparison to conventional scaffolds obtained with standard solvents.[144, 145]

142 | See Seidi et al. 2011.
143 | See Liao et al. 2006.
144 | See Liverani et al. 2019a.
145 | See Liverani et al. 2019b.

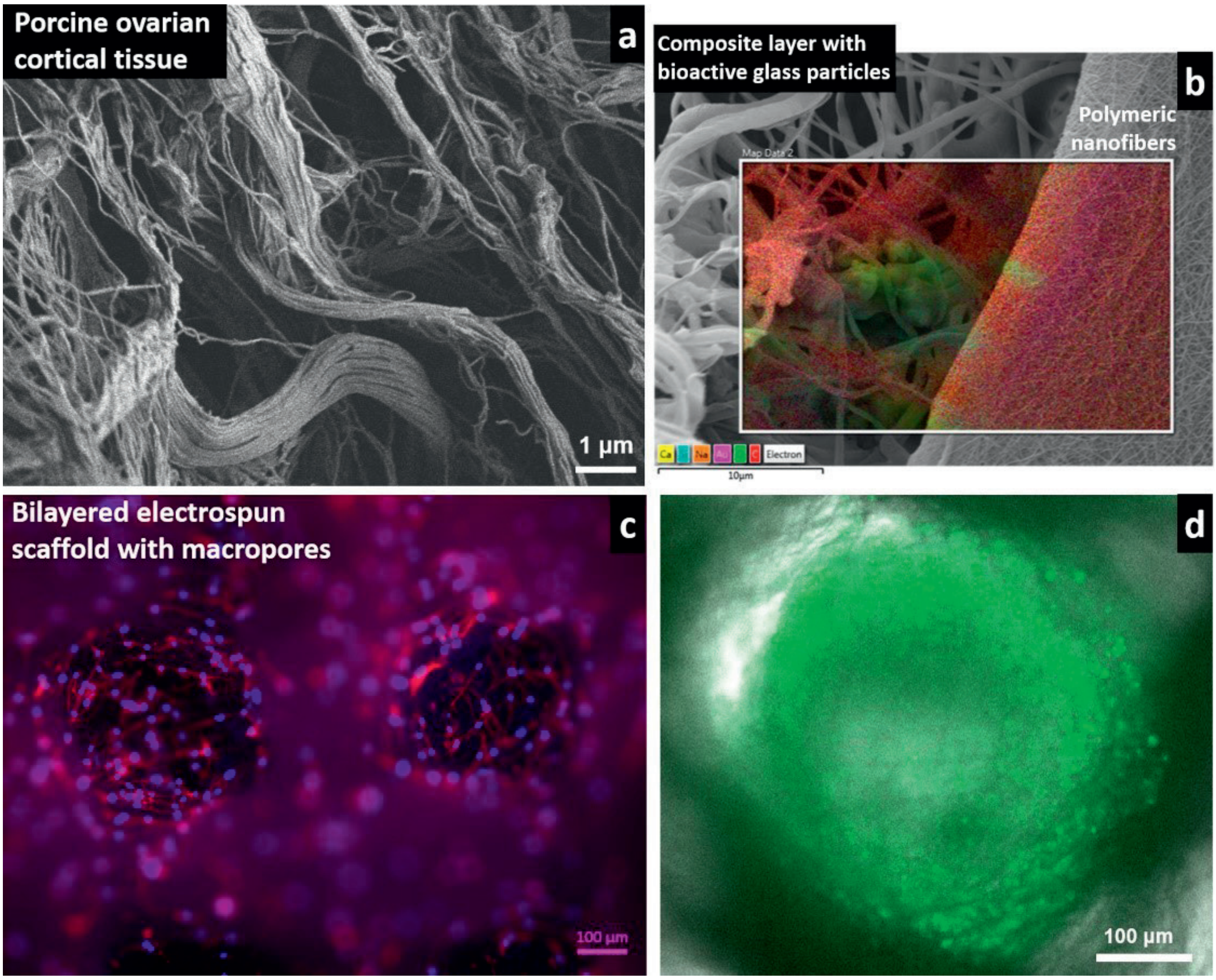

Figure 31: Biomimetic approaches based on electrospinning: (a) SEM micrograph of porcine ovarian cortical tissue; (b) SEM/EDX analysis of bilayered electrospun scaffold, with one polymeric nanofibrous layer and one composite fibrous layer containing bioactive glass particles; (c) bilayered patterned scaffolds seeded with cells, demonstrating suitable cell infiltration inside the scaffold;[146] (d) confocal image of PCL-patterned scaffold with porcine ovarian follicle (source: Institute of Biomaterials, Friedrich-Alexander University Erlangen-Nürnberg; a-c: Aldo R. Boccaccini; d: Aldo Leal-Egana)

Limited cell infiltration into electrospun scaffolds has been observed as one disadvantage of this technique.[147] This limitation might be overcome by changing the fabrication process and adding extra measures, e.g. use of patterned collectors, salt leaching as macropore former, gas foaming and the application of sacrificial polymers with a coaxial needle setup. The possibility of obtaining macropores in mats constituted by nano-/micrometric fibres, combined with the capability of controlling fibre orientation and the ability to obtain fibrous scaffolds from a combination of materials, e.g. nanoparticle-containing fibres, organic-inorganic hybrid systems, polymer blends, drug-loaded polymers, etc., have contributed to the expansion of the applications and higher quality scaffolds (see Figure 31).

In recent years, electrospinning has been used for the fabrication of nanofibrous scaffolds for a broad range of biomedical applications and some of the resultant products are already commercially available, for example coronary balloon-expandable stent

146 | See Liverani et al. 2019a.
147 | See Seidi et al. 2011.

systems, vascular access grafts and synthetic bone substitutes. Main applications are related to bone tissue engineering, hard-to-soft tissue interfaces (e.g. osteochondral segment, bone-ligament and bone-tendon interface), cardiac patches, vascular tissue engineering (considering the feasibility of obtaining 3D vessels with different layers, replicating the native structure of human blood vessels), scaffolds for nerve regeneration, patches for wound healing and dermal dressings, 3D scaffolds for tracheal tissue regeneration, membranes for corneal tissue engineering and, most recently, also 3D scaffolds for reproductive organ tissue engineering.[148] Loading fibres with bioactive molecules and drugs is leading to multifunctional scaffolds with drug delivery capability, including antibacterial fibrous structures for combating bacterial infections. Moreover, addition of bioactive (nano-particles enhances the functionality of fibres, where the size of particles can be selected according to the fibre diameter to achieve different configurations oriented for example to obtain mechanical reinforcement or to achieve enhanced exposure of the active particles on the fibre surface to facilitate ionic diffusion or drug delivery.[149]

8.4 Bio-inspired Medical Devices for Blood Treatment[150]

Dr. Markus Storr
Gambro Dialysatoren GmbH, Baxter International Inc., Germany

Medical devices currently in use in clinical practice for extracorporeal blood treatment are restricted to biopassive modules. These remove pathogenic target molecules from the bloodstream using membrane transport or adsorption mechanisms. These modules are currently used for example in chronic and acute renal replacement therapy, in organ support systems, such as liver and lung support systems, or in plasmapheresis for treating autoimmune diseases or severe hypercholesterolaemia. In general, the diseases addressed in this way are so complex that they are treated with a combination of extracorporeal blood treatment using medical devices and drug therapy. The necessary active ingredients are often administered using infusion therapies.

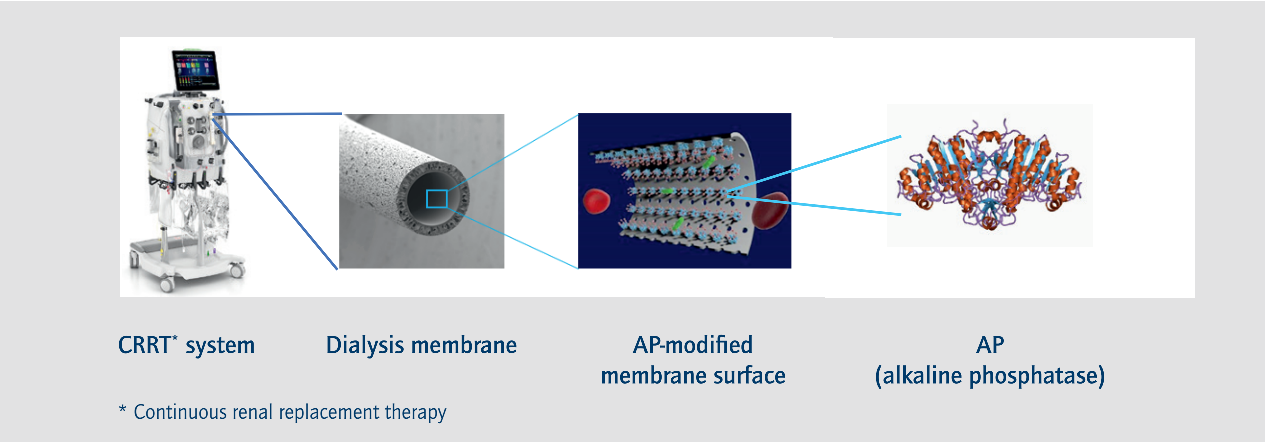

Figure 32: Therapy system for continuous extracorporeal blood treatment of septic acute kidney injury with active ingredient coupled to material surface (source: Baxter International Inc.)

148 | See Liverani et al. 2019b.
149 | See Tong et al. 2010.
150 | This contribution was translated from German into English.

In order to meet the associated requirements in an efficient manner, Gambro is looking into novel and innovative approaches to combining active ingredient therapy with mechanical blood treatment therapies: to this end we are working on coupling the active ingredients covalently to the blood-contacting surfaces and polymer materials of the blood treatment modules, e.g. to the surfaces of dialysis membranes, so that they no longer have to be infused into the bloodstream in dissolved form. Connecting the active ingredients to the surfaces prevents or slows down both degradation and metabolization of the substances, which takes place primarily in the liver or other organs, and thus leads to a marked increase in active ingredient stability and so to an improved pharmacokinetic profile of the active ingredient. Markedly lower quantities of active ingredient are needed to achieve a given average active ingredient level. Since this approach means organs and tissue are not exposed to active ingredients, the toxicity risk of the compounds is diminished significantly, so allowing on the other hand the use of larger and more effective quantities of active ingredient. The concept therefore also has a significant potential to bring about a marked reduction in the side-effects of therapeutic regimes. If suitable material treatment technologies are used, it is also possible to create a microenvironment on the surfaces which is optimized in terms of the activity of the active ingredient (e.g. in terms of electrical charge or pH).

One way in which Gambro is taking inspiration from biology when designing medical devices is the company's research into a novel therapy concept for extracorporeal blood treatment, in which purely physical blood treatment using filters is combined with pharmacological active ingredient therapies. This novel concept involves an enzyme with an anti-inflammatory effect being immobilized on polymer dialysis membranes, of the type currently used in continuous renal replacement therapy for acute renal failure. The active ingredient used is alkaline phosphatase. A recently published study of 301 patients with sepsis-associated acute kidney injury has shown that repeated intravenous administration of this enzyme leads to a significantly better patient survival rate than the administration of a placebo.[151] However, pharmacokinetic investigations on healthy test subjects have shown that, on intravenous administration, the phosphatase concentration in the blood drops to below 10 per cent of the initial peak concentration after just 4 hours.[152] As a result, relatively high infusion doses had to be selected to keep the blood concentration of the enzyme constantly above the minimum therapeutically effective level. Binding the alkaline phosphatase to the membrane surface of the dialysis module used for continuous renal function replacement in these patients would, however, significantly reduce degradation of the active ingredient, markedly reducing quantities of active ingredient compared with intravenous administration. The phosphatase needs to be coupled in such a way as to maintain biological activity, based on dephosphorylation of substrates in the blood (e.g. lipopolysaccharides and adenosine triphosphate). In addition, the material's surface characteristics have to be adapted to the optimum environmental conditions for phosphatase, which exhibits maximum activity in the alkaline pH range.

The above-described innovative concept, involving combining blood treatment modules and pharmaceutically active compounds in a single, biologically active medical device, also promises to be an advantageous approach in many other therapeutic fields.

8.5 The Bionic Ear – Restoring Hearing Through Bio-inspired Technology[153]

Prof. Dr. Thomas Lenarz
Hannover Medical School, Hanover, Germany

High-level hearing loss bordering on deafness entails a failure of auditory sensory cells. The function of these calls can be replaced in part by a "cochlear implant", which is an electronic neuroprosthetic device. The implant takes over the natural transformation process, in which acoustic information is converted into nerve action potential, the auditory nerve fibres being stimulated by a multichannel electrode which is introduced into the inner ear close to the auditory nerves. Current technology thus allows speech to be understood in quiet conditions, but only to a limited extent in a noisy environment, and listening to music is frequently impossible.[154] The main causes of this are the limited number of electrically isolated channels – the distance to the auditory nerve fibres and cell bodies is too great – and the fibroblasts surrounding the exploring electrode, which accordingly act as insulation.[155]

Biologicalization should be of assistance in overcoming these fundamental limitations. The aim is to link the electrically

151 | See Pickkers et al. 2018.
152 | See Peters et al. 2016.
153 | This contribution was translated from German into English.
154 | See Lenarz 2017.
155 | See Campbell/Wu 2018.

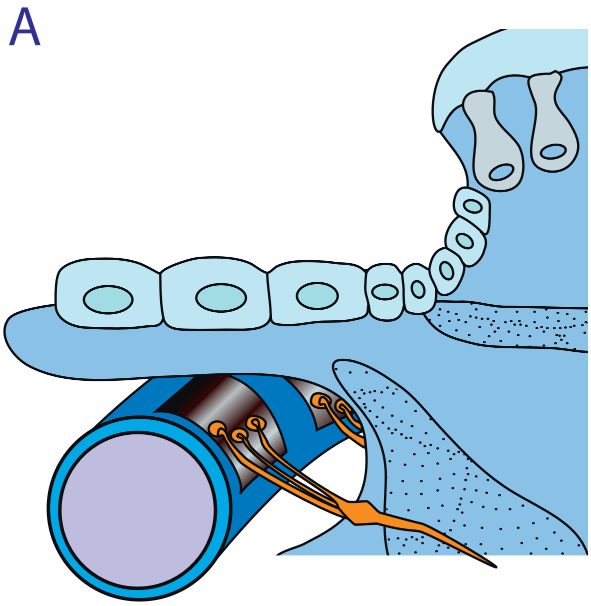

Figure 33: Electrode/tissue interface – desired dendrite growth from the spiral ganglion cells onto the electrode (source: Theodor Doll, Thomas Lenarz, Hannover Medical School, Department of Otorhinolaryngology – Head and Neck Surgery)

conductive contacts directly to individual nerve fibres via a multichannel electrode, so obtaining several hundred electrically isolated transmission channels.[156]

The following are possible individual steps:

- Functionalization of the surface by suitable micro- and nanostructures for selective cell growth (fibroblasts are kept away, peripheral nerve endings or dendrites, can grow).[157] In addition, a degradable polymer coating is conceivable which releases pharmacological active substances which support this cell-selective process and suppress insertion trauma. Examples are anti-inflammatory substances and nerve growth factors such as brain-derived neutrotrophic factor (BDNF).
- Cellularization of the electrode by suitable colonization of the surface with programmed fibroblasts or stem cells. Both are capable of permanently restoring autoproduction of nerve growth factors and thereby inducing regeneration of the peripheral nerve endings which grow onto and permanently contact the functionalized electrode surface.
- Partially filling the fluid-filled inner ear with an extracellular matrix between electrode and neuron ensures that the applied cells are nourished and is needed as a guide for renewable nerve growth.
- Application of suitable reservoirs for the release of nanoparticles, for example "adeno-associated viruses" (AAV) for transporting genetic information, which are infiltrated into the target cells (residual auditory sensory cells or auditory nerve cells). These are used in somatic gene therapy, to stop hearing loss from progressing, and optionally also for the regeneration of auditory sensory cells.

These four steps require intensive materials research into the development and processing of innovative materials representing the interface between technology and biology.[158]

This bionic ear with a markedly higher number of information and transmission channels is in a position to restore hearing virtually

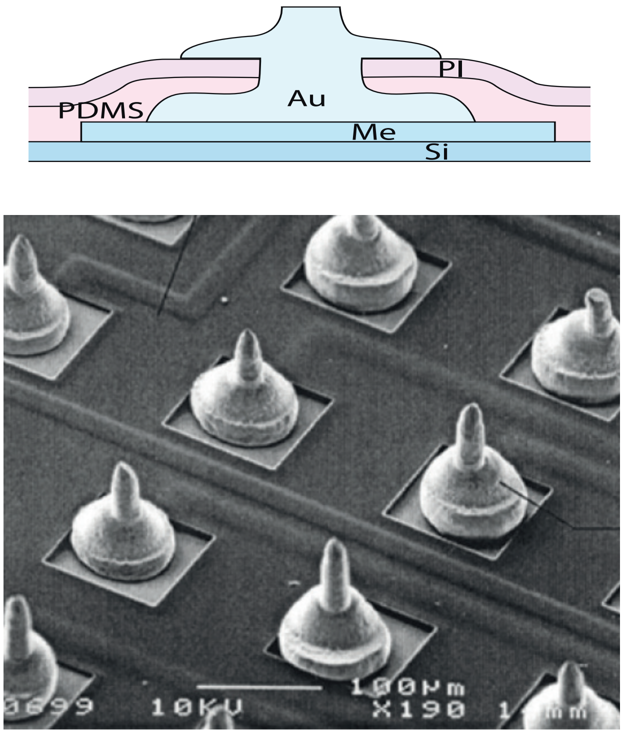

Figure 34: Electrode/tissue interface – fabrication of neural implants: stud ball method for fabricating flexible electrodes with high channel density (source: Thomas Stieglitz, Department of Microsystems Engineering – IMTEK, University of Freiburg)

156 | See acatech 2017.
157 | See McCreery 2004.
158 | See Glasmacher et al. 2020.

to natural levels, both in the case of prelingual deafness (children) and postlingual deafness (adults), and thereby to improve clinical results significantly.

8.6 Bio-inspired, Fibre-based Structures for Regenerative Medicine[159]

Prof. Dr. Chokri Cherif
Institute of Textile Machinery and High-Performance Material Technology, Technische Universität Dresden, Germany

The Institute of Textile Machinery and High-Performance Material Technology (ITM), TU Dresden is working to develop bio-inspired, fibre-based structures for regenerative medicine over the entire process chain from raw material to complex structure. Complex hybrid structures are being produced on the basis of predefined fibre arrangements and using textile production methods. Taking biopolymers, such as collagen, chitosan or silk, and biodegradable synthetic materials, such as polycaprolactone or polylactides, as basis, ITM is researching and developing fibrous materials with diameters, strengths and degradation kinetics tailored to requirements. A second development focus is on simulation-assisted design tools, geometric structural models and digital methods, which are needed if customized tissue-specific implants and scaffolds are to be designed for particular applications and patients. Examples of such implants and scaffolds are vascular prostheses, heart valves, stent grafts, hernia meshes and scaffolds for bone and cartilage regeneration.

Figure 35 shows a perfused geometric structural model of a woven heart valve (left) and a stent graft (centre), produced wholly on the basis of patient data. The stent graft contains stent rings, which are woven into the prosthetic structure, so as both to ensure reliable blood flow along the specified tube geometry and to keep the vessel patent. The right-hand part of Figure 35 shows a fluorescence micrograph of a bio-inspired short-fibre-based scaffold, which is manufactured using an additive textile printing method. The figure clearly shows successful colonization with bone- and vessel-forming cell types, which both grow completely through the open-pored structure and also form vascular structures for supplying the cells.

The Institute has clean rooms available with the most up-to-date machinery and equipment, so that it can carry out all the necessary processes from characterization of starting material to analysis of structures. Future research will include investigating novel smart structures which interactively support cell growth and thus tissue regeneration.

Figure 35: A perfused geometric structural model of a woven heart valve (left), an integrally fabricated stent graft with stent rings woven into the prosthetic structure (graft) (centre) and a fluorescence micrograph of a bio-inspired short-fibre scaffold (source: Institute of Textile Machinery and High-Performance Material Technology, Dresden)

159 | This contribution was translated from German into English.

9 Smart Material Systems and Artificial Intelligence

Prof. Dr. Peter Fratzl
Max Planck Institute of Colloids and Interfaces, Potsdam, Germany

The future of digital industrial applications will require materials that are no longer merely passive components of active devices, but become themselves operational as carriers of information. Indeed, information stored in smart materials no longer needs to be digitally processed by central information systems, this being both time- and energy-consuming. This is analogous to natural systems where structures over all length scales, from molecule to tissue, organ and the whole organism store information for the most varied activities. Many organs, such as liver, heart or muscles, operate autonomously to a certain degree, because the information about their mode of operation is stored directly in the tissue. To transfer such an approach to industry requires materials that react in a well-defined way to external stimuli, so that tasks can be subdivided hierarchically into repetitive operations. This makes it possible for sub-tasks to be carried out directly by programmable materials, with a coordinating unit, which is as a rule digital, assuming control.

Since natural systems have perfected this mode of operation through millions of years of evolution, they can provide conceptual visions for the development of programmable materials suitable for this type of information storage and processing. We can define two general concepts describing programmable materials, namely responsiveness and adaptability. Materials are responsive when they change their material properties depending on an environmental signal. A programmable material may additionally modify this reaction to the external stimulus in accordance with a rule and so adapt itself to the current situation An example from the plant world is humidity-responsive seed capsules: many seed capsules are dry containers that open or even propel themselves in response to a humidity change. The movement that these capsules perform is a direct function of the distribution and orientation of cellulose fibres inside the material, which guide the deformation upon water absorption and thus control movement. In a technological context, metamaterials, namely materials with a well-defined structure (e.g. in miniaturised trusses or porous materials), have been developed which are capable of changing their properties on demand, a responsiveness that can be of relevance for sensing and actuation, for example.

Adaptability is a more complex material property which is so far a long way from technical realization. In this case, the response of the material is not pre-programmed but modifies itself through "learning" by correcting the material response until a certain response is obtained. This adaptivity requires a feedback loop where the response of the material is modified according to a typical stimulus to which it is exposed. A typical example is adaptive growth of plants or bone adaptation through remodelling. When an organism has to carry large loads an extended period, bone reacts by thickening. When this typical load decreases, bone is slowly resorbed. In this way, the response is always to a certain extent "optimal". In the case of bone, this means sufficient strength at minimal mass.

Inspiration from Nature will, therefore, pave the way for responsive and adaptive materials and systems. Below, Christoph Eberl from the Fraunhofer Institute for Mechanics of Materials in Freiburg describes current research results about programmable materials that are very promising but still far from being adaptive (see section 9.1). Michael ten Hompel *et al.* describe the advantage of distributed adaptive systems in logistics (see section 9.2). While this is still realized with classical Artificial Intelligence approaches, transferring some of the more repetitive activities directly into materials systems might increase efficiency and save energy. Finally, Paschalis Gkoupidenis and Paul W.M. Blom discuss the potentials of neuromorphic computing which uses materials in a way inspired by the brain (see section 9.3). Finally, an interview with Henk Jonkers from the start-up "Green Basilisk", highlights the possibility of self-healing in everyday materials such as concrete (see section 9.4).

9.1 Metamaterials and Programmable Materials[160]

Prof. Dr. Christoph Eberl
Fraunhofer Institute for Mechanics of Materials IWM, Freiburg, Germany

Metamaterials and programmable materials have the potential to bring about a paradigm shift. Metamaterials can be given "unnatural" properties (e.g. the ability to steer light around people) by way of a complex internal design which the underlying physical material does not possess. Programmable materials go even further: local design of the internal structure from a homogeneous

160 | This contribution was translated from German into English.

material allows functionalities to be integrated which can currently only be produced using a large number of components. This allows functions to be integrated in a way never before achieved, while at the same time reducing the number of components and thus system complexity. Programmable materials therefore make highly integrated, functional systems possible, reducing our dependence on costly raw materials, and also open up the possibility of straightforward reuse, since in the best case scenario they consist of one homogeneous material. The process of decomposition can even be programmed into the structure.

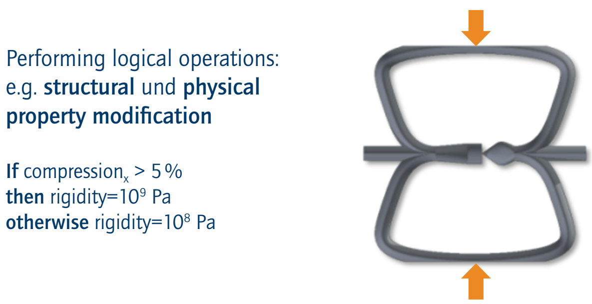

Figure 36: Individual elements can be enabled through their internal molecular or mesoscopic structure to respond to external stresses (arrows). The figure shows an individual element which has been designed to become soft as foam under a light load and rigid as wood under a heavy load (source: Matthew Berwind, Fraunhofer Institute for Mechanics of Materials IWM/University of Freiburg).

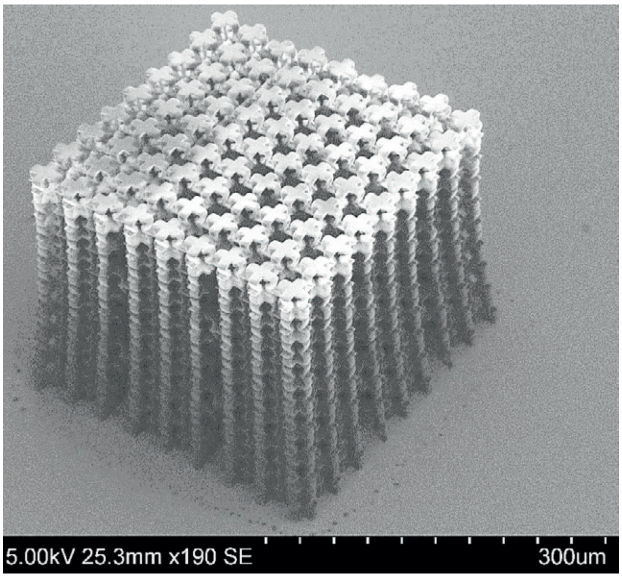

Figure 37: Mechanically programmable metamaterials consist of many individual elements which interact in concerted manner to perform system functions (source: Fraunhofer Institute for Mechanics of Materials IWM).

Programmable materials open up unique possibilities for novel system solutions, in which major parts of the system's functionality are provided by the material itself. Programmability stems from a deliberate combination of logical elements (e.g. if compression in the x-direction amounts to more than 5 per cent, rigidity should be equal to 10^9 pascals, otherwise only 10^8 pascals, see Figure 36), the material memory (e.g. bistable mechanical or molecular states) and the ability to process functions (e.g. lateral contraction as a function of elongation in the x-direction). This makes it possible to program in the response of a material to an external signal or a load. The material's responsiveness can then either be externally triggered (through application of an electrical field or by pressing on a specific location) or the programmable material can for example be automatically adapted in advance to modified conditions.

Programmable materials have immense application potential: programmable pore sizes enable self-cleaning membrane filters for water treatment systems, materials with programmable heat transmission ensure energy-efficient heat management in machinery or buildings, programmable friction allows smart control of coupling and positioning systems and programmable, speed-dependent changes in shape can result in aerodynamically or fluid-dynamically adaptable structures (as in the case of dolphins).

Fully functional, programmable materials require a combination of skills in material design, the production of complex components and product development. In material design, smart materials have to be combined with mechanical and optical metamaterials. Process technology has to make the production of architectured materials controllable, for example through additive manufacture or sheet-metal forming. To make full use of the potential on offer, a highly interactive, interdisciplinary process of application design is also needed.

Programmable materials may bring about a paradigm shift in materials handling by replacing technical multimaterial systems, consisting for example of sensor, controller, actuator and power supply, with a single, locally configured system. The key to this is programmable internal structure design, something over which Nature has unrivalled mastery.

9.2 Opportunities and Limits of Bio-intelligent Value Creation in Logistics[161]

Prof. Dr. Michael ten Hompel, Christian Prasse and Andreas Nettsträter
Fraunhofer Institute for Material Flow and Logistics IML, Dortmund, Germany

Over a decade ago, logistics researchers began to look into utilizing biological phenomena such as swarm intelligence in the development of innovative logistics solutions. The most recent insights into bio-intelligent value creation systems are enabling further systemic solutions to be derived from Nature and transferred to (primarily digital) technological systems. Current logistics research is working on investigating both the potential for transferring biological principles to logistical systems and the limits beyond which an adaptation of biological processes and methods is no longer possible in a sensible way.

The starting point for this these considerations is a systematic division of logistics and production into biological equivalents using the "tier model" (see Figure 38). In this model, logistical functional areas or system categories are compared with biological structures or interactions aiming at investigating the possibilities of transferring bio-equivalent methods more specifically:

- the lowest tier encompasses "protozoan" as genome carrier. Here, entities are transferred to logistics systems which can use a set of characteristics and abilities to perform specific functions within a "habitat".
- in the second tier, the "habitat", the protozoa act as a collective and reach a common target, for example the search for food. In logistics, "habitats" may be characterized by a range of tasks which are locally limited (to a warehouse or factory) but cross-functional (e.g. transportation, gripping, sorting, picking, negotiation, etc.).
- the third tier, the "biotope", merges multiple "habitats". In logistics and production, the biotope corresponds to different factories, warehouse sites or assembly facilities.
- finally, the fourth tier or "ecosystem" of logistics is the counterpart of global value creation networks consisting of different suppliers, producers, logistics service providers and customers.

So far, biological methods being transferred to logistics are currently represented particularly in the lower two tiers. At the "protozoan" and "habitat" level for instance, swarms of flexible transport vehicles imitate ants and their organizational principles (see Figure 39). However, there is no correspondence between logistics and biology in the upper two tiers. There seems to be a limit of transferability between "habitat" and "biotope" (see Figure 38: red line), beyond which the adaptation of biological or natural processes and methods to logistics is no longer possible in a sensible way.

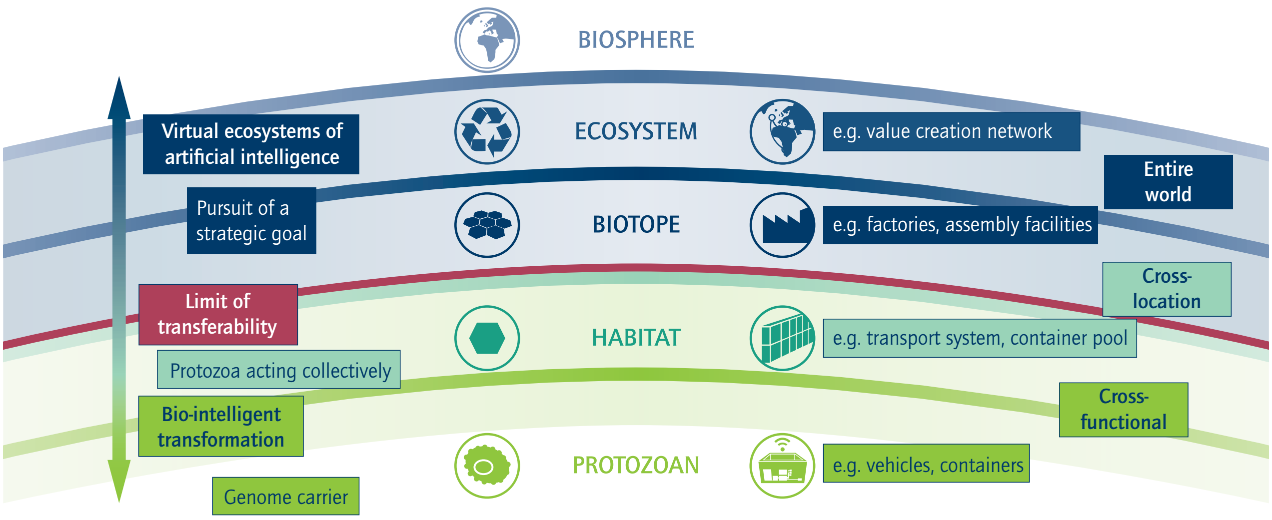

Figure 38: Bio-intelligent logistics as agile value creation ecosystem (source: Fraunhofer Institute for Material Flow and Logistics IML)

161 | This contribution was translated from German into English.

From a logistical point of view, the transition from "habitat" to "biotope" marks the point at which strategic and targeted design, planning and organization are required. As an example, the production of a complex product can be mentioned which must take place across several companies, i.e. on a cross-habitat basis. The coordination and optimization of companies with each other must pursue a strategic goal. At this level, biology cannot offer logistics any models. This is because no strategic goals are known in Nature beyond species preservation (unless, of course, these are as yet unknown to us). This also applies to the ecosystem level, where value creation networks have even more complex common strategic goals.

As promising as the transfer of biological principles in the "protozoan" and "habitat" level may be, logistics will have to seek other solutions at "biotope" and "ecosystem" level. Artificial Intelligence algorithms by definition address associated topics of design, planning, organization etc. and appear suitable according to today's state of research to analyse existing information and deduce or assist "sensible" decision making. If this idea is adopted, highly distributed AI systems will exist, negotiate, plan, learn and produce in an "ecosystem" in future. AI, therefore, pursues the goal of cross-system, multicriteria optimization, in terms of a new, bio-intelligent supply chain management. In this context, logistics research needs to investigate the mechanisms of biology and computer science for optimizing logistical value creation networks simultaneously and on an equal footing.

Figure 39: Cellular transport system with decentralized multi-agent control, in which software agents represent the individual vehicles and negotiate transport orders and routes, autonomously (source: Fraunhofer Institute for Material Flow and Logistics IML)

9.3 Organic Iontronic Devices for Neuromorphic Computing

Dr. Paschalis Gkoupidenis and
Prof. Dr. Paul W.M. Blom
Max Planck Institute for Polymer Research, Mainz, Germany

Information processing using software-based artificial neural networks, a field commonly known as Artificial Intelligence, is a popular approach with tremendous impact in everyday life. This approach relies on executing algorithms that represent neural networks on a traditional von Neumann computer architecture. An alternative approach is the direct emulation of the workings of the brain with actual electronic devices/circuits. The human brain consists of approximately 100 billion neurons communicating with each other in an interwoven network of almost 1000 times as many (10^{14}) synapses. Neurons are electrically excitable cells that collect, process and transmit information and are regarded as the processing units of the brain. Neurons are interconnected to each other through synapses in a complex network and their connection efficiency (synaptic plasticity) can be modified over a range of timescales. This complex network of neurons and synapses attributes unique properties to the human brain, such as a high degree of parallelism with inherent fault tolerant characteristics and low power consumption. These attributes render the brain an ideal model system for the implementation of information processing circuits of the future, also called neuromorphic computing. In the future, such neuro-inspired processing circuits are expected to result in breakthroughs in the way that computers analyze data, and conceive the real-world environment, as well as in the way that computers interact with humans.

Recently, organic electronic materials have been attracting increasing interest as a basic element for neuromorphic circuits. In addition to their ability to conduct electronic carriers, many organic electronic materials are also capable of conducting ions (which are either introduced into the film during synthesis, or are injected from an electrolyte). Due to the strong coupling of electronic and ionic carriers in a single material and their soft nature, these "iontronic" devices act in many cases as high efficiency, ion-to-electron converters and thus offer an interface between biology and electronics, otherwise known as "organic bioelectronics". The basic building block of organic bioelectronic circuits for neuromorphic applications is the organic electrochemical transistor (OECT), which converts ionic signals into electrical current. In neuromorphic architectures based on OECTs, electrolytes can play the role of connectivity media from device to device, as shown in Figure 40. This permits the definition of parallel "soft" connectivity between

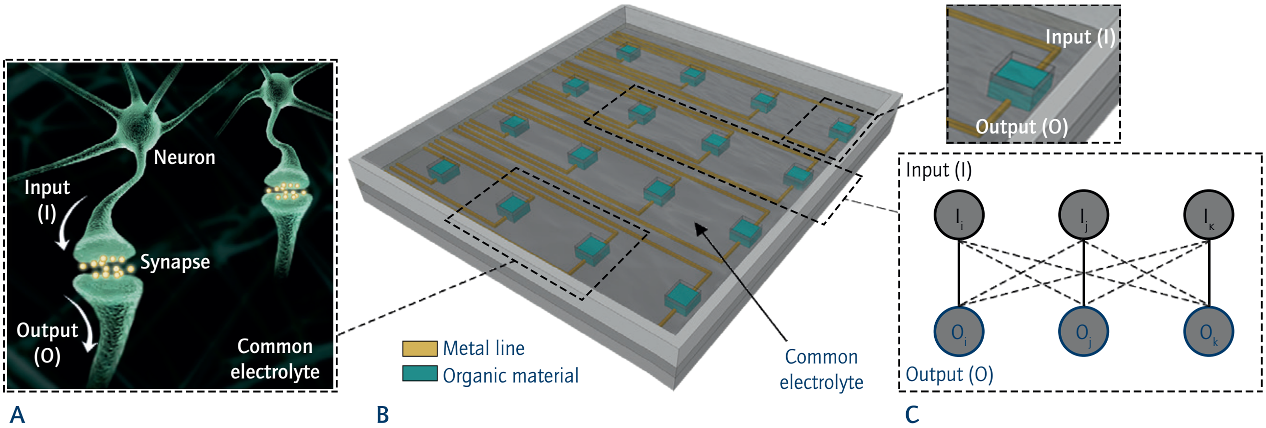

Figure 40: (A) Neurons and synapses in a biological neural network. The function/structure of a biological neural network is an ideal example for the implementation of neuromorphic circuits of the future. (B) Simplified illustration of an array of organic electrochemical transistors based on mixed conductors with neuro-inspired features in processing that is immersed in a common electrolyte. (C) Connectivity media for neuro-inspired architectures: complex interconnections are established though the electrolyte (dashed lines), when an array of organic electrochemical devices is immersed in a common electrolyte (source: Gkoupidenis et al. 2017 [CC BY 4.0]).

devices though the material continuum, as well as their global regulation through a common electrode, mimicking the global oscillations in the brain that synchronize neural populations.

Materials and devices that exhibit memory and have the potential to operate at the interface with biology will pave the way for novel data manipulation paradigms with bio-inspired features in information processing. The challenge is to develop organic devices/architectures capable of reproducing neuro-inspired information processing functions with the potential to operate at the interface with biology. Such architectures will have significant impact in applications that range from the brain-computer interface, through neuroscience and robotics to bioinformatics and the definition of novel computational paradigms at the interface with biology.

9.4 Interview with Henk Jonkers, Green Basilisk

Associate Professor Henk Jonkers chairs the Sustainability Group within the Materials & Environment section in the Faculty of Civil Engineering and Geosciences at the Delft University of Technology. His research focuses on the development of innovative, bio-based and sustainable construction materials and he is scientific adviser to the spin-off Green Basilisk.

Prof. Jonkers, what significance does the biologicalization of materials science and its innovation potential have for your country?

We are working on the assumption that bio-inspired and bio-based research will lead to processes or products which are more efficient than their traditional counterparts. So it is highly significant and has considerable potential, not only commercially but for society as a whole. As a country and region, we have made a start with the research into self-healing funded by the Dutch Ministry of Economic Affairs. The ministry believes our ideas can result in the development of new technologies and products which will not only be beneficial to society but also suitable for export.

Is this already happening?

We have our own start-up, Green Basilisk, which is commercializing self-healing concrete that is slowly finding its way into applications internationally. The interesting thing is that we see a difference between Europe and Asia in mentality. In Asia, they are much more open-minded to innovation and we have studied why this is. We have developed three different products, a self-healing concrete for new structures and two repair products for damaged structures. In Europe there is a lot of interest in the repair products, in Asia more in the concrete.

Why is this?

We believe it's because the many regulations and standards which apply to the European building sector make everyone keen to avoid the blame should anything go wrong. In addition, everything is standardized which completely blocks innovation. Innovation means doing something new, so it comes with risks and European investors are conservative so they carry out risk analyses. In Asia, on the other hand, they do "opportunity analyses" and evaluate the potential benefits. If you look at life-cycle costs from the outset, there is potential to save a lot of money and resources. Our product is a solution to a problem which the market sometimes can't even see. The Dutch government wants our economy to be over 95% circular by 2050.

How can a Circular Economy be achieved?

Companies have to be profitable and won't take a circular approach if it is costly. So, although there is a lot of innovation, it is not taken up by the market because it is costly. But there is a simple solution: politicians will have to come up with new regulations to nudge the companies. For example, a price could be put on using primary resources to spur commercial competition in order to cut the use of primary resources or reuse waste products. If you don't do that, innovative companies will be disadvantaged and nothing will happen.

Can you explain how your self-healing concrete works?

The bio-inspired part is of course the self-healing. In biology, you have organisms that can cope with a certain amount of damage because they can repair themselves, like our human bodies. Our aim was to develop materials and mechanisms that can be incorporated into traditional materials that have the potential to self-heal. Now, the problem with traditional concrete is that microcracks form under tension allowing water to penetrate, so ultimately shortening service life. Traditionally, this is solved by over-dimensioning structures and making unsustainable use of materials. This is why we developed a self-healing concrete based on bacteria which can survive being mixed into concrete. They are activated by water flowing into the microcracks, which is traditionally the problem but in our case is the solution. Once activated, the bacteria start to convert nutrients, which have also been incorporated into the concrete, into limestone, a concrete-like material, which seals the cracks. This is biomimicry at its best: on the one hand, we learn from Nature how to deal with a certain amount of damage and how to self-repair, and on the other, the approach is bio-based, since we are using natural bacteria. In addition, money and resources can be saved, both of which are important factors in Asia. The construction sector in Europe is keen on the repair products, for once the damage has already occurred.

So have structures already been built from your product in Asia?

One of our clients is a Japanese building contractor which is using self-healing concrete in most of its structures now and is already selling such buildings. In the Netherlands, we are so far still at the demonstration stage.

Figure 41: Henk Jonkers with a cube of bio-inspired, self-healing cement (source: Green Basilisk)

10 Interdisciplinary Aspects: Humanities and Creative Disciplines[162]

Prof. Dr. Peter Fratzl
Max Planck Institute of Colloids and Interfaces, Potsdam, Germany

The activity of systems is based on an interplay of energy, information and matter. The traditional image of this might be an industrial robot which is constructed from steel and aluminium (matter), is controlled by a computer program (information) and driven electrically (energy). However, maintaining a distinction between these three conditions for activity can no longer be justified from either a physical or technical or even a historical/cultural standpoint.

As long ago as the second half of the 19th century, the physicist Ludwig Boltzmann demonstrated that (dis)order is related to probability and therefore information. The resultant entropy is an essential component of a system's free energy. Einstein's special theory of relativity, in contrast, equates matter with energy by stating that mass can be converted into energy and *vice versa*. It must follow that matter and information are also more closely related than is generally assumed: as soon as matter is not in a completely amorphous state, it stores information as structure on many different size scales from atomic dimensions up to its external shape. Most technically usable material properties are based on structures which are introduced in controlled manner into the material and therefore constitute the "information" defining the behaviour of the materials. This applies just as much to control of the mechanical properties of metal alloys by inclusions and precipitates as to butterfly wing colours which originate from periodic pore arrangements. Due to the process of growth, natural materials are structured on many size scales which provides them with a high information content.[163,164] The unity of matter, information and energy is therefore a key concept which follows from the biologicalization of materials science.

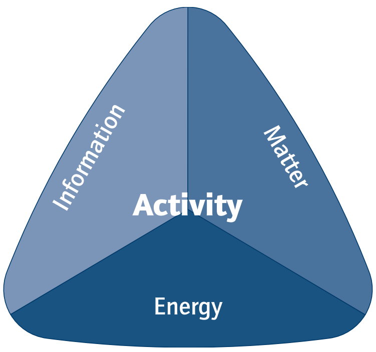

Figure 42: Activity as a combination of matter, energy and information (source: Wolfgang Schäffner, Department of Cultural History & Theory, Humboldt-Universität zu Berlin, and Peter Fratzl, Max Planck Institute of Colloids and Interfaces MPIKG)

Wolfgang Schäffner will firstly analyze the relationship between matter and information from the standpoint of cultural history and theory (see section 10.1). The literary scholar Karin Krauthausen and philosopher Michael Friedman (see section 10.2) will discuss what is meant by active matter. Markus Buehler from the Massachusetts Institute of Technology (MIT) will present the principle of "materiomics", in which organisms are viewed holistically as models for materials development (see section 10.3). The architect and designer Christiane Sauer will show examples of designing with fibre structures, a deeply bio-inspired approach since virtually all biological tissues are made up of fibres (see section 10.4).

The interdisciplinary interface between biology and engineering sciences is not only a challenge in terms of teaching and instruction, but also offers particular opportunities. The biologist Olga Speck will describe her experience in this connection (see section 10.5). Finally, the chemist Cordt Zollfrank and some colleagues will discuss issues around the bio-based economy (see section 10.6).

Interviews with representatives of BASF clarify some of the challenges (see section 10.7). On the one hand, conventional structural materials are already highly developed and of very good quality, so bio-inspired solutions will struggle here. There are major opportunities for more complex materials with highly integrated functionality, such as food packaging films which extend or verify the storage life of foodstuffs. Overall, it is more a matter of "mindset" than of direct transfer of solutions. BASF's design centre devises conceptual solutions, some of which may benefit from biologically inspired concepts, in cooperation with customers.

162 | This contribution was translated from German into English.
163 | See Fratzl/Weinkamer 2007.
164 | See Estrin et al. 2019.

In bio-inspired materials science it is essential to foster highly interdisciplinary approaches to research which take account of the humanities and design disciplines, so giving the latter the potential to bring about a paradigm shift in the use of materials and to have a long-term influence on industrial development.

10.1 Matter and Information[165]

Prof. Dr. Wolfgang Schäffner
Department of Cultural History & Theory, Humboldt-Universität zu Berlin, Germany

The humanities can contribute to the biologicalization of materials science by making it clear that, from a cultural history and theory standpoint, this process involves a great deal more than simply a new way of optimizing existing technologies. It is in fact a complete change of direction for our entire technological system which, especially since the late 19th century, has been characterized by viewing the underlying materials as providing a passive structure which merely carries out instructions which are externally encoded, activated and controlled. The passivity and inertia which was ascribed to matter in this way had a significant impact on material selection, choosing a maximally neutral material as the "hardware" for a machine being intended to ensure trouble-free operation. This applies not only to conventional mechanical but also digital technologies. The associated separation of matter and information is the technological counterpart to what is known from the history of philosophy as the separation of mind and matter,[166] a separation which not least in the 19th century led the humanities to turn resolutely away from technology.

The turnaround which is currently taking shape with regard to biological materials is a fundamental transformation which as a post-digital, material revolution enables a new relationship between matter and information. This situation is therefore also a fundamental challenge to the humanities: an epistemological and historical analysis is required if the possibility of resolutely turning away from this principle of matter being passive is to be made apparent in today's materials science. This is because biological materials are themselves proving to be active and thus no longer defined by this separation between passive matter and external activation and control. If the internal structure of materials encodes an intrinsic activity, then matter has itself become a system which integrates energy and information.

This inherent activity is not unknown historically: this material activity was put to practical technological use in Europe far back into antiquity and some other cultures have even maintained this understanding of active and intelligent materials right up until today. In the context of modern technology, however, this activity was not recognized as an energy store and encoding of an inherent nature but was instead treated as a dysfunction to be eliminated. The activity of wood has accordingly long been known, but was taken as a reason to neutralize it by forms such as plywood or indeed to replace wood as a material with other "more passive" building materials.

A central task would therefore appear to be to investigate this internal activity and encoding of matter: in contrast with our digital codes, active materials can be understood as the hardware of an analogue, geometric code, or in other words, as an operative geometry which the tangible and intangible, "mind", information and matter merge. A code would thus need to be described and developed which not only represents and simulates processes symbolically but at the same time embodies them in material form. The current turn towards matter and active materials could also eradicate the cybernetic separation between the mechanical properties of materials and the controlling information technology processes, which is a separation which also underlies digital technology. If active biological materials actually do establish an intrinsic connection between matter and information, the symbolic and the material, they constitute machine systems which present a fundamental challenge as a technological principle.

For the humanities, this means not only having to redefine themselves in relation to a new culture of the material world, but also entails a new synthesis of the humanities and materials science[167, 168] in the form of an interdisciplinary collaboration between the humanities and natural sciences, engineering and design in order to overcome the separation between matter and mind/information at an institutional level. This collaboration is the central focus of the "Matters of Activity" Cluster of Excellence at Humboldt-Universität zu Berlin.[169]

165 | This contribution was translated from German into English.
166 | See Schäffner 2017.
167 | See Schäffner 2016b.
168 | See Schäffner 2015.
169 | See Humboldt-Universität zu Berlin 2019.

10.2 Active Matter[170]

Dr. Michael Friedman and Dr. Karin Krauthausen
Cluster of Excellence 'Matters of Activity. Image Space Material' at Humboldt-Universität zu Berlin, Germany

How can this new concept of matter and materiality which has come to be known under the name "Active Matter" be understood? And just what operations does materials activity encompass? These questions can be approached by taking a look at the three-dimensional structure of materials because any kind of material has such a structure, irrespective of whether it is dead or living matter. Folding, which permits a change in shape and often brings about a change in function, is one fundamental operation of materials which is based on this three-dimensional structure. One simple example of this is the opening and closing of one or two planes along a one-dimensional axis, as is observed in pine cones: in dry weather, the scales rise up and the cone opens while in rain or humidity they sink down and the cone recloses. The scales can thus move and the shape of the cone changes and it is the unfolding and refolding dynamic structure which brings about the change in shape. This activity would appear counterintuitive when it is considered that the pine cone largely consists of dead matter.[171] However, there are further examples of folding activity in organic systems, for instance the unfolding of the pentagonal seed capsules of the brilliant stonecrop which likewise enables an ingenious self-sowing mechanism. A study by Lorenzo Guiducci and Khashayar Razghandi describes this mechanism of the seed capsule: "[T]heir fruit undergoes a reversible origami-like unfolding upon sufficient hydration [...]. The engine of the investigated movement was found to be the water adsorption and swelling of the cellulosic inner layer of the cell wall of the hygroscopic keel cells. The complex large-scale movement, however, could only be explained in terms of the sophisticated hierarchical design of the entire capsule."[172] The unfolding is therefore an example of "actuation systems [...] [which] do not depend on the active role of living cells [...]."[173] Just the two examples of the pine cone and the seed capsules of the stonecrop show that such three-dimensional material structures have an advantage (over static structures), since they enable a mechanism which brings about the emergence of the structural change in material space which is vital to life. The same may be concluded from studies into leaf growth: "[P]lant surface development, according to which the form of some biological surfaces is not genetically programmed in detail, but results from a coarse genetic control of growth rates, complemented by 'emergent processes' induced by geometric constraints of space and elasticity."[174, 175] All the stated examples indicate that the 'dead' matter is not 'dead' (defined as absolute passivity) or at least should not be considered so. Matter can itself be operative and understanding this opens up new horizons in order to take account of the activity of materials in all its various aspects, in other words without limiting the impact of this activity on living organisms. The focus should here not be on the 'folding' or 'folded' structure per se, but more fundamentally on the activity of the structure. This activity of the materials depends on the particular structural type and may for example likewise be based on weaving, braiding or knitting.[176, 177] Wolfgang Schäffner's understanding of natural materials as technology (specifically as "technologies of another kind") is informative and he concludes: "Nature is thus not opposed to technology, but would instead appear to be a storehouse of technical solutions."[178, 179] In the above-stated examples, technology takes the form of the material operation of folding which should be understood to be an active process and root cause of the immanent emergence of structural change. The present issue is not merely to overcome the opinion of matter being passive,[180] but instead additionally to connect the concept of active matter with the new production of novel, e.g. 'printed', materials in order to undermine the all too convenient conception of materials being passive here too. Folded or, specifically, folding materials serve as models here as they include the emergence of future structures within themselves, as Matthew R. Gardiner writes: The advantage of the new "processes of Fold Mapping and Fold Printing, [...] [that of printing]

170 | This contribution was translated from German into English.
171 | See Friedman/Krauthausen 2017.
172 | See Guiducci/Razghandi et al. 2016, p. 1f.
173 | See Guiducci/Razghandi et al. 2016, p. 2.
174 | See Prusinkiewicz/Barbier de Reuille 2010, p. 2121.
175 | See Guiducci et al. 2016.
176 | Woven structures are distinguished in that they convert a one-dimensional starting material (threads) into two- and three-dimensional objects with greater stability (while retaining flexibility). The research is attempting to understand these woven topologies and to transfer them onto a molecular level by using self-organizing threads. Possible applications might include catalysis, gas separation and storage.
177 | See Lewandowska et al. 2017.
178 | See Schäffner 2016a, p. 29.
179 | See Fratzl 2016.
180 | See Schäffner 2016a.

cohesive geometry and fabrication methods, is that previously impossible objects and concepts are now possible to design and fabricate."[181] In conjunction with the latest technologies, such as 3D printing, the material structures raise new issues and complexities for which they themselves provide the solution. This solution involves material programming which follows the three-dimensional structure of the materials and does not do so passively but is instead actively inspired by their own activity.[182]

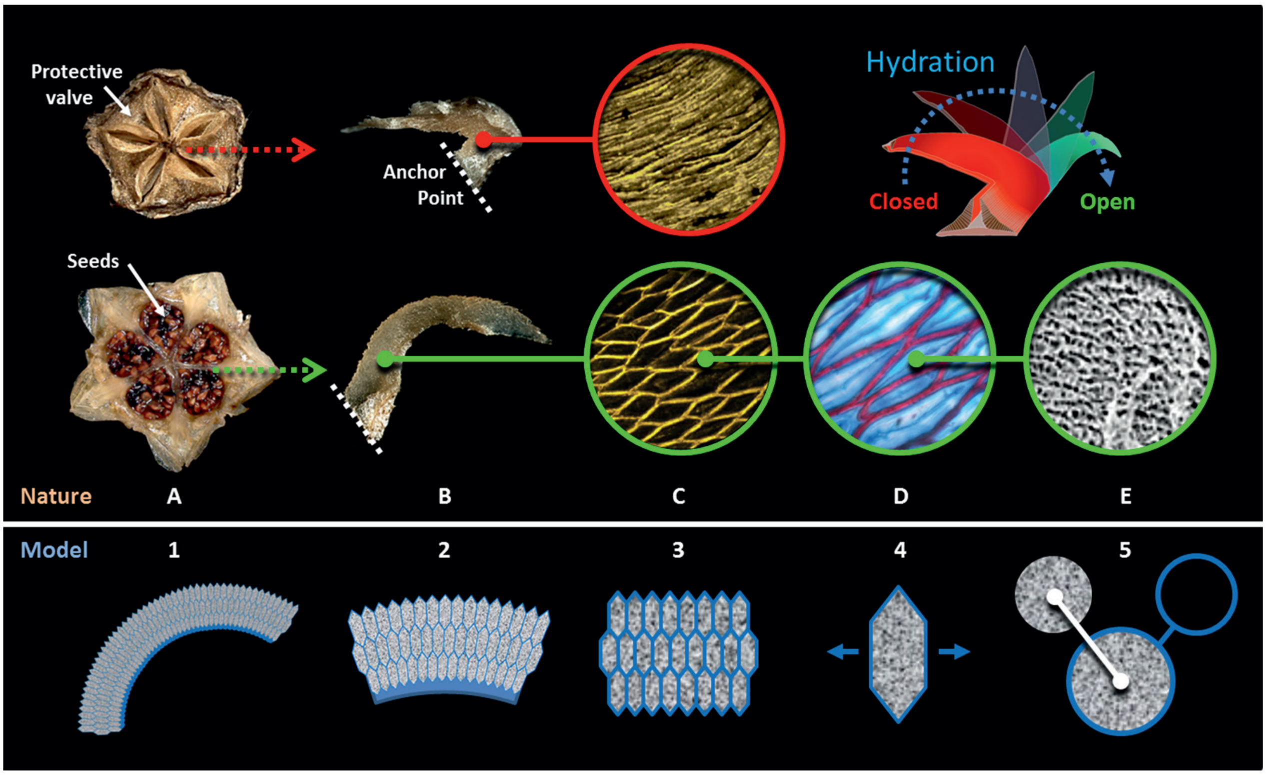

Figure 43: Top: The underlying architecture (on different length scales) enables reversible unfolding of the seed capsule of the brilliant stonecrop. Bottom: Abstract presentation of the activation principles on different length scales. Breaking away from the biological system while taking account of the underlying principles in simple models makes it possible to design bio-inspired active material systems. From right to left: Swelling of a highly swellable material within a closed cell results in a uniform change in volume of the cell. Directional deformation can be achieved by adapting the cell geometry; for example, an elongate hexagonal shape can lead to swelling in the direction of the long side of the cell. The deformation can be magnified by arranging such cells in a cell structure; for example, the honeycomb structure would expand on swelling. The resultant actuator can be adjusted in order to obtain different deformation modes; for example, if one side of such a honeycomb structure is restricted, this results in flexure of the entire structure (source: Guiducci/Razghandi et al. 2016 [CC BY 4.0]).

181 | See Gardiner 2018, p. 187.
182 | For an overview of the approaches to and topics of research into active materials or active material structures see Fratzl et al. 2020.

10.3 Bio-inspired Materiomics

Prof. Dr. Markus J. Buehler
Massachusetts Institute of Technology MIT, Boston, USA

The living world offers some of the most stunning materials as well as processes by which such materials are made – with prominent examples like silk, bone, or seashells.[183, 184, 185, 186] Of particular interest at the frontier of materiomics is the translation of insights from one domain to another, as in creating new materials designs that combine mechanisms seen in distinct natural materials. One such example could be the combination of properties of silk protein (known for its high strength and toughness) with that of elastin protein (known for its great elasticity and tunability). Although these proteins do not exist together in nature – they appear in different species and different places altogether – through bio-inspired process engineering it is possible to combine such materials into *de novo* proteins with novel properties by writing a new protein sequence that mixes patterns seen in silk and elastin.[187]

An exciting frontier in materials engineering inspired by nature is the way by which materials are evolved, made and actively controlled during their use. In a material like spider silk and complex webs made thereof,[188] the spider can be envisioned as an intelligent signal processing unit – a neural network – whereby the spider is an agent that gathers data through sensing vibrational signals of the web and making decisions about how to build and evolve the web based on these external inputs. For instance, a spider continuously monitors the web and decides where and how to build or repair its structure, acting as a sort of autonomous 3D printer that deposits various types of materials on demand. This view of neural network-based material manufacturing offers a new avenue of exploration for materials scientists, by which the natural neural network (the insect) may ultimately be replaced by Artificial Intelligence, or artificial neural networks.[189, 190, 191] In this paradigm, the bio-inspired design approach does not merely copy geometries found in nature but also mimics the process by which materials are built and how they evolve in the context of the living system and the ecological principles in which they function. It can lead to autonomous systems where manufacturing and repair mechanisms are built into the material.

This expanded bio-inspired materiomics approach focuses on transcending the manifestations of matter, looking more deeply into design principles of ways by which properties of disparate functional systems are created by living organisms – not just materials, but expressions of language, art and other manifestations by which living systems project themselves to the world. For instance, both biological materials and human expressions of art can be understood as hierarchical systems that build up complexity and function through a designed arrangement of building blocks across length- and time-scales (see Figure 44A). In recent work we have, for example, explored the interface of material and sound, and shown how we can transcend scales in space and time to make the invisible accessible to our senses and to manipulate matter from different vantage points, using innovative agents such as AI interacting with human creativity.[192, 193, 194]

The online audio file[195] shows the transformation from western classical music as one example of a hierarchical system to music created from an interplay of hierarchical sounds created by the vibrations of protein molecules. One impact of this work could be the design and making of new materials, new art and music, and the development of a deep mathematical understanding of the functional underpinnings of disparate manifestations of hierarchical systems, where design concepts from one domain can be used in the manifestation of another (see Figure 44B).

To give a specific example for this paradigm-shifting approach to design materials, one can translate the patterns of protein

183 | See Fratzl/Weinkamer 2007.
184 | See Barthelat et al. 2016.
185 | See Buehler 2013.
186 | See Cranford/Buehler 2012.
187 | See Yeo et al. 2018.
188 | See Su et al. 2018.
189 | See Silver et al. 2016.
190 | See Schmidhuber 2015.
191 | See He et al. 2016.
192 | See Qin/Buehler 2019.
193 | See Yu et al. 2019.
194 | See Hesse 1943.
195 | Markus J. Buehler: https://soundcloud.com/user-275864738/a1-1.

designs originating from their amino acid sequences into sound, and then manipulate material design in the audio space by composing new music, and then translating the newly generated sounds back into proteins (see Figure 44C). One may also use existing musical compositions and extract hierarchical patterns from them that can be directly used in materials design. This approach of exploiting hierarchical system design across different manifestations of matter (in material, sound, words, and so on) offers an unusual way to design new materials which expands our ability to manipulate matter in a domain where structural variations (such as amino acid sequence mutations) can be understood through different senses (e.g. the auditory system) and alternative theoretical models (e.g. music theory), utilizing a cross-platform approach to studying biological materials using materiomics.

The insights from this cross-platform approach explain practically relevant issues such as the strength of silk or the emergence of disease, the creation of new art, and the exploration of the underpinning philosophy of what constitutes material and imagination. The translation from various hierarchical systems into one another poses a new paradigm to understand the emergence of properties in materials, language, visual art, music, and similar systems, an array of which can offer new research directions in materiomics. Data driven methods, complemented by mathematical approaches such as category theory, offer the sort of tools that now allow us to advance these fields in a unified manner.

Online audio file[195] hierarchical systems in sound;[196] example showing the transition from classical western music to music composed from the vibrations of protein molecules (see Figure 44A). The classical music heard at the beginning is composed of a hierarchy of sounds using a variety of classical instruments (violin, viola, cello, etc.). The protein-based music heard towards the second half of the piece is created based on the sonifications of three proteins: 1) 5iom protein: Nucleoside Diphosphate Kinase from *Schistosoma mansoni* (a water-borne parasite of humans which belongs to the group of blood flukes), 2) 1sve protein: Protein Kinase A in *Oryctolagus cuniculus*, *Bos taurus* (rabbit and bovine). The enzyme catalyzes the transfer of a phosphate group from adenosine triphosphate (ATP) to a specified molecule. ATP is a complex organic chemical that provides energy to drive many processes in living cells. 3) 4rga protein: Phage 1358 receptor binding protein (rare group of phages infecting *Lactococcus lactis*).

196 | See Qin/Buehler 2019.

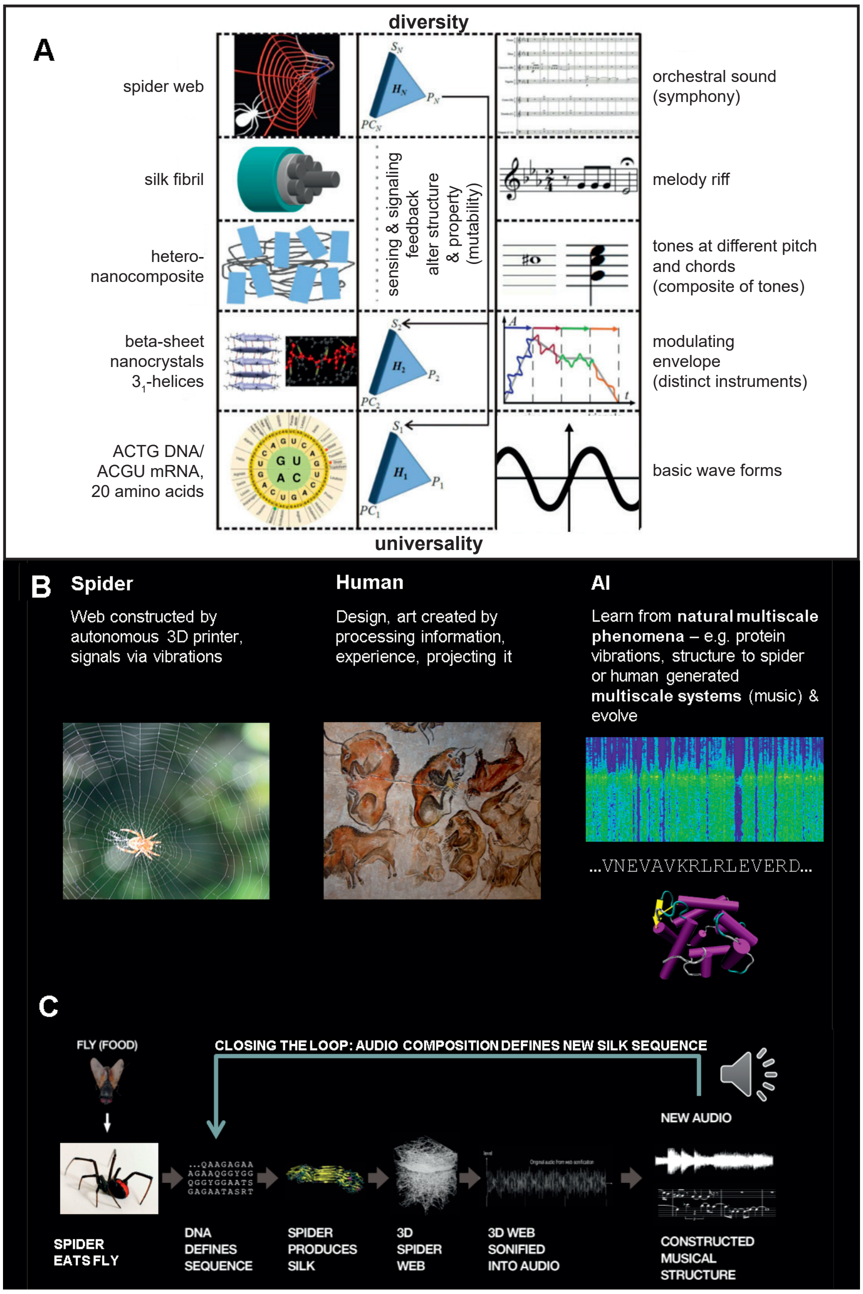

Figure 44: A: Hierarchical systems in materials and sound (example audio online[197]). B: Neural networks, whether found in insects or humans, are the agents behind the design of hierarchical systems such as materials (spider web construction), art (paintings, music, etc.). The natural neural network can be replaced with artificial models, enabling the use of AI to design hierarchical systems of various kinds including sound, which can be translated to the material domain. Artificial Intelligence thereby acts as a neutral arbiter and translator between various manifestations. The inset of the protein showcases a new material designed through the musical representation of proteins.[198] C: Closing the loop between audio and material manifestations offers a new way to interpolate between biological designs seen in materials and those created through human expression of art, and can provide a new mechanism to manipulate materials through the use of sound[199, 200] (sources: Markus J. Buehler, Massachusetts Institute of Technology; single images: cave art by Thomas Quine [CC BY-SA 2.0], spider web by Stephencdickson [CC BY-SA 4.0] and redback spider by Laurence Grayson from Suffolk, UK [CC BY 2.0]).

197 | Markus J. Buehler: https://soundcloud.com/user-275864738/a1-1.
198 | See Yu et al. 2019.
199 | See Qin/Buehler 2019.
200 | See Dubus/Bresin 2013.

10.4 Design with Fibre Structures[201]

Prof. Christiane Sauer
weißensee kunsthochschule berlin, Germany

In design or architecture, design processes start by identifying ideas or concepts which, on the basis of a particular task, put form and function in relation to one another. A suitable materiality is often sought and applied only after the design has already been completed.

Designing with fibre structures turns this principle on its head and applies a bottom-up approach. The fibre or its processed form as roving, yarn or strand encompasses form, function and materiality in one and becomes the starting point for design. Together with the properties of the fibre (e.g. of glass, mineral, animal or plant origin), the manner in which the fibre is further processed (e.g. as a non-crimp, knitted, woven or nonwoven fabric) generates specific functionalities which can be tailored to the intended purpose. The material thus becomes a focus of the design process.

This paradigm shift in the approach to materiality opens up completely new possibilities, the properties of a surface or object being deliberately "designed." Material gradients, for instance between resilient and rigid or between transparent and opaque, can be achieved and different functionalities can be produced with the same material.

"Stone Web" is based on the natural material basalt which occurs in large quantities in the Earth's crust. In an industrial process, the lava rock is melted, drawn into filaments and converted into rovings or yarn which, in a reversal of the original nature of rock, can then be used to produce lightweight, filigree fibre structures. Very good mechanical and thermal properties make this rock-based textile material attractive for many applications. Nevertheless, it has not yet established itself on the market on a broader basis and is virtually unknown among designers.

The modular system, "Stone Web" consists of truncated octahedrons made of wound and resin-reinforced basalt yarns (see Figure 45 and Figure 46). As a honeycomb system inspired by biological models, the modules can be assembled and repeatedly reconfigured. Elements of different levels of transparency, load-bearing capacity or resilience can be combined depending on the desired function, e.g. privacy screen or seating. Varying the winding density and geometry means that even different areas of a single module, such as stiff edges and resilient seating surfaces, can be produced with one and the same yarn, in a similar way to biological materials which create specific properties by arranging fibres differently in their structure. The system can thus create a broad range of shapes and performances while using little material. The result is an adaptable system with a variety of functions.

This design project, developed in a Master Studio at weißensee kunsthochschule berlin, has clearly struck a chord among professionals, reflecting the great interest in such fibre-based

Figure 45: "Stone Web", a modular lightweight construction system made of wound basalt fibres, weißensee kunsthochschule berlin, Natascha Unger, Idalene Rapp, Design and Experimental Materials Research, Prof. Christiane Sauer (source: weißensee kunsthochschule berlin/Natascha Unger, Idalene Rapp)

Figure 46: "Stone Web" spatial modular system (source: weißensee kunsthochschule berlin/Natascha Unger, Idalene Rapp)

201 | This contribution was translated from German into English.

approaches to design. It has been exhibited in various settings including the "Disruptive Materials – Changing the Future" innovation show at the Interzum Cologne 2019 trade fair, in the Exempla special exhibition, "Textiles - material of the future", at the International Craft Trades Fair, Munich 2019, and in the 2017 "Neue Stoffe, New Stuff" exhibition at the Textile Museum, St. Gallen, Switzerland. "Stone Web" also won first prize in the materials innovation category in the "Textile Structures for New Building" student competition at the Techtextil trade fair in Frankfurt am Main, 2017.

Conventional fibre composite materials are based on a polymer matrix in which reinforcing fibres are embedded. By reversing the matrix to fibre ratio "Stone Web" attempts to improve the environmental compatibility of such a composite structure. Since the geometry of the fibres provides a large proportion of the strength, it has proved possible to keep the polymer matrix content very low, with the fibres merely being impregnated with resin prior to processing. Although the starting material basalt is one hundred per cent natural and disposal thus presents no problems, the use of a reinforcing resin still results in a composite material which does raise issues regarding disposal and recycling. Central challenges facing the future of fibre-matrix composites will therefore include the improvement of processes for recyclability or the development of applicable environmentally friendly, plant-based resins.

10.5 Education at the Interface between Biology and Materials Science[202]

Dr. Olga Speck
Plant Biomechanics Group at the University of Freiburg, Competence Network Biomimetics, Germany

Biomimetic materials systems: today we live in a world shaped by science and engineering in which interdisciplinary thinking and working are an integral part of lifelong learning.[203] In recent years, the interface between biology and materials science has turned out to be a rich source for the development of biomimetic materials and materials systems and has brought about a blossoming of knowledge about the biological models which serve as inspiration.[204]

Biomimetic approaches: research and development projects in biomimetics[205] on the one hand require a solid grounding in natural sciences and engineering, specifically in addressing biological (e.g. hypothesizing) or technical issues (e.g. requirements profile), in investigating biological models (e.g. experiments to elucidate the interrelationship between form, structure and function) and in technical implementation (e.g. laboratory, pilot and production). On the other hand, interdisciplinary transfer capabilities are also required both for identifying and transferring the functional principle (on the basis of the underlying mathematical, chemical and physical laws) and at the abstraction step (e.g. functional models, simulations, construction plans).

Previous successes: recent years have seen the publication of numerous teaching and learning modules about biomimetics in the form of conventional printed publications, electronic media (e.g. Bionik-Online[206] and Bionik-Vitrine[207]) or kits (e.g. BionicsLab,[208] Bionics4Education[209]) in German and English, whose common didactic theme is the hub between natural sciences and engineering. Extracurricular places of learning (e.g. botanical gardens and zoos, science centres) direct their biomimetics offerings, such as guided tours, educational trails and experiments, to anyone who is interested, from small children to adults. In schools, basic scientific subjects are also being complemented by subject combinations for teaching biomimetics, while independent biomimetics courses have been set up at universities of applied sciences and universities are offering interdisciplinary Bachelor's, Master's and PhD thesis in disciplines such as biology, chemistry, physics, mathematics, architecture and design.

Critical view: Although biomimetics can be described vividly, some misunderstandings persistent. These include constant demands for "biomimetic experiments" for teaching which cannot exist in the sense of biomimetics definition. More what is meant are experiments which demonstrate the functional principle of the biological model or in the biomimetic product.

202 | This contribution was translated from German into English.
203 | See Speck/Speck 2007.
204 | See VDI-Gesellschaft Technologies of Life Sciences 2011.
205 | See VDI-Gesellschaft Technologies of Life Sciences 2012.
206 | See Plant Biomechanics Group Freiburg 2016b.
207 | See Plant Biomechanics Group Freiburg 2013.
208 | See Plant Biomechanics Group Freiburg 2016a.
209 | See Festo Didactic SE 2019.

Moreover, biomimetic developments are not simple analogies which, due to the same functional principle (e.g. suction cups), have to be regarded as parallel developments in Nature and technology. A biomimetic approach instead means systematically transferring the functional principles identified in the biological model to a biomimetic product.[210] Furthermore, due to the flow of ideas from biology to technology, biomimetic products are often considered more sustainable than conventional products. This blanket application of a biomimetic promise[211] is not tenable, but must instead be verified in comparative sustainability assessments, whereby the selection of the comparative product is of decisive importance for the result.[212]

Future visions: thanks to the internet, data, information and knowledge have become a public good, the increasing significance of which, in today's knowledge society, is placing new demands on (continuing) education for people of every age. Expertise, contextual understanding and team working are in demand precisely at the interfaces between disciplines, as in the case of biomimetics between natural and engineering sciences.

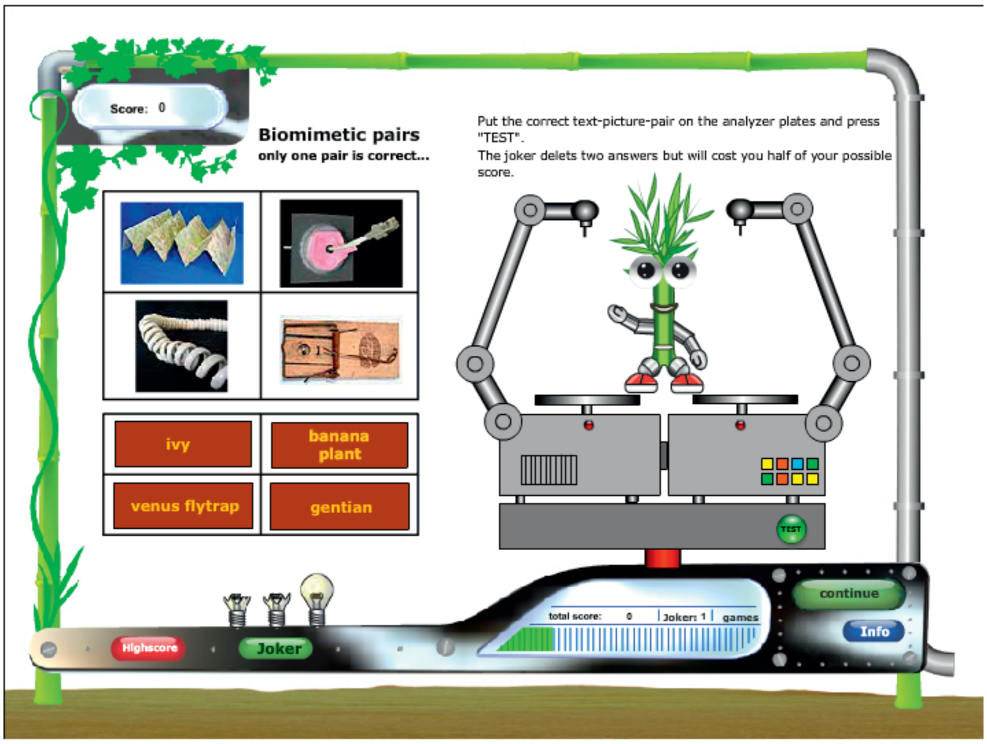

Figure 47: Billy Bamboo is the guide to the Biomimetics-Quiz which can be played online[213] in standard German, English and Swabian dialect (source: Olga Speck, University of Freiburg).

210 | See Speck et al. 2017.
211 | See von Gleich et al. 2007.
212 | See Antony et al. 2012.
213 | See Plant Biomechanics Group Freiburg 2016c.

10.6 Economics and Bio-inspired Materials Research[214]

Prof. Dr. Magnus Fröhling, Prof. Dr. Claudia Doblinger, Prof. Dr. Sebastian J. Goerg, Prof. Dr. Cordt Zollfrank
TUM Campus Straubing for Biotechnology and Sustainability (TUMCS), Technical University of Munich, Germany

The biologicalization of materials science and the establishment of a bio-based economy in general are expected to have a high potential for innovation, including new properties and functions of biologically inspired materials as well as positive effects in terms of sustainability and the transformation to renewable resources. One such example is the use of nacre (mother-of-pearl) as a model for the sustainable production and high-tech application of bio-inspired structural or construction materials. The hierarchical structure of nacre consisting of calcium carbonate (aragonite) and biopolymer phases (chitin, proteins) across several length scales determines its remarkable properties, which engineering materials are yet to match. In order to make a statement on the potential of such applications and its full use, the creation of close links between technological/scientific and economic research is necessary. From a scientific/technological point of view, basic and applied research are necessary for providing these bio-inspired structural materials and for demonstrating their major technical suitability and superiority. The replacement of conventional construction materials such as concrete by bio-inspired materials might serve as an example.

The direct sustainability impact of such bio-inspired materials and their industrial implementation can be evaluated using the methods of the techno-economic assessment, a life-cycle assessment (LCA) and a social LCA (S-LCA). In this way, key variables in terms of business, economic and social sustainability criteria can be identified. The bio-inspired materials and their process development can be guided by research and development.

Furthermore, innovation research provides important insights into the successful adoption and dissemination of bio-inspired materials for new consumable and high-performance materials and the associated contiguous processes. Moreover, defining novel business models can contribute to successful commercialization of the innovation. It is also possible to identify the user groups that should be addressed at different points in time as part of the adoption curve.

Method development in economic sciences is required if the anticipated socioeconomic effects are to be investigated in a predictive way, which may arise from the dissemination of new methods (e.g. on introduction and use of bio-inspired structural materials). This applies not only to the replacement and substitution of existing

Figure 48: Bio-inspired materials in their socio-technological and environmental setting (source: Cordt Zollfrank, TUM Campus Straubing for Biotechnology and Sustainability TUMCS)

214 | This contribution was translated from German into English.

products and value chains, but also to the development and implementation of new ones. The dynamic adaptation of the systems into which these methods are to be embedded and their mutual interaction with regard to sustainability criteria (see Figure 48) needs to be considered. Macroeconomic factors such as price fluctuations on international markets or national and international regulatory efforts (e.g. potential CO_2 tax and CO_2 certificates) will also get highly relevant as they directly or indirectly influence relevant trade-offs for production and development. In addition to its innovation potential, rigorous biologicalization or the more targeted exploitation of the full potential of bio-inspired materials will also result, in structural changes and potential negative consequences for some individual stakeholders during the transformation to a bio-based economy. There is a strong need to develop predictive measures in order to boost opportunities and to mitigate risks. This would help to create a wider social acceptance for bio-inspired materials.

Creating close links between technological/scientific research on the one hand and economic research on the other will allow these fields of research to complement one another in many ways with regard to bio-inspired materials: technological/scientific research will benefit from socioeconomic insights while economics will obtain more detailed knowledge, making its work a more accurate reflection of reality. Bio-inspired materials science and engineering can be implemented in a targeted and efficient manner through the sustainable use of biogenic resources and through input from economic research.

10.7 Interviews with Staff of BASF SE

10.7.1 Interview with Jens Rieger, BASF SE[215]

Dr. Jens Rieger, a physicist by training, retired in 2019 after over 30 years' experience in materials research at BASF.

Dr. Rieger, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

One great example is our understanding of "super surfaces", i.e. surfaces with superhydrophobic or superhydrophilic properties which have many different exciting applications. Another one is hybrid materials, i.e. materials comprising organic and inorganic components. This is a huge topic, even if materials researchers at BASF are not at present trying to directly replicate seashell, a well-known example of a natural hybrid material. Nature can provide inspiration. Our research is directed at gaining an understanding of how Nature obtains specific property profiles, which we will then, where appropriate, apply to the development of new materials. There are already specific examples of application in architecture and construction, for example the minimal surface geometries of the Olympic stadium roof in Munich. Topologically optimized materials are another fascinating topic, but the BASF designfabrik® designers will be able to tell you more about them; they have developed a chair with a very filigree design in which the concept of saving material by optimum load distribution is inspired by Nature, which is certainly able to point the way forward in this respect by achieving maximum effect with minimum use of materials.

What, in your opinion, are the major hurdles and challenges for development and implementation?

One obstacle is, I think, that we already have very good materials for many conventional applications. We should therefore take a broader view and identify major issues of social relevance, such as sustainability and energy management, and work out from this standpoint what contribution might be made by greater biologicalization of materials science.

One technical obstacle is the fact that Nature has time to generate materials and structures (e.g. during plant growth) while we don't have such amounts of time in typical production processes. Moreover, Nature is "living", i.e. structures such as skin or other surfaces can be renewed, a phenomenon which is not straightforward to mimic.

What would you like to see happen for headway to be made?

BASF's research and development activities are making good headway, but we could go one step further by drawing greater public attention to the topic. Biomimetics or materials biologicalization can open doors and that's a useful starting point.

215 | The interview was originally conducted in German.

10.7.2 Interview with Andreas Mägerlein and Alex Horisberger, BASF designfabrik®[216]

Andreas Mägerlein is an engineer, industrial designer and head of BASF designfabrik® and Alex Horisberger is an industrial designer and member of staff at BASF designfabrik®.

Mr. Horisberger, how would you rate the innovation potential of knowledge derived from Nature?

We have been using such knowledge for years, for example to create an economic advantage in product development by consuming less material and making products lighter.

What's your view, Mr. Mägerlein?

Getting to that point is costly, however. As a conventional engineer, you can sometimes be surprised by simulation results which address biomimetic considerations. The computational tools are relatively costly which means that smaller SMEs cannot necessarily afford to work in this way. Biomimetics still plays virtually no part in conventional engineering training, at best you might have read a book about it. However, things are changing slowly with computer-aided design and 3D printing becoming increasingly important.

Indeed, so what do you consider to have been one of the most important developments in biologicalization in recent years, Mr. Horisberger?

3D printing has certainly created the greatest design freedom. But it has also brought difficulties: the materials were initially too weak and the result could not be mass-produced. However, material properties are slowly improving and are approaching those of injection-moulded plastics. 3D printing technology also allows me to reproduce growth structures and hollow articles and go far beyond what is possible with traditional moulds.

And what do you consider to have been one of the most important developments here, Mr. Mägerlein?

Resource loops are also very interesting. For example, we have developed a material which can be degraded in an industrial composter at a very specific temperature and moisture level. The requirement is for the degradation process to begin only once a product has been used and for it to be possible to determine the end of useful life on an individual basis. All that remains at the end is a pure biomaterial that can be returned to the ground.

Digitalization is another major topic. Only now, for instance, do we have sufficient computing capacity and the appropriate tools to be able to reproduce biomimetic structures, for example to "fast forward" bone growth mechanisms for the virtual development of complex components. Growth is always an optimization process and a bone fracture for example results in the fracture location becoming stiffer and stronger because of the bone responding to the load. Software also does the same thing, optimizing in iterative computing steps. This had been known for some time but now we can finally carry out the computation at an economic speed. It has not previously been possible to manufacture such parts which have ribs and branches at the correct locations. Thanks to 3D printing, I'm now also able to manufacture anything I can design on the computer. In my opinion, and I'm sure it will happen at some point, the next step will in future be for a component to grow itself with the assistance of simulations and 3D printing. Of course, it will take some time until this can happen on a mass production scale. But in the case of 3D printing too it was still thought ten years ago that its market was too small and now huge effort is being put into getting in on the act.

All in all, I don't think that there will be any development in future which will not involve biomimetic thinking, not least because we have to find a way of managing and optimizing our resources. And optimization, including in relation to materials usage, is something Nature has already been doing for millions of years. How material is recycled to generate reusable and new products is also biomimetics. Unfortunately, we still have a lot of catching up with Nature to do here. It is not yet even certain that there is a consensus around this issue, but advocacy is slowly developing.

So I'm convinced the innovation potential of Nature-derived knowledge is essential and that it is important for us to build on this potential. For example, Nature has of course not yielded a chair, but we can use natural principles and apply them to our human products, for example when designing a chair. Using our expertise and simulation skills, we have helped to design a chair based on conventional, organic principles. We have taken tree growth as our model of how to optimize materials usage and nevertheless ensure that particular loads can be borne, so that's a classic biomimetic principle while taking account of shapes specified by the designers.

216 | The interview was originally conducted in German.

Mr. Mägerlein, what, in your opinion, are the major hurdles and challenges for development and implementation in biomimetics?

Both feasibility and economic viability, since as we know one of the most important material properties is after all its price. But I'm optimistic that the public is interested in the use of resources. While it is indeed always difficult to bring new ideas onto the market, perhaps biomimetic structures should be used as a marketing principle and shouted from the rooftops. Festo for instance is doing a very good job here and soft robotics and Artificial Intelligence are of course in any case major future issues.

What would you like to see happen for headway to be made in the field, Mr. Horisberger?

Regulations are always a wonderful motivator. If biodegradable bags were required by law, then we would no longer have any problems competing with conventional materials on price. But I also believe that the material's properties should be convincing rather than its price. That's also the case with some new materials.

And what's your take on this, Mr. Mägerlein?

The focus should be on an interdisciplinary approach and that's something which needs to begin during a student's studies. It must be made clear that an engineer could well occasionally need to talk to a biologist when it comes to materials development. And a designer should attend an engineering course now and again. That's the idea behind our designfabrik®, where we provide an extremely broad and interdisciplinary network. On the other hand, course content is also becoming ever more complex, requiring constant further specialization. The need for an interdisciplinary setup is almost a contradiction in terms and a dilemma. Ultimately, the widest possible range of different experts should be able to have a direct conversation among themselves. At designfabrik®, we provide a table for the right people to sit down around. We are only as clever as the people who are right there in the room. A basic understanding of the problem is, of course, vital here, which is why you need to know the right people you would like to come and sit down at the table.

10.7.3 Interview with Andreas Wüst, BASF SE[217]

Andreas Wüst is Head of Dynamic Structural Analysis at BASF SE.

Mr. Wüst, what is your job at BASF?

I help our customers who buy materials from us to design parts properly. Factors to be taken into account are not only material properties, but the production process and the desired design. As long ago as the nineteen nineties, I came across numerical methods in this connection which were based on bionic principles. For me, bionics doesn't simply mean slavishly copying from Nature and building something which looks similar, but instead involves understanding how something actually works. It's utterly irrelevant whether the final outer appearance is reminiscent of a biological system.

What exactly do you mean here? Do you have a good example of what that means for a product?

One example is a lower bumper support which we designed jointly with Opel with the assistance of bionically inspired methods. Biologically inspired topology optimization has made its arrival in industry. We no longer have any structurally loaded components in which these methods are not used. We are continuing to develop the methods and the developments in 3D printing are of assistance here because they make the process much more flexible. The difficulty with topology optimization is that Nature's optimized design cannot be straightforwardly implemented with an injection moulding machine. For example, hollow structures occur in Nature which require major effort to produce using traditional manufacturing processes. Compromises thus always have to be made and the outcome of a bionic investigation has first to be interpreted and made transferable. "Generative Design", which smooths and improves the results and converts them directly into a 3D print instruction, is a further development of topology optimization.

So, in your opinion, has 3D printing been one of the most important developments of recent years in this field, or have there been others?

217 | The interview was originally conducted in German.

Not 3D printing, but our increased understanding of Nature, for instance that there is an intrinsic flow of power in a component which we can only get away from by copying how Nature would do it. So we're making use of evolution. Transferring this understanding that there are higher-order laws is in my opinion the central point of this biologicalization, if that's what you want to call it.

What enabled the breakthrough in understanding?

Firstly, the knowledge and understanding also has to get to the engineers. The first usable papers on topology optimization were published in the late nineteen eighties, when I was a student, but the topic did not feature on the curriculum. It has taken 15 to 20 years or so and it's still not fully established on the curriculum. On the other hand, the growth of computing resources has been helpful - today's students can carry out 2D topology optimization with an app on their mobile phones. I always have a problem with the word "simulation", which appears to be in opposition to design engineering. What we do is "Virtual Engineering"!

What would you like to see happen for headway to be made?

I'm always struck by how there are good engineers and good biologists but the link between the two is often missing. We can start addressing this in schools. I give presentations about bionics to trainee biology teachers at the teacher training college in Heidelberg where these teachers of the future have a seminar on bionics. What I would have appreciated both at school and at university, and I'm exaggerating a bit here, would have been for the biology teacher to have explained something, then left the room only for the physics teacher to come in and pick up from where the biology teacher left off. A systemic viewpoint is simply inadequate. If people have a question and are looking for a solution then they will naturally only look in their own disciplines which they are really familiar with. If they simply don't know that such methods exist, then they won't look for them. I would like to see interdisciplinary education and also the creation of corresponding professorships.

Another possibility for putting bionic methods in place is co-creation, i.e. joint component development projects with companies which haven't previously worked with such methods. We are currently expanding our Creation Center at BASF in Ludwigshafen where we put new methods innovatively into practice with customers. In this way, we increase acceptance when biology ultimately makes a positive contribution to a product's economic success.

From a long-term standpoint, this is a matter of resource conservation: if I make a component which lasts twice as long, I've saved a component. However, this requires a paradigm shift and a different optimization goal. At present, the goal is to minimize manufacturing costs. Resource conservation and sustainability, i.e. so to speak the "societal costs", should instead also be included.

11 Bibliometrics, Funding Programmes, Associations

This section brings together details of previous publications and patents in the field of bio-inspired materials research. It will also mention examples of existing or completed funding programmes, and comments from various associations and institutes.

In the analysis of publications, the graphs include not only the actual number of publications but also the number of times they have been cited, so as also to take account of their impact within the scientific community. One noteworthy aspect is the considerable increase in publications since the mid nineteen nineties (see Figure 49). When it comes to publication impact, the USA is a long way in front of China, with the three major European countries of Germany, England and France in third, fourth and fifth place respectively (see Figure 50).

Patents filed in this field also show a very marked increase from the mid noughties, making them about a decade behind publications (see Figure 51). What is noteworthy in this respect is that China is significantly in front of the USA and Europe (see Figure 52). This could point to a trend which is also addressed in some of the company interviews, i.e. that Asia is happier to implement bio-inspired technologies than is the West.

11.1 Literature Search

The literature search was carried out using Web of Science.[218]

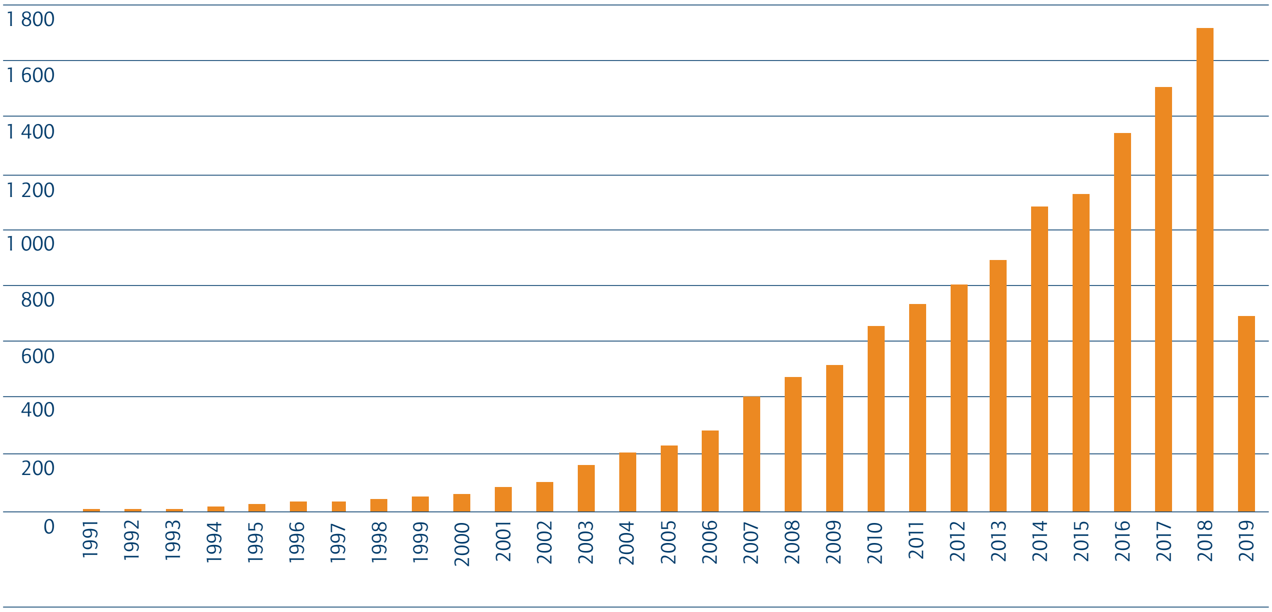

Figure 49: Total publications per year since 1991. The key search words were: TOPIC = ((“bio-inspired” OR bioinspired OR biomimetic OR “nature-inspired” OR biomimicry” AND (material* OR biomaterial*)), (source: own presentation based on Clarivate Analytics 2019, as at 29 May 2019).

218 | See Clarivate Analytics 2019.

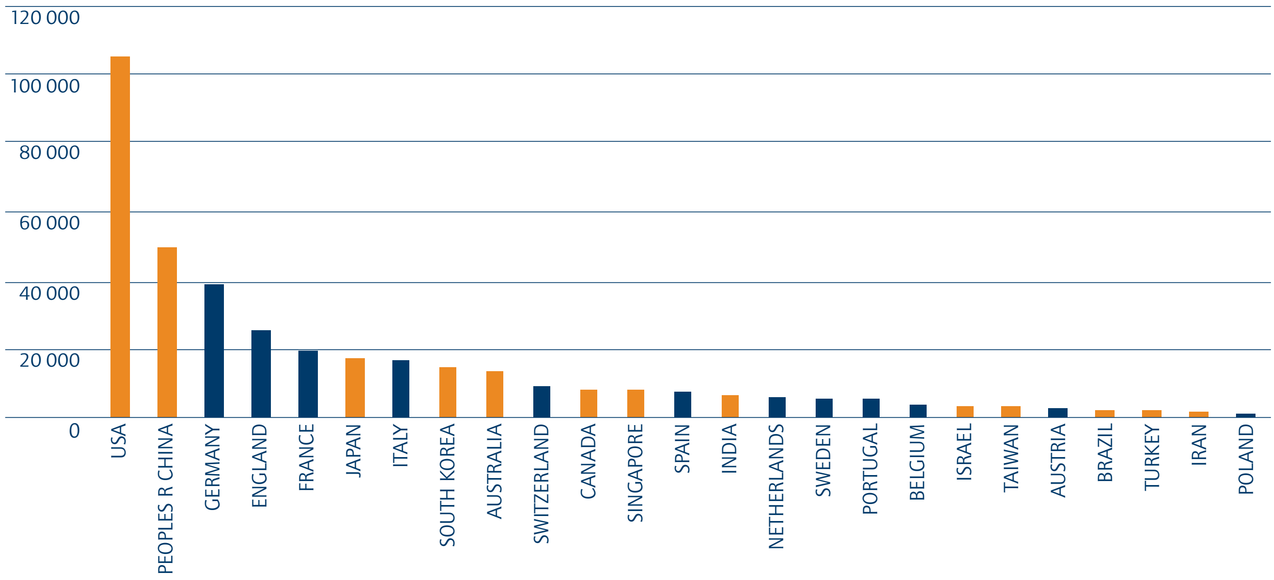

Figure 50: Total citations by country, European countries shown in dark blue. The key search words were: TOPIC = (("bio-inspired" OR bioinspired OR biomimetic OR "nature-inspired" OR biomimicry" AND (material* OR biomaterial*)), (source: own presentation based on Clarivate Analytics 2019, as at 16 April 2019).

11.2 Patent Search

The patent search was carried out on DEPATISnet (the German Patent and Trademark Office online worldwide patent search facility) using similar key words to the literature search.

The search revealed a total of 877 filings (after correcting the total of 2,900 patent filings for patent families).

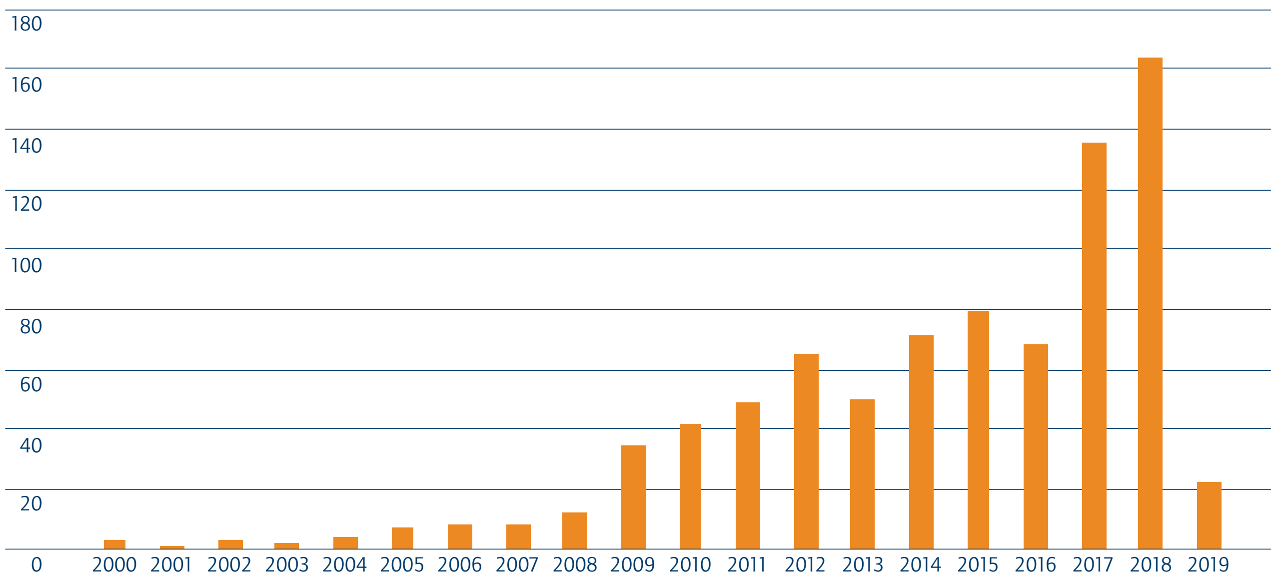

Figure 51: Number of patents filed per year – corrected for patent families. The key search words were similar to those used for the literature search: abstract = ((bio#mim? OR bioni? OR bio#inspir? OR nature#inspir#) AND (material? OR bio#material")), (source: own presentation based on DEPATISnet, the German Patent and Trademark Office's online document archive, as at 5 June 2019).

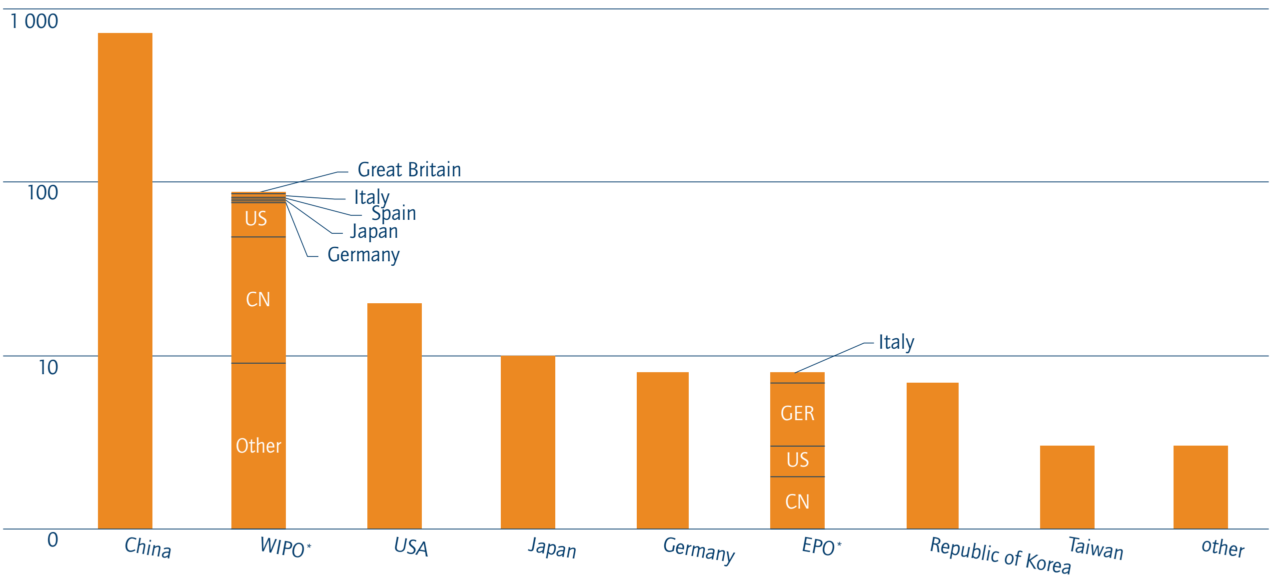

Figure 52: Number of patents accepted worldwide by national and international patent offices presented logarithmically after correction for patent families. The key search words were similar to those used for the literature search: abstract = ((bio#mim? OR bioni? OR bio#inspir? OR nature#inspir#) AND (material? OR bio#material?)). *WIPO and *EPO respectively denote World Intellectual Property Organization and European Patent Office. For these two offices, the columns are additionally divided into the most frequent applicant countries of origin (source: own presentation based on DEPATISnet, the German Patent and Trademark Office's online document archive, as at 5 June 2019).

11.3 Selected DFG Funding Programmes

DFG, the German Research Foundation, has been funding bio-inspired materials science for some years. Three particular Priority Programmes (SPPs) can be singled out; their descriptions from the GEPRIS - Projects Funded by the DFG information system are reproduced below. There are also three newly approved clusters of excellence and a number of other Priority Programmes, Collaborative Research Centers and Research Units (see Table 1).

Generation of Multifunctional Inorganic Materials by Molecular Bionics

(SPP 1569)

Joachim Bill, term 2012 to 2019

Inorganic functional materials have a tremendous impact on key technologies relevant for the further development of future fields like information technology or energy generation and storage. In this connection, complex-structured multifunctional inorganic materials as well as their hybrids with organic components play a main role. The generation of such materials with defined structure and stoichiometry via conventional processing is limited, since such processes require increased temperatures and/or pressures as well as major technological efforts. Accordingly, there are worldwide research activities to overcome such limitations and to search for new procedures, which allow the manufacturing of new materials under ambient conditions with reduced processing efforts. Living nature provides impressive evolution-optimized processes, which lead to complex-structured multifunctional inorganic solids. Their formation occurs via biomineralization in aqueous environments under ambient conditions and is genetically determined. During these processes biopolymeric templates that control the mineralization and the structure formation of the inorganic components play a main role. These processes also involve molecular self-assembly and finally yield composites made of non-metallic inorganic solids like calcium phosphate or carbonate and bioorganic components. Such inorganic/bioorganic hybrids exhibit unique multifunctional features and in particular, their performance and property spectrum is further tuned and expanded by the incorporation of the bioorganic fraction. Even though many of the technically relevant materials are not generated by the processes developed by biological evolution, the consideration of biomineralization principles provides promising prospects for the generation of inorganic functional materials via the interaction between bioorganic and inorganic components. The Priority Programme's main scientific objective is to apply the principles of biomineralization to the generation of complex-structured multifunctional inorganic materials as well as of their hybrids with bioorganic portions. In order to achieve this goal, the Priority Programme addresses research work on (1) the *in vitro* and *in vivo* generation of such materials directed by biomolecule-based templates with a main focus on 2D and 3D structures, (2) the characterisation of the formation mechanisms as well as of the structure of the materials, and (3) the investigation and design of the physical and chemical properties of the materials. Furthermore, these experimental studies are accompanied by computational modelling of the formation, structure and properties of the materials.

"Design and Generic Principles of Self-healing Materials"
(SPP 1568)
Ulrich Schubert, term 2011 to 2018

Biological materials are evolutionarily optimized functional systems. One of their most outstanding properties is the ability to self-heal and regenerate a function upon the infliction of damage by external mechanical loads. In nature, self-healing can take place either at the level of the individual molecule or at macroscopic level, e.g. merging of broken bones, closure and healing of injured blood vessels and tissue. Man-made materials generally do not have this healing ability, as all current engineering materials were and are being developed on the basis of the 'damage prevention' paradigm rather than a 'damage management' concept.

However, self-healing materials offer enormous possibilities, in particular for applications where long-term reliability in poorly accessible areas, such as tunnels, underground infrastructure, high-rise buildings or space applications, is important. In addition, self-healing would be ideal for applications which are prone to damage, such as surface coatings. However, up to now only few strategies exist for the development of self-healing materials, and those which exist are focussed on only one material class and one type of application.

A dedicated fundamental approach to the self-healing concept addressing repair mechanisms and strategies relevant for implementation to all material classes is still lacking. For this reason, the objective of the Priority Programme is the conceptual design of synthetic self-healing materials and the elucidation of generic, fundamental material-independent principles (e.g. following a sequence of crack generation and propagation, mobility and transport of material, interface bonding and immobilization of the transported material). Respecting the intrinsic nature of each class of materials, generic approaches to self-healing will be formulated, tested and ultimately implemented in new materials design.

The vision of the Priority Programme is that novel materials with self-healing capability will enable access to new fields of application including biomedical implants, ultra lightweight engineering metals and ceramics as well as high-performance polymers and composites.

Biomimetic Materials Research: Functionality by Hierarchical Structuring of Materials
(SPP 1420)
Peter Fratzl, term 2009 to 2016

The aim of the Priority Programme is to explore the possibility of generating new material classes of great potential by combining the degrees of freedom of hierarchical structuring inspired by nature with the variety of materials offered by engineering. The goal of this biomimetic approach is to obtain new or unusual combinations of material functions and properties. This is to be achieved by structuring a given material, rather than by changing its chemical composition ("function by structure"). The long-term vision of the Priority Programme is to fill in blanks in material property charts by hierarchically structured materials, and to obtain the function-form relationship in organs or plant bodies with predominantly mechanical function to improve the understanding of living systems.

There is no restriction on the choice of constituent materials, as long as the principle of hierarchical structuring over at least two levels is followed. Typically, (at least) one of the material properties is mechanical; the other one may be also mechanical or acoustic, electrical, optical or thermal, to name but a few options, and the hierarchical structure is crucial in obtaining this property combination. Passive mechanical properties (such as stiffness, strength, toughness etc.) are considered as well as active properties connected to actuation or motility.

A variety of challenges are being addressed. First, it is necessary to study some natural materials as examples of how hierarchical structuring is used by nature to achieve unusual property combinations. Furthermore, theoretical and experimental tools of materials science need to be developed to address the issue of hierarchy. New approaches for synthesis of hierarchical materials and demonstrators have to be developed. The scope of the Priority Programme is thus divided into three focus areas: (1) characterization of natural hierarchical materials as a kind of "idea park", (2) development of principles to design, simulate and manufacture hierarchical materials with property-relevant structural features, (3) development of manufacturing technologies for materials solutions based on hierarchical structures.

	Title	Spokesperson	Term	URL: DFG GEPRIS - Projects Funded by the DFG
TRR 141	Biological Design and Integrative Structures. Analysis, Simulation and Implementation in Architecture	Jan Knippers	2014 to 2019	https://gepris.dfg.de/gepris/projekt/231064407
EXC 2025	Matters of Activity. Image Space Material	Wolfgang Schäffner	since 2019	https://gepris.dfg.de/gepris/projekt/390648296
EXC 2193	Living, Adaptive and Energy-autonomous Materials Systems (livMatS)	Anna Fischer, Jürgen Rühe, Thomas Speck	since 2019	https://gepris.dfg.de/gepris/projekt/390951807
EXC 2068	Physics of Life - The Dynamic Organization of Living Matter	Suzanne Eaton, Stephan Wolfgang Grill	since 2019	https://gepris.dfg.de/gepris/projekt/390729961
EXC 1027	Image Knowledge Gestaltung. An Interdisciplinary Laboratory	Horst Bredekamp, Wolfgang Schäffner	2012 to 2018	https://gepris.dfg.de/gepris/projekt/194453117
SPP 1117	Principles of Biomineralization	Peter Behrens	2001 to 2007	http://gepris.dfg.de/gepris/projekt/5471129
SPP 1100	Interface between Biomaterial and Biosystem	Roger Thull	2000 to 2006	http://gepris.dfg.de/gepris/projekt/5470550
SPP 2100	Soft Material Robotic Systems	Annika Raatz	since 2019	https://gepris.dfg.de/gepris/projekt/359715917
SFB 599	Sustainable Bioresorbable and Permanent Implants of Metallic and Ceramic Materials	Thomas Lenarz	2003 to 2014	http://gepris.dfg.de/gepris/projekt/5485789
SFB 1027	Physical Modelling of Non-Equilibrium Processes in Biological Systems	Heiko Rieger	since 2013	https://gepris.dfg.de/gepris/projekt/200049484
FOR 1405	Dynamics of Electron Transfer Processes within Transition Metal Sites in Biological and Bioinorganic Systems	Gerald Henkel, Sonja Herres-Pawlis	2011 to 2017	https://gepris.dfg.de/gepris/projekt/159419156
FOR 548	Polysialic Acid: Towards the Evaluation of a New Bio-identical Scaffold Material	Rita Gerardy-Schahn	2004 to 2010	https://gepris.dfg.de/gepris/projekt/5471076

Table 1: Selected funding programmes from GEPRIS – Projects Funded by the DFG (source: DFG)

11.4 Selected German Federal Funding Activities

Unlike with biotechnology, where the know-how from diverse key engineering technologies have been put to intensive use since the early nineteen nineties, funding policy regarding knowledge transfer from the biosciences to materials is so far rather weak.

The Federal Ministry of Education and Research (BMBF) has addressed this gap in the funding system with the national funding programme "From Material to Innovation". Consequently, the programme picks up the increasing trend towards "biologicalization".

"The functionality and complexity of biomaterials has increased greatly in recent years. Where first generation biomaterials provided purely mechanical assistance, such as in implants or artificial joints, modern variants are already interacting purposefully with their surroundings. This may be achieved by coating with an active ingredient, patterning or by using a bio-based material. This trend towards "biologicalization" will continue to grow over the next few years with biomaterials opening up whole new potential pathways and not only for regenerative medicine."[219]

Given this context, the national Framework Programmes attach particular importance to bio-inspired or biomimetic materials modelled on Nature.

Some of the applications described in this acatech DISCUSSION, such as the clarification and utilization of natural structural and functional principles or the use of biogenic starting materials, are also to be found amongst other things in further BMBF Framework Programmes. One example is the funding of imaging methods through the Framework Programme "Photonics Research Germany - Light with a Future" which has enhanced the gain in knowledge in the life sciences. In 2001, the German government established a multidisciplinary biophotonics research programme: a multidisciplinary program for the development of optical solutions for biological and medical issues.

The funding of biogenic raw materials is of particular importance. In this context, the "National Research Strategy BioEconomy 2030" under the auspices of the Federal Ministry of Education and Research (BMBF) should be mentioned in particular. The focus is both on renewable raw materials and bio-based process solutions, which draw on the entire range of biological resources down to microorganisms and cells and individual biological constituents. For instance, the BMBF initiative launched in 2010 and entitled "Next Generation Biotechnological Processes – Biotechnology 2020+" will attempt to emulate biological material and energy conversion processes by bringing together engineering and life sciences, e.g. in research projects into microbial fuel cells and artificial photosynthesis.

The "Renewable Raw Materials" programme of the Federal Ministry of Food and Agriculture (BMEL) aims to promote primarily applied research and development in the field of sustainable production and the use of renewable resources. The programme covers a) agricultural and forestry crops and aquatic biomass as raw materials, b) biogenic residues (reusable waste, secondary products) from agriculture and forestry, aquaculture, processing industries, commerce and domestic sources, c) production, provision, processing and use of renewable resources, d) resource-efficient and environmentally responsible production of bio-based products and bioenergy carriers and e) overarching topics including social dialogue.

BMBF's funding initiative "BIONA – Bionic Innovations for Sustainable Products and Technologies" supported initial approaches to translating natural structures and functions to engineering applications. In the context of two calls for proposals (2007 and 2008),[220] funding has been provided for practical, sustainable developments using a bionic approach.[221] The aim of this funding initiative was to convert innovative bionic approaches into prototypes and demonstration models in order to open up the way to economically viable industrial application. To this end, the intention was to translate structural, functional and process engineering principles from living Nature into engineering or other application-focused disciplines and continue development towards competitive products and methods. The BIONA initiative was established as part the FONA Research for Sustainable Development[222] Framework Programme, which was set up to deal with the global challenges relating to climate research and resource conservation. Key technologies, such as materials research and nanotechnology, are major research fields for sustainable developments. The aim is to make smarter and much more efficient use of economically strategic raw materials and thus contribute to the sustainable and secure supply of raw materials in Germany.

219 | See Bundesministerium für Bildung und Forschung 2015, p. 34.
220 | See Bundesministerium für Bildung und Forschung 2006.
221 | See BIONA 2019.
222 | See Bundesministerium für Bildung und Forschung 2019.

Further subject-specific connecting points of biologized material and materials research can be found, among other things, on the Federal Government's Framework Programme for Health Research, which aims to integrate research results more quickly into medical care for patients. At the interface of biology and technology, materials research provides solutions, for example durable implants, which make a critical contribution to opening up the potential of personalized medicine.

This brief analysis of research funding available for application-oriented basic research makes it clear that, while funding for basic research has enabled decisive progress to be made in recent years in "bio-inspired materials research", only selected aspects of this research priority are taken into consideration in current government Framework Programmes, despite its innovation potential for Germany as a location for research and industry.

One possible approach to giving "bio-inspired materials research" greater weight in the funding policy context is to mention the topic in the cross-departmental agenda "From Biology to Innovation", which is set out in Chapter IV of the Coalition Treaty for the 19th legislative period. This agenda's objective is to integrate biological knowledge, biological principles, bio-based materials and biotechnological processes to a greater degree into all areas of our economy and our lives.

This acatech DISCUSSION is an important blueprint for the research and funding parameters which are as yet to be defined for the materials research agenda process.

11.5 Interviews with Associations and Institutes

11.5.1 Interview with Frank O. R. Fischer, DGM[223]

Dr.-Ing. Frank O.R. Fischer is General Manager and CEO of the DGM (German Materials Society).

Dr. Fischer, in your opinion, what does the biologicalization of materials science mean for Germany and how great do you consider its innovation potential to be?

These bio-inspired materials have enormous potential, but implementing the knowledge gained from basic research is still problematic.

In your opinion, how can this translation be improved?

This subject has already come up to a certain extent at the Federal Ministry of Education and Research (BMBF) and I am expecting that the appropriate decisions will be made, and maybe a funding initiative set up, to speed this process up, not least on the basis of this study.

What would you see as the hurdles to translation?

I think that science has a certain obligation to help industry, especially SMEs, to understand the research results. SMEs have fewer technology scouts who might introduce them to new technologies of this kind. I also think that interdisciplinary seed funding or BMBF funding can play a major part.

In your view, what will be the biggest challenges for development and implementation over the next few years?

With the DFG (German Research Foundation) having funded three major Priority Programmes in the last few years, it is now time for the BMBF to invest in an implementation phase. I think it has been demonstrated that the potential is there and now appropriate long-term programmes are needed to develop prototypes, as has been done for resource efficiency. This will be driven partly by seed funding from the Federal Ministry of Economic Affairs and Energy, but I do think that the BMBF could make a significant contribution too.

How do you think Germany is doing compared to other countries?

So far as I can see, Germany would definitely seem to be among the top five! As far as basic research is concerned, I would say we were in pole position, and if we were to take the right steps at this point we could translate our research excellence into jobs and economic wellbeing.

And how is Germany doing compared to other countries when it comes to innovation potential?

We're too conservative and too scared to experiment! The result of this has been that many technologies end up being implemented elsewhere, despite their having first seen the light in Germany. I think we need start-ups in the field of bio-inspired materials science, then things stand some chance of actually being implemented.

223 | The interview was originally conducted in German.

In your opinion, how can we ensure that Germany makes progress in this field of research and stays at the top?

Up to now there's not been a continuing programme which picks up the knowledge from the last three big DFG Priority Programmes and obtains BMBF funding for it. Examples where this has been done, such as functionally gradient materials, which were translated from basic research into application-related research, have been very successful. We need to follow that model.

11.5.2 Interview with Kurt Wagemann, DECHEMA[224]

Prof. Dr. Kurt Wagemann is Executive Director of the DECHEMA Gesellschaft für Chemische Technik und Biotechnologie e.V.

Dr. Wagemann, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

There have been three developments which seem important to me. One is cell cultures and cell adhesion. A lot of progress has been made into keeping cells alive. This is less about learning from Nature than about using living structures in engineering systems. Secondly, the switchable functionalization of surfaces, for example hydrophilic and hydrophobic, is also exciting. And finally, I think hierarchical patterning of structures, e.g. Gecko feet and adhesion (see section 7.1) is a promising topic.

What is the significance of this for Germany and how do you rate the associated innovation potential?

Biotechnology is definitely becoming ever more important for the production of chemicals and materials. In the context of biologicalization as a whole, I would rate its significance and its innovation potential as medium. I think it's well worthwhile researching the subject, but I think that the number of breakthroughs we can expect is limited. There will certainly be some, but as with nanotechnology 25 years ago, which was seen as the solution to all our problems, expectations of biologicalization are similarly high, maybe too high.

What are the major hurdles and challenges for implementation?

I can't see any fundamental hurdles. Research and development need support, of course, but the framework is in place for that. Genetic engineering, for example, has to deal with very different regulatory hurdles and issues of acceptance. Indeed, if acceptance by the general public is a major hurdle, then biologicalization is well-placed.

How would you rank Germany globally?

High to very high. In basic research definitely very high, as for application-oriented research the Fraunhofer Gesellschaft has championed the cause and you can't ask for much more. I don't see much activity in industry though. I think people are waiting to see what new ideas come up. But, with some honourable exceptions, this is industry's usual approach to this sort of thing.

In your opinion, how can we ensure that Germany makes progress in this field of research and stays at the top?

The subject of translation is currently of very great concern to policymakers and there are certainly shortcomings, though I wouldn't say they were specific to Germany. The influence of technology ambassadors, i.e. enthusiastic and above all well-trained people from the research institutions who introduce know-how to industry, should not be underestimated. However, this type of technology enthusiasm is ultimately associated with start-ups, and we are short of those in Germany.

Any ideas how that could be improved?

There are some places where lots of things are happening, I'm thinking for example of TU Munich, which is good at launching start-ups. Others should follow their example. I think that a funding programme explicitly earmarked for such efforts should be launched by BMBF. The EXIST programme, set up by the Federal Ministry for Economic Affairs and Energy (BMWi) already provides a lot of support once a concept for a start-up has been devised. If BMBF were to speak of "biologicalization" in connection with materials research, but also for the associated process development, that might help get the topic noticed more. The concept of interdisciplinary research also seems to me to be important in this respect. My standpoint is that conventional subjects should be studied, but that then there should be incentives to take an interest in and engage with issues from neighbouring fields. In general, it's a case of bridging gaps, whether between different subjects or between the laboratory and market maturity.

224 | The interview was originally conducted in German.

11.5.3 Interview with Ljuba Woppowa, VDI[225]

Dr. Ljuba Woppowa is Managing Director of VDI Society Technologies of Life Sciences and VDI Society Chemical and Process Engineering.

Dr. Woppowa, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

I would say there are two major topics. The first is bioprinting. We organized a VDI Expert Forum in June 2019 and published several articles in the VDI nachrichten, German Weekly for Technology and Business. Just the development of additive manufacturing of plastics and the printing of metallic materials was a big step, but the additive manufacturing of biological material and tissue is a spectacular innovation in materials development and a huge technological step into the future. These processes open up important opportunities and possibilities in medical technology. The second topic, also driven by additive manufacturing, is lightweight construction in general. For some time, biomimetics have allowed us to calculate resource-efficient lightweight structures and optimize them using Nature as a model. Now, new printing processes are enabling production as well.

How significant do you think the topic is in Germany and how do you rate the potential for innovation?

For me, biologicalization and the bio-based economy in Germany are a very high priority and I am aware that we are setting many innovative trends that no other country is working on as intensively as Germany. For example, five years ago digitalization was still very nebulous, but the concrete implementation and practical applications have only become clear in recent years with the efforts of industry, associations and NGOs. Biologicalization is much the same.

What are the specific hurdles which need to be overcome?

Bio-based materials are still too expensive compared with traditional, i.e. petroleum-based materials, and are therefore not very competitive. Compared with cheap coal from China and shale gas from the USA, biotechnology has still not found any way of mass-producing products sufficiently inexpensively for them to become established on the market. Nonetheless, it is my opinion that these technologies need to develop in precisely this way, so we don't find ourselves at a disadvantage when raw materials run short. So we must also put our best efforts into biological processes and stay at the heart of research and technology! Interdisciplinary work is becoming ever more important. The multi-way exchange of biotechnology with conventional chemistry and process engineering promotes development. In addition, Artificial Intelligence and big data need to be integrated into classical subjects' curricula.

How do we go about implementation?

There is a real need for interministerial funding policy: BMBF has for instance been funding bionics for ten years under the BIONA initiative. Important topics and lighthouse projects which arose from this were not pursued, however, because interministerial funding wasn't possible. BMBF's Bio-Agenda is a step in the right direction, but other initiatives are needed if the funding "Valley of Death" is to be bridged and research projects transferred to industrial application. A continuous research funding process is needed to ensure "upscaling" and for this a new funding concept needs to be established. The jump cannot be made directly from test tube to mass production, rather closing this gap requires an interdisciplinary approach and the participation of all stakeholders from research, industry and users.

11.5.4 Interview with Viola Bronsema, BIO Deutschland e.V.[226]

Dr. Viola Bronsema is Managing Director of BIO Germany, the sector association for the biotechnology industry.

Dr. Bronsema, what do you consider to have been one of the most important developments in biologicalization in materials science in recent years?

These days, innovations are no longer measured only in terms of novelty value and current demand but also of sustainability. What I find exciting is the combination of bio-inspiration and sustainability, which we must not lose sight of when discussing bio-transformation and the Bio-Agenda. When these aspects come together, our old friends biotechnology and the bio-based economy are not far off. AMSilk's spider silk developments are a classic example of bio-inspiration and sustainability: this robust material is suitable for a wide range of uses, including as an industrial fibre, as a wound dressing or as a transplant coating,

225 | The interview was originally conducted in German.
226 | The interview was originally conducted in German.

while at the same time being sustainable. It is biodegradable and does not make our plastics footprint even worse.

Another example is 3D printing, which can now be used to produce customized prostheses for patients, possibly even from bio-based materials. I find this fascinating. And completely new fields are opening up, in medical informatics, digitalization and e-health as a whole, leading to progress of real relevance to our society. I say this because, interesting as self-cleaning surfaces or space shuttles are, the real challenge at present is to live as biologically and environmentally as possible and to get the circular economy embedded in everyday life.

Another important factor is the discussion around what exactly is a new material. Often a "new material" fundamentally just replaces an old one, for example where a fossil-based material is replaced by a material made from biomass. However, we must also discuss what new materials with specific physical and chemical properties we actually need to meet future challenges. At the moment, there are "nice to haves" and "need to haves" and we need to prioritize.

In your opinion, how significant is this topic in Germany, and how do you rate the associated innovation potential?

There's always something we can learn from biology. Aircraft and aerodynamics in general were originally based on bird flight. We've been using biotechnology for millennia to produce and upgrade foodstuffs. The potential for innovation is nowhere near exhausted. There are various estimates as to what percentage of global chemical production will be bio-based by 2030, ranging from 25[227] to 40[228] per cent, so the potential is great in any case. BDI, The Federation of German Industries, of which we are a member, has now added the topics of biologicalization, the bio-based economy, life sciences and biotechnology to its agenda, a step we feel was necessary. Innovation only functions when we achieve a convergence of technologies and manage to win over traditional industries to these new approaches, materials and processes. We have the "*technology push*", and have made progress on many fronts, but we are still lacking "*market pull*", before we can establish new value chains.

So what are the hurdles and challenges?

The dogged insistence on the old "claims" and paths: "good is the enemy of great". We have joined the BDI to demonstrate that global developments in the bio-based economy, with the associated need for new sensors, machinery and production lines, also provides opportunities for traditional industries – we just need to tackle things together. These new methods will also enable us to get closer to meeting climate targets. We know that it is going to get more expensive to produce CO_2, and companies will need to adjust. The sticking point at the moment is "upscaling": it is risky to build larger facilities on the off-chance, for example to illustrate feasibility and economic viability on an industrial scale. So the market is failing and investment is needed. If we want to move ahead together, we have to convince policymakers and society, but as I said earlier, we don't want innovation at any price, but rather innovation with sustainability potential.

Are there shortcomings in the way the bio-based economy and sustainability are communicated?

Communication has failed somehow with the term "bio-based economy". Obviously a cotton shirt is bio-based, but that's not really what we're talking about at the moment, is it? The crucial factor is that we produce knowledge- and bio-based innovations and think through future challenges. We must not forget that a bio-based economy is not necessarily sustainable. Sustainability is something we have to actively pursue.

How do we make headway?

Funding of industrial research needs to continue. And research funding must be designed so as to promote the best possible collaboration between start-ups, SMEs, academia and major industry. It is also important that we look at value chains as a whole. And of course political decision-makers and the authorities have to be brought on board where a regulatory framework is needed, for example.

How is Germany doing compared to other countries?

I should like to emphasize, since everyone is talking about digitalization, that biologicalization and in particular engineering and biotechnological approaches suit Germany very well. We are after all the country of beer brewing and hundreds of types of bread – we're good at that sort of thing. And we have very good engineers. Biologicalization suits our mindset perfectly! The disadvantage is that we have become very weary of it all, and the terms sustainability and bio-whatever are more likely to be associated with going organic, eating shrivelled carrots and

227 | See Road to Bio 2019.

228 | The projection was drawn up in the context of an internal workshop.

doing without plastic bags and steak. Society and policymakers do not realize that "bio" can also be associated with innovation and a high-tech economy. Maybe it's also "bio" when Artificial Intelligence learns from neural networks or a machine can climb a wall like a gecko (see section 7.2). It just needs to be sustainable, otherwise it's not in keeping with the times.

11.5.5 Interview with Alexander Böker, Fraunhofer IAP[229]

Prof. Dr. Alexander Böker is Director of the Fraunhofer Institute for Applied Polymer Research IAP in Potsdam-Golm and Chair of "Polymer Materials and Polymer Technologies" at the University of Potsdam. Fraunhofer IAP is developing bio-based and synthetic polymers which are efficient, smart and sustainable – from the laboratory to the near-industrial scale.

Prof. Böker, what do you understand by the phrase "biologicalization of materials science"?

Well, in very general terms, principles are being transferred from Nature to materials. This includes biogenic resources being used for materials, for instance. Looking purely at the biomaterials side, a classic example is everything that can be obtained from wood: cellulose, lignin, etc. We at Fraunhofer IAP are working on one hand on these more traditional developments, on the other hand also alternative processing methods such as 3D printing or the biological functionalization of surfaces and their interaction with the surrounding environment are also important research topics here.

We are thus providing materials with biological functions. To this end, we are introducing biological building blocks developed by Nature millions of years ago to a surface or also directly into materials. For instance, we're working on novel polymer films into which natural proteins or enzymes have been integrated with the intention that they will work the same way as in their natural surroundings. Such systems are of great interest for example in the pharmaceutical sectors for the development of medicines and in the packaging industry too. Proteins and enzymes can be biotechnologically modified to make them more stable, which is necessary as they have to withstand polymer material processing, for example. We can also impart other functions to biomolecules which they don't have naturally, in a type of "directed evolution". That is our approach to new "biologicalized" materials.

Also of interest are the approaches where the starting point is "growing Nature", the intention being to construct tools and machines that can regenerate themselves and which are no longer subject to wear. That is still a long way off in the future, but a start will be made at some point.

How do you rate the associated potential for innovation?

The biologicalization or biological transformation of production and materials research is one of the Fraunhofer Gesellschaft's main strategic initiatives for good reason: it has the potential for disruptive innovation. On the one hand, we can draw inspiration from Nature when it comes to developing new material functionalities, while on the other hand biocompatibility and biodegradability help in tackling the waste issues associated with certain materials. It is true that with respect to biodegradability we have to decide on a case by case basis whether biodegradation or a closed recycling cycle makes more sense. Ultimately, however, every newly developed "bio-inspired" material leads to a whole new class of materials, since we are going beyond the conventional chemical and physical properties of a material and adding a biological activity or property.

In your view, are there also hurdles or challenges?

The opportunities offered by a completely new class of materials (with biological functions) are incredible. However, as with every new technology, it will be a while until it will be implemented on a large scale. One issue are acceptance problems. Another hurdle, in my opinion, is the interdisciplinary nature of biologicalization. To generate these new materials for application in products or indeed just to move in this direction, I need biotechnologists and microbiologists, and also physicists, specialists in physical chemistry, chemists and lastly engineers and designers. This means that many complex disciplines which are not necessarily used to working together have to collaborate from the very beginning if long-term success is to be achieved. Ultimately, this emphasizes a need to make scientific education more interdisciplinary.

229 | The interview was originally conducted in German.

12 International Perspectives

This section presents selected international centres for bio-inspired materials research on the basis of interviews.

12.1 Interview with Donald Ingber, Wyss Institute at Harvard University, Boston, USA

Prof. Dr. Donald E. Ingber, is the Founding Director of the Wyss Institute for Biologically Inspired Engineering at Harvard University, the Judah Folkman Professor of Vascular Biology at Harvard Medical School and the Vascular Biology Program at Boston Children's Hospital, and Professor of Bioengineering at the Harvard John A. Paulson School of Engineering and Applied Sciences.

Prof. Ingber, could you tell us what you are doing differently at the Wyss Institute and describe your approach to creating innovation?

We started the Wyss Institute over ten years ago and the challenge was to think where bioengineering would be moving 30 years ahead. We looked back and we saw that in the past, engineering had already transformed medicine and the world by applying engineering principles to solve medical problems. However, we felt that we had already begun to uncover enough about how Nature builds, controls and manufactures from the nanoscale up, that we were now in a position where we could use biological principles to develop new engineering innovations. That's what we call "Biologically Inspired Engineering". Nature doesn't have separate departments of Chemistry, Biology, Physics or Arts. So, why does academia organize itself this way? We ignore disciplinary boundaries and we are more than a fundamental science institute. We are more like a translation institute as we believe that our ideas will not change the world unless they get out of the lab. So, our measures of success for the institute included from the beginning: our intellectual property portfolio, corporate alliances, licence agreements, start-ups and actually having products in the commercial pipeline! We had a five year gift of 125 million dollars to start with, the largest gift in Harvard's history at that time, we doubled it five years ago, and we just recently announced that we tripled it. It has been quite an amazing adventure!

So you put all these measures of success in place, can you explain how things work in practice now?

We have a novel structure here and we have written a review article[230] on the Institute model itself. One of the most novel things we did was to hire over forty full-time permanent staff from industry, many with product development experience, who ideally have some management experience and team management skills; we call them our Advanced Technology Team (ATT). Some institutes hire people from industry to work in their core facilities, but our people are in the trenches with students and fellows and faculty, and they come from all sorts of companies. This brings a level of interdisciplinarity, as well as a translation focus, you usually don't get in academia. We have people who know how to deal with milestones and timelines. And that's a real game changer, to have that in academia. We give enough funding to our core faculty to hire one to two students or fellows, and we give them complete creative freedom to just play. This turbocharges what I call it the skunkworks of academia, and we don't have faculty take time to write grants or apply for funding. We just chose people that we think are visionaries and we bring them together around problems that no single faculty can solve on their own, and collaborations arise spontaneously. The relatively small level of funding we provide to individuals is to help keep the ideas coming up, and to fuel the pipeline. In the end, everything is about people.

We also launched the Institute by creating what we call Enabling Technology Platforms in which we gave visionaries in our key focus areas a pot of money each, and provided them with total control over it, but demanded that they use those funds to also enable activities of other faculty, and to bring them all together in a collaborative way. Importantly, we don't give individual faculty lab space; we give projects and platforms space, which we call "Collaboratories" and we then bring staff from multiple collaborating labs working on the same projects into this common space. We also have later stage Validation Projects and Institute Projects that are more staff driven and focused on technology validation as well as business development. It's really a different model for academia, it really is. Success is all about which team members work well together. You have to bring the right people together, give them creative freedom, and try to get out of their way; that's our innovation model.

230 | See Tolikas et al. 2017.

Yes, it sounds like you are facilitating interdisciplinarity and creativity with a focus on innovation.

That was the goal! And it's working! We have published one paper in *Science* or *Nature* every month on average for the past ten and a half years. And we only have 18 part-time faculty because all our faculty keep their academic appointments in their home schools at Harvard or at collaborating universities and hospitals. They have to teach at their home institutions, serve on the usual committees, and they have some their research activities at both sites. However, they locate their work that is more translational, and their more entrepreneurial staff at the Institute. That keeps it vibrant. You know, the level of impact has been amazing. We've done 31 start-up companies, 57 licences, and more than 2000 patents.

What would you see as the main hurdles and challenges for innovation?

Institutional jealousy and competition. We can't ignore the fact that we live in a competitive world, but the trick is to make it a win-win for both sides.

Do you have a good example of a bio-inspired material science start-up?

One of my start-ups, which is called Emulate Inc.,[231] is commercializing our "Organs-on-Chips" technology, which are microfluidic devices the size of a computer memory stick lined by living human cells (see Figure 53). These devices recreate the

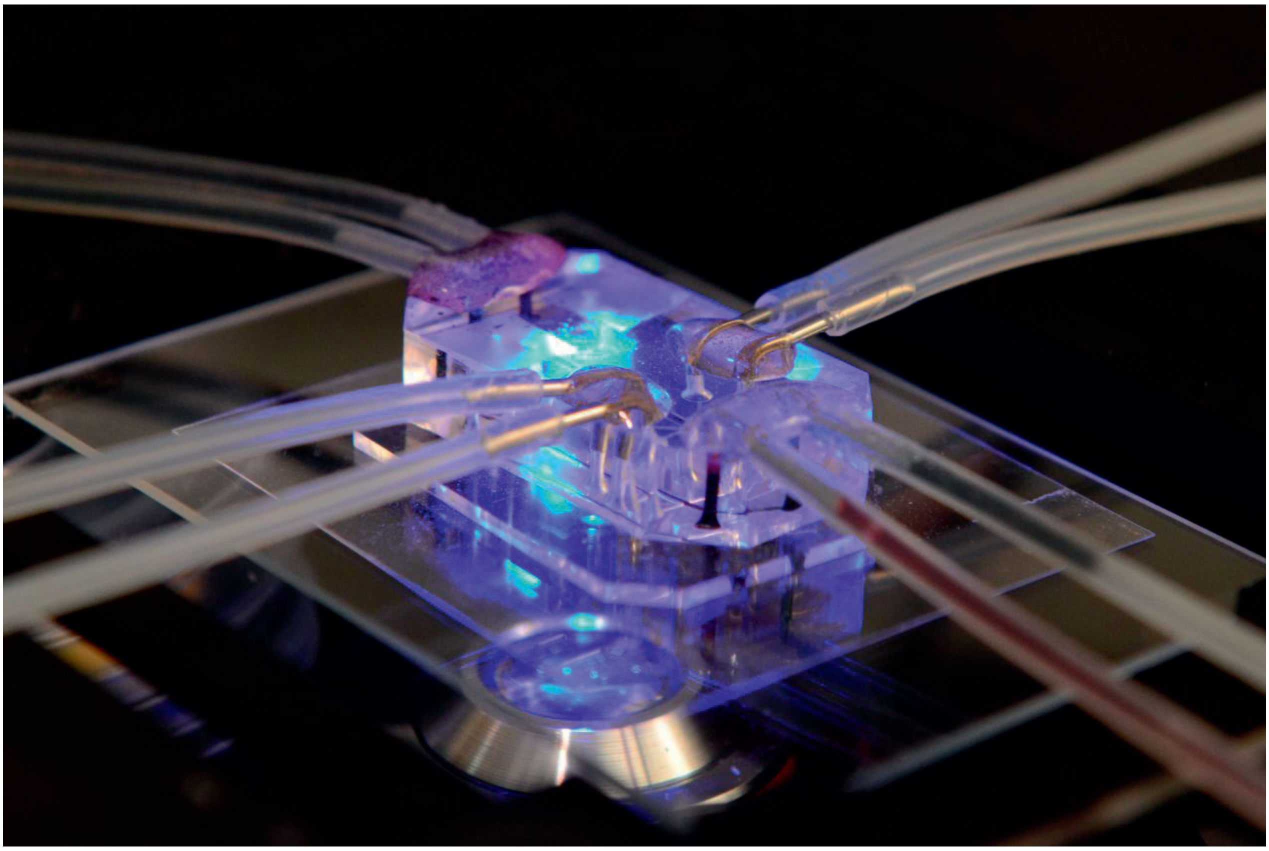

Figure 53: Organs-on-Chips are microengineered systems lined with living human cells that emulate the function of a number of organs, including lung, intestine, liver, kidney and brain. These systems enable better prediction of drug safety and efficacy in humans, provide insights into mechanisms of disease that enable development of new therapeutics, and have the potential to advance personalized medicine (source: Wyss Institute at Harvard University).

231 | See Emulate Inc. 2019.

tissue-tissue interfaces, organ-level structures, and pathophysiological responses of living human organs. Emulate is selling products around the world that are being used to replace animal testing for drug development and cosmetics, as well as for fundamental research. Joanna Aizenberg has a company called Advanced Material Technologies, Inc., which is selling omniphobic surfaces to prevent sticking of everything from barnacles to blood. The Wyss also licensed Conor Walsh's soft exosuit technology to Rewalk Robotics, which recently obtained FDA[232] approval to begin sales of this wearable robotic clothing as a rehabilitation suite for stroke patients.

What recommendations would you make to German decision-makers?

Don't put your money through your existing university infrastructure, do something totally new. What skunkworks originally referred to was when a big company would take a small group of the most creative people and move them outside of the usual organizational and reporting structures, with different funding, so that they could create something totally out there. In terms of areas to look in the bio-world, I think there are many places where major advances remain to be made. The microbiome is one as it plays such a huge role in health and disease, yet we are still learning how to study it. I think synthetic biology is huge. 3D printing and other types of material printing are going to be other exciting areas to explore as there is so much room to make new advances. You need government to invest in organizations that are willing to pursue high-risk – potentially high pay off type of work. You have to take great people out of their old institutions, and bring them together with best people within an organizational structure that best enables them to work with each other. I personally think that this needs to be built from the bottom-up by the scientists and engineers who have the vision and the passion. So, the approach has to be a little different from just funding the most successful mainstream scientists. You have to break the mould and find the troublemakers and mavericks who question the established ways of doing things, but also have demonstrated that they can be effective and work well with others!

12.2 Interview with Robert Full, UC Berkeley, USA

Prof. Dr. Robert J. Full is a Howard Hughes Medical Institute Professor in the Department of Integrative Biology[233] at the University of California at Berkeley. He is the founder and director of CiBER, the Center for Interdisciplinary Biological Inspiration in Education and Research. The focus here is on discovering fundamental principles of biology that inspire novel engineering while engineers provide biologists with new hypotheses, approaches and techniques. Professor Full is the Editor-in-Chief of the journal *Bioinspiration and Biomimetics*.

Prof. Full, what do you mean when you talk about the biologicalization of materials science?

We try to really understand the principles of biological materials and make use of them. Once you extract those principles it doesn't mean in any way that you simply copy them, which is what people think. We know that evolution works on a "just good enough principle", not an "optimizing" or "perfection" principle. So, you figure out the principles of these materials and then you look on the engineering side. If there is already something that does it better, you don't need to look to Nature. Nature is just another source of design ideas. But in some cases, they are spectacularly good!

What is your view of upcoming developments and their innovation potential?

Biomaterials are incredibly hierarchical, they go up from tiny scales to very large superstructures and more and more we want these materials to do more than one thing: we want them to be multifunctional, we want them to sense, actuate, compute and communicate. That was a dream ten years ago. And now you are seeing all sorts of engineered materials that can do all of those things. We have techniques like biomineralization, we can use self-assembly, we can do freeze-casting and vacuum casting and all kinds of incredible developments like laser engraving and 3D printing. The additive manufacturing field has simply exploded. Now, with these manufacturing techniques, you can do all of these things and use Nature's principles. So it's just a revolution!

232 | Food and Drug Administration, the United States government authority responsible for the approval and market surveillance of foods, drugs and medical devices.

233 | See Poly-PEDAL Lab 2019.

What are the hurdles and challenges which have to be overcome?

The challenge for all the major companies is to make their products inexpensive and in large volumes. You can do those wonderful things, but they are very costly. So, you need a whole new view of manufacturing at the nanotech level, it's really a multi-scale problem. But whoever figures out the automated factory processes to pull this off, will accelerate innovations from medical devices to building houses and architecture. We will have to determine where the transitional spots are, where there is sufficient interest in purchasing and buying to get you to the point where you can leverage what you built and you can design a whole new market. However, it is really difficult to identify these spots, but some will probably be in medicine, because more people, more governments, more insurance companies are willing to pay more initially for medical products. But if you can find a broad consumer application of these bio-inspired materials that will allow you to leverage building all that capacity then I think this will take off even faster.

Figure 54: A gecko-inspired robot named "Stickybot" climbing next to its inspiration, the tokay gecko that uses a fibrillar adhesive (source: Robert J. Full, UC Berkeley)

Education is another vital area and we have to realize the future potential of bio-inspired design by very strong educational programmes. Courses merging discovery-based approaches with design-based learning are the future. I have 200 students in my class, half of them are not science majors, half of them are just beginning students, they've never taken another science course, yet we have them read scientific papers, so we make them understand where the biological discoveries come from and once they get the principles, they make designs on that basis. For example, we are just submitting a grant application with Thomas Speck[234] with the aim of offering a version of a course like ours in every college. The key here is that the class really focuses on work competencies that involve creativity, collaboration, and communication skills that any country is going to need, because in most cases, for the students of today, the jobs they will have don't even exist yet. If you don't invest in this field now and quickly, it will be too late! But with Peter Fratzl as a leader, Germany already has a good lead in many respects.

Does communication with society have a role to play here?

Yes and I'm very optimistic, I give a lot of TED talks for example. These talks capture the imagination of the public and show the societal benefits of learning from Nature. However, I think there is also a risk that some people are pushing too hard on the "green-ness" of this. We should really understand and communicate the fundamental principles of sustainability, so we don't get diverted by "green washing", where companies get the public excited about a product when it's really not making the environment better. In fact, we're really concerned about unsubstantiated claims in this field.

So, how do you rate the innovation potential for the US, or is this innovation already a reality in the US?

We're still right at the beginning but biomedical applications, such as drug delivery, dentistry, and health monitoring, will be the first area to really get going. But the consumer market for

234 | Prof. Thomas Speck is head of the Plant Biomechanics Group and Director of the Botanic Garden at the University of Freiburg. See his article on lightweight construction (section 4).

wearables is big too. Bolt Threads[235] for example, they work with spider silk where they go from genes to a product. Adhesives, protective coatings, self-healing materials and antimicrobials inspired by Nature are coming as well. And finally, soft robotics is taking over the country (see section 5) and soft materials in relation to robotics are being studied at every university, especially ours and at Harvard and MIT too.

What recommendations would you make to German decision-makers?

If you want strong entrepreneurship, a Silicon Valley for Germany, you need to have the educational support, train students and get them into innovation incubators! But it has to be politicians supporting it together with business and with scientists from multiple fields, working from the molecules all the way up to the whole structure. You must support the basic research and then facilitate its transition to market, so avoiding the loss of novel inventions that do not have an immediate return on investment. For politicians it's simple: it's a win-win, people will have more jobs and more money, contributing more to a sustainable society.

12.3 Interview with Lei Jiang, Beihang University, China

Prof. Dr. Lei Jiang is the dean of the School of Chemistry of Beihang University and an expert in bio-inspired smart interfaces. He has been a member of the Chinese Academy of Sciences since 2009, of the "World Academy of Sciences for the advancement of science in developing countries" since 2012 and is also a foreign academician of the American Academy of Engineering.

Prof. Jiang, what's the significance of bio-inspired research for China?

It's highly significant. China has many research groups working in this field and the government is investing in the new "Bio-inspired interfacial science and future technology" research centre which I lead.

Is industry also involved and do you see innovation potential?

There are some companies already and some are starting up right now. We will see very fast growth in the near future. For example, the latest unmanned aerial vehicle designed by Boeing is bio-inspired, specifically from a stingray and not, as usual, from birds.

What are the current research priorities in your institute and in China?

I am focusing on superwettability, for example on the question as to why lotus leaves are so clean. It's because they are superhydrophobic which means a droplet rolls on their surface like a ball. How does this work? Or why are our eyes superhydrophilic? It makes them clear. Or how does spider silk collect water from a mist? Or why can a cactus collect water from mist? These are the questions we are interested in answering.

Do you think such innovations will come onto the market in the coming years?

Of course! People are already producing artificial spider silk (see interview 2.6). Or there are projects where water is collected at the beach in the morning and evening and then used to irrigate plants. Or you can generate electricity on an island by collecting fresh water and mixing it with salt water.

In your future institute, are you planning to work with industry, or will it be purely a fundamental research institute?

Both. We want to carry out in-depth research and transfer it to industry. But in China, we don't have to approach industry, it comes to us. We are planning to start joint projects, which are funded by the government and the companies. In China, we combine the advantages of socialism and capitalism.

What do you think are the major challenges and hurdles facing the development of this kind of technology?

The problem is the lack of communication with industry: when a scientist starts a project, industry should be involved from the outset to ensure that it's application driven.

Do you think the Chinese government has acknowledged the importance of this field?

My work is the leading research in China and others are following. Funding is available for learning from Nature and there are also lessons to be learned from the US, Germany and Japan. Learning from Nature is endless, after all what is science but an investigation of the natural world? You cannot invent a crystal

235 | See Bolt Threads 2019.

without modelling it on Nature. That's how it will always be, not just for China or Germany, but for the whole world. Understanding this is vital.

How would you assess Germany in this context?

I think Germany has great strengths, but innovation and transfer to industry must happen incrementally.

12.4 Interview with Xiaodong Chen, Nanyang Technological University, Singapore

Prof. Dr. Xiaodong Chen is President's Chair Professor in Materials Science and Engineering at Nanyang Technological University (NTU), Singapore, director of the Innovative Centre for Flexible Devices (iFLEX) and Co-Director of the Max Planck–NTU Joint Lab on Artificial Senses.

Prof. Chen, what are the research priorities in the field of bio-inspired materials science in Singapore right now?

Singapore is a tiny country, but is really innovation oriented. We don't have major resources, so we try to make sure that our

Figure 55: On-skin, silk-based electrodes with high skin conformability and high conductivity developed by Prof. Chen and his group (source: School of Materials Science and Engineering, Nanyang Technological University)

research really has an impact on our society, so that the tax payer sees the benefit. I see a lot of impact and there is considerable interest in this field, for example in mimicking hydrophobic materials. Another question is, what are sustainable natural resources? The issue of CO_2 emissions is very important right now.

And what are the major challenges here?

We need more scientists like Peter Fratzl who are focusing on how we can learn from Nature. But then, there are so many different research topics. You have to focus on the promising areas and have a few flagship projects! You have to have a business case for a successful model and then more people and industry will automatically follow. Overall, the area is really promising and has the potential for low investment and great results. Also from a global perspective, it's about time we made use of sustainable resources! If we find a way to mimic Nature we will solve this problem.

How do you promote innovation in Singapore?

We have a lot of connections. We start from fundamental science and seek to create a link with industry. How can industry benefit from our research? We ask them: what questions do you have? You cannot just raise your own questions, you have to find a common question with industry, and then you find a solution. Singapore is pretty small, about the size of Berlin. This means you can't do everything but have to focus. The government does this from the highest level, which obviously wouldn't be possible in the same way in Germany.

12.5 Interview with Olli Ikkala, Aalto University, Finland

Prof. Dr. Olli Ikkala heads the Molecular Materials laboratory at the Department of Applied Physics at Aalto University in Greater Helsinki and the Academy of Finland's Centre of Excellence in Molecular Engineering of Biosynthetic Hybrid Materials Research (HYBER). He develops functional materials based on hierarchical self-assembly, biomimetics, and natural materials such as nanocellulose.

Prof. Ikkala, what is the significance and innovation potential of bio-inspired materials science for Scandinavia?

There are two areas of relevance. Firstly, the use of plant-based materials (celluloses, hemicelluloses, and lignins) for conceptually new applications and, secondly, the emerging potential of biotechnology (synthetic biology) for materials science.

In relation to the first topic, for historical reasons Finland (like Sweden) is very active in the forest industry which is under great pressure to move its product portfolio away from conventional paper products and cardboards towards wood-based advanced materials. In future, the aim is increasingly to replace oil-based polymers in the most varied applications with more sustainable wood-based starting materials. Sooner or later, we will have to limit processing of oil-based polymers because the costs of extracting oil will inevitably increase if we are to maintain a continuous supply of oil. There are fields where plant-based materials might be the solution, for example in addressing the micro plastics issue. Attempts are thus being made to make use of forest-based resources not only for bulk polymer applications but also for new advanced materials. This is certainly no easy matter, as conventional polymers have been developed and optimised over a number of decades, and, while recycling them may make them sustainable, this would require well-developed infrastructure, something that is not a given in every country. On the other hand, a vigorous political debate is under way in Finland about cutting CO_2 emissions and about how to provide and restore CO_2 sinks which are capable of absorbing and storing carbon. This has created a groundswell of alternative political opinion that there should be no increase in the use of forest-based materials. Opinions are thus completely at odds. Achieving rational solutions requires in-depth and objective life-cycle analyses for different scenarios rather than emotionally driven opinions. In our major flagship project, FinnCERES, the Competence Centre for the Materials Bioeconomy, the Finnish Academy is investing in the investigation of various scenarios and the development of appropriate technical solutions in collaboration with existing and emerging companies. This is a considerable challenge. We can see that companies are starting to invest in investigating the possibilities for advanced non-oil-based sustainable materials.

On the other hand, while we think that synthetic biology holds huge promise for the long-term future, there is still a need for concrete further action for larger scale technologies. Various Finnish universities are conducting research into biotechnology and VTT Technical Research Centre of Finland in particular is working on relatively large-scale industrial biotechnology. Commercial processes, for example for degradable polymers, have already been developed for global industry.

How do you involve industry from an early stage?

That is a key question. To date, our experience is that strong research-oriented competitive funding is still needed before companies start making major investment in the actual product-oriented research and development. The aim of our FinnCERES project is to support the transformation of plant-based materials into commercial innovations and products ("translational" research). We are researching in various areas, such as food formulations, materials for construction, photonics, clean air, food, clean water, lightweight materials, wearables, carbon materials, coatings, adhesives, energy, and others. Importantly, a broad selection of companies is now involved, not just the cellulose industry. FinnCERES uses its funding as seed money to encourage companies increasingly to carry out joint innovative development projects. In particular, there are promising start-ups working in small-scale niche markets.

So what are the major hurdles and challenges?

They are pretty much the same as in any field in which new products are being brought onto the market: their price has to be lower than or at least the same as and their properties better than those of established products. In plant-based materials, one potential route is to use industrial waste to reduce costs. In Finland, this has opened up new business opportunities, especially for SME's.

Another potential hurdle are the different types of customers from the materials industry and the forest industry, who have different expectations and backgrounds. How can these differences be overcome? In addition, the forest industry typically produces large volume products, while entry onto the advanced materials science market may initially require a focus on small-volume speciality products. In some cases, the forest industry has already brought specialized products onto the market, for instance UPM Biomedicals which commercializes wood-based solutions for biomedical applications.

What's needed for headway to be made?

Invariably, multidisciplinary research methods are essential for growing a new generation of experts with a new working culture and new networks. This entails seamless collaboration between chemists, physicists, materials scientists, biochemists, modelling experts, and engineers. This is the working culture which has been adopted in our Centre of Excellence in Molecular Engineering of Biosynthetic Hybrid Materials Research. Over the past six years, we have brought together physicists, biologists and chemists and have learned to speak the same language. It is also interesting to see how IT has become such a significant force for cultural change: at the outset, there was a culture of hacking where people were programming just for fun and building all kinds of devices. We need to develop a similar culture of "bio-hacking" in synthetic biology. This is why my colleague Prof. Merja Penttilä has just received funding of one million euro to set up a "bio-hacking lab".

To create a garage lab like in the early days of Microsoft?

Exactly, we even call it the "bio-garage"! The students are invited to make their own discoveries and we think this is really important, although we are clearly quite a long way from innovation here. It is modifying the culture, however.

What is your assessment of the developments in the coming years?

I think it is important to rethink the materials basis within the polymer industry from the ground up. One interesting point is of course sustainability and the various opinions around it. Sustainability can be achieved by using oil-based plastics within an efficient re-circulation infrastructure. However, there will be always societies where recycling won't work. The oil-based economy is based on extremely optimized processes which put every fraction to good use. This is now happening in the plant-based sector too, where it's called bio-refining and we can replace ever more of the chemicals obtained from oil. It may not be competitive in every case, but plant-based products are tending to become cheaper, while oil will become more expensive in the long run, so a tipping point will come, sooner or later.

Moreover, bio-inspired materials can be complex, still allowing multifunctionality. This is why we believe we have to incorporate more machine learning and Artificial Intelligence to design bio-inspired materials properly. We need to screen a large parameter space where some kind of big data handling could bring benefits. One challenge is to create suitable data libraries. Machine learning has so far only worked in very simple cases. Therefore conceptual developments are needed. Another potentially attractive development would be directed evolution for materials science. Drawing inspiration from the biological world, ever more complex functionalities will be mimicked, in particular including dissipative non-equilibrium systems. My personal interest is in how to go beyond responsive and shape-memory materials towards materials that incorporate "learning" elements, such as algorithmically mimicking classical conditioning, which is among the simplest forms of psychological "learning". These approaches are highly promising and our first article based on our second ERC grant has just been published. In general, one of the next steps in bio-inspiration will be to mimic not only "dead" materials like silk, bone, teeth or nacre, but also dynamic, non-equilibrium materials which exhibit more and more "lifelike" behaviours.

Is there anything else we should discuss here?

As one specific example, in Finland, there is considerable interest in replacing cotton. You may well think that cotton is sustainable, but it needs lots of water which is increasingly becoming a limited resource. There is a long tradition of replacing cotton with cellulose, for example with viscose, but this often involves using toxic solvents. So, even if initially bio-based materials are used, the process is not sustainable. Ionic liquid solvents can open up new ways forward here, one good example being the Ioncell project, which covers every aspect "from birch to catwalk". It's still at the pilot stage but is very promising and could come onto the market in the next few years.

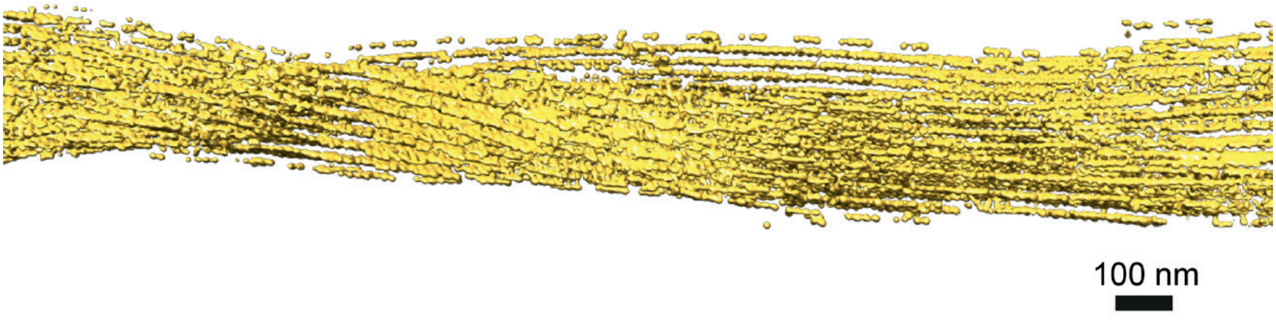

Figure 56: Electron tomogram of gold nanoparticles templated on tobacco mosaic virus self-assemblies for chiral assembly as an example for biomimetic templating for new functions (source: Dr. Nonappa, Aalto University, School of Science, Finland)

12.6 Interview with João Mano, University of Aveiro, Portugal

Prof. Dr. João F. Mano is a full professor at the Department of Chemistry of the University of Aveiro (Portugal). He is the director of both the Master's and Doctoral Degree Programmes in Biotechnology at the University of Aveiro. He is the director of the COMPASS Research Group at the associated laboratory CICECO – Aveiro Institute of Materials.[236]

Prof. Mano, what is the significance of biologicalization in materials science and what is its innovation potential for Portugal?

It's very important in general, not just for my country but also for Europe and the rest of the world, not least because it is associated with sustainability and resource conservation. Biologicalization also provides highly innovative solutions which may sometimes be more economically attractive than currently used technologies.

Which are the major research institutions in this field in Portugal and what areas do they focus on?

At the University of Aveiro, there is CICECO, Portugal's largest materials research institution with almost 500 researchers. There is great interest in ceramics and we are working hard on bio-inspired materials, using bioactive glass and composites in biomedical applications. We also have strengths in bio-based research, making use of resources from forests and the sea. Our research group is investigating cellulose and marine-derived polysaccharides together with advanced chemical routes for modifying them. Starting from such polymers of natural origin, we can also draw inspiration from Nature to develop novel biomaterials and strategies for tissue engineering and culturing applications. We are also strong on inorganic materials and metal-organic frameworks.

What do you see as being the trends in Portugal in the coming years, not only at your institute but also in general? Is there a bio-inspired "industry" and are there products which are commercially available?

Various industries use materials derived from renewable sources, from forestry, the sea and agriculture. There is great potential in terms of industrial applications because these technologies have been increasing in complexity, and require more highly skilled professionals. Portugal does, however, still lack biomedical companies and a major pharma industry. Nevertheless, we are seeing growth in this field, and we have more and more professionals and spin-offs. For example, we formed a spin-off to commercialize human-derived proteins that can be turned into hydrogels and used for 3D cell culture and this has clear potential in therapeutics and targeted drug release. Portugal is also launching a new "Collaborative Laboratories" programme where industry, technology transfer agencies and universities join forces in large consortia to solve major societal issues, such as energy resources.[237] The issues addressed include food, construction materials, means of transport or biorefineries. Corporate participants are expected to top up the government funding. At the moment, this is Portugal's most important programme for bringing industry and academia together. Following the crisis in 2008 in Portugal, our country is now back on the up, thanks to higher levels of investment in science in recent years, especially in scientific jobs.

Should the European Union play a role here?

Definitely! There is a need for specific calls from the Commission to facilitate interdisciplinary research. There should be a focus on transferrable science, such as bio-inspired adhesives. But your study would appear to be going in the right direction. If we take the European flagships[238] on graphene or the brain, for example, it would be worthwhile to have such a major programme on biologicalization or whatever one might want to call it.

236 | See COMPASS 2019.
237 | See Fundacao para a Ciencia e a Tecnologia 2019.
238 | See European Commission 2019.

12.7 Interview with Sybrand van der Zwaag and Santiago Garcia Espallargas, Delft University of Technology, Netherlands

Prof. Dr. Sybrand van der Zwaag is professor of Novel Aerospace Materials (NovAM) at Delft University of Technology. Among other things he is the Scientific Director at the Delft Centre for Materials and the driving force behind the Innovation-Oriented Research Programme (IOP) Self-Healing Materials.

Prof. Dr. Santiago Garcia Espallargas is currently Associate Professor in the Novel Aerospace Materials Group and team leader in self-healing polymeric materials research at Delft University of Technology.

Prof. van der Zwaag, can I ask what your country's current research priorities are in this field?

We are in the middle of a transition from fixed wing aircraft, where the wings are rigid because of the rigid aluminium they are made of, to morphing wing structures. A bird can fly thanks to the morphing shape of its wings and mimicking this is a major technical challenge. The idea is that morphing wings will improve efficiency. There are two bio-inspired materials developments in connection with this theme, the first being the self-healing materials program launched in 2003 with participation by 85 companies and five universities. Funding to the tune of 30 million euro was provided by the Dutch government together with a matching programme from DFG, the German science and research funding body. The second is a smaller, more focused programme on the use of biological substances in aircraft coatings which Prof. Garcia is currently setting up.

Prof. Garcia, what is your role in this programme?

For over a decade, we have been focusing on learning how to modify polymer chemistry in order to produce strong but healable polymers and how to properly characterize healing in polymers and coatings. We will continue working on these topics but also on more application-oriented areas. At the same time, we have started up a new programme focusing on the production of materials from microorganisms. Two successful initial concepts we are working on are the use of algae exoskeletons (see Figure 57) for anticorrosive paints and the development of

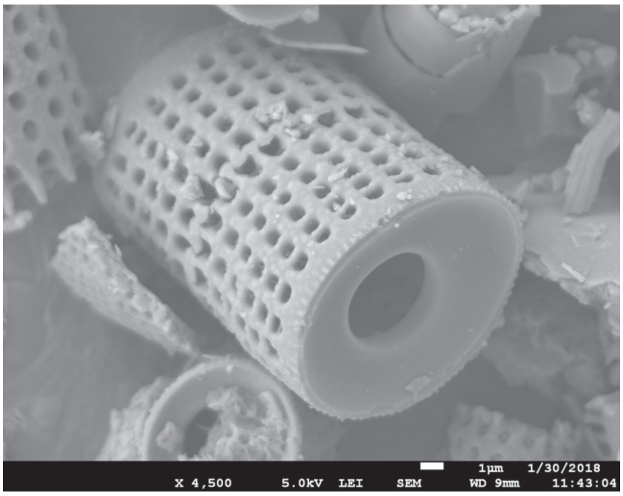

Figure 57: Scanning electron microscope image showing the porous outer skeletons of diatoms used for inhibitor storage (source: P.J. Denissen, Novel Aerospace Materials Group, Delft University of Technology)

bacterially-derived nacre-like coatings in work led by Dr. Meyer and Dr. Aubin. The initial results look very promising. We expect to develop these programmes in the relatively near future with the help of industry and other academics.

Prof. van der Zwaag, are you working with spin-offs or larger companies?

We prefer to work with larger companies but if they are too slow we do look for alternatives. This is why we have founded two companies which develop and market biomaterials, "Slimy green stuff"[239] and "Green Basilisk" (see section 9.4). Both use bio-inspiration to create highly functional new materials with applications in civil engineering. Although the civil engineering industry has a reputation for being very conservative, once the innovation is accepted the impact can be huge. Successfully scaling up from the gram-scale in the laboratory to the tonne volumes required to convince industry has so far proved to be the greatest hurdle.

Prof. van der Zwaag, does it make sense to give up completely on traditional systems or is your aim to replace them in part and come up with smart combinations?

We shouldn't try to replace everything traditional right now, but perhaps in future, who knows? We have to consider the actual value of using such systems.

239 | See Slimy Green Stuff 2015.

Prof. Garcia, what's your take on this?

We have to be realistic: some man-made material systems outperform biological materials by orders of magnitude. For instance, in terms of strength and stiffness and formability, there is simply no biological system that can compete with metals. Concrete can't be replaced either and it is unlikely that high-performance fibres will be, although spider silk is a nice example (see section 2.6). Carbon fibres are extremely stiff and way outperform biological systems. Biological materials might not be capable of completely replacing synthetic engineered materials but they might facilitate implementing novel and improved properties which are otherwise difficult to achieve with synthetic materials. This is the approach we referred to as "biotouch" in a recent report.[240] However, other fields, such as informatics, will certainly also benefit from biological concepts like neural networks and even self-healing. And there are also materials for data processing and for functional properties in the energy sector. The production of oxygen and hydrogen is one area where bio-inspired and bio-based materials may well have a word or two to say.

Prof. van der Zwaag, what is your view of developments in the Netherlands over the coming years, not only in science but also with regard to innovation?

With self-healing materials, it is getting increasingly difficult to make the transition from a good concept to industrial reality because, except in a few specialized areas, the conditions to make it happen just aren't in place. We have to make politicians realize that university research may create new jobs and be of benefit to existing businesses. However, if we want to make change happen, we need to start focusing on a lower level of fundamental science again, allow more time for research and make sure that the transition is covered. I'm not suggesting that we should all go back to the roots, but there should be separate fundamental research programmes to complement the current trend of involving industry from the outset of concept development. Our national self-healing materials programme got funded due to a very clear message from the Dutch materials sector that our concept was really interesting and worth funding but too far away from their current interests to have a chance of receiving financial support from industry.

Prof. Garcia, what are the greatest challenges for implementation and innovation?

Working out how to scale up existing ideas is a major challenge in many cases, since most laboratory developments still only involve milligram volumes.

Where to you see the potential for bio-inspired materials, Prof. van der Zwaag?

Dairy products are a very important resource for the Netherlands as we have lots of expertise, and the second major area is water-related. If you look at the Netherlands and in particular at Delft University of Technology and its biotechnology know-how, we lead the world in purifying water by removing harmful and other unwanted substances. This tradition of extracting the right molecule from biological and non-man-made mixtures is one of our major strengths and that's where I see the best opportunities for the Netherlands.

12.8 Interview with Hisashi Yamamoto, Chubu University, Japan

Prof. Dr. Hisashi Yamamoto is an organic chemist who is a member of faculty at the University of Chicago, a university professor at Nagoya University and a professor and director at Chubu University in Japan. His research primarily focuses on acid catalysis chemistry.

Prof. Yamamoto, what is the significance and innovation potential of bio-inspired materials?

I think they are of amazing significance, which is why I'm now working in peptide chemistry. Peptides are an important and sustainable natural product for the drugs industry. In this century, increasing numbers of people have developed an interest in developing new high-performance biomaterials, such as artificial spider silk, which has excellent strength and tear-resistance. Scientists had long struggled without success to synthesize spider silk until a breakthrough was made: spider silk proteins have now been sequenced and the silk is being produced by a small Japanese company using bacteria.

240 | See Montano et al. 2018.

What are the major hurdles and challenges in this field?

We still face various difficulties in peptide synthesis. Almost every week some new peptides are reported in biological journals, but unfortunately synthesizing these peptides on a relatively large scale is extremely costly and complicated. This constitutes a bottleneck for the pharmaceuticals industry. In addition, there is no longer any huge interest in peptide synthesis among synthetic chemists because everyone thinks it is a classical problem that was solved half a century ago. This means we still don't have any modern synthetic technology for peptides. My aim is to reduce the price of peptides by a thousandfold or even more. If I'm successful, peptides will become a major focus for pharmaceutical companies in the coming century.

Upscaling peptide synthesis, however, also remains a challenge. Moving from milligram to kilogram volumes will revolutionise the world of drugs. We need to make radical and fundamental changes because these new technologies inspired by Nature will differ fundamentally from existing technologies. This applies not only to chemistry but possibly also to biology or physics.

Appendix

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Editors:

Prof. Dr. Peter Fratzl
Max-Planck-Institut für Kolloid- und Grenzflächenforschung
Potsdam Science Park
Am Mühlenberg
14476 Potsdam
Germany

Prof. Dr. Karin Jacobs
Universität des Saarlandes
Campus E2 9
66123 Saarbrücken
Germany

Prof. Dr. Martin Möller
DWI – Leibniz-Institut für Interaktive Materialien e. V.
Forckenbeckstr. 50
52074 Aachen
Germany

Prof. Dr. Thomas Scheibel
Universität Bayreuth
Lehrstuhl Biomaterialien
Prof-Rüdiger-Bormann-Str. 1
95447 Bayreuth
Germany

Prof. Dr. Katrin Sternberg
Aesculap AG
Am Aesculap Platz
78532 Tuttlingen
Germany

Series editor:

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Munich Office
Karolinenplatz 4
80333 Munich | Germany
T +49 (0)89/52 03 09-0
F +49 (0)89/52 03 09-900

Berlin Office
Pariser Platz 4a
10117 Berlin | Germany
T +49 (0)30/2 06 30 96-0
F +49 (0)30/2 06 30 96-11

Brussels Office
Rue d'Egmont/Egmontstraat 13
1000 Brussels | Belgium
T +32 (0)2/2 13 81-80
F +32 (0)2/2 13 81-89

info@acatech.de
www.acatech.de

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Materials play a crucial part in virtually all products and areas of technology. Demographic change, greater shortages of resources and climate change require a more sustainable economy, while changing requirements are also increasing the levels of complexity to be managed in materials science. The biologicalization of materials research – that is to say taking inspiration from Nature as to how biological resources, principles and methods can be used – in particular holds major innovation potential for Germany as a location for research and business.

The acatech DISCUSSION uses examples to demonstrate the multiplicity of different possible structural, functional and synthesis principles with which Nature is already inspiring and will in future continue to advance materials research. Examples of novel material-based innovations at the interface of biology and technology which will benefit both society and the economy are presented from various fields of application.