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Biologicalisation in manufacturing – Current state and future trends

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ABSTRACT

Biologicalisation as the convergence of biology, engineering and information technology offers the prospect of dramatic step change scenarios for future innovative development. A large number of highly stimulating and potentially very valuable solutions, created over millions of years of evolution, are available in nature's solution space and waiting for application in technology. Transfer methods linking the biosphere and the technosphere are classified as functionalities which assume: bio-inspiration from nature, bio-integration combining biological and technological solutions, and bio-intelligence. The latter aims at achieving developments towards living systems based on the (reasonably) high level of appreciation of the environment, the system's capability and the specific task to be undertaken using decision making or self-reasoning. The use of large numbers of different sensors is involved together with sensor fusion strategies, self-healing and self-organising properties, along with functional integration. Moreover, to derive maximum benefit, the key enabling technologies will play a crucial role going forward. The impact on industry of unique and outstanding solutions will radically change the way manufacturing is performed today by building on new levels of latency, interconnectivity and communication. This paper aims at supporting the comprehension of these developments and revealing future trends, research needs and educational requirements in manufacturing science and technology as the biosphere and the technosphere converge to create the new levels of global sustainability.

1. Introduction

Biological systems have always served as a source of inspiration for mankind. With the progression of industrialization in the early days, discrete manufacturing and especially production machines shifted away from using biological materials or biological systems. Evidence for this can be seen in the distinct change of materials which have been finding application in the more recent era of industrial development. Since some decades biological structures have found interest for the development of technical products. It is only in very recent times that integrated biological functionality has re-emerged and is now of central interest. An early approach in this direction stems from [236], who coined in 1997 the term "biological manufacturing system" (BMS), which is defined as a system that adapts to non-predetermined changes in the environment by self-growth, self-adaptation, artificial intelligence (AI) and evolution. While at that time the computational performance was too weak, limiting the application of BMS in industry and artificial intelligence as such, a new boost for adopting biological functionalities started at the CIRP General Assembly in 2017, which driven by the white paper of Byrne et al. [49] rapidly spread throughout the manufacturing scientific community. Recently a collection of important papers for the biological transformation in discrete part manufacturing appeared as a special issue of the CIRP Journal of Manufacturing Science and Technology in late 2021. This is also the framework which has been adopted in this keynote area. Also covered are technologies that adopt in the sense of convergence methods and tools of discrete manufacturing.

Biologicalisation in Manufacturing is defined as the use and integration of biological and bio-inspired principles, materials, functions, structures and resources from living nature for intelligent and sustainable manufacturing technologies and systems with the aim of achieving their full potential. In [48] a classification of the different approaches of bio-inspiration, bio-integration and bio-intelligence to adopt solutions from nature is given, as shown in Fig. 1. The terms *Biologicalisation* and *Biological transformation* are often used synonymously. *Bio-inspiration* means the transfer of natural phenomena for value creation through a process of analysis, abstraction and technical realisation. The underlying idea is to technically replicate concepts/characteristics of nature.

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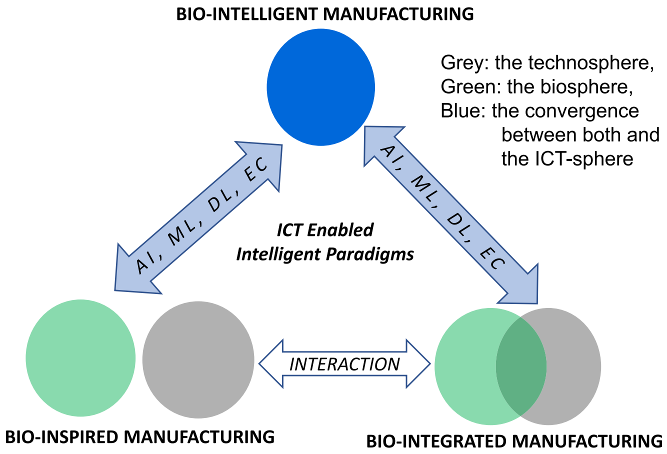

Fig. 1. Classification of methods in biological transformation [48].

Bio-integration seeks combinations of technical and biological components or processes (i.e., biotechnology) in traditional value creation environments, to get the best of both worlds, where often an increase of sustainability is the focus. Examples include: Use of microorganisms to recover rare earth elements from magnets; functionalisation of polymers; recovery of bioplastics from CO_2 waste streams; utilisation of microorganisms as lubricant components in cutting fluids.

Modified definitions are given in [121,169], where especially the definition of bio-intelligence is different. The definition of bio-intelligence as it is used in this paper here is given as: “*Bio-intelligent manufacturing is realised through merging artificial Intelligence with bio-inspired and/or bio-integrated manufacturing solutions, incorporating information channels, sensor and actuator systems. A special form of bio-intelligent manufacturing is when co-existence, mutual interactions and co-evolution of technical, informational and biological elements (or sub-systems) take place, with the potential of converging towards living systems.*” [48].

Bio-interaction has been introduced as a term by [170] as the development mode leading towards bio-intelligent systems, where elements of biosphere and technosphere are integrated together with an information system.

Biological transformation or in short biologicalisation is seen in manufacturing as a breaking frontier of industry 4.0, especially in relation to the applied ICT field (information and communication technology) by [48,49]. Recently the 2022 Horizon Europe Call “Development of technologies/devices for bio-intelligent manufacturing” (HORIZON-CL4-2021-DIGITAL-EMERGING-01-27) has been launched and focuses on the use of biological elements as key enabling technology for manufacturing as an emerging trend. Fraunhofer society in Germany has taken up this topic in the EVOLOPRO project.

The development of technologies towards the new paradigm of biologicalisation therefore profits from the rapid development of digitalisation. As a consequence, changes in manufacturing are happening at dramatic speed nowadays and ideas and visions at an even faster pace, leaving policy makers and stakeholders in a state of high uncertainty about future developments. The paper aims at collating material and solutions, indicating the actual standpoint and unravelling future benefits and requirements from the competitiveness and innovation perspectives. Especially the discussion of the enabling technologies, developing in parallel and independent of manufacturing offer the possibility of anticipating future manufacturing methods. With the help of *bio-simulation* the extent to which manufactured systems can act or react like living structures can be analysed [171].

Learning from nature and evolution, and covering methods, structures and functionalities opens up a vast field of intelligent solutions. It must though be kept in mind that these are often intertwined with other properties and functions because a biological system is typically a highly integrated organism. The lotus leaf surface structure, for example, cannot function continuously without its healing capability.

Malshe [160] presented nature’s toolbox of fascinating individual solutions presented in Fig. 2 and showed parallels between nature and manufacturing, providing archetypes for technical developments in the fields shown in Fig. 3. Simply copying from nature is not the right approach – understanding and then adopting is the way to deal with nature’s solutions and methods. Distinguishing real opportunities from wishful thinking is a major task though. Table 1 compares the performance of biological systems with those of technical systems.

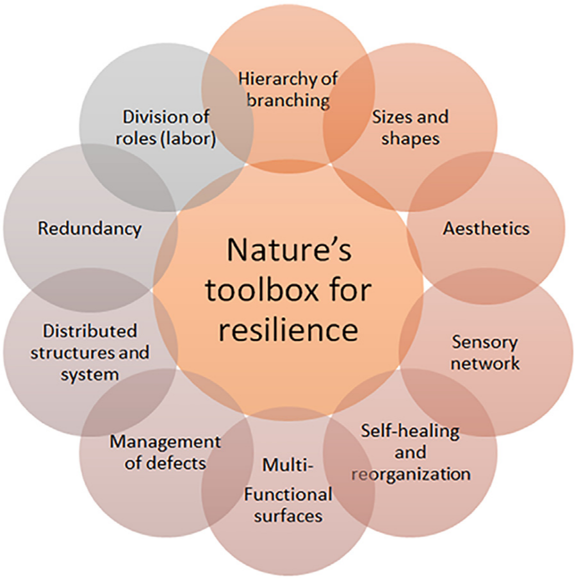

Fig. 2. Nature‘s toolbox for resilience according to [160].

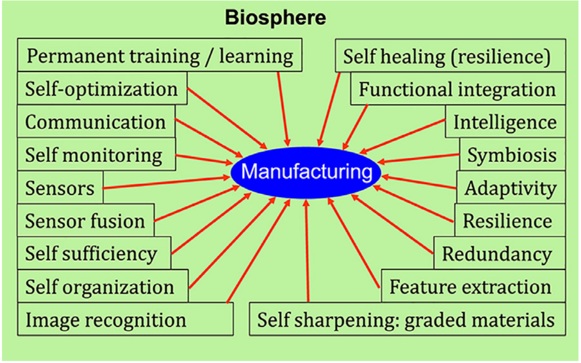

Fig. 3. Application fields of bio-inspiration.

The great adaptability of biological systems for instance is not an adaptability of the individuum to the changing environmental conditions but rather is the result of the dying out of generations of species, which is not what scientists and engineers intend for their systems. Also, biological systems themselves are not sustainable, at least not in the manner in which engineers think about sustainability. Fig. 4 shows a comparison of the circular economy in the biosphere and in technosphere. Parallels can be clearly seen and it is demonstrated that neither biological systems nor nature have a superior circular economy. Oil, coal and limestone are the waste dumps of biological systems of millions of years ago. Nature has invented additional creatures that live with the waste of others, which has parallels with industrial symbiosis. Also, efficiency is not a principle of biological systems; the energy efficiency of mammals is only a few percent. On the other hand, the human brain, for example, is highly energy efficient as can be estimated with the information from [53,88,90,128,232]. It uses about 15 W for 2000 teraflops compared to the largest supercomputer in 2021 (Fugaku, Japan) that requires ~30,000 kW for 442,000 teraflops. A bird’s brain is the best computing system in a performance to

Table 1
Performance of biological systems compared to technical systems.

Superiority of biological systems	Superiority of technical systems
Intelligence reasoning, strategy development, store experience, enhance results, identification of features and patterns	**Power** Different forms of power (electrical, mechanical, thermal) available rapidly and scalably
Abundance of Sensors Broad band sensors like vision, sound image of environment	**Flexibility** Extensibility, replacement of components, large portfolio of technical systems to individually apply optimum level of force e.g. levers, gears
Exchange of information exchange with other colleagues and other species, on very different channels optic, acoustic, gestures etc. → recognition	**Speed** Technical sensor technology, production and transport processes
Self healing and health reserve partly redundancy and redistribution of functionalities. Fault tolerance and resilience	**No Exhaustion** Ability to provide services virtually without interruption
Functional integration combining information channels and alimentation with structural elements	**Energy Efficiency** Electrification enables highest efficiencies
Reproduction generating new species and growth	**Survival without nutrients** only for functioning supply of media and energy required

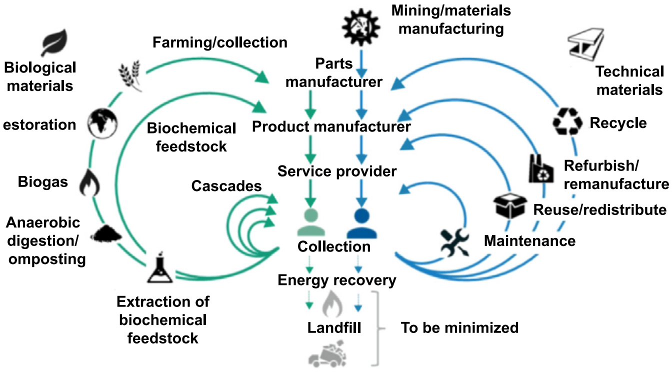

Fig. 4. Circular economy in the biosphere compared to the circular economy in the technosphere [78].

weight respect. This demonstrates the magnificient superiority of natural intelligence.

Sustainability and efficiency can be gained by convergence between the biosphere and the technosphere and setting biological solutions relative to their inspired technical counterparts in a different context. Sustainability, being today one of the most critical objectives, cannot be extracted from bio-inspiration, bio-integration or bio-intelligence alone. It requires the careful adaptation of biological solutions to technical needs.

This paper considers the superiority of biological systems according to Table 1 and shows possible solutions and results in the technosphere in this respect. After presenting the vision of living production machines in Chapter 2 and the discussion on the convergence between the three spheres (technosphere, biosphere and the cybersphere) shown in Fig. 1, the state of the art in communication technology and established cognition systems is dealt with in Chapter 3. Self-monitoring and subsequentially self-healing and self-organisation principles are discussed in Chapters 4 and 5. This is done on different levels from the material scale up to mechanical components, production machines and then in Chapter 6 for production organisations. Chapter 7 demonstrates the integration of biological materials in technical systems and Chapter 8 shows the integration of biological and technical functionalities. Chapter 9 deals with artificially generated bio-inspired metamaterials and thus connects to different fields of biologicalisation by functional properties and healing characteristics, needing the understanding for the integration and the functional purpose. They might also influence the development of enablers for living production systems, like cheap and versatile sensors and miniaturised or functionally integrated actuators. Bio-intelligence is considered in Chapter 10 through the symbiotic co-existence and co-evolution of the technical, information and communication, as well as biological ingredients in production of living materials. Enablers for the aspects of biologicalisation developed independently in the technosphere are presented in Chapter 11. The paper closes in Chapters 12 and 13 with a discussion of the visible and possible future impacts on the manufacturing industry. Trends are revealed and the role of manufacturing science for a convergence between the three spheres, biosphere, technosphere and cybersphere is outlined. Ethical considerations and strong governance aspects clearly become indispensable in biologicalisation.

In the converging worlds of biosphere and technosphere as characteristics of biologicalisation especially in manufacturing, definitions, clarifications, explanations and classification of single terms, vocabulary expressions and even linguistic communication understandable and acceptable by researchers and operators are needed. A dedicated activity was thus carried out jointly between the CIRP Collaborative Working Group on biologicalisation and the CIRP Committee on Terminology with the aim of providing proposals and solutions useful to tackle terminology issues and fill definition gaps in this new and rapidly developing discipline from a manufacturing engineering perspective. General terms and specifications of the field are given according to [48,49] while other terms are defined and used consistently in the following chapters.

2. Towards a living production/manufacturing system

The discussion of biologicalisation inevitably requires the discussion and the consideration of living systems. In terms of production engineering, Monostori et al. expect the transition “from the old, lifeless manufacturing systems to the manufacturing systems being alive: self-learning, cognitive, communicative, self-healing, self-assembling: in short, towards a “Living Manufacturing System” [173]. This has the characteristics of [98]: cellular organisation; metabolism; homoeostasis; complexity; stimulation & communication; reproduction; inheritance (heritage, legacy, heredity) and development; movement and evolvability. From this, the authors compare various aspects of living systems and production systems. Accordingly, no technical system has ever achieved the fulfillment of all principles of life. The purpose of biologicalisation is therefore not the transformation towards a living system as an end in itself, but rather the fusion of biosphere and technosphere in the sense of superior production goals. This chapter attempts to clarify what an efficient innovation process looks like with regard to a convergence of the technosphere and the biosphere in order to resolve the conflict between sustainability and competitiveness.

The vision of the biologicalisation process and thus the achievement of a living technical system requires a continuous convergence of the technosphere and the biosphere. Historically, the convergence of different disciplines is nothing new in the field of production engineering and this has been seen in the various industrial revolutions to date as the convergence of cyber-physical systems and production systems [173]. The sheer scale of technical problems as well as the biological solution space requires a complete rethinking of innovation processes.

2.1. The different roles of life sciences within biologicalisation

The definition of biologicalisation assigns a central importance to the life sciences and biological understanding, but these have very different roles depending on the context of application. Overall, according to [4] four different functions of the biosphere in the transformation process of biologicalisation can be identified in addition to the degree of integration (cf. Fig. 1), whereby the first three functions remain primarily at the level of bioinspiration and the fourth one in particular includes both biointegration and biointeraction:

1) A narrative and identity-forming function: By drawing parallels with nature the concept of biologicalisation is illustrated. The process of development and innovation does not build on life science approaches itself (e.g., the general concept of recycling).
2) Nature providing impulses for novel solutions: By studying and

understanding biological concepts, novel ideas for technical solutions may arise, but these are subsequently implemented in an analogical technical system, which does not build on the biological principle of actions (e.g., self-healing materials, Chapter 5).

3) Biology as a blueprint for technical solutions: The biological mechanisms underlying natural phenomena are rebuilt in a technical system that mimics the biological principle of action. Therefore, the innovation builds on in-depth knowledge from life and technical sciences (e.g. mobile machine tools, Chapter 6). This is also known as *Bio-Inspired Design*, which is the use of bio-inspired principles, functions and structures for developing more sustainable manufacturing systems, relying on the transfer of the underlying principle from biology to engineering to create innovative ideas [241,268].
4) Biological concepts as an integral part of the technical system: Components and principles from living nature are integrated in technical systems, making use of their functions and properties. The biological functions can also be optimized in a technical environment. This requires interdisciplinary cooperation and the physical combination of biological and technical components (e.g., biosensors or industrial biotechnology. Chapter 7 and 8).

All four principles involve biology acting as a donor and manufacturing technology acting as an acceptor, from which the biology push and manufacturing pull idea has evolved. The perspectives two to four focus on a very technical approach, which purely intuitively implies looking for fundamental analogies between the bio-sphere and the technosphere, for example in materials, but also in sensors and actuators (see Fig. 5). By this means, analysing bio-based principles can help find a solution to an existing engineering problem (top down), or it can trigger an idea for a new product (bottom up) [23,49,116,142,241,243,268]. Both variants require that the underlying properties be formalized so that the "translation process" into the respective other domain can succeed (horizontal arrows in Fig. 5)

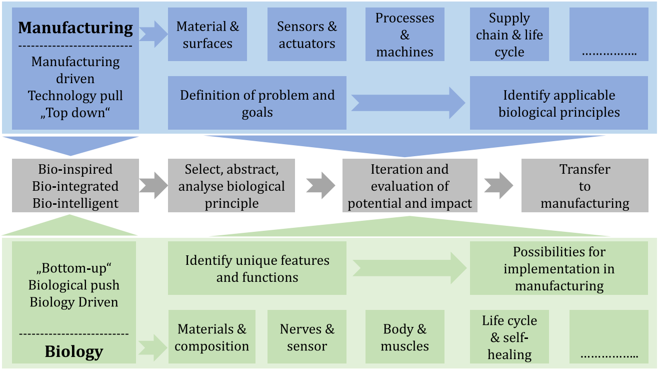

Fig. 5. Concept of manufacturing pull and biology push [49,72].

Since there is more than one potential solution from nature for most problems in production engineering, the matching process must be designed in order to find a global optimum from the solution space of biology. Several approaches as shown in Fig. 6 are compared in [268].

Scientific papers as compiled by biologists over the past centuries contain substantial knowledge about the way natural evolution in flora and fauna has conceived solutions for often complex problems, allowing the described species to more efficiently thrive under the boundary conditions imposed upon them by their respective environments. The vocabulary utilised by biologists to describe the solution concepts, the underlying physical principles, the working principles, the embodiment details and the resulting functionality, typically substantially differs from the terminology used by designers to describe an engineering problem. A simple query system using natural language processing (NLP) techniques such as stemming or lemmatisation thus cannot be effective to mine the available scientific biology literature as an available resource. In [216] a number of approaches to overcome this hurdle are described. Thereby, the scalability of these methods and solutions is still a concern since mining the large databases of scientific publications still requires interactive preprocessing instead of being able to use automated methods. The works [242,243] and [268] present methods to overcome this barrier by using dimensional reduction techniques, which are statistical methods from machine learning, in the vocabulary used in both the biology and the technical domain. Different mapping techniques then allow to project a query emerging from an engineering problem domain into the vector space representing the repository of the considered biological publications. Structured clustering of the matches found in this solution space enables the avoidance of high redundancy and information overflow problems, thus providing a selection of publications describing potentially relevant species offering solutions to the engineering problems to be solved [268].

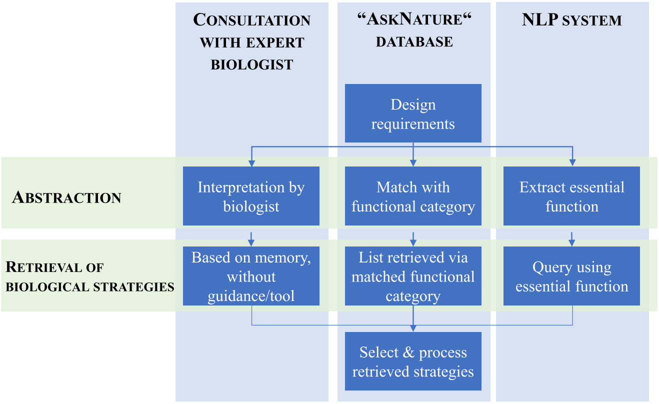

Fig. 6. Different matching methods for manufacturing problems and biological solutions according to [268].

2.2. The transformation process as an overall system

Conceptionally, biologicalisation is a transformation process having the dilemma of a technology-driven approach with a strong mission orientation. By doing so, on the one hand, it aligns with well established technological concepts (biotechnology, bionics etc.). On the other hand, biologicalisation itself contributes to larger mission-oriented economic concepts like circular economy and the bioeconomy which is built on a broad spectrum of technologies. Especially against this mixed background, which is both technology-driven and mission-oriented, the resulting solutions must serve all three dimensions of sustainability - social and environmental, and also economic.

Therefore, cross-disciplinary exchange in an open-minded way needs to be intensified taking into account not only the knowledge and achievements already present within the different disciplines but also their distinct research interests [4].

For promoting cross disciplinary interactions, a common mission based on a common perspective should be defined. One of the most urgent fields of activity is the establishment of an environmentally sustainable society as this factor is the foundation for a high quality of life and a prospering economy [99]. In this context, [121] discusses the biological transformation as a pathway for environmental sustainability presenting a perspective in which the transformation of manufacturing systems offers disruptive opportunities for a symbiotic alignment of the exchanged substances between the biosphere and technosphere, see Fig. 7. Here, biological principles, technologies and methods add functional units (e.g. damage remediation or CO_2 sequestration), reduce the resource consumption and lower the emissions to the biosphere, having the vision of a zeroed environmental impact of manufacturing systems.

Therefore, biologicalisation may take every element of the manufacturing system (starting from products up to far reaching factory networks) into account independent of its substance and nature [49,121]. By increasing the connectivity of the energy and material flows within the system, the synergy between the biosphere and technosphere and by this the effectiveness of the manufacturing process may be enhanced or even a positive environmental impact may be achieved [105,120]. Based on this, the biologicalisation process can for example foster circular economy in all its facets by providing new recycling or sorting processes (see Chapter 1). However, in nature circularity

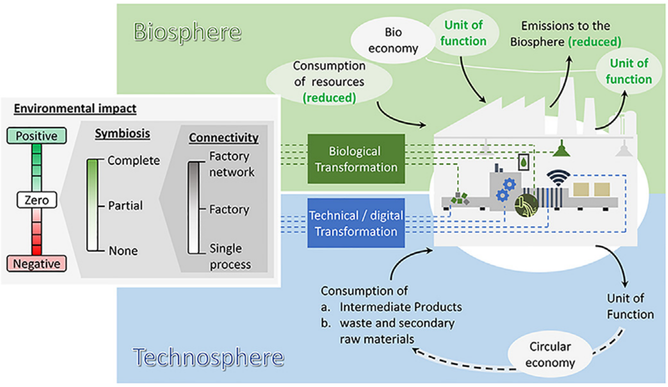

Fig. 7. Interaction of a biological transformed manufacturing system between the biosphere and technosphere according to [105,121].

takes place on a large scale, by many interacting systems, so the same systemic thinking must take place when applying biologicalisation.

3. Communication and cognition

Communication, in terms of interaction and cognition, is a central systemic prerequisite for harvesting the potential of biologicalisation. Interaction and cognition are two of the fundamental properties of living nature. In the biosphere, communication can be intracommunication within an organism or intercommunication between several organisms. On a systemic level, this distinction shows a high level of similarity to communication forms in the technical spheres. For example, intracommunication occurs within one machine, which means that for instance the control algorithms are set up according to the model of nature [172]. A next level arises summarizing any kind of communication between multiple machine tools or production systems. Exchange protocols exist with limited functionalities but still giving headroom for further developments [188]. At this stage, it is already becoming clear that the technical realisation of biologicalisation needs to be built upon the principles of Industry 4.0, e.g. the interconnectivity of IoT. While intercommunication means communication of two same species, trans-organismic communication focuses on the interaction between different species, for instance different bird species [264]. From the point of view of biologicalisation, this form is significant, since numerous interfaces are inherently evolving or newly emerging, like for example:

- Human-Machine Interface (Chapters 6, 8)
- Taking data from biosensors and transferring it to technical ICT systems (Chapters 7, 8, 10) and
- Control of biological processes, etc. (Chapters 4, 5, 8, 10)

On the pathway towards living manufacturing systems, an effective and efficient communication between all system elements including the human at the centre of the loop will be the key element, and states an integral part of human-cyber-physical systems to arise to highly productive environments [32]. In this regard, biological systems, especially humans, can serve as a blueprint, but in the first instance need to be understood, secondly translated to a model and finally integrated into the technical systems.

In order to cope with the emerging complexity of production systems the cognitive abilities of the human have come into the focus in context of biologicalisation. The leap in complexity results from the increasing number of possible solutions, the growing dynamics as well as the interconnection. But also increasing requirements strongly contribute to the complexity leap as more and more influences need to be taken into account. The cognitive systems engineering as described and discussed in [123] and [270] has to deal with the systems' complexity, for instance in manufacturing processes and a design for simplicity towards the operator. In [123] the approach of a joint cognitive system integrating operators and machines also allows for redistribution of the tasks. Former experiences of leaps in complexity, such as the introduction of cyber-physical production systems, showed that it is increasingly necessary to consider complexity as a relevant influencing variable in production systems, and cognition becomes decisive [207].

Cognition as a collective term for conscious and unconscious processes as well as structures related to the reception, processing and storage of information in living beings as structured in [2], will be a central building block to deal with this emerging complexity. Development stages of how cognitive transformation necessarily builds upon digital transformation is shown in Fig. 8. Humans as cognitive beings are thus able to process (thinking, decision-making) a stimulus coming from outside by receiving information (perception, attention) and to transform it into knowledge (thought patterns, memory) or to perform an action (behaviour, language). Conversely, cognitive processes affect human behaviour by making plans (thinking), making decisions or judgments, or generating ideas for a solution to a problem (creativity). Moreover, this is not limited to specific problems or the single individual: Humans have the ability to adapt their knowledge to other, similar problems or to adopt ways of acting on identical problems from other people and to pass on their knowledge to them.

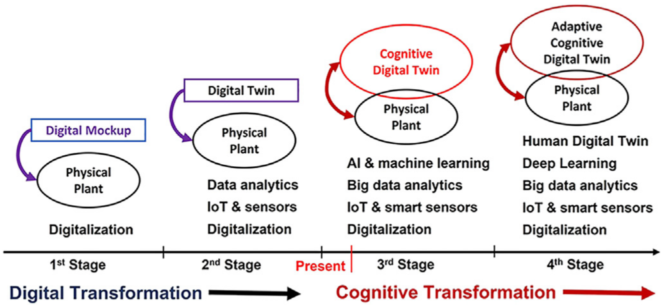

Fig. 8. Development stages of cognitive transformation [79].

Transferred to cognitive technical systems, this means that they are able to take in digital information from sensor data and networks, derive conclusions and actions, and execute them (partially) autonomously. This includes in any case:

- Perceiving: The basis of the adaptivity of current systems is data about the process, the current state of the product, the means of production and the environmental conditions, which are obtained via sensors.
- Processing: For the realisation of self-optimizing processes, networking of controls from the field level to the enterprise level is essential in order to significantly expand the information content for decision-making.
- Understanding: In this context, understanding means automatically analysing machine, plant and process data and linking it with other data sources for trend analysis and optimisation of value networks. Machine learning methods provide extensive options for this.
- Strategy development, deciding and acting: The goal is context-adaptive procedures and decisions based on a link between statistical learning methods and large knowledge representations. The state of development can be represented by a stage model (comparable to Fig 8). To reach the next level in each use case and linked production process, close cooperation between process specialists, automation and IT experts, and specialists in the field of AI is required.

The transfer of knowledge gained during the life cycle to subsequent product generations is defined in [68] as “Gentelligence”, which means a system with genetic and intelligent properties. It enables the transfer of biological principles such as technical inheritance to provide information for new component generations and lifelong learning. The use of gentelligence in manufacturing opens up new possibilities for planning, control and monitoring of production processes [92].

The performance of biological systems is then to combine information from different channels to first gain a complete image of the situation with internal and environmental components, then derive a decision from this. In [260] the concept of a biointelligent SLM machine with the major channels of information is presented. Communication with a fleet of machines and communication with human operators together with a modern self learning expert system based on ontologies for storage and inference is shown. The communication with human operators imposes some requirements: The information given to the machine is a mere instruction, information is normally unstructured and incomplete. The system therefore needs elements for gaining understanding, needs to combine new information with older information, needs plausibility, checks etc. Furthermore, humans do not want to get bored by standard questioning. Therefore, human machine teaming is explored and exposed in [261]. Different protocols for machine-to-machine communication exist. Also, the concept of federated learning is discussed and exemplified for thermal compensation. This is elaborated in more detail in [224], where a cloud-based learning approach is proposed for a phenomenological thermal compensation model.

As pointed out the trans-organismic communication is key part of biologicalisation, in a consequence human-machine communication will be leveraged to a novel level of mutual understanding. Control by gestures instead of keyboard and mouse is discussed for instance in [52,180]. Speech recognition which has grown in maturity in the meantime will enable a more intuitive communication with the machine. Direct coupling of machine controls with the nervous systems of humans is a necessary step for the development of bio-integration and is discussed in Chapter 8 as an application of bio-interaction. Furthermore, virtual reality and augmented reality (AR) developments help humans experience the physical reality of the machine, by making magnetic fields, wear states, and error sources visible or audible for humans, which means that translators to the senses of human operators are developed [140,200]. Already today AR is frequently used in the maintenance of complex production systems [166,205].

The machine will become easier to set up and use for the operator. The communication will become more adapted to the intuitive communication of humans. This means that from the information uptake and processing the machine develops similar behaviour patterns to humans.

4. Self-monitoring

Self-monitoring, or as used synonymously, *self-sensing* is defined as the basic function of manufacturing systems to capture the data and the critical information from the environment, the physical process and/or the production system involving products, quality, materials, machines, tools, etc. [196]. While self-sensing as it is used here ends with the captured signals that may be transformed into electrical signals, self-monitoring on the other hand has a component of data processing and preparation for decision making, strategy development etc. The cognitive machine then needs a self-*deciding* function for data-driven decision making in manufacturing, including identification, collection, communication, analysis, sharing, retrieving, and learning. This function solves certainty and indeterminacy questions in the manufacturing systems to achieve autonomy and precise decisions, which are based on Big Data, including historical and real-time data [196]. Finally, the actions taken require *self-adaptivity*, the function to change the system based on self-monitoring and self-deciding.

Machines are becoming increasingly complex and integrated and will perhaps become difficult or even impossible to be debugged or maintained at a reliable level. The Smartface project of VW [31] might serve as an example, where the assembly system is controlled by the product. The assembly line reconfigures itself according to the production program, which means that a service person may have to interact with a different assembly line every day. The topic of reliability and maintainability (RAM) is a critical topic in modern manufacturing industries and the central goal is to increase autonomy. Self-monitoring requires the exploitation of as many signals as possible that are produced within the control systems, which must analyse a selection of them accurately. But it also requires additional sensory input, which itself introduces possibilities of failure and needs to be treated as the myriads of sensors in a human body with plausibility checks so that sensor signals that fail can be muted and their information be generated by observer models from remaining sensors. The robustness of self-monitoring systems is also discussed in [201], for instance, requiring that sensors must be capable of detecting any exceptional circumstances in neighbouring sensors. This means that the detection coverage must at least overlap between different sensors. Complementarity and redundancy must be carefully balanced to gain maximum information about the system and its environment, and maximum coverage of failures under a maximum number of possible states of the monitoring system and machine states. This requires a completely new approach to the setup of monitoring systems. Self-monitoring requires further diagnostic tools and a cognition system over and above the sensors, according to [43,201]. The term *self-engineering system* is introduced in [201], which has self-monitoring as its important prerequisite. This is further demonstrated and elaborated in [43], where the self-X-terms for the monitoring branch are introduced as follows:

- Self-diagnosing – A system which can identify the cause of a fault in the system. The findings of the system can inform further responses, but a self-diagnosing system does not have a response action built-in.
- Self-modelling – A system which can simulate system performance or behaviour and normally provides a basis for a system to decide on a solution or action. This is often used in
- robotics.
- Self-evaluating – The system can perform assessments and make judgements about itself using the resources or information available.
- Self-inspection – The system can perform checks or investigations on its internal states. Self inspection can involve comparison to an ideal or target state.
- Self-awareness – The system knows current and previous states.
- Self-testing – A system can monitor or observe its state and recognise when a fault has occurred.

Monitoring in terms of observing everything available helps reduce the chances of missing degradation or failure. However it becomes expensive and complex. The decision has therefore to be made which components of a system shall be monitored and with which effort. The field sensors, cameras and microphones, which are typically also used by biological systems, gain in importance where increasing amounts of information are required [258]. The term *Bio-optics (subset of bionics)* refers to optical components that mimic either living optical systems or biological systems used to control light [171]. Field sensors are capable of detecting time and space (direction and phase) and resolution, and contain frequency and volume information. The signal content is thus extremely rich, but the filtering of the right information requires sophisticated mathematical or AI tools, which involves a broad field of bio-inspired solutions, as shown for instance in [213], and [103] for AE sensors and microphones. A survey on acoustic monitoring is presented in [258] and an overview on process monitoring can be found in [228,229]. Both of these references and also [215] show the vast opportunities that can be gained from AI evaluation of sensor systems and of any sensor fusion approach. Further, bio-inspired sensors are gas sensors calibrated on specified chemical substances, which is for instance demonstrated in [159] for the detection of overheating in grinding. The monitoring concepts are described in a stage-like approach and are shown in Fig. 8.

Fig. 9 shows that data capturing is only the starting point of the data chain ending with real influences on the system by self-X (also compare Chapter 3). Important and often bio-inspired is the feature extraction, using different kinds of sensors combining them in mathematical functions and transforming them into the frequency domain. Fig. 10

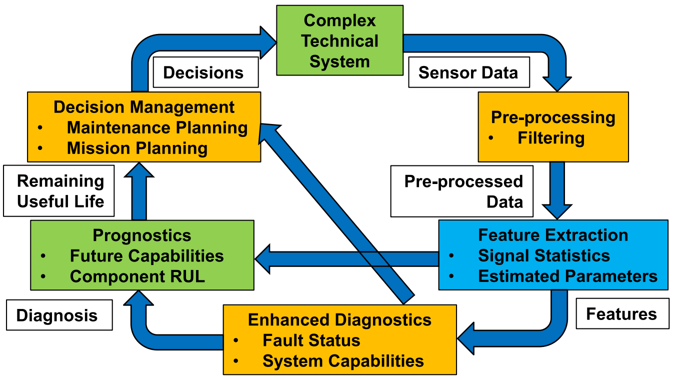

Fig. 9. Monitoring cycle [201].

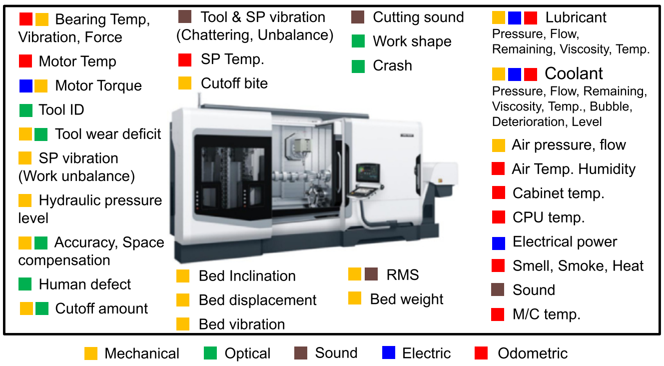

Fig. 10. Monitoring on machine tools by DMG Mori Co Ltd [209].

demonstrates the sensor coverage on a milling machine being composed of signals from the drives and inverters, the measuring system and the control system, which are in any case available and additionally installed sensors. The possibilities of feature extraction and anomaly detection are completely underutilised in today's machine tools.

In [285] a sensor network for the thermal compensation of machine tools is introduced for self-monitoring and self adaptation to enhance the accuracy. Different temperature sensors are distributed over the machine as shown in Fig. 11, which measure the environmental conditions as well as internal machine temperatures.

The temperature signals are clustered for an input selection and fed into a phenomenological compensation model, which is adapted to different external and internal situations. In case of strong imbalance of the signals in time or from each other the cross checking is done by probing an artefact at the expense of some minutes of production loss. This is automatically triggered and so the autonomy of the system is safeguarded, which is an example for a system capable for self-inspection.

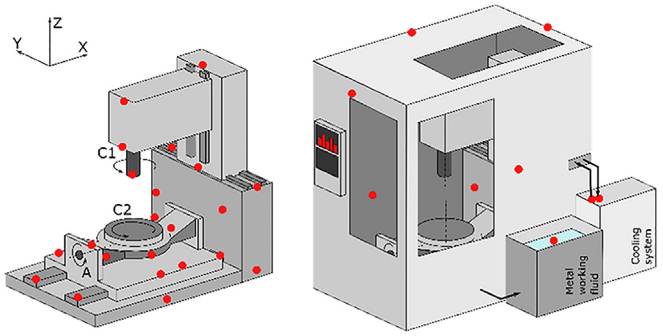

Fig. 11. Temperature sensor location for self adaptive thermal compensation of a 5-axis milling machine [285].

Sensors integrated in materials as discussed in Chapter 8 are used for structural health monitoring in case no characteristic failure mode can be foreseen and a distributed survey is required.

5. Self-healing and self-repair

5.1. General considerations and terminology

An important advantage of biological systems over technical systems is the handling of exceptions that occur from the outside or internally. Increasing the autonomy of technical systems is the driving force behind adopting procedures from nature. As flora and fauna have a huge portfolio of different strategies to regenerate their functionality, they are a valuable blueprint for inspiration for technical systems. Nevertheless, it is not useful to copy the strategies and mechanisms of nature, as the time scales are completely different. This holds true for development (evolution), growth and also healing. In addition, the materials and the growth and development principles are different.

A principle of nature is composition from smaller sub-systems as the building blocks (cells). According to [160] this principle is also the basis for the reorganisation, repair and healing mechanisms during operation. It is also the underlying principle for any management of defects, for instance in relation to all the strategies of crack stopping and crack scattering. In the technosphere shorter time scales prevail, which excludes the utilisation of buildup (growth) from elementary building blocks and subsequently requires different approaches for self-healing and self-organisation.

[43] introduces the term *Self-engineering (SE) System,* which utilises techniques such as self-healing, self-repairing, self-adapting and self-reconfiguration to enable a system to respond autonomously to a loss or potential loss in its function. In [44] examples of bio-inspired SE systems are presented and analysed with respect to complexity. Five design rules for bio-inspired SE-systems are presented. The complexity of SE systems is analysed in [42].

SE-systems have four key characteristics. They must:

1) restore or partially restore lost functionalities
2) have built in health reserves which are not added in case of failure from outside
3) avoid maintenance and increase life time
4) have autonomy, i.e., do not require human interaction

Fig. 12 introduces a landscape of self-X-terminology where the terms are conveniently compiled albeit in a reasonably unstructured manner. A taxonomy extracted from the literature distinguishes the terms self-repair, self-organisation and self-healing. Whilst self-healing takes place at the material level, self-organisation and self-repair arise at the component level. Self-repair uses spare parts provided from outside, whereas self-organisation uses inbuilt redundancies, which then coincides with the structuring proposed by [22] and summarised in Fig. 13. Self-adaptability has been added as a fourth element of self engineering, because it provides a system which had not been previously present, while the others restore the functionality. In this respect also the term cognitive adaptability coined by [79] but mostly used for production programs also needs to be considered for machines, emphasizing the automatic strategy development. Fig. 13 provides a process chain for self correction and the link to self-monitoring presented in Chapter 4. Detection of functional loss though happens in the field of self-repair, often without real awareness of the system, namely at the level of material structural elements. For instance a crack directly releases a healing agent. Self-healing systems dealing with unforeseen failures require a large array of sensors in order to allow for the neces-

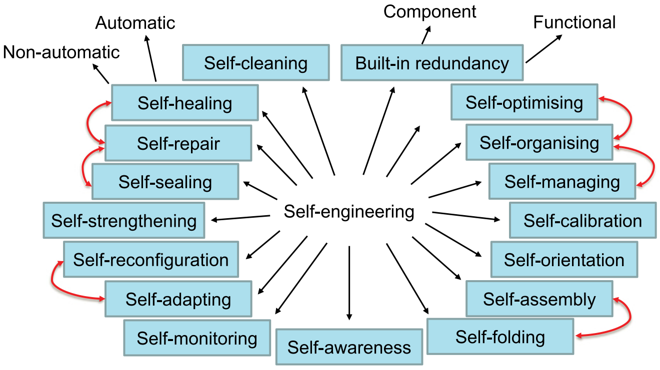

Fig. 12. Structure of self-engineering [43].

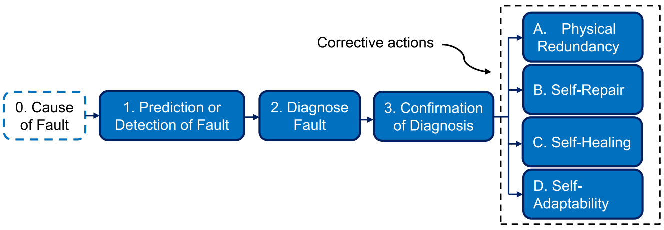

Fig. 13. Process chain from fault detection to corrective actions [22].

sary cognitive capabilities to detect disturbances and unwanted behaviour. [100] gives an overview of appropriate monitoring approaches as enablers for self-healing methods in machine tools.

The different aspects of self-repair and self-healing are also outlined and structured in [89]. The publication also provides a survey of self-healing in different fields, like self-healing electronics, self-healing materials, self-healing and self-repairing mechanics, self-healing MEMS and self-healing robots.

A stem cell-like approach is referred to, where pre-manufactured elements are finalized for the individual function upon request.

An example of a simple self-repairing system would be the exploitation of the ability of robots in an assembly line to repair neighbouring robots, for instance exchanging drive motors, sensors, etc.. Autonomy over time is realised through the provision of spare parts based on self monitoring, RUL (remaining useful lifetime) estimation and the resulting request for exchange. Swarms of robots that are capable of reconfiguring themselves according to changes in their environment and changing tasks are proposed by [150]. The robots have different tasks and are capable of reproduction, whereby larger robots assemble smaller ones.

Reconfigurable systems contain major elements for self-repair. However, although typically human interaction is required according to [33], nevertheless systems with self reconfiguration capabilities exist. Functional elements can be added to take over deinstalling and subsequent reinstallation of damaged elements.

While in self-repair systems a repair occurs as a response to a failure leading to damage or loss of function, an SE system can also take preventive action before the failure occurs and can at minimum offer a strategy for automatic preventive maintenance.

Strict redundancies are rare within biological systems, if they exist at all. All components are always used and are not idle until the failure situation occurs. Real redundancy is observed in nature especially with regard to reproduction. The conservation of species is ranked higher than the survival of the individuum. Natural systems typically use all available means and where loss of functionality arises, reorganise themselves such that necessary functionalities can still be fulfilled, albeit with less efficiency. Redundancy is only realised by functional elements that additionally take over the tasks of failed elements. Different variants of redundancy can be imagined and are described as a taxonomy in [43]:

- Component redundancy – identical components are available to fullfill the function
- Functional redundancy – the same function typically with less performance can be performed by other components in cases of failure.
- Active redundancy – different components share a function; if one (or more) is lost, the others maintain the function.
- Partial active redundancy – various system functions are maintained by all components or materials and can be maintained even after some components are damaged.
- Passive redundancy – spare components and materials are inactive and can be activated to replace those that fail.

Exploiting partial redundancy and reaction to failed joints or loss of extremities in robots that can adapt to their situation are shown in [62]. The demands for resilience towards disturbances and the possibilities of failures require inbuilt redundancies or health reserves, which means that each failure is followed by a redistribution of functionalities such that the main functions of the systems are secured as much as possible. But each failure / disturbance creates a loss in functionality and a degradation of the health of the system, but retains the main function in analogy to biological systems. In the end an external interaction is inevitable to re-establish the full functionality.

Fig. 14 shows the retained functionality after the healing cycles. This approach was developed in [61] for self-healing, but is also applicable to self-organisation. This demonstrates different approaches for the health reserves of a system and distinguishes between 100% recovery in the first failure cycles $f_b(H)$ against only partial recovery from the beginning $f_a(H)$. Furthermore, as metric for cumulative healing a life cycle healing efficiency L_H is introduced as ratio between the areas below $f(H)$ and bounded by $\eta_h=1$. It is nevertheless important for sustainability considerations to estimate the expenditures necessary for the self-healing or the self-organisation approaches. A mapping of damage types to possible restoring mechanisms was introduced by [89].

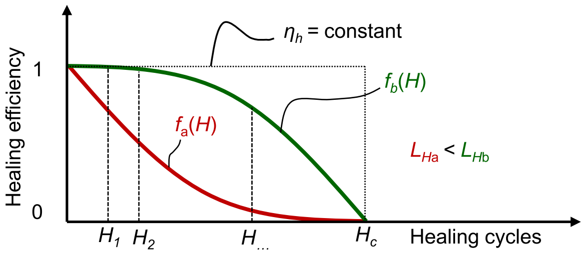

Fig. 14. Healing efficiency and life cycle healing efficiency [61].

Wells [262] provides an analogy beween a biological immune system and quality assurance in the assembly line of sheet metal structures. Antigenes to be counteracted are parts which have a lack of dimensional accuracy. The concept of an *Engineering Immune System (EIS)* inspired by the human immune system was developed in [146] and is closely related to SE. An EIS is designed to improve the robustness and resilience of the system, and it can use automatic control in response to disturbances to return the system to a stable state. The approach of a resilient and self-maintaining system seems like a promising approach for future research.

Systems are defined as self-organizing systems when they have the capability of adapting to changing conditions by the selection of different available elements or different process sequences to be used. An extension of self-organisation for the design of electronic circuits is presented in [24]. Faulty lines are detected and eliminated, and an alternative path which fits with the functionality requirements is sought, as presented in Fig. 15. This behaviour is described in Chapter 6.

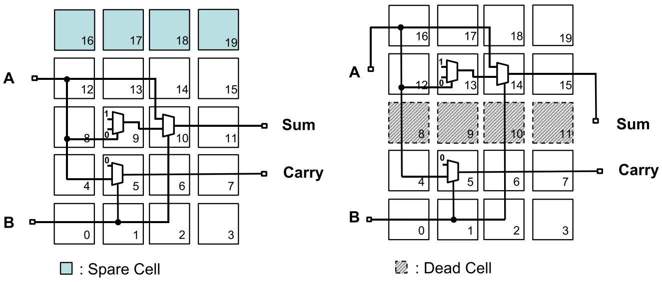

Fig. 15. Self-organizing electronic circuit [24].

5.2. Self-healing

5.2.1. Self-healing systems

Systems are able to reconfigure, identify and repair themselves autonomously following faulty behaviour, failure or error. In biological systems self-healing is necessarily combined with the living nature of the system.

Systems fulfilling the following characteristic traits can be defined as an actual self-healing system:

- a priori unbound disturbance and solution space,
- retention of a functional state not entirely dependent on redundancies,
- ability to reconstitute an original desirable state, and
- distinct cognitive capabilities allowing intrinsically or heuristically developed solutions to a previously undefined disturbance.

A strong body of research has been published on self-healing for materials and structures, comprising some excellent review papers [43,251,271] and also several books on this topic providing a systematic overview over the field, [67,94,106,240]. A number of different applications of self-healing are discussed in [43] together with their technology readiness level (TRL). The related principles can also of course be used beneficially in manufacturing. A review of bio-inspiration in the materials sector for self-healing is presented in [45]. They show how cells process environmental signals and transform them into properties and functions of the materials. This biologicalisation of materials provides an insight as to how cells can be engineered to produce precursors of the material used for healing and an overview of the resulting self-healing mechanisms. They also show that not only the replication of known materials but materials with unique properties arise.

Self-healing of materials has been reported on in literature for ceramics, especially concrete, for polymers and to a lesser extent also for metals. *Self-healing materials and Self-repairing materials* are defined differently for different materials, and sometimes used synonymously (and contrary to the definition used here).

A condensed terminology is shown in the morphological box of Fig. 16. The trigger for healing can be extrinsic or intrinsic for healing initiation (extrinsic – coming from outside and intrinsic – coming from inside the damaged area itself) [211]. While internal triggers operate on a local basis and thus do not reveal the self-repair action to a monitoring system of the machine state, external triggering requires a self-monitoringapproach including sensors, data processing, fault detection, strategy development, and communication. For ceramic materials a taxonomy is also in use that distinguishes the materials provenance, namely autogenic and autonomic. The first means that healing material is directly embodied in the material to be healed, while autonomic means that additional material is added into the microstructure for the healing of damage [133].

Self Healing

Healing trigger	Extrinsic external	Intrinsic internal	Mixed intrinsic material, reaction with water and oxygen		
Healing material	Extrinsic autonomic	Intrinsic autogenic			
Healing reaction	Physical (electro)	Two components	Chemical else	Bio-chemical	
Base material	Concrete	Ceramics	Polymers	Reinforced plastics	Metals
Provision of healing material	Microcapsule	Microcapillaries	Microstructure	Microvascular	
	Environment	Mixed environment/matrix	In situ material		

Fig. 16. Morphological box for self-healing of materials.

It is pointed out in [183] that self-healing only can be initiated if total consideration of the second law of thermodynamics and the principle of minimum free enthalpy in equilibrium are fulfilled, as this directly corresponds to a degradation of health reserves. To enhance the self-healing efficiency for multiple healing cycles a transportation system for bringing the healing agent to the place of action is required. The microvascular systems for this purpose are directly inspired from the biosphere.

For polymers 2-component healing is frequently applied, requireing a 2-vessel system as shown in Fig. 17. The vessels are made of hollow fibres which fracture with the developing crack and release resin and hardener into the crack space. Different solutions are found in [108,144,147,164].

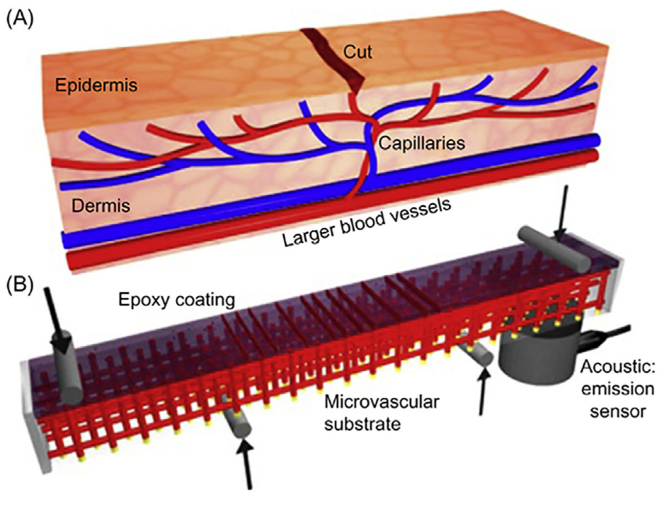

Fig. 17. Microvascular system to transport the healing agent [164].

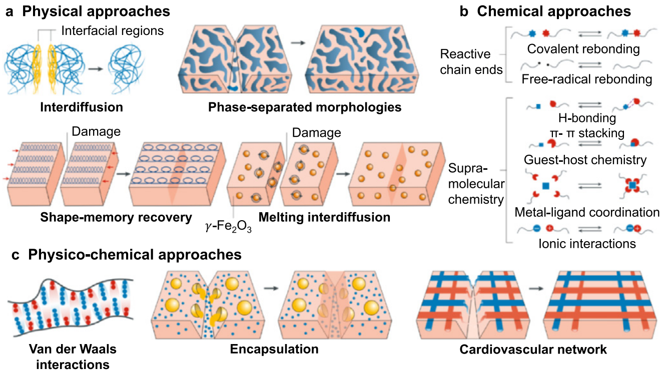

Fig. 18. Rebonding mechanisms in polymers according to [251].

Different rebonding mechnisms for polymers are shown in Fig. 18, which allow them to be classified as smart polymers according to [237]. [46] and [280] distinguish the healing mechanisms as shown in Fig. 16. A limitation of healing efficiency is also that typically the self-healing agents are capable of curing the matrix, but the self-healing of carbon fibres cannot be found in the literature. Self-healing of fibre reinforced composites is shown in [135] and promises success when healing starts already at the early stage of damage initiation [135].

Due to their brittleness, damage and cracks are inevitable in ceramic components. With the migration at high temperatures of the composing elements or elements from the environment, ceramics offer the possibility of generating new phases with volume augmentation. This can be used for closing cracks as shown for one example in [246]. [281] presents a good overview of self-healing routes in concrete, which already exists in industrial applications. Of particular interest here are autogenic reactions and reactions utilizing material from the environment such as water, oxygen and CO_2. Healing approaches based on microbial actions are discussed for different materials. In some instances, biological systems can be directly used for manufacturing purposes. This is the case of biomorphic mineralisation, which is a technique that produces materials with morphologies and structures resembling those of natural living organisms by using bio-structures as templates for cross-linking, reported by [60]. Especially for concrete, a system was proposed in [66], where dormant bacteria are embedded within the concrete structure. Upon cracking, oxygen activates them operationally during which they produce the healing material. Also [8] addresses crack healing by biomineralisation, where micro-organisms provide the healing substance by transforming material from the crack surfaces as shown in Fig. 19. Compared to other methods of material production, biomorphic mineralisation is facile, environmentally benign and economical [82].

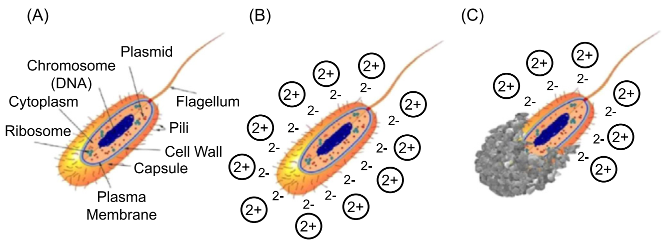

Fig. 19. Bio-mineralisation: negatively charged outer hull of the microbia attracts Calcium [8].

As stated in [43] self-healing in metals is much more difficult than in concrete or polymers and always requires thermal input. A survey of self-healing in metals is found in [240] for Al-Cu-Mg-Ag-alloys [154].

Surfaces provide the interface of a system to the hostile outside world. In biological systems they always have important additional functions as collated by [161]. Also in the technosphere, surfaces are especially prone to wear, corrosion and deterioration. Although the biological system is capable of re-establishing the surface, in the technosphere the growth of structures has not yet been realised. This means that the wear of the surface needs to be such that the same geometry required for the function is preserved. Solutions to this challenge are not yet available.

The release of an anticorrosive agent upon change of pH value from microcapsules is described in [77]. A possible application case for self-healing compensation of wear on surfaces inspired by biology was published by [183]. Sealing and resealing of surfaces is discussed in [158] and [176].

Deposition of material at the right place to keep gap sizes in i.e. guideways and bearings might be a possibility in the future for to counteract wear. Approaches with a lubricant bringing the material precursor and depositing it using localized electro-discharge deposition are under discussion.

5.3. Self sharpening tools

In manufacturing processes tool wear severely limits productivity and autonomy of machines, wear of functional elements for biological systems limits the lifetime of the elements. In the biosphere as well as in the technosphere approaches are taken to cope with this challenge. Tool exchange or stabilisation of the wear profile of the tool are the approaches that also prevail in the biosphere. Stabilisation in the utilisation of graded materials is a direct inspiration from the beaver tooth and is shown in Fig. 20. This was developed by [117,118,247,248] for the cutting of CFRP (carbon fibre re-inforced polymers). While the profile of the tool remains unchanged the regrowth of materials is emulated with the repositioning of the cutting edge by the CNC drive.

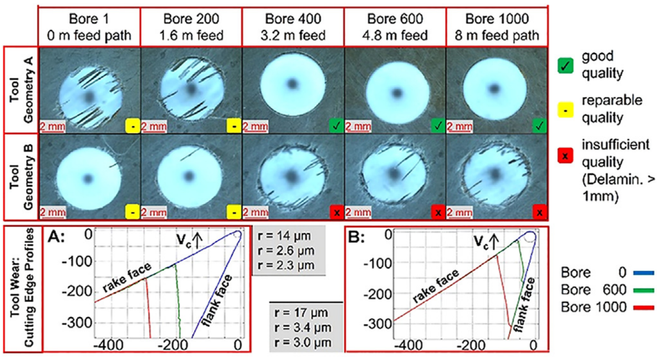

Fig. 20. Self-sharpening tools with cutting in CFRP [248].

The shark teeth approach shown in Fig. 21c is widely used in industry as tool changer for geometrically defined cutting edges and for self sharpening of grinding wheels. Worn grains break out of the wheels and new ones become active in the process. This principle was proposed by [129] and [161] (also for tools with defined cutting edge geometries) and is presented in Fig. 21a, b, where hard cubic boron nitride particles break out and reveal new ones.

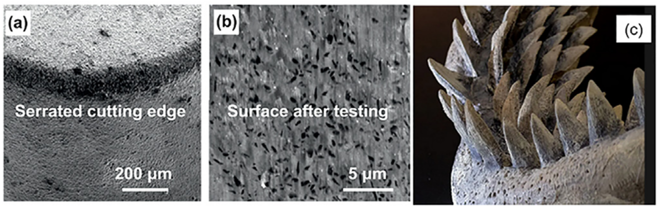

Fig. 21. Permanently stable serrated tool surface with the help of CBN – TiN composition of the coating by [161]. Regrowing teeth of shark example Megalodon [198] as biological analogue.

6. Bio-intelligent production organisations

Future production must be agile in reconfiguration, efficient in commissioning and during operation as well as resilient towards environmental conditions. It is currently under investigation in the two main branches "bio-intelligent production architectures" and "evolution inspired learning". In addition, the integration of the human worker plays a significant role in living production organisations.

6.1. Biologically inspired production architectures

Nature masters agile adaptation to specific tasks. Particularly, its flexibility is interesting for production architectures. One example for transferring biological principles to production architecture is cell-inspired factory layouts. Fig. 22 shows a factory layout which concentrates immobile production sources in the centre – analogous to a cell nucleus. These could be large forming and casting machines or rolling mills. All other production resources (resource input, energy supply, cutting and assembly cells and shipping stations) are situated radially around the nucleus and are therewith more flexible in quantity (compare Fig. 22). This leads to an adaptability in throughput and process chains and makes the setup feasible for different manufacturing tasks, as is necessary in a cyber-physical matrix production according to [114]. Here, the analogy of a biological cell becomes visible, since they are also flexible concerning their task (e. g., muscle cell, skin cell) by, for example, numbers of mitochondria.

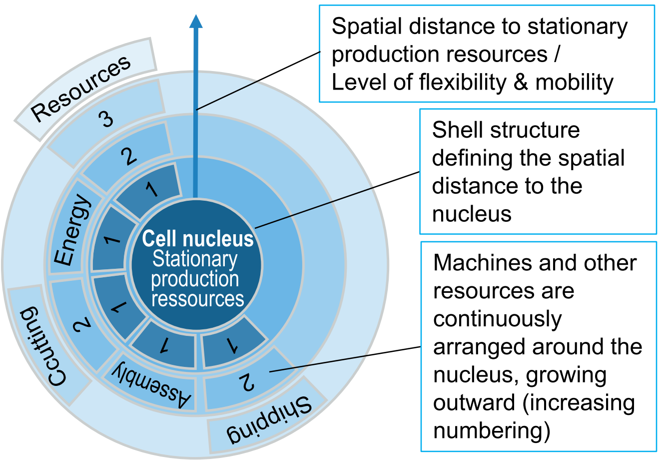

Fig. 22. Concept of a future factory according to [115].

Biological cell-inspired factories comprise different kinds of manufacturing units [115,231]. Besides stationary machines, a large number of highly flexible units such as robot cells (ressources 1–3 in Fig. 22), cutting machines (cutting 1–2 in Fig. 22) or adaptable storing devices enhance the setup. The stationary units can remain more or less unchanged when a factory layout is transformed, for example, to a more cutting-oriented process chain by adding cutting cells. However, the position and also the manufacturing or storage task of flexible cells can vary widely. To completely enable such a bio-inspired factory setup, several requirements need to be fulfilled:

- new design solutions for the overall layout (see Fig. 22),
- new approaches of power, air and information supply,
- new IT solutions in interlinkage and information distribution (compare Chapter 3),
- new optimisation paradigms in facility layout planning as well as production optimisation,
- new approaches of supervision and condition monitoring, as well as,
- a new paradigm of PLC programming.

The arising requirements are transferrable between the mentioned bio-inspired layouts and cyber-physical matrix production structures as introduced by [234]. A study [114] of the Industry 4.0 Platform, systemized these requirements and developed them into a capability maturity model, comprising 13 aspects. Main enablers for flexible but still efficient production architectures are:

- the basic structure of the production system,
- the design of the process modules,
- operational production planning and –control,

- the control of the process modules

followed by nine additional aspects in the fields of hardware definition and software enablement.

A main enabler of nearly all intelligent and bio-inspired approaches for future production is the digitalisation with focus to cognitive production as pointed out in Chapter 3. Self-description of the production assets including their capabilities and digital twins of production resources and products are topics that arose with industry 4.0 regarding constantly adapting architectures like for the cell-inspired factory or similar approaches as for matrix production.

Another role model that can be adopted from nature is the behaviour of animals in swarms and packs, comprising the idea that complex tasks are decomposed and segmented. Subsequently, a multitude of agents with self-description is capable of partially solving the tasks, leading to an overall sufficient result. The vision behind this swarm-approach is that by transferring swarm activities from a reactive to a cognitive manner, the swarm can develop from a swarm of hunted individuals to a collaboratively acting swarm as hunter.

Transferred to production a major emerging field of technology, with ample prospects, is Swarm Robotics, i.e., the design, construction, and deployment of large groups of robots that coordinate and cooperatively solve a problem or perform a task [70,150]. Swarm Robotics commonly takes inspiration from natural self-organizing systems as defined in Chapter 5. The collective behaviour of biological swarms is dependent on local interactions amongst members of the group. This is based on the repeated decision making of the individual, which, in turn, requires accurate and constantly updating information of the social environment (Chapter 3). Research questions currently being investigated are the hierarchical dissemination of intelligence in the swarm or pack on different levels, the information distribution and gathering as well as the development of an architectural model for this kind of approach [110]. The results are validated on use cases such as the manufacturing of large parts with small machines or the flexible and mobile transport of automobile parts by robots in a self-organized, dynamic, and workload-optimized manner. Furthermore, the assembly and manufacturing of large high-precision parts are addressed [110]. To date, a key challenge in the successful deployment of multiple robotic systems in technological applications is that of the autonomous data acquisition and decision making of the individual agent or robotic device. Ample research is focused on acquiring and applying related knowledge from living organisms (from Bacteria swarms, all the way to groups of apes or humans). One such example is the ongoing study of locust swarms (compare Fig. 23), a quissetential example of collective behaviour, in which laboratory experiments are complemented by computer simulations to generate testable hypotheses regarding the swarming mechanisms [10,11,70,136,137].

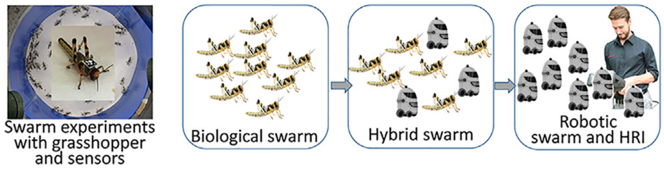

Fig. 23. Swarm investigation for organisation of manufacturing systems.

Based on this, there are many new possibilities for combining flexible production architectures with the agility of swarms as mobile autonomous machining units. Mobile machining solutions use autonomous machining units which usually possess a significantly smaller workspace than the dimensions of the workpiece [238]. Thus, they are temporarily positioned at or directly coupled to the work piece covering a limited area. Due to their usually small dimensions they can be easily repositioned, therefore being able to iteratively cover the whole work piece. The principle of mobile machine tools itself is inspired by biological counterparts and can possess different levels of mobility (Fig. 24) [241].

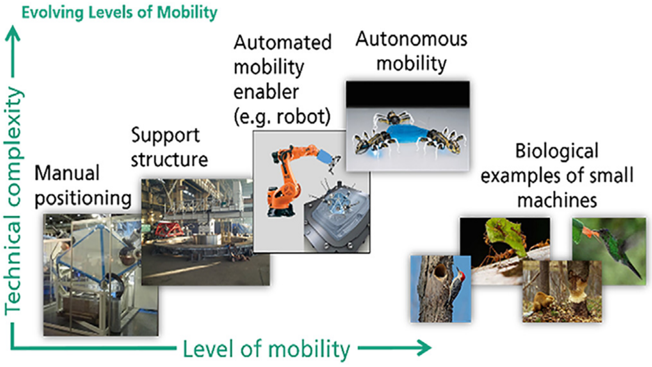

Fig. 24. “Biological small machines” and machine tools or systems with different levels of mobility and complexity according to [241].

While mobile machines originally were intended to be used as solitary manufacturing assets for (re-)manufacturing and maintenance operations of large industrial components, their basic principle allows for their use in swarm-like autonomous and cooperative machining operations deploying multiple units. This would allow for agile and resilient production strategies due to the given scalability in quantity and flexibility in time as well as location domain. Single machining units can be universal in their base structure, but dedicated to specific tasks via interchangeable process modules. In order to facilitate the use of mobile machines within a swarm manufacturing strategy, single machines have to provide four basic capabilities which are illustrated in Fig. 25:

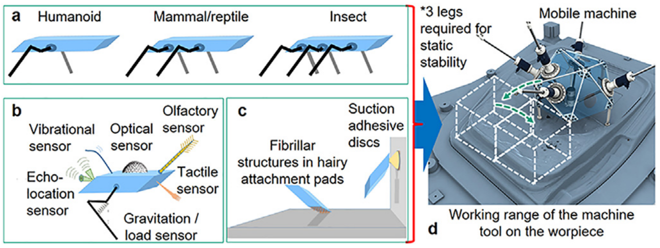

Fig. 25. Insect-based bio-inspiration for the mobile machine tool, a) stability and mobility, b) sensors and control system, c) mounting and adhesion, d) Mobile machining unit fixed on the large workpiece according to [241].

- Kinematics for autonomous mobility and adaptive interface devices enabling machines to move along and adhere to various work piece surfaces and geometries [241]
- Miniaturisation and lightweight design to ensure stable application of the machine, even in case of fragile structures [93]
- Smart self-calibration and self-orientation to navigate within the work environment and prevent collisions
- Self-awareness in terms of system capabilities in a changing work environment [93].

An according swarm must be able to coordinate, self-organize and allocate tasks (combined with location and time domain) to autonomous machining units to achieve a process, which has to fulfil the base requirement of suitability for production as well as consider aspects like:

- Minimizing continuous geometric features across segment borders to ensure high quality
- Detecting self-similarities of geometric features or tasks to minimize diversity

- Scheduling sequential and simultaneous manufacturing steps for maximum productivity
- Making efficient usage of space and ensuring a nearly uniform distribution of workload to the different entities

Research within the fields of computational biology, developmental biology, evolutionary biology, molecular biology, systems biology, and cognitive science has shown that regardless of the level of biological organisation, certain aspects of the behaviour and design of biological systems can always be found that promote their flexibility [27]. These aspects are mainly explorative behaviour, conserved core processes, weak coupling and invisible anatomy [27].

Some of the elements, like hierarchy or modularity, are frequently used in the design of current technical systems. Others, such as degeneracy and weak links, can be found rarely but their potential for enabling flexibility has not yet been widely recognized. For all elements, research is more in the early stages of understanding how these elements can be used to build more powerful and flexible systems of interacting intelligent agents. The goal of these developments is the establishment of intelligent, flexible and self-adaptable products as well as processes that lead to a new level of machine autonomy [27] All in all, there are a number of points of connection between production architecture and biology, but in this consideration primarily at the level of bio-inspiration. There are, however, further open points of connection that extend the consideration. Firstly, a production is again only one part in a superordinate system, such as an energy network. For this case of energy networks, there are approaches to applying the concept of biologicalisation [91], so that production approaches with flexible energy utilisation are also conceivable. Secondly, humans are an elementary component of a production architecture, which is why their role in the context of biologicalisation will be analysed below.

6.2. Human in the loop

Production organisations are per se living, as they are steered by human intelligence, and operated by a team of human coworkers. From this perspective, human-in-the-loop (HITL) is a middle course between full automation and complete manual processing. At each automation interval of this approach, a simple question must be asked: "Can a human add more value to this step?" If the answer is yes, then this step gets a junction for human intervention. The term "human in the loop" in artificial intelligence refers to systems that allow humans to provide direct feedback on AI-model predictions that are below a certain confidence level, so that the final decision is made by the human. This necessarily requires means of communication as described in Chapter 3. Furthermore, the human intervention can start at the training phase by labelling the data to give high quality training data. It can end up by testing and validating data through scoring the output to improve the model's performance. This feedback action to the AI model makes it smarter, more confident and more accurate. In the field of human-machine-interaction, "human in the loop" approaches give the collaborative tasks between humans and robots new aspects. Unlike the independent and fully autonomous system, this approach could be integrated into the robotic manipulation planner [197]. This makes the robot system completely flexible and fullfills the requirements of human-centred design approaches. Automated planning tools of the robotic system will make the first suggestion to subtask distribution between the coworker and themselves according to their pre-defined advantages in a collaborative task. However, the human operator can adapt and optimize the divided subtasks situationally. Some advanced approaches of "Human-in-the-loop", e. g. [47], propose a hybrid shared controller for assisting human novice users or even a partially automated process learned from modelled skills of human experts. In this case, the automation chain could interact with human users in two styles: it knows how to optimally control the system from the expert's demonstrations in the offline computation, or it assists the novice in real time based on the inference of the novice's skill level. Such approaches require modelling human behaviour and skill settings. [165] proposed neuroscientific models of human behaviour as a stochastic dynamical system. The human-driven models could be implemented for adaptive control of a robotic system in human-robot-interaction HRI tasks. [20] and [21] have gained a unique type of database which can be used for modelling the variance of human body motion and the mental states of the human during the interaction with heavy-duty industrial robots. This data aims to assist the human novice users during the planning phase of complex HRC (human-robotic-collaboration) applications considering the coworker-centred workspace design. In addition, it improves the human-centred cyber-physical systems by increasing the safety, efficiency and flexibility of the HRC systems.

7. Integration of biological materials

The utilisation of biological materials in technical systems has been practised by humans for millenia. Wood has been used for implements, tools and structures and natural straw and clay composites for building materials. More recently, the utilisation of natural and renewable resources has received increased attention, driven by the imperative to reduce anthropogenic impacts on climate change and in the search for new functionalities.

There are four different types of bio-integration:

- Direct utilisation of biological material in technical systems, e.g., biological materials as the main functional element in cutting fluids (section 7.3);
- Integration of biological and technical systems into a single system (Section 8.2);
- Living elements as the product of technical systems, such as the automated production of stem cells controlled with bio-inspired algorithms (Section 10).
- Utilisation of technically modified biological material (chapter 7)

Polymers started in the beginning of 20th century as modified biological materials initially used to imitate valuable natural materials, to develop into their sophisticated technical importance today. From that development, the borderline between biological materials, modified biological materials and artificial materials cannot clearly be drawn. Polymers can be biological like spider webs, mo-dified biological such as shellac, amber, wool, silk, and natural rubber that have been used for centuries, and artificial synthetics like bakelite, nylon, neoprene, synthetic rubber, and silicone. Bio-identical materials are discussed here, and bio-inspired materials are discussed in Chapter 9.

7.1. Integration of biological bulk material in technical systems

Typically, natural resources such as wood have greater randomness of properties than technical materials. Technologies to equalize natural products to enhance their reliability might be key success factors for their more intense utilisation and also as a contribution to capture CO_2 and store carbon for a longer time. It shall also be investigated whether in civil engineering an exchange of energy intensive products (concrete) with modified renewable ressources can be a valid option. Scaffolds from bamboo are frequently used in civil construction in eastern countries, for example, and more intensive utilisation of wood or modified wood as seen in Fig. 26 are under discussion today. Other biological materials might find beneficial utilisation in technical systems not only as structural materials, but to provide other functions as has been explored in [64] and [227] for lubrication as metal working fluids. It may be the case that silk, spider webs, other biological material and modified materials play a future role in manufacturing technology.

The mycelium of fungi has the property to grow over large distances and also fill hollow spaces because it comprises the filamentous cells of a fungus, and it is a very broad biological material class on its own, which is also able to react to certain trigger signals, making it useful for the interaction stage of biologicalisation. Several use cases and

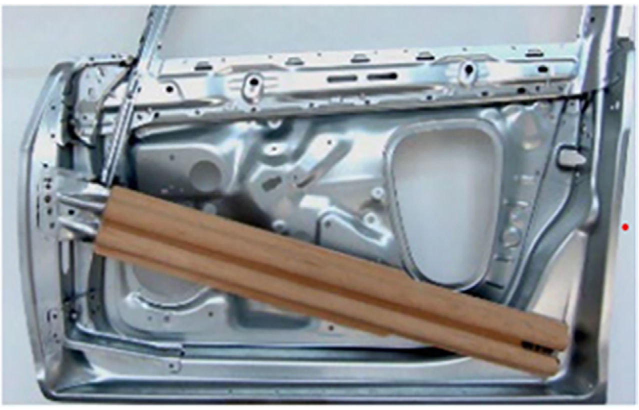

Fig. 26. Wood as construction material in automotive application [139].

industrial production methods for this material are examined in [111]. One research vector is to use the material as thermal insulation for the construction industry. For this purpose, the mycelium must have both high thermal insulation and fire protection properties which are provided by bio-based additives. Furthermore, the infestation of additional toxic moulds by other fungi must be prevented. Of course, this poses challenges for the production process, since normal mould protection would also hinder the desired growth of the mycelium. One solution is encapsulated essential oils. The second research vector seeks for possibilities of the mycelium to grow into moulds in a targeted manner and also to print mycelium 3D via the substrate. Furthermore, the possibility to introduce targeted local electrical conductivity into the mycelium by additives in the substrate to integrate conductive traces directly into a device is analysed. For industrial utilisation, regulatory issues also need to be solved as mycelia must comply with toxic limits in both the production and use phases, as well as be REACH-compliant [203], etc.

Micro-organisms, (e.g., bacteria) can be useful for different tasks at the molecular level and due to their large number are capable of providing significant benefits in production. Gluconacetobacter xylinus can be used for the production of zellulosis capsula with, for instance, some pharmaceutical contents [192]. Gentechnologically modified Cyanobacteria create hydrogen with sun light, which can be used for solar cells that directly produce hydrogen and are capable of self-repair and self reproduction. Shewanella oneidensis can generate Molybdenum sulfide in nanosize and monoatomic layers. This material can be used as superconducting material. Recycling of Co, Li, Nd and In from electronic scrap can be done by different kinds of bacteria. Also, bio-leaching of Cu and Co from meagre ores but especially from electronic waste achieved with the help of bacteria might become a breakthrough for circular economy [273].

7.2. Utilisation of biological materials for machining systems

In [167,227], a bio-integrated industrial breakthrough is presented to develop sustainable micro-organism-based (bacteria, yeasts, microalgae) cutting fluids for greener machining processes. The principal goal is to exploit the high sustainability potential of substituting oil-containing fluids with microbial-based fluids for machining, where microorganisms have an effective lubricating function. The expected benefits for the industry can be summarised as: (i) Machine tool building industry: increased sustainability of machine tools functioning with new microbial-based cutting fluids instead of conventional mineral-oil based cutting fluids. (ii) Industrial end users of machining processes: reduction of environmental impact and related costs for disposal of spent cutting fluids. (iii) Cutting fluid industry: market advantage following the development of new, highly eco-compatible microbial-based cutting fluids. (iv) Other industrial fields: any industry where microbial-based lubricant fluids may substitute oil-based lubrication can exploit the advantage of the associated sustainability improvement. (v) Green manufacturing: the sustainable bio-innovation impacts notably the flow of environmental waste with the goal of reducing and ultimately minimising environmental impact while also maximising resource efficiency.

In [227] *Spirulina Platensis*, which is a multicellular filamentous cyanobacterium (blue-green algae) consisting of an unbranched cylindrical filament of cells was selected in [63] for turning operations. Its employment is therefore fully sustainable regarding environmental impact and entirely risk free for human health [95]. For cutting AISI 1045 C steel with uncoated WC it performed equally well as oil-based fluids.

Two yeast strains, *Saccharomyces cerevisiae* and *Metschnikowia pulcherrima*, both of which are non-pathogenic and widely used in food and beverage industries, were selected for high-speed milling trials. *S. cerevisiae* was selected as a baseline material for the milling trials, since this strain has previously shown lower cutting forces and similar tool wear compared to conventional cutting fluid [167]. The yeasts were used as the primary compositional element in custom-prepared metalworking fluids (MWF) and tested in full-scale high-speed milling of a Ti6Al4V alloy with flood cooling delivery, representative of industrial applications [64].

It was shown that both yeast strains provided similar or better performance in terms of cutting forces, tool wear and workpiece surface finish compared to a mineral oil-based reference MWF. The results provide early-stage evidence of the significant potential to reduce or even eliminate mineral oils in metalworking fluids.

In [227] the implementation of a bio-integrated machining cell with on-site production of microbial-based cutting fluids with all ancillary equipment was conceptualized and is shown in Fig. 27. This concept combines production, regeneration of biological material as described in Chapter 10 and on-site utilisation, which is often required by living materials.

Fig. 27. Concept of a machine tool with bio-integrated cutting fluid on the basis of *Spirulina platensis* and generation / regeneration of the fluid on site [227].

8. Integration of biological and technical functionalities

While Chapter 7 deals with the integration of materials, this chapter is dedicated to the integration of biological and technical functions. These described technologies, products or materials have implications for manufacturing since relevant industrialised manufacturing processes and techniques need to be developed; and the materials/products themselves may find application in a manufacturing context, e.g. as anti-fouling coatings, sensors, or novel human-machine interfaces. The human in the loop concept is discussed in Chapter 6 and concerns living production organisations for which the human operator and supervisor play a significant role. *Bio-interaction* describes the kind of integration as a characteristic of manufactured systems that respond to biological changes in their operational environment [171], which might be the product or the biological subsystem.

8.1. Bio-functionalisation of technical materials

The combination of biological and technical materials can be employed to achieve new levels of functionality. One example is the bio-functionalisation of technical material surfaces with surface coatings inspired or derived from nature, to produce biological functionalities. The modification of surfaces with antimicrobial peptides (AMP) has been explored as a promising alternative to biocides. AMPs form a key part of innate immunity in all living organisms and function as a first line anti-infective defence against a wide spectrum of bacteria, fungi, and enveloped viruses [18]. Various approaches have been described for the realisation of stable, active and highly adherent AMP coatings on stainless steel, polymers and ceramics, for application in medical devices and implants [7,134,278]. The translation of this approach to technical systems such as tanks and pipelines has also been explored for the control of microbiologically induced corrosion [222].

In [241] and elaborated further in [27] a paradigm change in coating technology is presented which will facilitate a shift from oil based to biologically based surfaces. Special material binding peptides are used that stick to material surfaces and are capable of binding other proteins giving the desired property, for instance antifouling as demonstrated in [51], anti-microbial, super-hydrophobicity, self-healing etc. This opens the door for directed protein evolution and new surface treatment technologies offering a vast amount of possible combinations and properties [27,210], (Fig. 28).

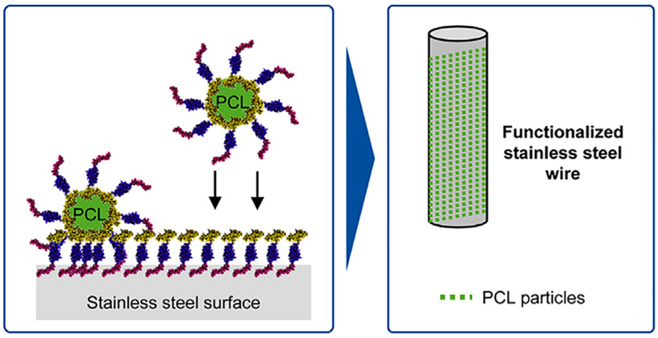

Fig. 28. Engineering of biological coatings with material binding peptides and polycaprolactone (PCL) releasing antibiotics [9,27].

Peptides are commonly employed to bind cells and other biological materials to solid surfaces. Examples are shown in [9] and [59] . This technology could be utilised for a wide range of medical stents, implants, or catheters.

8.2. Bio-electronic systems

The term bio-electronics has become more popular in recent years to describe the convergence between electronics and biology, driven by advances in bio-technologies and nano-electronics for applications such as organic light emitting diodes (OLED) and advanced pace makers.

Bio-electronic devices are characterised by an intimate interface between electronics and biological systems [54]. As inorganic electronic materials like metals or semiconductors have major limitations for achieving a close coupling between cells, tissue and organs [230], an increased interest in organic bio-electronic materials for flexible and stretchable biosensors [28,151] emanates.

Living organisms depend on a multitude of sensors which provide information on key parameters including temperature, light, chemicals, sound and mechanical forces [221]. Nature's sensor toolbox offers a rich source of inspiration for the realisation of artificial bio-sensors.

As in nature, an artificial biosensor comprises two functional parts – a biological receptor to recognise a stimulus and an electronic transducer that translates and amplifies the stimulus into an electrical signal. The sensing elements can contain biological materials such as enzymes, antibodies, microorganisms, tissues and receptors and can be tailored to make the sensor selective and sensitive to the targeted analyte [195]. The immobilisation and binding of the biological materials to the solid material substrates (metals, polymers, ceramics, semiconductors, insulators) is of particular importance, as is the communication across the biological-technical interface [170].

In the Horizon Europe Project "BioMeld" biohybrid machines (BHMs) consisting of catheters with bio-actuators and sensors are fabricated via a self-monitoring and self-controlling bio-intelligent manufacturing cell [76]. To make BHMs, material science (catheter construction), cell physiology (bio-actuators integrating muscle cells), bioreactor (ensuring muscle cell contraction) and organic bio-electronics (bio-actuators/sensors integration) are applied.

The food industry is one of the leading application areas of bio-sensors. Traditional analytical techniques such as high-performance liquid chromatography and gas chromatography are time-consuming and require expensive equipment and skilled operators [153]. Bio-sensors are a more convenient, portable and less skill-intensive potential alternative to many analysis tasks (Fig. 29).

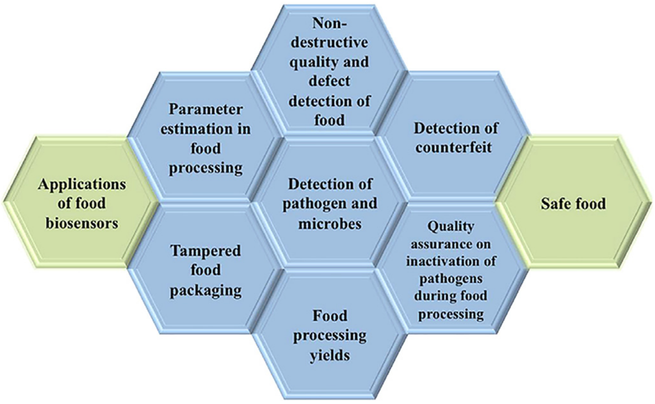

Fig. 29. Application of bio-sensors in food industries [153].

In nature, many flying insects and animals rely on their ability to detect and follow scents in order to find food or a mate. A technical system that could replicate this ability could potentially be used to detect explosives, gas leaks, incipient fires, or find disaster survivors. A live moth antenna was integrated into a drone to produce a flying odour-sensing biohybrid robot ([6], Fig. 30). The insect antennae were found to respond much quicker than metal oxide gas sensors. The authors anticipate that the utilisation of recent advances in gene editing may offer a feasible pathway towards achieving improved chemical specificity and sensitivity of the antennae [6].

Fig. 30. Moth antenna on odour localizing nano-drone [6].

Olfactory receptors in biology are gene-coded to respond to a particular odour molecule. The characterisation of olfactory receptor gene families is enabling the development of electronic smell sensors or bioelectronic noses [257]. These utilise engineered olfactory receptor cells of nanovesicles as the biological sensing component, which are bound and immobilised on sensor material substrates with adhesive peptides. Optical, piezoelectric and electrochemical methods are utilised to detect and convert the biological signals into usable electrical or optical signals. Visualisation of the different odour responses has been used as one signal analysis technique [138]. Bio-electronic noses may find application in the detection of explosives and drugs, monitoring of air, water quality, detection of effluents, development and quality control of odour-relevant products (e.g. coffee, wine), and quality monitoring of food products (e.g. detection of oxidation and spoilage).

The skin is the largest organ in the human body and is endowed with a wide range of properties including stretchability, mechanical toughness and self-healing. Numerous sensory receptors in the dermis and epidermis enable the sensing of stimuli such as temperature, pressure, strain, vibration and pain. Artificial electronic skin (e-skin) refers to devices that mimic the properties of skin for application in wearable electronics, medical devices, prosthetics and robotics. Research into suitable sensors has increased dramatically in recent years and various kinds of sensors (tactile, chemical, electrophysiological) have been developed [190,225,274]. An auditory skin is presented in [148]. Its use to search, translate and control devices by voice commands was successfully demonstrated.

Some e-skin products have already found their way into applications, especially in the biomedical field. For example, the BioStamp nPoint^{TM} is a sticking plaster-sized wireless biometric sensor system that can be attached to the skin. It is intended for use by health care professionals and researchers to monitor physiological parameters of patients like heart rate, respiratory rate, and body movement [30].

In future, e-skin could endow prosthetics and robots with human-like senses such as touch for human-robot interaction and cooperation. Human operators would also be able to «feel» what a robot arm or gripper is doing, thus greatly enhancing real-time remote-control possibilities.

8.3. Bio-integration of humans and technical systems

The classical example of this type of bio-integration is the functional prosthetic limb. A breakthrough for functional integration, termed the Cyborg experiment, was achieved by Warwick [107,254,255,256], who integrated a chip in his arm and used the electric signals detected by the chip to move a wheelchair or a robotic hand synchronously to his biological hand. With rapid advances in electronics, digital technologies, battery technologies, advanced lightweight materials, and 3D printing, such prosthetics have evolved from the simple passive leg, hand and arm prostheses to functional and affordable devices that are controlled via the user's own muscles or nerve interfaces for intuitive control (Fig. 31). In [109] a technology was reported that transforms colour information into sound to help colour-blind persons perceive the beauty of colors. A further step in bio-technical systems integration is the direct interfacing of the brain and computer (BCI). Electroencephalography (EEG) is a well-known, non-invasive BCI that dates back to 1924 [104]. EEG measures the brain's electrical activity via external electrodes and its main application remains as a medical diagnostic and research tool. However, EEG technology has also been demonstrated for sensing helmets to increase the safety of the operators in [50], for machine control in [189], for the control of computer cursors [269], robot arms, [35-38,166] and prostheses [69,193]. Remote control of virtual helicopter-like systems through BCIs has been investigated in [71,145].

Fig. 31. 3D printed bionic arm (©Open Bionics, 2018).

Partially invasive and invasive BCI implants promise better resolution and more accurate readings and have been shown to be capable of capturing complex brain signals, such as handwriting recognition from imagined hand movements [266,265]. BCIs implanted into the brain carry additional costs and risks and to date, the Utah microelectrode array originally developed in 2004 remains the only such implant that is FDA (Food & Drug Administration) approved for temporary human use [202]. However, this area of research is attracting great interest and funding [177,186]. In the medium term, it is likely that invasive human brain BCIs will find application in the medical field.

It is more likely that non-invasive BCIs may find practical application in future manufacturing systems. Non-verbal user-to-user communication through analysis of neural signals from non-invasive BCIs [75] is still in a very early stage of development, but is an interesting communication concept.

9. Bio-inspired meta-materials and surfaces

9.1. General considerations with illustrative examples

The idea of a bio-inspired meta material seems to be an oxymoron as metamaterials are defined as "any material engineered to have a property that is not found in naturally occurring materials". How-ever, nature is a master of functional integration. The inspiration from nature behind metamaterials is to achieve a certain functionality by a defined material structure. This is part of functional integration in development, which is used, for example, to increase material utilisation, integrate different functionalities or simplify assembly processes.

Two main approaches for new bio-inspiration based developments can be identified [97]: (i) A more traditional approach based on the relationship between biological structures and their functions especially in the area of lightweight design (Fig. 32 bottom right). This approach has been proven to be successful when the function is more related to the biological structure characteristics and less to the biological material properties. (ii) A more recent approach represented by inspirations at very small scale. This type of bio-inspiration is more related to the material and material surface characteristics (Fig. 32 left and top) than to the achieved geometrical structure.

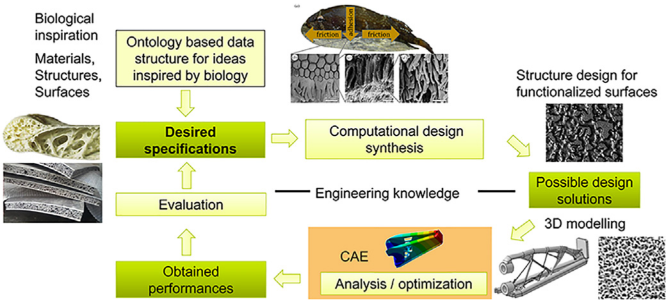

Fig. 32. Process of functional integration: new methodology to design mobile machine tools including examples of optimized component structures and functionalized surfaces [241].

The combination of biologically inspired design approaches [58] with manufacturing processes that enable a functional integration [72,284] is a key factor for the design of biologically inspired mechatronic systems, [73] for example. Only through the integration of functional elements or functional (smart) materials into supporting structures can the high functional density inherent in biological systems be achieved.

Since function integration normally takes place in the design phase of a component, an "engineering pull" occurs in the majority of cases in the context of biologicalisation. (Fig. 32).

The limiting constraint in the past was that the components had to be producible by conventional manufacturing processes. With the emergence of additive manufacturing processes, a multitude of further biological principles can be technologically anticipated. Recent development of additive manufacturing technologies enables the design of artificial materials to achieve global structures with new properties [96,245]. These include multi-functionality, providing economy of space and mass, and structural hierarchy, influencing the materials' mechanical properties [245].

Up to now, research in metamaterials focusses on polymer and ceramic materials [55,127,199,279] and only a few papers are available on metal structures [5,102]. There are still challenges concerning the manufacturing of multi-scale and multi-material structures. Multi-functional components require the combination of complementary additive manufacturing processes to include electronic and thermal features [155], examples of which are developed in [81] and [156].

For the combination of strength and toughness, bones represent a unique lightweight structural material, copied by a multitude of metallic foams, sandwich, and lattice structures. A hard and dense external structure, strongly resistant to compression and distortion, surrounds a porous, lightweight, load-adapted material with a high energy absorption potential [132,276]. Sandwiches made of aluminium foam with steel cover sheets drastically reduce the bending of movable transverse gantries of milling machines for large tool and mould making [72]. Open-cell metallic foams exhibit an excellent density-to-strength ratio, high energy absorption and permeability, and high inner surface areas. Potential applications include filtration elements, diffusers for gaseous media, permeable heat exchangers, bone implants, porous electrodes, and catalytic surfaces.

Functional (smart) materials, such as energy-converting materials [175], are of great importance, because they can provide sensory and actuator functions. Structurally compliant integration results in material composites, which enable intelligent components that can sense their own state or the ambient conditions [74] or specifically adapt their shape depending on the actual needs [74,119].

New ceramics have been developed in [277] to imitate the properties of the conch seashells, which, due to the nanolaminae and biopolymer layers of their unique hierarchical microstructures, exhibit a remarkable ferroelectric behaviour and account for a huge polarisation with extremely high pyroelectric coefficients 2–3 orders of magnitude larger than those of conventional ferroelectric materials.

Integrated condition and health monitoring works in many ways in nature, one example being the periosteum in the endoskeleton of vertebrates, which can also be used as a model from nature in the technosphere. While the skin surrounding the bone contains nerve cells that perform sensory tasks in order to send electric signals to the nervous system, the bone itself has no sensory function, however, it takes on a load-carrying task. This approach is transferred to technical implementation using a lightweight metal structure surrounded by an outer skin of fibre-reinforced polymer (FRP) composites with integrated fibre-Bragg-Grating (FBG) sensors for monitoring tasks [253]. Furthermore, no additional cables for power supply or evaluation are needed [13]. Focusing on vibration analysis, after external excitation of a component, damages in the form of delamination can be successfully detected taking parameters such as frequency, location, as well as excitation direction into account. The integration of FBG sensors for structural health monitoring enables needs-based replacement or maintenance of components only when necessary (compare Chapter 4).

Another example is the integration of several optical elements in one single lens presented by [85,86] for the design and manufacturing of the compound eye based on the biomimicry approach shown in Fig. 33. Fig. 33(b) shows the special lens made by nanometric cutting [3]. With this unique lens design, an imaging system with a wide view angle up to 120° was developed as shown in Fig. 33(c). Using the biomimicry approach or even biologicalisation, production engineering can also be developed towards atomic and close-to-atomic scale manufacturing (ACSM), which is the core competence of Manufacturing III level introduced in [84,250], namely the new paradigm of manufacturing advancement.

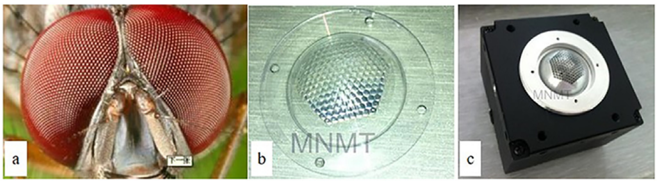

Fig. 33. Lens design with a wide angle inspired by the eye of a fly (a) Compound eye of a fly; b) Freeform lense element; c) System and application according to [83,84].

9.2. Programmable materials

Programmable materials, as part of the family of functional materials, are materials that can upon stimuli (e.g. electric) modify their shape. In nature stimuli can be light, temperature, or temperature difference. They allow functional integration as inspired by nature, combining load carrying capacity and shape adaptation. Periodically arranged unit cells with different geometric features allow the control of material properties and thus the shape, e.g., by strain-dependent Poisson's ratio [263] (see Fig. 34), which significantly enlarges the design space.

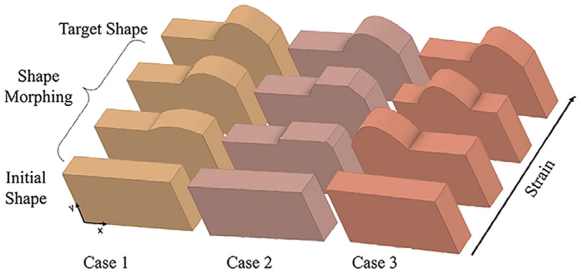

Fig. 34. Schematic representation for three cases of shape morphing behaviour under axial strain. Case 1: The target shape is reached by (linearly) increasing the amplitude of the lateral deformation. Case 2: The filling of a target shape is adjusted until a complete fitting of the target is achieved. Case 3: A shape (bulge) is shifted through the material until the target position is reached [263].

Some applications in production, but also in automotive, aerospace, medical and other fields require temporarily different functional shapes. In the future, for example, bio-inspired soft robots can be developed on the basis of programmable materials. Another example is the so-called growing structures that enable the temporary availability of structures or the development of locomotion systems and strategies for, e.g., difficult-to-access, sensitive environments. In nature, examples of such structures can be found, amongst others, in many creatures that have the ability to form body parts in the form of everting tubular structures for the temporary performance of functions, such as the extension of the snail eye.

The development of highly flexible metamaterials, e.g., in the form of net structures based on flexible polymers [34] which can repeatedly endure these high deformations, enables the transfer of the eversion principle to a technical application.

Superelastic shape memory alloys [119], which allow reversible deformations of up to 10% without significant strain hardening or failure, allow, in addition, higher actuator forces. Research activities in this field demonstrate that transfer of this biological principle requires these innovative materials and strongly simulation-based development and design.

9.3. Sustainability and implications for manufacturing

Bio-inspired metamaterials should provide new functional solutions and/or increase the sustainability of a product. The two topics are closely intertwined and it is therefore important to integrate biologicalisation as well as sustainability requirements early in the design process. This requires that the topic becomes an essential part of design theory.

From the production technology point of view additive manufacturing is a key enabler for the roll-out of bioinspired meta-materials, as certain structures cannot be achieved by classical machining processes (e.g. Fig. 32). Nevertheless, additive manufacturing is also limited in regard to sustainability, considering the necessary amount of energy for the melting of the material for example, which shifts the sustainability requirement to the use phase (benefit of 3rd type). The high prevalence of additive manufacturing is not a primary limitation for bio-inspired meta-materials but opens the design space from the feasibility point of view. Both a functional expansion of components as a technological uniqueness and a reduction of material diversity will be achieved in the future. Both lie within the focus of the biologicalisation agenda. The manufacturing of shape memory alloys and programmable materials using additive manufacturing has also been summarized as 4D-printing. Thereby the 4th dimension refers to the time domain.

Graded materials are a speciality of nature, adapting the properties to the local requirements, which can beneficially, if not only, be achieved through additive manufacturing. This can,for instance, be used for controlling the wear behaviour in self sharpening tools as discussed in Chapter 5. Functional integration as one of the assets of biological systems for self-healing and self-monitoring requires the availability of additive manufacturing technologies. But biological systems are able to regrow material on site, being an application of additive manufacturing not yet implemented in technical systems.

9.4. Biologically inspired materials, approaches and solutions

Biological solutions of interaction with the environment through surfaces is especially interesting for bio-inspiration. A number of solutions and their technical counterparts are presented here.

One promising industry related development in biologicalisation is the development of modular functional assemblies based on biological building blocks to functionalize surfaces as presented in the project “BioHyb” [26]. The example shows the potential impact of interdisciplinary collaboration of biotechnology, soft matter nanotechnology, polymer chemistry and production engineering for a promising solution. For instance, one of the most pressing challenges in dentistry is inflammation. Biohybrid coating can alleviate this by preventing the bacterial colonisation of the implant together with an additional microstructure to increase the robustness and longevity of the coating.

Realizing robust underwater surface bonding remains very difficult, if not unfeasible, using present techniques because of surface contamination and hydration layer properties. Inversely, marine mussels have an exceptional ability to stick and anchor tightly to rocks and other surfaces under the sea, even in case of rough waters, due to the interfacial mussel foot proteins (mfp) rich of amino-acid substances providing strong underwater adhesion. Based on bio-inspiration and bio-imitation, mfp substances have been adopted to functionalize synthetic polymers for high wet adhesion at multiple length scales, including nanofabrications in electronics, lithography and biomedicine [3].

Diverse manufacturing solutions were suggested in order to develop bio-inspired fibre materials capable to mimick the spider silks and reproduce their multipurpose capture/dragline properties of high water collection, stickiness, mechanical strength, elasticity, supercontraction and torsional shape memory [25]. Dragline spider silk was artificially obtained by spinning recombinant dragline silk proteins (ADF-3; 60 kDa) generated in mammalian cells under low conditions of shear and coagulation [214]. In [283], synthetic fibres capable of directional water collection, characterised by periodic nanofibrils spindle-knots separated by aligned nanofibrils joints, were fabricated. In [56], artificial spider silks were manufactured by employing β-sheet nanocrystals in combination with amorphous parts.

Bio-inspired surface technologies have been developed for realising nanoporous material coatings on metal, ceramic or polymeric substrates in order to produce superhydrophobic surfaces. To imitate the rice leaves’ anisotropic wetting function, rice leaves-like aligned carbon nanotube films were obtained by controlling surface deposition on the catalyst anisotropic behaviour [272]. In nature, colours are produced by pigmentation, iridescence (structural colouring) or their combination. Colouring effects are generated by the surface of the Morpho butterfly wings through incident light wave reflection at particular wavelengths, producing vivid colours via multilayer and thin film interference, diffraction and scattering phenomena [14]. Butterfly wing scales are composed of microstructures like ridges, cross-ribs, ridge-lamellae and microribs which determine structural colouring via light interference. This effect can be mimicked by employing metal oxides like TiSO4, ZrO2 and Al2O3. Bio-inspired technologies have been researched regarding surface tension in order to develop hydrophobic or hydrophilic coatings. Bio-inspired surface treatment solutions have been proposed to realise air and water repellent surfaces capable to avoid fluid entry, like in [80] where biofilm colonies of bacillus subtilis have been employed for their notable water and gas repellent properties as a consequence of chemical composition and nanoscale topography.

Bio-mimicking shark skin properties by nanotechnology surface development can allow for more effective movement in water. By analysing the shark skin texture, which repels barnacles or other biofouling differently from boat hulls and further smooth surfaces in the sea., it was found that shark skin also prevents microbial activity. Bio-inspired nanoscale textured surfaces were realised on plastic sheets to obtain the same kind of property combination. Geckos are well known for being extraordinarily capable to stick to and travel on vertical and even upside-down surfaces, despite the fact that there are no chemical adhesives under their feet to make them sticky. As a matter of fact, the bottom of the gecko’s toes is characterised by ridges covered with uniform ranks of setae and every seta is additionally subdivided into a very high number of split ends and flat tips named spatulas [15]. Gecko’s feet stick to any surface due to Van der Waals forces between setae and surface molecules. As the number of setae on a gecko’s foot is higher than 1.5 million, exceptionally high adhesion forces can be exerted on surfaces. Artificial setae have been manufactured by MEMS techniques such as photolithography, electron beam lithography, plasma etching, deep reactive ion etching, chemical vapour deposition (CVD) and micro-moulding. The application of synthetic setae, commonly called “gecko tape”, has concerned area as diverse as nanotechnology, military, health care and sport.

10. Production of living elements

The production of living elements is discussed in the context of this paper because the convergence between advanced manufacturing and ICT technologies especially AI tools today enables a more sensitive treatment of high value biological products.

Regenerative medicine deals with the "process of replacing, engineering or regenerating human or animal cells, tissues or organs to restore or establish normal function" [163]. By stimulating the organism’s own repair mechanisms, tissues and organs previously considered as irreparable can be healed.

In regenerative medicine some of the biomedical approaches involve the application of stem cells [206]. The properties of pluripotent stem cells (PSCs) such as embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), lie in the fact that they can undergo self-renewal while maintaining their capacity to differentiate into multiple types of functional cells [141,218]. Examples for the biomedical approaches are the injection of stem cells obtained through directed differentiation (cell therapies); the induction of regeneration by infused cells (immunomodulation therapy); and transplantation of in vitro grown *organs* and *tissues* (tissue engineering) [223].

The number of iPSCs required for clinical use can be estimated as $7{\cdot}10^7$ cells per treatment [182]. According to [125], for pancreatic islet transplantation, at least $6{\cdot}10^8$ β cells are needed per patient, while about $6{\cdot}10^{10}$ hepatocytes per patient are required for producing of 30% liver tissue. The above facts underline the importance of the production of stem cells of different types. This is why the main focus in this chapter is on their production, knowing, however, the range of biopharmaceutical, food supplements and biotechnological products is immense.

10.1. Stem cell production

The essence of the stem cell production is the cultivation of the iPSCs' samples under controlled conditions. In present days the production of stem cells proceeds with significant human involvement by following adaptive protocols taking the growth behaviour and the quality of the stem cells into account.

In conventional biopharmaceutical production a well-defined biomolecule is generated by an appropriately designed and run cell line. In contrast, in iPSC production the product is the living cell itself. Moreover, the input raw cells are derived from the patients themselves or from donors, resulting in high batch-to-batch variation [112], which makes a significant difference compared with traditional manufacturing processes. The varying growth rate of the cells results in varying processing times, which needs regular process checking and adaptation and calls for a mixed-initiative production control scheme [172].

The production of an appropriate number of iPSCs efficiently, reproducibly, with consistent quality and in a cost effective way is a real challenge [29,174,185,208].

With the development of novel production technologies in the context of Industry 4.0, automation solutions are now increasingly developed and adopted [39], which remove all direct interactions between the user and the product from the process, reduce the risk of human failure and enable reproducible processes [143]. In addition to improvement in the quality and quantity of cells produced, automation enables a more comprehensive monitoring of processes and the generation of an extensive data record, which helps manufacturers to align with the strict regulatory requirements.

Examples of robot-assisted systems that allow fully automated processing of stem cells include the following: the *AutoCulture*® automated cell processing machine [131], the *CompactT SelecT* automation platform [218], the *AUTOSTEM* [12], the *StemCellFactory* [1], the *StemCellDiscovery* [172], and the *iCellFactory* [40,41].

Long-term maintenance of IPSCs was reported on in [141]. The undifferentiated states of the cells were maintained for 60 days by using the developed automated cell culture systems.

One of the key requirements of the automated cultivation of stem cells is regular, non-invasive checking of their conditions. As part of the *StemCellFactory* system, the fully automatic recognition of the cells' states by using phase contrast microscopy and deep learning algorithms is described in [194]. In [122], a deep learning-based automated cell tracking (DeepAct) technology based on Kalman filters is reported.

A distinctive feature of the iPSC production is the symbiotic co-existence and co-evolution of the technical, information and communication, as well as biological ingredients in production structures. The application of biologically inspired control algorithms represents a promising way to overcome the issues of automated production of stem cells. For this purpose, an approach combining digital, agent-based simulation and reinforcement learning is described in [172] by using the The *StemCellDiscovery* testbed (Fig. 35). The applicability of the proposed approach is demonstrated by the results of a comprehensive investigation.

The research reported in [172] is an exemple of biologicalisation in its own right, i.e. the use of bio-inspired algorithms for controlling a manufacturing system which produces biological material. The first results indicate that a well-fit growth model of cell cultures, combined with an agent-based simulation model of all the main objects and resources in this micro-world of production, can provide a reliable basis for a reinforcement learning-based control scheme. This novel approach, even though it is data-intensive, gives room for incorporating existing background knowledge of the application domain, and, at the same time, can enhance the performance of actual solutions using rule-based control.

Fig. 35. The StemCellDiscovery testbed [172].

Though significant developments in the automation of stem cell processing have been achieved in the past years, there are important further challenges to cope with, as indicated in [65,125]. To avoid or to minimize heterogeneity across different labs, appropriate, standardised *quality control methods* are to be developed. *Deep learning* offers a powerful tool for quality control, and the inclusion of *expert knowledge* is essential to establish effective quality control solutions. Further investigations are needed to clear how the operation parameters influence the *cell properties. Cooperation* of representatives from different disciplines, such as biology, mechanical engineering, physics, and computational engineering is essential. Naturally, the *cost effectiveness* of the solutions is also a target [182] and *ethical issues* cannot be neglected in this field [57].

In [267] the need for an increased understanding of the underlying biological processes and their interaction with approaches to manufacturing technology is stated.

10.2. Future protein production

According to a recent report of the United Nations the current global population is near to 8 billion, and about 20% increase can be estimated by 2050 [179]. Therefore, protein production needs to be significantly increased in the coming years. Though plant-derived protein sources are widely available, animal meat maintains its popularity and is considered as a high-quality and savoury protein source [124]. However, as it became clear in the past few decades, traditional animal production causes severe problems, e.g. environmental, social, and animal welfare concerns.

Cultured meat, with other words in vitro *meat* can be produced by cell culture technology, where the animal cells are primarily gained through muscle biopsy. Comparisons of the production and the characteristics of traditional meats and cultured meats underline the high potential of the latter in feeding the growing population [124]. However, the consumer acceptance of cultured meat is low. In order to increase its consumer acceptance, the pluripotent stem cells come into focus, as they could differentiate into muscle, fat and other types of cells and this way a real meat flavour could be reached. The manufacturing related challenges and opportunities are similar, and were considered in Section 10.1.

Production engineering challenges of living materials are intensively researched in [87]. The large-scale production of mealworms as a protein source is significantly developed. Appropriate automation and equipment for proof-of-concept are under development. For breeding, a system will be developed for sorting and detecting mealworm larvae by using optical, non-invasive inline sensor technology in combination with evaluation algorithms for monitoring, intelligent control and documentation of the growing process. With inline sensor technology to be established accordingly, data can be generated that can be easily logged and support product tracking & tracing. This data can also be used to perform targeted, complex optimisation analyses to efficiently adjust insect feeding and rearing strategies. At the end of the production process, automated cleaning systems can ensure reproducible hygienic conditioning of the module.

10.3. Further industrial production of biological materials

Increasing importance is being placed on industrial automated processes controlling the breeding conditions and taking into account the success of the process in a closed loop manner. For the utilisation of mycelia to fill hollow spaces in technical systems as pointed out in Chapter 7 they must be triggered to grow in the intended manner. The reaction on certain trigger signals could be proven, which makes it useful for the interaction stage of biologicalisation. Breeding of microorganisms in a breeding tank under conrolled conditions for technical use as described in Chapter 7 is another application field of bio-integration where the biosphere and technosphere meet. Additive manufacturing with living cells can be used for the generation of additive organs like skin, bone etc. and is presented in [16].

11. Enabling technologies

Biologicalisation does not develop spontaneously but is facilitated by a number of key enablers. The movement of industry towards Industry 4.0 and the rapid development of ICT technologies, particularly the consumer product driven mass production of small, cheap electronic devices is one of these enablers. In addition, recent advances in the key technology fields of manufacturing, materials, and biotechnologies are enabling the convergence of the fields technosphere, biosphere, and cybersphere (ICT) (Table 2).

Table 2
Key enabling technologies.

Field	Enabling technologies for biological transformation
Information and Communication Technologies	High performance, cloud computing - Big Data analytics, multi-scale simulation - Artificial Intelligence (AI), Machine Learning (ML), Artificial Neural Networks (ANN) Microelectronics - high computing power in small packages - small, low cost sensors and actuators - integrated, organic bioelectronics - *flexible, stretchable, biocompatible, biodegradable*
Manufacturing & Materials Technologies	Micro- and nano-manufacturing - MEMS, photolithography,micro-moulding Additive manufacturing - multi-materials, bioprinting, 3D printing of electronics Bioreactors and biorefineries Composite materials - functional integration, biopolymers Metamaterials Battery materials (e.g. Li-ion)
Biotechnologies	Genetic engineering - gene editing, programmable Biosynthesis microorganisms Biochemical engineering

11.1. Information and communication technologies

Rapid developments in mass-produced microelectronics, small, cheap sensors and actuators enable digitalisation and underpin their integration into cyber-physical and bio-intelligent manufacturing systems. The emergence of organic, carbon, and polymer based electronics is enabling the development of flexible, stretchable sensor systems (e.g. for wearable devices), and is also expected to lead to new applications in flexible electronic memories [149], chemical and biological sensors [233], ionizing radiation detectors [17,101], and solar cells [275].

Biologically-inspired AI and ML approaches and Artificial Neural Networks (ANNs) open up new possibilities for managing complex, integrated production systems, supply chains and organisations, as discussed more fully in [48] and [260]. Low-cost high-performance cloud computing technologies underpin big data analytics and larger-scale simulations of complex systems and processes. Multi-scale simulation of natural materials, processes and systems drives their translation into technical and production systems [130,249]. High throughput screening enables rapid gene sequencing and coding, and directed evolution in materials science and manufacturing [244].

The integration of new technologies such as 5 G/6 G, Blockchain and quantum technologies with “traditional” Industry 4.0 technologies (e.g. IoT, cyber-physical systems) is foreseen to lead to a higher evolution of Industry 4.0 in the longer term, with new possibilities in data analysis, simulation, information security, and traceability [212,217].

11.2. Manufacturing and material technologies

MEMS fabrication (such as LIGA) is an important technique that is routinely used to manufacture devices such as micro-mechanical accelerometers with integrated electronics [282]. Other micro- and nano-manufacturing technologies such as micro-moulding, micromachining, lithography, and physical vapour deposition have been used to realise bio-inspired materials and surface structures, such as gecko tape and lotus leaf-inspired surface coatings as described earlier. Micro-fluidics technologies significantly contribute to miniaturisation of bio-sensors, owing to substantially smaller dimensions and limitation of the number of bio-sensitive elements utilised as well as the reduction of sample volume [28,235]. Nano and close-to-atomic manufacturing and self-assembling technologies [83] are required for the further development of bio-chips.

Additive manufacturing (AM) is a key technology for realising structures and material combinations that are not possible to manufacture by other means, e.g., biologically inspired, structurally optimised components and structures, and functionally graded materials. Electronic components such as thin film transistors (TFT), diodes and LEDs can be printed [178], while 3D printed, flexible microcontrollers with onboard memory have been demonstrated in [157]. This opens up new possibilities for integrating such microcomputers in soft robotics, wearables, and industrial systems. Bio-printing of biological materials and electronics is a fast-developing area of research that could open new potentials in sensor, bioprocessing, and medical device applications [191].

Key material technologies include:

- nanostructured materials such as carbon nanotubes, graphene for bio-sensors,
- renewable and/or bio-degradable materials (e.g. bio-polymers, bio-based fibres) and
- affordable battery materials with high energy and power densities for mobile and distributed devices.

11.3. Bio-technologies

Bio-technology encompasses the exploitation of biological processes for industrial and other purposes, especially the genetic manipulation of microorganisms for the production of useful materials and products [187]. Key application areas are medical (development of medicines, vaccines), industry (use of microorganisms and enzymes to create products), agriculture (improving agricultural product yields and qualities through, e.g., genetically modified plants and crops), and environment (waste treatment, mitigation of water and land contaminants). Genetic engineering and gene editing are key technologies that enable the modification of organisms to express particular materials, properties or behaviour. In the context of biologicalisation, examples include the engineering and manufacture (bio-synthesis) of proteins and peptides for the bio-functionalisation of solid surfaces for bio-sensors (Chapter 8), or the modification of microalgae using various recombinant DNA techniques to ensure higher yields of the targeted metabolite (Chapter 7). Advances in synthetic biology high throughput screening technologies enable techniques such as directed evolution strategies, thereby greatly accelerating progress [162,252].

12. Scaling up for industrialisation

12.1. Potential from the end user's perspective

In manufacturing, biologicalisation is typically associated with the potential to provide solutions to central challenges and current trends such as automation, flexibility and individualisation, but also with increasing energy and resource efficiency. A survey amongst end-users [19] revealed that there is a high level of acceptance of the relevance of these trends. Thereby, the sustainability potential of biologicalisation is most likely achievable if it is compatible with the more classical economic goals in industry. In this context the utilisation phase of products has also to be considered, as it can be more relevant regarding the life cycle analysis than the efforts associated with the manufacturing phase alone [4]. For that reason in [129] and [161] an extended sustainability centred flow chart for the biologicalisation process is presented (shown in Fig. 36).

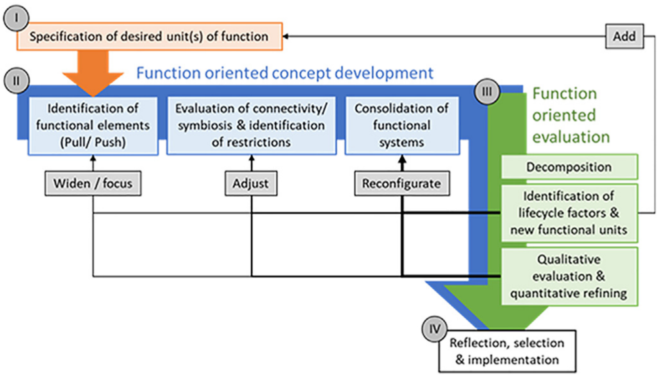

Fig. 36. Flow chart for a function oriented and ecological sustainability centred biological transformation process according to [105,114].

In [19] the status quo as well as the potential up to 2035 for companies were surveyed in 10 different fields of action as a preliminary investigation on the topic. A more detailed analysis shows that the solutions having high disruptive potential have a very low level of technological maturity and are still being developed today within the category of the lower Technology Readiness Level basic research [110]. Industrialisation needs to follow a two-step strategy a) harvesting "quick wins" in the short term and b) in the medium- and long-term developing turnkey disruptive solutions to fully leverage the potential of biologicalisation.

It is necessary to adopt new and nearly mature solutions in the short term. For the long term it is vital that methods and standardised procedures for an industrial transformation process be developed. In doing so, individual solutions can be combined for an even better cost/benefit ratio to develop highly attractive disruptive solutions more rapidly.

12.2. From partial stand-alone to full scale industrial solutions

The development of specific use cases in the context of the biologicalisation fundamentally result in either direct or indirect benefits of technologies. An increase of tool life due to friction-minimizing microstructure [226] or reduced material costs due to load-optimized bionic component structures [259] are examples of direct benefits. Indirect benefits are property changes or adaptations of existing products and processes, such as the substitution of mineral cutting fluids by completely biodegradable fluids thereby minimizing disposal costs [215] and health risks to employees [220].

It is currently very challenging to measure the economic benefit of bio-inspired, bio-integrated or bio-intelligent systems [168] directly, because the change costs and risks in comparison to possible gains are difficult to estimate in advance. This can change abruptly, if the availability of primary raw materials deteriorates significantly and the costs for additional production technologies are reduced [121].

For this reason, it is planned that the economic viability as well as the technological and ecological superiority of biologicalisation be shown on a completely transformed machine tool as an overall solution within the framework of the Fraunhofer BIOMANU III project. The machine concept is optimized with respect to various functionalities and selected examples of the biological transformation based on a cyber physical system. This includes the optimisation of the tool system by sensory acquisition of tool data directly at the tool or tool holder and tool optimisation by the integration of surface structures (Fig. 37b, [226]) for optimized wear resistance and cutting fluid supply in the cutting zone (Fig. 37d, [105]), integration of anti-adhesive surfaces (Fig. 37f), use of new insulating materials (Fig. 37a, [204]), use of biological cutting fluids (Fig. 37c, [215]) and AI-supported thermal compensation (Fig. 37e). This biologically transformed machine concept which is under development will serve as a research and development platform to study the interaction of the individual solutions and will demonstrate the benefits of biologicalisation to industry.

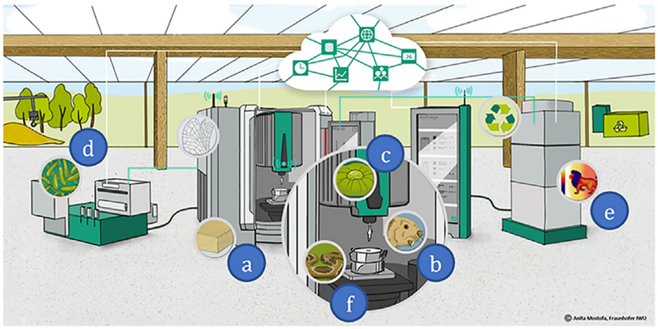

Fig. 37. Schematic representation of a biologically transformed machine tool according to [110].

It is expected that biologicalisation in industry will lead to profound and economic change processes [169,181], which must be addressed in a fundamental manner in order to meet the ambitious goals of climate neutrality and sustainability. The scaling of individual stand-alone to full scale solutions will help to solve the trade-off between sustainability and economy.

12.3. Change processes in industry

With each new paradigm in production technology - e.g., Lean and Industry 4.0 - suitable metrics have been created to make the degree of penetration and implementation quantifiable. In this area, for example, the Industry 4.0 Readiness Check was developed to help companies determine their own position with regard to Industry 4.0 [126].

For implementing biologicalisation the industry also needs methods and tools to determine their own position in relation to this new paradigm. Although there is no established tool today, the basic methodology and experience with Industry 4.0 can at least be transferred to a certain extent, based on the Industry 4.0 Readiness Check for example [152]. Together with the more advanced process models for example from [121], the necessary planning and analysis tools to develop appropriate individual transformation roadmaps are available.

13. Conclusion: trends and future developments

Trends follow the requirements of mankind, and thus biologicalisation must be seen in a general trend stream where the potential impacts are environmental issues. The latter include sustainability, circular economy, reduction of adverse environmental effects, especially the CO_2 footprint, and the enhancement of industrial production in terms of cost reduction, an increase of autonomy, quality increase, lean six sigma, and zero fault production. Therefore, biologicalisation is considered to be the continuation or a part of a breaking frontier of industry 4.0. In particular, developments in Industry 4.0 are the primary enablers for biologicalisation. The Gartner hype cycle, shown in Fig. 38, provides a trend estimation for the expected development and implementation of biologicalisation topics updated from 2018 [49]. This new hype cycle is based on a survey made by the authors, including developments and applications described in this paper. Some developments, such as supervised learning and advanced optical sensory, already identified in 2018 in the so-called “Plateau of productivity “of the diagram, have already been implemented. A few developments, such as self-cleaning, superhydrophilicity, E-skin, structural colouring, and self-organisation systems, have advanced in the direction of industrial application. Human-robot collaboration has already been tested in industry, while other developments such as machine- and factory cognition and autonomous mobility are expected to be applied in a 5-to-10-year timeframe. Implementing BCI (brain-computer interface), sensing helmets, or living production and organisations may take more than 10 years. General trends and future developments are presented in the following sections.

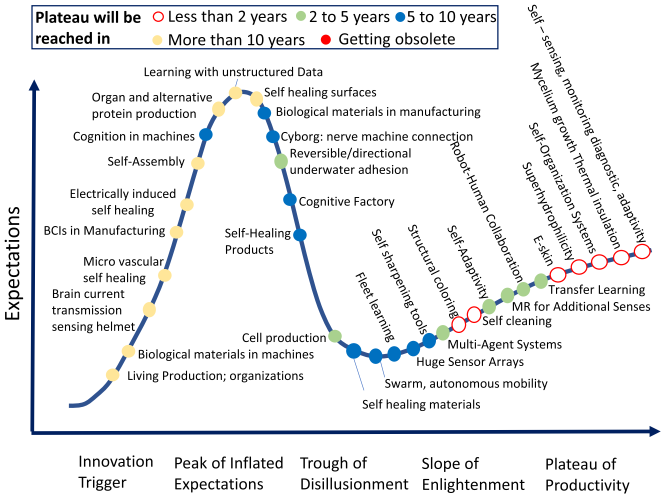

Fig. 38. Gartner hype cycle 2022 for biological transformation (update of the hype cycle 2018 in [49]).

13.1. Design space for biologicalisation

Using extensive analysis, future scenarios and new challenges can result in bio-intelligent technologies and product innovation.

The solution space of the biosphere is vast, and unless a comprehensive, structured, and systematic approach is adopted, it is almost unexplorable. In the past, most of the solutions taken from the biosphere just happened by accident or intuition. Systematic search and design methods for biologicalisation in manufacturing are currently in development. Some successful discoveries are described in [113,219].

Different obstacles to the adoption of biological solutions need to be overcome. Even excellent or exceptional solutions within the entity of the biological system need to be adopted in an integrated manner. The lotus leaf effect is only sustainable together with the self-healing function. Scaling is often impossible because the underlying functional principles work only within the scale of the biological solution [15]. Due to the entirely different principles of growth in the biosphere, the application might be limited by current manufacturing technologies. Finally, the time scales are different, which means that the biological generation takes time, and the durability over time might not meet technical requirements.

Two high-level categories [216] for systematic utilization of the biological design space are under development: (a) methods to support the search and retrieval of biological material solutions; (b) guidelines to assist manufacturers during the transfer process.

13.2. Biological and bio-inspired metamaterials

It has been shown that new material developments are one of the most significant areas of bio-inspired and bio-integrated R&D, comprising smart materials, surface texturing, material superstructures, and materials with targeted applications. Available bio-based materials and material combinations provide a very large number of solutions for direct imitation (biomimicry) or bio-integration. The relevant literature reveals numerous solutions provided by microorganisms such as microalgae, bacteria, or fungi. The industrial applications include lubrication, storage of energy and CO_2, enriching solutions with certain elements, building structures, enhancing surface properties, and providing healing effects. Bio-integration of microorganisms is expected to play a more significant role in the future. Furthermore, mesoorganisms such as worms or insects are investigated for producing materials such as proteins, quinine, and others. Producing cells for the medical treatment of humans, such as stem cells, and producing additive organs, such as the liver and skin, comprise a novel upcoming technological discipline. This production of biological organisms presents a new and difficult challenge, as the products and the process must be exactly defined and carefully monitored.

The combination of biologically inspired design approaches with manufacturing processes enabling functional integration, form the basis for a new group of bio-inspired metamaterials. The continuous progress in manufacturing technologies will enable the development of pioneering products, such as innovative bio-inspired lenses. Programmable materials are another disruptive solution field which will allow completely new designs, such as shape-morphing structures and features.

13.3. Biologicalisation change in production systems

New production systems are being developed with increased autonomy. Biologicalisation offers a unique approach towards a more holistic production system which can be implemented across the entire production chain. However, despite all efforts, the vision of a living system with an integrated operator still lies in the distant future. Nevertheless, the trend towards living production systems is accelerating as it helps to meet the existing challenges of autonomous production technology. The variety of possible solutions in nature enables scientists to find new individual solutions based on different biological methods or principles, which can be transferred to manufacturing. Yet, the innovation process of biologicalisation requires a continuous and systemic approach to find an optimum solution. Technologies such as sensor coverage, automatic decision-making, artificial intelligence, and modern ontology-based expert systems are currently used for developing production technologies. As indicated in the Gartner diagram (Fig. 38), current developments include novel ways of collaboration between humans and machines, human and machine control, and even direct transfer of commands via coupling between human nervous systems and machine controls. The development of sensor fusion solutions with careful balancing of redundancy for robustness and coverage of signals and economics is frequently discussed in the literature. Signal processing becomes increasingly sophisticated, especially by utilising full field sensors such as optical cameras and sound sensors, especially due to their rich signal content inspired by human sensing technologies of data processing.

Self-healing and self-organisation of biological systems offer significant advantages over technical systems, particularly for applications of functional surfaces. However, this approach is restricted by limited health reserves, unachievable full strength, and strength reduction due to embedding the healing system. The sustainability of self-engineering systems concerning material utilisation is still under examination. It extends over the system's lifetime and increases autonomy while increasing complexity and resource consumption. A system like blood vessels initiating wear compensation by depositing liquid carried precursor material, for instance in bearings, is not yet available.

Considerations of robustness and RAM (reliability and maintainability) need to be directly integrated into the design phase for biologicalisation.

Future production must be agile in reconfiguration, efficient in commissioning and operation, and resilient towards environmental conditions. The transformation process within the biologicalisation mainly takes place at the level of bio-inspiration. The existing approaches, such as cell-inspired factory layouts, swarm organisations, and mobile production units in combination with the human-in-the-loop, show the high potential of living production systems.

The interplay between biology and production technology offers a vast and new field of innovations. Specific use cases in biological transformation fundamentally result in exploitable possibilities for industrial companies to achieve technological superiority with improved sustainability. It should be possible to transfer and scale up the solution to a finished product or a ready-to-use technology to be economically viable while simultaneously providing stand-alone solutions. Therefore, companies must determine their vision, position, and roadmap toward biologicalisation.

13.4. Resource efficiency by biologicalisation

Resource efficiency and the ambition to gain more functionality with lower investment, especially in materials, resources, and energy, with a lower CO_2 footprint and improved sustainability, continues to drive technology, for example, by miniaturization, recycling, and reuse of materials and components on a global scale.

Biological systems alone are not necessarily sustainable on all scales. Large sediments of coal, oil, and other materials are the waste of ancient biological species. They became valuable after millions of years with the development of homo sapiens, who are capable of exploiting this waste. However, at the same time, humans produce new waste. Sustainability is a matter of symbiosis of larger reuse cycles. It should be considered and will be the content of a planned forthcoming CIRP publication on industrial symbiosis. The waste streams from industries must find applications in some other industries. Furthermore, it can be expected that the prudent integration of biological solutions and technical solutions, and the convergence between technosphere and biosphere as described above, will contribute to solving the sustainability problem.

13.5. Ethical issues

As reported in Chapter 2, a transition is expected "from the old, lifeless manufacturing systems to the manufacturing systems being alive: self-learning, cognitive, communicative, self-healing, self-assembling: in short, towards Living Manufacturing Systems". The Cyborg experiment, as reported in [255,256] and outlined in Section 8.3, is a good example where a chip was integrated into a human arm, and the electric signals detected by the chip were used to move a wheelchair or a robotic hand in synchronization with the biological hand. A sensing helmet and other developments increasing the sensing capabilities of humans have demonstrated a major breakthrough in functional integration [50,71]. These solutions clearly show great benefits, expanding the capabilities of humans, yet at the same time also present possible misuses. The implications of such developments are far-reaching. It is well recognised that numerous new challenges in applied ethics [184] will arise to a much greater extent than in the past as rapid scientific/technological advances are being made. A significant number of implications exists along with open questions associated with such new developments, for example:

- Machines developing capabilities similar to those of human beings,
- The integration and utilisation of biological living materials into the manufacturing environment,
- The production of living systems and elements (including, for example, human organs such as the liver and skin),
- The changing relationship between machines and humans as bio-intelligence grows to become more mainstream,
- The new forms of communication between human workers and the new living manufacturing systems and
- The changing role of the human workers in the new manufacturing environment and to what extent the machines take over the role of the human workers.

The deeper aspects of these challenges largely concern the unknown and unintended consequences of converging the engineering, materials science, biological sciences, and ICT disciplines. It is noted that, despite this topic's scientific, technical, and particularly societal importance, only minimal scientifically based literature has been published to date in this field. [184] provides a set of recommendations for the further development of biologicalisation in manufacturing, taking the emerging ethical challenges into account.

Declaration of Competing Interest

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References

[1] https://www.stemcellfactory3.de/. Retrieved on 23.07.2019.
[2] Adams N (2015) Bloom's Taxonomy Of Cognitive Learning Objectives. *J National Library of Medicine* 103(3):152–153.
[3] Ahn BK, Das S, Linstadt R, Kaufman Y, Martinez-Rodriguez NR, Mirshafian R, Kesselman E, Talmon Y, Lipshutz BH (2015) High-Performance Mussel-Inspired Adhesives Of Reduced Complexity. *Nature Communications* 6:8663–8669.
[4] Aichinger H., Pullmann L., Wydra S., Heyen N., Hüsing B., Sartorius C., Reiß, T. (2021) Biological Transformation - Technology Assessment In Production Under The Aspect of Resource Efficiency. A Study Conducted By Fraunhofer ISI For The Fraunhofer Society.
[5] Alkhatib A.J. (2022) Biologically Inspired Designs for Additive Manufacturing of Lightweight Structure. In: Praveen Kumar A, Sadasivuni KK, AlMangour B, Abdul bin Majid MS (2022) High-Performance Composite Structures. Composites Science and Technology, Springer, Singapore.

[6] Anderson MJ, Sullivan JG, Horiuchi TK, Fuller SB, Daniel TL (2020) A Bio-Hybrid Odor-Guided Autonomous Palm-Sized Air Vehicle. *Bioinspiration & Biomimetics* 16:026002.

[7] Andrea A, Molchanova N, Jenssen H (2018) Antibiofilm Peptides And Peptidomimetics With Focus On Surface Immobilisation. *Biomolecules* 8(2):27.

[8] Ansari A, Siddiqui VU, Khan I, Akram MK, Siddiqi WA, Khan A, Asiri AM (2020) Effect Of Self-Healing On Zeolite-Immobilized Bacterial Cementitious Mortar Composites. *Self-Healing Composite Materials*, Elsevier Inc, https://doi.org/10.1016/B978-0-12-817354-1.00014-4.

[9] Apitius L, Buschmann S, Bergs C, Schönauer D, Jakob F, Pich A, Schwaneberg U (2019) Biadhesive Peptides for Assembling Stainless Steel and Compound Loaded Micro-Containers. *Macromolecular Bioscience* 19(9):e1900125.

[10] Ariel G, Ayali A (2015) Locust Collective Motion And Its Modeling. *PLoS Computational Biology* 11(12):e1004522. https://doi.org/10.1371/journal.pcbi.1004522.

[11] Ariel G, Ayali A, Be'er A, Knebel D (2022) Variability and Heterogeneity in Natural Swarms: Experiments and Modeling. *Active Particles* 3:1–33.

[12] AUTOSTEM – Stem Cell Manufacture (2020). http://www.autostem2020.eu/. Retrieved on 22.07.2022.

[13] Ball A, Gelman L, Rao BKN (2020) *Advances in Asset Management and Condition Monitoring: COMADEM 2019*, Springer. https://doi.org/10.1007/978-3-030-57745-2 ISBN: 978-3-030-57744-5.

[14] Ball P (2012) Nature's Colour Tricks. *Scientific American* 306:74–79.

[15] Bartlett MD, Croll AB, King DR, Paret BM, Irschick DJ, Crosby AJ (2012) Looking Beyond Fibrillar Features To Scale Gecko Like Adhesion. *Advanced Materials* 24 (8):1078–1083.

[16] Bartolo P, Malshe A, Ferraris E, Koc B (2022) 3D Bioprinting: Materials, Processes, And Applications. *CIRP Annals* 71(2):577–597.

[17] Basiricò L, Ciavatti A, Fraboni B (2021) Solution-Grown Organic And Perovskite X-Ray Detectors: A New Paradigm For The Direct Detection Of Ionizing Radiation. *Advanced Materials Technology* 6(1):2000475.

[18] Battersby AJ, Khara J, Wright VJ, Levy O, Kampmann B (2016) Antimicrobial Proteins And Peptides In Early Life: Ontogeny And Translational Opportunities. *Frontiers in Immunology* 7:309.

[19] Bauernhansl T, Brecher C, Drossel W-G, Gumbsch P, ten Hompel M, Wolperdinger M (2019) *BIOINTELLIGENZ – Eine neue Perspektive für nachhaltige Industrielle Wertschöpfung*, Fraunhofer Verlag.

[20] Bdiwi M, Hou S, Winkler L, Ihlenfeldt S (2021) Empirical Study For Measuring The Mental States Of Humans During The Interaction With Heavy-Duty Industrial Robots. 2021 IEEE Conference on Cognitive and Computational Aspects of Situation Management (CogSIMA). https://doi.org/10.1109/CogSIMA51574.2021.9475939.

[21] Bdiwi M, Harsch A, Reindel P, Putz M (2020) VariPath: A Database for Modelling the Variance of Human Pathways in Manual and HRC Processes with Heavy-Duty Robots. 2020 IEEE International Conference on Robotics and Automation (ICRA): 1821–1826.

[22] Bell C, McWilliam R, Purvis A, Tiwari A (2013) Concepts of Self-Repairing. *Measurement and Control* 46:176–179.

[23] Ben Hanan U, Weiss A, Zaitsev V (2017) Jumping Efficiency Of Small Creatures And Its Applicability In Robotics. *Procedia Manufacturing* 21:243–250.

[24] Benkhelifa E, Pipe A, Tiwari A (2013) Evolvable Embryonics: 2-In-1 Approach To Self-Healing Systems. *Procedia CIRP* 11:394–399.

[25] Benyus J (1997) *Biomimicry: Innovation Inspired By Nature*, William Morrow & CompanyNew York, USA.

[26] Bergs T, Schwaneberg U, Apelt S, Jakob F, Emmenegger C, Beckers A, Yayci A, Nöth M, Sarmiento M, Barth S (2022) Structure Protects Function - An Enabler For The Functionalisation Of Component Surfacesby Biohybrid Coatings. *Procedia CIRP* 110:133–138.

[27] Bergs T, Schwaneberg U, Barth S, Hermann L, Grunwald T, Mayer S Biermann F, Sözer N (2020) Application Cases Of Biological Transformation In Manufacturing Technology. *CIRP Journal of Manufacturing Science and Technology* 31:68–77.

[28] Bettucci O, Matrone GM, Santoro F (2022) Conductive Polymer-Based Bioelectronic Platforms Toward Sustainable And Biointegrated Devices: A Journey From Skin To Brain Across Human Body Interfaces. *Advanced Materials Technologies* 7:2100293.

[29] Biermann F, Mathews J, Nießing B, König N, Schmitt RH (2021) Automating Laboratory Processes By Connecting Biotech And Robotic Devices – An Overview Of The Current Challenges, Existing Solutions And Ongoing Developments. *Processes* 9:966.

[30] BioStamp nPointTM Instructions for Use. Retrieved on 17.08.2022.

[31] Bochmann LS, Gehrke L, Gehrke N, Mertens C, Siess O, et al. (2016) Innovative Konzepte einer sich selbstorganisierenden Fahrzeugmontage am Beispiel des Forschungsprojekts Smart Face. in Schindler M, (Ed.) *«Einführung Und Umsetzung von Industrie 4.0 – Use cases Aus Der Praxis»*, Springer; 2016. https://doi.org/10.1007/978-3-662-48505-7_4.

[32] Bocklisch F, Packowski G, Zimmermann S, Lampke T (2022) Integrating Human Cognition In Cyber-Physical Systems: A Multidimensional Fuzzy Pattern Model With Application To Thermal Spraying. *Journal of Manufacturing Systems* 63:162–176.

[33] Bortolini M, Galizia FG, Mora C (2018) Reconfigurable Manufacturing Systems: Literature Review And Research Trend. *Journal of Manufacturing Systems* 49:93–106.

[34] Boxberger L, Weisheit L, Hensel S, Schellnock J, Mattheß D, Riedel F, Drossel W-G (2020) Development of Everting Tubular Net Structures Using Simulation for Growing Structures. *Appl Sci* 10(18):6466.

[35] Bozinovski A, Bozinovska L (2009) Anticipatory Brain Potentials In A Brain-Robot Interface Paradigm. *4th International IEEE/EMBS Conference on Neural Engineering*, IEEE, 451–454.

[36] Božinovski A, Stanko T, Velimir I, Liljana B (2011) Robot Control Using Anticipatory Brain Potentials. *Automatika* 52(1):20–30.

[37] Bozinovski S. (1990) Mobile Robot Trajectory Control: From Fixed Rails To Direct Bioelectric Control. In O. Kaynak (ed.) Proc. IEEE Workshop on Intelligent Motion Control: 63–67.

[38] Bozinovski S, Sestakov M, Bozinovska L. (1988) Using EEG Alpha Rhythm To Control A Mobile Robot. In G. Harris, C. Walker (eds.) Proc. IEEE Annual Conference of Medical and Biological Society: 1515–1516

[39] Brecher C, Malik A, Blanke P, Herfs W. (2019) Dynamic Integration Of Manual And Automated Biological Process Skills Into MES. *24th IEEE International Conference on Emerging Technologies and Factory Automation (ETFA)*, Zaragoza, Spain, 10-13 September: 1069-1076.

[40] Brecher C, Pieske S, Malik A, Storms S (2019) Modelling Of Devices In An Adaptive And Dynamic Environment. *Procedia CIRP* 86:210–215.

[41] Brecher C, Wein S, Xu X, Storms S, Herfs W (2019) Simulation Framework For Virtual Robot Programming In Reconfigurable Production Systems. *Procedia CIRP* 86:98–103.

[42] Brooks S, Roy R (2020) A Complexity Framework for Self-engineering Systems. *Smart Sustain Manuf Syst* 4:254–259.

[43] Brooks S, Roy R (2021) An Overview Of Self Engineering Systems. *Journal of Engineering Design* 32:397–447.

[44] Brooks S, Roy R, Dirks JH, Taylor D (2022) An Analysis Of Complexity Of Self-Engineering Function In Biology. *Journal of Engineering Design (UNDER REVIEW)* .

[45] Burgos-Morales O, Gueye M, Lacombe L, Nowak C, Schmachtenberg R, Hörner M, Jerez-Longres C, MohseninH Wagner HJ, Weber W (2021) Synthetic Biology As Driver For The Biologisation Of Materials Sciences. *Materials Today Bio* 11:100115.

[46] Burhan H, Saygili S, Sen F (2020) *Principal and Mechanism of Self-Repair of Polymer Matrix Composite materials. Self-Healing Composite Materials*, Elsevier Inc, . https://doi.org/10.1016/B978-0-12-817354-1.00011-9.

[47] Byeon S., Sun D., Hwang I. (2021) Skill-level-based Hybrid Shared Control for Human-Automation Systems. IEEE International Conference on Systems, Man and Cybernetics (SMC): 1507–1512.

[48] Byrne G, Damm O, Monostori L, Teti R, van Houten F, Wegener K, Wertheim R, Sammler F (2020) Towards High Performance Living Manufacturing Systems—A New Convergence Between Biology and Engineering. *CIRP Journal of Manufacturing Science and Technology* 34:6–21.

[49] Byrne G, Dimitrov D, Monostori L, Teti R, van Houten F, Wertheim R (2018) Biologicalisation: Biological Transformation in Manufacturing. *CIRP Journal of Manufacturing Science and Technology* 21:1–32.

[50] Campero-Jurado I, Marquet-Sanchez S, Quintanar-Gomez J, Rodriguez S, Corchado JM (2020) Smart Helmet 5.0 for Industrial Internet of Things Using Artificial Intelligence. *Sensors* 20:6241.

[51] Cao P, Liu D, Liu Y, Wang H, Zhang C, Yuan D, Liu X (2023) Marine Antifouling Behavior Of The Surfaces Modified By Dopamine And Antibacterial Peptide. *Journal of Oceanology and Limnology* 41(1):174–188.

[52] Carfì A, Mastrogiovanni F (2021) Gesture-Based Human–Machine Interaction: Taxonomy, Problem Definition, and Analysis. *IEE Transactions on Cybernetics* : 2168–2267.

[53] Carlsmith J (2020) How Much Computational Power Does It Take to Match the Human Brain? *Open Philanthropy.* https://www.openphilanthropy.org/research/how-much-computational-power-does-it-take-to-match-the-human-brain/ accessed July 29, 2022.

[54] Carrara S, Iniewski K (2015) *Handbook of Bioelectronics*, Cambridge University Press, 1–569.

[55] Cera L, Gonzalez GM, Liu Q (2021) A Bioinspired And Hierarchically Structured Shape-Memory Material. *Nature Materials* 20:242–249.

[56] NjA Chan, GuD, S Tan, Fu Q, Pattison TG, O'Connor AJ, Qiao GG (2020) Spider-Silk Inspired Polymeric Networks By Harnessing The Mechanical Potential Of B-Sheets Through Network Guided Assembly. *Nature Communications* . 11 Nr. 1630.

[57] Charitos IA, Ballini A, Cantore S, Boccellino M, Di Domenico M, Borsani E, Nocini R, Di Cosola M, Santacroce L, Bottalico L (2021) Stem Cells: A Historical Review About Biological, Religious, And Ethical Issues. *Stem Cells International* :9978837.

[58] Cianchetti M. (2021) Embodied Intelligence In Soft Robotics Through Hardware Multifunctionality. Frontiers in Robotics and AI 8, Article 724056, https://doi.org/10.3389/frobt.2021.724056.

[59] Clauder F, Möller S, Köhling S, Bellmann-Sickert K, Rademann J, Schnabelrauch M, Beck-Sickinger AG (2020) Peptide-Mediated Surface Coatings For The Release Of Wound-Healing Cytokines. *J Tissue Engineering and Regenerative Medicine* 14:1738–1748.

[60] Cribb W, Lin C-L, Rintoul L, Rasch R, Hasenpusch J, Huang H (2010) Hardness In Arthropod Exoskeletons In The Absence Of Transition Metals. *Acta Biomaterialia* 6:3152–3156.

[61] Cseke A, Haines-Gadd M, Mativenga P, Charnley F (2020) A Framework for Assessing Self-Healing Products. *Procedia CIRP* 90:283–312.

[62] Cully A, Clune J, Tarapore D, Mouret JB (2015) Robots That Can Adapt Like Animals. *Nature* 521(7553):503–507.

[63] D'Addona DM, Conte S, Teti R, Marzocchella A, Raganati F (2020) Feasibility Study of Using Microorganisms as Lubricant Component in Cutting Fluids. *Procedia CIRP* 88:606–611.

[64] Damm O, Bezuidenhout M, Uheida E, Dicks L, Hadasha W, Hagedorn-Hansen D (2021) Yeast-Based Metalworking Fluid For Milling Of Titanium Alloy —An Example Of Bio-Integration. *CIRP Journal of Manufacturing Science and Technology* 34:47–60.

[65] Daniszewski M, Crombie DE, Henderson R, Liang HH, Wong RCB, Hewitt AW, Pébay A (2018) Automated Cell Culture Systems And Their Applications To Human Pluripotent Stem Cell Studies. *SLAS Technology* 23(4):315–325.

[66] De Belie N, Gruyaert E, Al-Tabbaa A, Antonaci P, Baera C, Bajare D, Darquennes A, Davies R, Ferrara L, Jefferson T, Litina C, Miljevic B, Otlewska A, Ranogajec J, Roig-Flores M, Paine K, Lukowski P, Serna P, Tulliani JM, Vucetic S, Wang J, Jonkers HM (2018) A Review Of Self-Healing Concrete For Damage Management Of Structures. *Adv Mater Interfaces* 5:1–28.

[67] de Rooji M, Van Tittelboom K, De Belie N, Schlangen E (2013) *Self-Healing Phenomena in Cement-Based Materials. State-of-the-art-Report of RILEM Technical Committee 221-SHC*, Springer.

[68] Denkena B, Dittrich M-A, Stamm S, Wichmann M, Wilmsmeier S (2021) Gentelligent Processes In Biologically Inspired Manufacturing. *CIRP Journal of Manufacturing Science and Technology* 32:1–15.

[69] Do AH, Wang PT, King CE, Chun SN, Nenadic Z (2013) Brain-Computer Interface Controlled Robotic Gait Orthosis. *Journal of Neuroengineering and Rehabilitation* 10(1):111.

[70] Dorigo M, Theraulaz G, Trianni V (2021) Swarm Robotics: Past, Present, And Future [Point Of View]. *Proceedings of the IEEE* 109(7):1152–1165.

[71] Doud AJ, Lucas JP, Pisansky MT, He B (2011) Continuous Three-Dimensional Control Of A Virtual Helicopter Using A Motor Imagery Based Brain-Computer Interface. *PLoS One* 6(10):e26322.

[72] Drossel W, Dani I, Wertheim R (2019) Biological Transformation And Technologies Used For Manufacturing Of Multifunctional Metal-Based Parts. *Procedia Manufacturing* 33:115–122.

[73] Drossel W, Meinel F, Bucht A, Kunze H (2018) Smart Materials For Smart Production – A Cross-Disciplinary Innovation Network In The Field Of Smart Materials. *Procedia Manufacturing* 21:197–204.

[74] Drossel W, Schlegel H, Walther M, Zimmermann P, Bucht A (2015) New Concepts For Distributed Actuators And Their Control. *Soft Robotics: Transferring Theory to Application* : 19–32.

[75] Drummond K. (2009) Pentagon Preps Soldier Telepathy Push. Wired, Retrieved on 17.08.2022.

[76] EC Call HORIZON-CL4-2021-DIGITAL-EMERGING-01, Project Name/Acronym: A Modular Framework for Designing and Producing Biohybrid - “BioMeld” (2022-2025), https://biomeld.eu.

[77] Eduok U, Ohaeri E, Szpunar J (2020) Self-Healing Composite Coatings With Protective And Anticorrosion Potentials: Classification By Healing Mechanism. Self healing composite materials. *Elsevier Inc* : 123–162. https://doi.org/10.1016/B978-0-12-817354-1.00008-9.

[78] Ellen Mac Arthur Foundation(2022) https://www.ellenmacarthur-foundation.org/the-circular-economy-in-detail-deep-dive, Retrieved 7.5.2023.

[79] ElMaraghy H, Monostori L, Schuh G, ElMaraghi W (2021) Evolution And Future Of Manufacturing Systems. *CIRP Annals* 70(2):635–658.

[80] Epstein AK, Hochbaum AI, Kim P, Aizenberg J (2011) Control Of Bacterial Biofilm Growth On Surfaces By Nanostructural Mechanics And Geometry. *Nanotechnology* 22:494007.

[81] Espalin D, Muse DW, MacDonald E, Wicker RB (2014) 3D Printing Multifunctionality: Structures With Electronics. *International Journal of Advanced Manufacturing Technology* 72:963–978.

[82] Fan T-X, Chow S-K, Zhang D (2009) Biomorphic Mineralisation: From Biology To Materials. *Progress in Materials Science* 54(5):542–659.

[83] Fang F (2022) *Laboratory of Micro/Nano Manufacturing Technology*, Tianjin UniversityChina.

[84] Fang FZ (2014) *Manufacturing III (Invited Lecture)*, University College Dublin. Dublin, Ireland November 11.

[85] Fang FZ (2020) Atomic And Close-To-Atomic Scale Manufacturing: Perspectives And Measures. *Int J Extreme Manufacturing* 2(3):030201.

[86] Fang FZ, Cheng Y, Zhang X (2013) Design Of Freeform Optics. *Advanced Optical Technologies*, 445–453.

[87] Fraunhofer (2021) https://www.ivv.fraunhofer.de/en/press/fraunhofer-light-house-project-futureproteins.html retrieved 23.8.2023

[88] Fischetti M (2011) Computers versus Brains. *Scientific American* . https://www.scientificamerican.com/article/computers-vs-brains/ accessed July 29, 2022.

[89] Frei R, McWilliam R, Derrick B, Purvis A, Tiwari A, DiMarizio Serugenda G (2013) Self-Healing And Self-Repairing Technologies. *International Journal of Advanced Manufacturing Technology* 69:1033–1061.

[90] Fujitsu Limited. *Supercomputer Fugaku retains First Place Worldwide in HPCG and Graph500 Rankings*, Press ReleaseTokyo, Japan May 30, 2022 https://www.fujitsu.com/global/about/resources/news/press-releases/2022/0530-01.html accessed July 29, 2022.

[91] Full J, Miehe R, Kiemel S, Bauernhansl T, Sauer A (2019) The Biological Transformation of Energy Supply and Storage – Technologies and Scenarios for Biointelligent Value Creation. *Procedia Manufacturing* 39:1204–1214.

[92] Gartner P, Jacob A, Haluk A, Löffler J, Gammak J, Lanza G, Sang-Gook K, et al. (2022) Manufacturing Genome: A Foundation for Symbiotic, Highly Iterative Product and Production Adaptations. in Andersen, et al., (Ed.) *Towards Sustainable Customization: Bridging Smart Products and Manufacturing Systems. CARV MCPC 2021*, Springer Intern, ; 2022. https://doi.org/10.1007/978-3-030-90700-6_3.

[93] Georgi O., Rentzsch H., Blau P. (2018) Miniaturized Parallel Kinematic Machine Tool For The Machining Of Small Workpieces. 18th Int Conference of the European Society for Precision Engineering and Nanotechnology (EUSPEN International Conference), Venice, Italy.

[94] Ghosh SK (2009) *Self-Healing Materials: Fundamentals, Design Strategies, and Applications*, Wiley WCHGmbH.

[95] Gilroy D, Kauffman K, Hall RA, Huang X, Chu FS (2000) Assessing Potential Health Risks From Microcystin Toxins In Blue-Green Algae Dietary Supplements. *Environmental Health Perspectives* 108(5):435–439.

[96] Giorgio I, Spagnuolo M, Andreaus U, Scerrato D, Bersani AM (2021) In-Depth Gaze At The Astonishing Mechanical Behavior Of Bone: A Review For Designing Bio-Inspired Hierarchical Metamaterials. *Mathematics and Mechanics of Solids* 26 (7):1074–1103.

[97] Gleich A, Pade C, Petschow U, Pissarskoi E (2002) *Potentials and Trends in Biomimetics*, Springer.

[98] Goertz I-D, Brummer F (2012) *Biologie Fuer Ingenieure*, Springer SpektrumBerlin.

[99] Goodland R (1995) The Concept of Environmental Sustainability. *Annual Review of Ecology and Systematics* 26:1–24.

[100] Goyal D, Pabla BS (2015) Condition Based Maintenance Of Machine Tools — A Review. *CIRP Journal of Manufacturing Science and Technology* 10:24–35.

[101] Griffith MJ, Cottam S, Stamenkovic J, Posar JA, Petasecca M (2020) Printable Organic Semiconductors For Radiation Detection: From Fundamentals To Fabrication And Functionality. *Frontiers in Physics* 8. https://doi.org/10.3389/fphy.2020.00022.

[102] Gu D, Shi X, Poprawe R, Bourell DL, Setchi R, Zhu J (2021) Material-Structure-Performance Integrated Laser-Metal Additive Manufacturing. *Science* 372 (6545):eabg1487.

[103] Gutknecht K, Cloots M, Sommerhuber R, Wegener K (2021) Mutual Comparison Of Acoustic, Pyrometric And Thermographic Laser Powder Bed Fusion Monitoring. *Materials & Design* 210:110036.

[104] Haas LF (2003) Hans Berger (1873-1941), Richard Caton (1842-1926), And Electroencephalography. *Journal of Neurology, Neurosurgery & Psychiatry* 74 (1):9.

[105] Hagen J, Arafat R, Abraham T, Hermann C (2022) Function Oriented Biological Transformation Of A Lubrication Process System. *Procedia CIRP* 110:26–31.

[106] Hager MD, van der Zwaag S, Schubert US (2016) *Self Healing Materials*, Springer.

[107] Hameed J, Harrison I, Gasson M, Warwick K. (2010) A Novel Human Machine Interface Using Subdermal Implants. Proc. IEEE 9th International Conference on Cybernetic Intelligent Systems: 106–110.

[108] Hansen CJ (2015) *Microvascular-Based Self-Healing Materials. In Recent Advances in Smart Self-Healing Polymers and Composites*, Elsevier Ltd, 129–157. https://doi.org/10.1016/C2013-0-16515-4.

[109] Harbisson N (2008) *Painting By Ear. Modern Painters*, The International Contemporary Art Magazine, New York 70–73.

[110] Harst S, Früchtl M, Neugebauer R (2022) Biological Transformation of Manufacturing – From a Vision to Industrial Transfer – Interim Evaluation from the Perspective of Applied Research. *Procedia CIRP* 107:925–930.

[111] Harst S, Früchtl M, Aichinger H, Kemter-Esser C, Volkert B (2023) Mycelium – From Funghi to products. *Procedia CIRP* . in preparation.

[112] Heathman TRJ, Rafiq QA, Chan AKC, Coopman K, Nienow AW, Kara B, Hewitt CJ (2016) Characterisation Of Human Mesenchymal Stem Cells From Multiple Donors And The Implications For Large Scale Bioprocess Development. *Biochemical Engineering Journal* 108(15):14–23.

[113] Helfman Cohen Y, Reich Y, Greenberg S (2014) Sustainability Strategies In Nature. *Int J Design & Nature and Ecodynamics* 9(4):285–295.

[114] Hellmich A, Foith-Förster P, Zumpe M, Zumpe F, Münnich M, Berkhan P, Ranke D, Trierweiler M. (2022) Umsetzung von cyber-physischen Matrix-Produktionssystemen.

[115] Hellmich A, Sai B, Süße M, Schreiber M, Wiese T, Ihlenfeldt S, Bauernhans T, Putz M, Reinhart G. (2020) Bio-inspired Factories of the Future. In: Proceedings of the Conference on Production Systems and Logistics CPSL 2020: 426–437.

[116] Helms M, Vattam S, Goel A (2009) Biologically Inspired Design: Process and Products. *Design Studies* 30:606–622.

[117] Henerichs M (2015) *Bohrbearbeitung von CFK unter besonderer Berücksichtigung der Schneidkantengeometrie* Ph.D. thesis ETH Zürich No. 22629.

[118] Henerichs M, Voss R, Kuster F, Wegener K (2015) Machining of Carbon Fiber Reinforced Plastics: Influence Of Tool Geometry And Fiber Orientation On The Machining Forces. *CIRP Journal of Manufacturing Science and Technology* 9:136–145.

[119] Hensel S, Boxberger L, Weisheit L, Schellnock J, Thielsch J, Riedel F, Drossel W-G (2021) Everting of Tubular Net Structures Based on Shape Memory Alloys. *IOP Eng Res Express* 3(2):025028.

[120] Hermann C, Blume S, Kurle D, Schmidt C, Thiede S (2015) The Positive Impact Factory - Transition from Eco-efficiency to Eco–effectiveness Strategies in Manufacturing. *Procedia CIRP* 29:19–27.

[121] Herrmann C, Cerdas F, Abraham T, Büth L, Mennenga M (2021) Biological Transformation Of Manufacturing As A Pathway Towards Environmental Sustainability: Calling For Systemic Thinking. *CIRP Journal of Manufacturing Science and Technology* 34:157–170.

[122] Hirose T, Kotoku J, Toki F, Nishimura EK, Nanba D (2021) Label-Free Quality Control And Identification Of Human Keratinocyte Stem Cells By Deep Learning-Based Automated Cell Tracking. *Stem Cells* 39:1091–1100.

[123] Hollnagel E, Woods DD (2005) *Joint Cognitive Systems – Foundations of Cognitive Systems Engineering*, CRC Press Taylor and Francis. ISBN 10: 0-8493-2821-7.

[124] Hong TK, Shin D-M, Choi J, Do JT, Han SG (2021) Current Issues And Technical Advances In Cultured Meat Production: A Review. *Food Science of Animal Resources* 41(3):355–372.

[125] Horiguci I, Kino-oka M (2021) Current Developments In The Stable Production Of Human Induced Pluripotent Stem Cells. *Engineering* 7:144–152.

[126] Impuls-Stiftung (2016) Industry 4.0 Readiness - Online Self-Check for Businesses, https://www.industrie40-readiness.de/?lang=en. Retrieved on 29.07.2022.
[127] Islam MK, Hazell PJ, Escobedo JP, Wang H (2021) Biomimetic Armour Design Strategies For Additive Manufacturing: A Review. *Materials & Design* 205:109730.
[128] Jabr F (2012) Does Thinking Really Hard Burn More Calories? *Scientific American* : 2022. https://www.scientificamerican.com/article/thinking-hard-calories/ , accessed on July 29.
[129] Jiang W (2014) Bio-Inspired Self-Sharpening Cutting Tool Surface For Finish Hard Turning Of Steel. *CIRP Annals* 63(1):517–520.
[130] Jagath K, Burela RG (2019) Multi-Scale Modelling And Simulation Of Natural Fiber Reinforced Composites (Bio-composites). *Journal of Physics Conference Series* 1240(1):012103.
[131] Kami D, Watakabe K, Yamazaki-Inoue M, MinamiK Kitani T, Itakura Y, Toyoda M, Sakurai T, Umezawa A, Gojo S (2013) Large-Scale Cell Production Of Stem Cells For Clinical Applications Using The Automated Cell Processing Machine. *BMC Biotechnology* 13:102.
[132] Kamps T, Gralow M, Schlick G, Reinhart G (2017) Systematic Biomimetic Part Design for Additive Manufacturing. *Procedia CIRP* 65:259–266.
[133] Kanellopoulos A, Quereshi TS, Al-Tabbaa A (2015) Glass Encapsulated Minerals For Self-Healing In Cement Based Composites. *Construction and Building Materials* 98:780–791.
[134] Kazemzadeh-Narbat M, Cheng H, Chabok R, Alvarez MM, La Fuente-Nunez C, Phillips KS, Khademhosseini A (2021) Strategies For Antimicrobial Peptide Coatings On Medical Devices: A Review And Regulatory Science Perspective. *Critical Reviews in Biotechnology* 41:94–120.
[135] Kessler MR, Sottos NR, White SR (2003) Self-Healing Structural Composite Materials. *Composites Part A Applied Science and Manufacturing* 34:743–753.
[136] Knebel D, Ayali A, Guershon M, Ariel G (2019) Intra- Versus Intergroup Variance In Collective Behavior. *Science Advances* 5(1). https://doi.org/10.1126/sciadv.aav0695.
[137] Knebel D, Sha-Ked C, Agmon N, Ariel G, Ayali A (2021) Collective Motion As A Distinct Behavioral State Of The Individual. *IScience* 24(4). https://doi.org/10.1016/j.isci.2021.102299.
[138] Ko HJ, Park TH (2016) Bioelectronic Nose And Its Application To Smell Visualisation. *Journal of Biological Engineering* 10:17.
[139] Kohl D., Böhm S. (2016) Holzformteile als Multi-Materialsysteme für den einsatz im Fahrzeug Rohbau (HAMMER); Forschungsprojekt, gefördert durch die FNR (Fachagentur für nachwachsende Rohstoffe. FKZ: 13N12039.
[140] Kollatsch C, Klimant P (2021) Efficient Integration Process Of Production Data Into Augmented Reality Based Maintenance Of Machine Tools. *Production Engineering* 15:311–319.
[141] Konagaya S, AndoT Yamauchi T, Suemori H, Iwata H (2015) Long-Term Maintenance Of Human Induced Pluripotent Stem Cells By Automated Cell Culture System. *Scientific Reports* 5:16647.
[142] Kroll E, Buchris E (2018) Weight Reduction of 3D-Printed Cylindrical And Toroidal Pressure Vessels Through Shape Modification. *Procedia Manufacturing* 21:133–140.
[143] Kulik M, Ochs J, König N, Schmitt R (2016) Automation In The Context Of Stem Cell Production – Where Are We Heading With Industry 4.0? *Cell Gene Therapy Insights* 2(4):499–506.
[144] Kumar R, Hynes NRJ, Senthamaraikannan P, Khan A, Rangappa SM, Singchien S, Barathi SRS, Asiri AM, Khan I (2020) *Self-repairing Fibre Polymer Composites: Mechanisms And Properties. In self Healing Composite Materials*, Elsevier Inc., 71–85.
[145] LaFleur K, Cassady K, Doud A, Shades K, Rogin E, He B (2013) Quadcopter Control In Three-Dimensional Space Using A Noninvasive Motor Imagery-Based Brain-Computer Interface. *Journal of Neural Engineering* 0(4):046003.
[146] Lee J, Ghaffari M, Elmeligy S (2011) Self-Maintenance And Engineering Immune Systems: Towards Smarter Machines And Manufacturing Systems. *Annual Reviews in Control* 35:111–122.
[147] Lee MW, An S, Yoon SS, Yarin AL (2018) Advances In Self-Healing Materials Based On Vascular Networks With Mechanical Self-Repair Characteristics. *Advances in Colloid and Interface Science* 252:21–37.
[148] Lee S, Kim J, Roh H, Kim W, Chung S, Moon W, Cho K (2022) A High-Fidelity Skin-Attachable Acoustic Sensor For Realizing Auditory Electronic Skin. *Advanced Materials* 34(21):2109545.
[149] Lee S, Seong H, Im SG, Moon H, Yoo S (2017) Organic Flash Memory On Various Flexible Substrates For Foldable And Disposable Electronics. *Nature Communications* 8(1):725.
[150] Levi P, Meister E, Schlachter F (2014) Reconfigurable Swarm Robots Produce Self-Assembling And Self-Repairing Organisms. *Robotics and Autonomous Systems* 62:1371–1376.
[151] Li T, Li Y, Zhang T (2019) Materials, Structures, And Functions For Flexible And Stretchable Biomimetic Sensors. *Accounts of Chemical Research* 52:288–296.
[152] Lichtblau K, Stich V, Bertenrath R, Blum M, Bleider M, Millack A, Schmitt K, Schmit E, Schröter M. (2015) IMPULS - Industrie 4.0-Readiness. Impuls-Stiftung des VDMA
[153] Lima SA, Ahmed MU. (2017) Introduction to Food biosensors. Food Chemistry, Function and Analysis No. 1, Food Biosensors, Edited by Minhaz Uddin Ahmed, Mohammed Zourob and Eiichi Tamiya, The Royal Society of Chemistry: 1–21.
[154] Lumley RN, Polmear IJ. (2007) Advances in Self Healing of Metals. Proc. First International Conference on Self Healing Materials, Schmets AJM Zwaag Svan der (Eds.), Springer, Dordrecht.
[155] Macdonald E, Espalin D, Doyle D, Muñoz J, Ambriz S, Coronel Jr J, Williams A, Wicker R (2018) Fabricating Patch Antennas Within Complex Dielectric Structures Through Multi-Process 3D Printing. *Journal of Manufacturing Processes* 34:197–203.
[156] MacDonald E, Wicker R (2016) Multiprocess 3D printing for increasing component functionality. *Science* 353:aaf2093.
[157] Machine Design (2018) 3D-Printed Flexible Chip Offers 7,000X More Memory. https://www.machinedesign.com/3d-printing-cad/article/21836322/3dprinted-flexible-chip-offers-7000x-more-memory. Retrieved on 29.9.2022.
[158] Maes M, Van Tittelboom K, De Belie N (2014) The Efficiency Of Self-Healing Cementitious Materials By Means Of Encapsulated Polyurethane In Chloride Containing Environments. *Construction and Building Materials* 71:528–537.
[159] Maier M, Gittler T, Weiss L, Bobst C, Scholze S, Wegener K (2019) Sensors As An Enabler For Self-Optimizing Grinding Machines. *MM Science Journal HSM2019-89* : 3192–3199.
[160] Malshe A, Bapat S, Rajurkar K, Melkote S (2021) Biological Strategies From Natural Structures For Resilience In Manufacturing. *CIRP Journal of Manufacturing Science and Technology* 34:146–156.
[161] Malshe A, Rajurkar K, Samant A, Hansen HN, Bapat S, Jiang W (2013) Bio-Inspired Surfaces For Advanced Applications. *CIRP Annals* 62(2):607–628.
[162] Markel U, Essani KD, Besirlioglu V, Schiffels J, Streit WR, Schwaneberg U (2020) Advances in Ultrahigh-Throughput Screening For Directed Enzyme Evolution. *Chemical Society Review* 49:233.
[163] Mason C, Dunnill P (2008) A Brief Definition Of Regenerative Medicine. *Regenerative Medicine* 3(1):1–5.
[164] Mauldin TC, Kessler MR (2010) Self-Healing Polymers And Composites. *International Materials Reviews* 55:317–346.
[165] Medina JR, Borner H, Endo S, Hirche S (2019) Impedance-Based Gaussian Processes for Modeling Human Motor Behavior in Physical and Non-Physical Interaction. *IEEE Trans Biomed* 66(9):2499–2511.
[166] Meng J, Zhang S, Bekyo A, Olsoe J, Baxter B, He B (2016) Noninvasive Electroencephalogram Based Control Of A Robotic Arm For Reach And Grasp Tasks. *Nature Scientific Reports* 6:38565.
[167] Meyer D, Redetzky M, Brinksmeier E (2017) Microbial-Based Metalworking Fluids In Milling Operations. *CIRP Annals* 66(1):129–132.
[168] Miehe R, Bauernhansl T, Beckett M, Brecher C, Demmer A, Drossel W-G, Elfert P, Full J, Hellmich A, Hinxlage J, Horbelt J, Jutz G, Krieg S, Maufroy C, Noack M, Sauer A, Schließmann U, Scholz P, Schwarz O, ten Hompel M, Wrycza P, Wolperdinger M (2020) The Biological Transformation Of Industrial Manufacturing – Technologies, Status And Scenarios For A Sustainable Future Of The German Manufacturing Industry. *Journal of Manufacturing Systems* 54:50–61.
[169] Miehe R, Bauernhansl T, Schwarz O, Traube A, Lorenzoni A, Waltersmann L, Full J, Horbelt J, Sauer A (2018) The Biological Transformation Of The Manufacturing Industry – Envisioning Biointelligent Value Adding. *Procedia CIRP* 72:739–743.
[170] Miehe R, Fischer E, Berndt D, Herzog A, Horbelt J, Full J, Bauernhansl T, Schenk M (2019) Enabling Bidirectional Real Time Interaction Between Biological And Technical Systems: Structural Basics Of A Control Oriented Modeling Of Biology-Technology-Interfaces. *52nd CIRP Conference on Manufacturing Systems, Procedia CIRP* 81:63–68.
[171] Miller J., University of North Carolina at Charlotte, USA. Contribution to: “Terminology Issues/Gaps Related to Biologicalisation in Manufacturing”, 2nd CIRP CWG Meeting, 22 Aug. 2019.
[172] Monostori L, Csáji B, Egri P, Kis K, Váncza J, Ochs J, Jung S, König N, Pieske S, Wein S, Schmitt R, Brecher C (2021) Automated Stem Cell Production By Bio-Inspired Control. *CIRP Journal of Manufacturing Science and Technology* 33:369–379.
[173] Monostori L, Váncza J (2020) Towards Living Manufacturing Systems. *Procedia CIRP* 93:323–328.
[174] Mount NM, Ward SJ, Kefalas P, Hyllner J (2015) Cell-Based Therapy Technology Classifications And Translational Challenges. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences* 370:1680.
[175] Müller M, Müller B, Hensel S, Nestler M, Jahn SF, Müller R, Drossel W (2016) Structural Integration Of Piezoceramic Fibers In Deep Drawn Sheet Metal For Material-Integrated Health Monitoring. *Mechatronics* 34:100–110.
[176] Murakami T, Ahn TH, Hashimoto T, Ogura N, Kishi T (2011) A Study On The New Water Leak Repair Method For Subway Tunnels Using Crack Self-Healing Repair Method. *Journal of Ceramic Processing Research* 16:95–97.
[177] Musk E, Neuralink (2019) An Integrated Brain-Machine Interface Platform With Thousands Of Channels. *Journal of Medical Internet Reearch* 31(10): e16194.. 1.
[178] Nano Dimension (2019) 3D Printing Integrated Circuits: What’s Possible Now and in the Future? https://www.nano-di.com/resources/blog/2019-3d-printing-integrated-circuits-whats-possible-now-and-in-the-future. Retrieved on 29.9.2022.
[179] N.N. (2022) World Population Prospects 2022, United Nations, New York, USA
[180] Nemec J, Alba-Flores R. (2022) Unmanned Aerial Vehicle Control Using Hand Gestures and Neural Networks. Int IOT, Electronics and Mechatronics Conf (IEMTRONICS) 978-1-6654-8684-2/22.
[181] Neugebauer R, Ihlenfeldt S, Schliessmann UD, Hellmich A, Noack M (2019) A new Generation of Production with Cyber-Physical Systems – Enabling the Biological Transformation in Manufacturing. *Journal of Machine Engineering* 19 (1):5–15.
[182] Nießing B, Kiesel R, Herbst L, Schmitt RH (2021) Technoeconomic Analysis Of Automated iPSC Production. *Processes* 9:240.

[183] Nosonovsky M, Bhushan B (2010) Surface Self-Organisation: From Wear To Self-Healing In Biological And Technical Surfaces. *Applied Surface Science* 256 (12):3982–3987.

[184] O'Brolchain F, Gordijn B, Byrne G, Dunne N (2021) Ethical Aspects of the Biologicalisation of Manufacturing. *CIRP Journal of Manufacturing Science and Technology* 34:178–185.

[185] Ochs J, Biermann F, Pietrowski T, Erkens F, Nießing B, Herbst L, König N, Schmitt RH (2021) Fully Automated Cultivation Of Adipose-Derived Stem Cells In The StemCellDiscovery – A Robotic Laboratory For Small-Scale, High-Throughput Cell Production Including Deep Learning-Based Confluence Estimation. *Processes* 9:575.

[186] Oxley TJ, Yoo PE, Rind GS, et al. (2021) Motor Neuroprosthesis Implanted With Neurointerventional Surgery Improves Capacity For Activities Of Daily Living Tasks In Severe Paralysis: First In-Human Experience. *Journal of NeuroInterventional Surgery* 13:102–108.

[187] Oxford Languages. Retrieved on 17.08.2022.

[188] Panda S, Mondal S, Kumar N (2022) SLAP: A Secure and Lightweight Authentication Protocol for machine-to-machine communication in industry 4.0. *Computers and Electrical Engineering* 98:107669.

[189] Papadelis C, Braun C, Pantazis D, Soekadar SR, Bamidis P (2013) Using brain waves to control computers and machines. *Advances in Human-Computer Interaction* 2013:802063. Article ID.

[190] Park J, Lee Y, Hong J, Lee Y, Ha M, Jung Y, Lim H, Kim SY, Ko H (2014) Tactile-direction-sensitive and stretchable electronic skins based on human-skin-inspired interlocked microstructures. *ACS Nano* 8(12):12020–12029.

[191] Pavan Kalyan BG, Kumar L (2022) 3D Printing: Applications In Tissue Engineering, Medical Devices, And Drug Delivery. *Aaps Pharmscitech* 23:92.

[192] Pepicelli M, Binelli MR, Studart AR, Rühs PA, Fischer P (2021) Self-Grown Bacterial Cellulose Capsules Made through Emulsion Templating. *ACS Biomater Sci Eng* 2021:3221–3228.

[193] Pfurtscheller G, Müller GR, Pfurtscheller J, Gerner HJ, Rupp R (2003) Thought-Control Of Functional Electrical Stimulation To Restore Hand Grasp In A Patient With Tetraplegia. *Neuroscience Letters* 351(1):33–36.

[194] Piotrowski T, Rippel O, Elanzew A, Nießing B, Stucken S, Jung S, König N, Haupt S, Stappert L, Brüstle O, Schmitt R, Jonas S (2021) Deep-Learning-Based Multi-Class Segmentation For Automated, Non-Invasive Routine Assessment Of Human Pluripotent Stem Cell Culture Status. *Computers in Biology and Medicine* 129:104172.

[195] Prasad K, Ranjan RK, Lutfi Z, Pandey H (2009) Biosensors: Allications And Overview In Industrial Automation. *International Journal on Applied Bioengineering* 3 (1):66–70.

[196] Qu YJ, Ming XG, Liu ZW, Zhang XY, Hou ZT (2019) Smart Manufacturing Systems: State Of The Art And Future Trends. *The International Journal of Advanced Manufacturing Technology* 103:3751–3768.

[197] Raessa M, Chen J, Wan W, Harada K (2020) Human-in-the loop Robotic Manipulation Planning for Collaborative Assembly. *IEEE Transactions on Automation Science and Engineering* 17(4):1800–1813.

[198] Rafferty JP (2022) Megalodon. *Encyclopedia Britannica* . https://www.britannica.com/animal/megalodon Retrieved on 17.07.2022.

[199] Raheem AA, Hameed P, Whenish R, Elsen RS, Aswin G, Jaiswal AK, Prashanth KG, Manivasagam G (2021) a Review on Development of Bio-Inspired Implants Using 3D Printing. *Biomimetics* 6(4):65.

[200] Rahman M, Pan R, Ho J, Tseng T-L. (2022) A Review of Augmented Reality Technology and its Applications in Digital Manufacturing. Available at SSRN: or https://doi.org/10.2139/ssrn.4068353.

[201] Rajkumar R, Brooks S (2020) Self-Engineering – Technological Challenges. in Karabegović I, (Ed.) *New Technologies, Development and Application III. NT 2020. Lecture Notes in Networks and Systems 128*, Springer, Cham; 2020. https://doi.org/10.1007/978-3-030-46817-0_2.

[202] Rapeaux AB, Constandinou TG (2021) Implantable Brain Machine Interfaces: First-In-Human Studies, Technology Challenges And Trends. *Current Opinion in Biotechnology* 72:102–111.

[203] REGULATION (EC) No 1907/2006 Of The European Parliament And Of The Council of 18 December 2006.

[204] Reibert D, Sydow S, Abraham TG (2022) Integration of Bio-based Insulation Materials as a Contribution to the Biological Transformation of Production Technology. *Procedia CIRP* 110:305–310.

[205] Reljić V, Milenković I, Dudić S, Šulc J, Bajči B (2021) Augmented Reality Applications In Industry 4.0 Environment. *Applied Sciences* 11:5592.

[206] Riazi AM, Kwon SY, Stanford WL (2009) Stem Cell Sources For Regenerative Medicine. *Methods in Molecular Biology* 482:55–90.

[207] Riesener M, Kuhn M, Keuper A, Schuhmacher J, Schuh G (2022) Complexity-Oriented Design For Cyber-Physical Systems. *Proc CIRP* 109:203–208.

[208] Robinton DA, Daley GQ (2012) The Promise Of Induced Pluripotent Stem Cells In Research And Therapy. *Nature* 481:295–305.

[209] Roy R, Stark R, Tracht K, Takata S, Mori M (2016) Continuous Maintenance And Future – Foundations And Technological Challenges. *CIRP Annals* 65 (2):667–688.

[210] Rübsam K, Weber L, Jakob F, Schwaneberg U (2018) Directed Evolution of Polypropylene and Polystyrene Binding Peptides. *Biotechnology and Bioengineering* 115/2:321–330.

[211] Sankaranarayanan R, Hynes NRJ, Kannan PS, Khan A, Asiri AM (2020) Mechanical Behavior Of Self-Healing Polyethylenimine/Polyacrylic Acid Multilevel Polymer Films. *Self-Healing Composite Materials*, Elsevier Inc., 405–414.

[212] Saura JR, Ribeiro-Soriano D, Palacios-Marqués D (2021) Evaluating Security And Privacy Issues Of Social Networks Based Information Systems in Industry 4.0. *Enterprise Information Systems* : 1–17.

[213] Sauter E, Winter M, Wegener K (2022) Analysis Of Robustness And Transferability In Feature-Based Grinding Burn Detection. *International Journal of Advanced Manufacturing Technology* 120:2587–2602.

[214] Scheibel T (2004) Spider Silks: Recombinant Synthesis, Assembly, Spinning, And Engineering Of Synthetic Proteins. *Microbial Cell Factories* 3:14–28.

[215] Selbmann E, Preiß M, Ben Achour A, Teicher U, Hänel A, Ihlenfeldt S (2022) Investigation Of Bio-Based Cooling Lubricants For The Machining Of Aircraft Stainless Steels. *Procedia CIRP* 110:47–52.

[216] Shu LH, Ueda K, Chiu I, Cheong H (2011) Biologically Inspired Design. *CIRP Annals* 60(2):673–693.

[217] Sigov A, Ratkin L, Ivanov LA, Xu LD (2022) Emerging Enabling Technologies For Industry 4.0 And Beyond. *Information Systems Frontiers*, Springer. https://doi.org/10.1007/s10796-021-10213-w.

[218] Soares FAC, Chandra A, Thomas RJ, Pedersen RA, Vallier L, Williams DJ (2014) Investigating The Feasibility Of Scale Up And Automation Of Human Induced Pluripotent Stem Cells Cultured In Aggregates In Feeder Free Conditions. *Journal of biotechnology* 173:53–58.

[219] Solga A, Cerman Z, Striffler BF, Spaeth M, Barthlott W (2007) The Dream of Staying Clean: Lotus and Biomimetic Surfaces. *Bioinspiration & Biomimetics* 2 (4):126–129.

[220] Somashekaraiah R, Suvin PS, Gnanadhas DP, Kailas SV, Chakravortty D (2016) Eco-Friendly, Non-Toxic Cutting Fluid for Sustainable Manufacturing and Machining Processes. *Tribology Online* 11(5):556–567.

[221] Stieve H (1983) Sensors Of Biological Organisms – Biological Transducers. *Sensors and Actuators* 4:689–704.

[222] Stillger L, Müller D (2022) Peptide-Coating Combating Antimicrobial Contaminations: A Review Of Covalent Immobilisation Strategies For Industrial Applications. *Journal of Materials Science* 57:10863–10885.

[223] Stoick-Cooper CL, Moon RT, Weidinger G (2007) Advances In Signaling In Vertebrate Regeneration As A Prelude To Regenerative Medicine. *Genes & Development* 21(11):1292–1315.

[224] Stoop F, Mayr J, Sulz C, Kaftan B, Bleicher F, Yamazaki K, Wegener K (2023) Cloud-Based Thermal Error Compensation With A Federated Learning Approach. *Precision Engineering* 79:135–145.

[225] Suen M-S, Lin Y-C, Chen R (2016) A Flexible Multifunctional Tactile Sensor Using Interlocked ZnO Nanorod Arrays For Artificial Electronic Skin. *Procedia Engineering* 168:1044–1047.

[226] Teicher U, Baumann R, Bouraoui Y, Ben Achour A, Lasagni AF (2022) Laser Structuring With DLIP Technology Of Tungsten Carbide With Different Binder Content. *Procedia CIRP* 111:601–604.

[227] Teti R, D'Addona DM, Segreto T (2021) Microbial-Based Cutting Fluids As Bio-Integration Manufacturing Solution For Green And Sustainable Machining. *CIRP Journal of Manufacturing Science and Technology* 32:16–25.

[228] Teti R, Jemielniak K, O'Donnell G, Dornfeld D (2010) Advanced Monitoring Of Machining Operations. *CIRP Annals* 59(2):717–739.

[229] Teti R, Mourtzis D, D'Addona D, Caggiano A (2022) Process Monitoring Of Machining. *CIRP Annals* 71(2):529–552.

[230] Tian B, Xu S, Rogers JA, Cestellos-Blanco S, Yang P, Carvalho-de-Souza JL, Bezanilla F, Liu J, Bao Z, Hjort M, Cao Y, Melosh N, Lanzani G, Benfenati F, Galli G, Gygi F, Kautz R, Gorodetsky AA, Kim SS, Lu TK, Anikeeva P, Cifra M, Krivosudský O, Havelka D, Jiang Y (2018) *Physical Biology* 15:031002.

[231] Tinello D, Winkler H (2017) Überlegungen zur Übertragung bionischer Systemdesignmuster auf die Fabriklayout- und Materialflussplanung. *Logistics Journal: Proceedings* 2017.

[232] TOP500 (June 2022), https://www.top500.org/, accessed on July 29, 2022.

[233] Torricelli F, Adrahtas DZ, Bao Z, Berggren M, Biscarini F, Bonfiglio A, et al. (2021) Electrolyte-Gated Transistors For Enhanced Performance Bioelectronics. *Nature Review Methods Primers* 1(1):1–24.

[234] Trierweiler M, Foith-Förster P, Bauernhansl T (2020) Changeability of Matrix Assembly System. *Procedia CIRP* 93:1127–1132.

[235] Trotta IG, Volpe A, Ancona A, Fassid I (2018) Flexible Micro Manufacturing Platform For The Fabrication of PMMA Microfluidic Devices. *Journal of Manufacturing Processes* 35:107–117.

[236] Ueda K, Vaario J, Ohkura K (1997) Modelling of Biological Manufacturing Systems for Dynamic Reconfiguration. *CIRP Annals* 46(1):343–346.

[237] Urban MW, Davydovich D, Yang Y, Demir T, Zhang Y, Casabianca L. (2018), Key-And-Lock Commodity Self-Healing Copolymers, 225/October: 220–225.

[238] Uriarte L, Zatarain M, Axinte D, Yagüe-Fabra J, Ihlenfeldt S, Eguiaa J, Olarraa A (2013) Machine Tools For Large Parts. *CIRP Annals* 62(2):731–750.

[239] Van der Zwaag S (2007) *Self-Healing Materials: An Alternative Approach to 20 Centuries of Materials Science*, SpringerThe Netherlands.

[240] van Dijk N, van der Zwaag S (2018) Self-Healing Phenomena in Metals. *Advanced Materials Interfaces* 5(17):1–13.

[241] van Houten F, Wertheim R, Ayali A, Poverenov E, Mechraz G, Eckert U, Rentzsch H, Dani I, Willocx M, Duflou JR (2020) Bio-Based Design Methodologies For Products, Processes, Machine Tools And Production Systems. *CIRP Journal of Manufacturing Science and Technology* 32:46–60.

[242] Vandevenne D, Verhaegen P, Dewulf S, Duflou J (2015) SEABIRD: Scalable Search for Systematic Biologically Inspired Design. *Artificial Intelligence for Engineering Design Analysis and Manufacturing* 30/01:78–95.

[243] Vandevenne Dennis (2014) *Methods and Algorithms for Systematic Biologically Inspired Design*, KU Leuven. PhD-thesis.

[244] Vanella R, Kovacevic G, Doffini V, Fernández de Santaellaab J, Nash MA (2022) High-Throughput Screening, Next Generation Sequencing And Machine Learning: Advanced Methods In Enzyme Engineering. *Chemical Communications* 15:2455–2467.

[245] Velasco-Hogan A, Xu J, Meyers MA (2018) Additive Manufacturing as a Method to Design and Optimize Bioinspired Structures. *Advanced Materials* 30(52):1800940.

[246] Verga F, Makowska M, Cellerai G, Florio K, Schmid M, Wegener K (2021) Crack-Healing, A Novel Approach for a Laser-based Powder Bed Fusion of High-performance Ceramic Oxides. *Additive Manufacturing Letters* 1. https://doi.org/10.1016/j.addlet.2021.100021.

[247] Voss R (2017) *Fundamentals of Carbon Fibre Reinforced Machining* Ph.D. thesis ETH Zürich 24283.

[248] Voss R, Henerichs M, Harsch D, Kuster F, Wegener K (2017) Optimized Approach For Characterisation Of Cutting Edge Micro-Geometry In Drilling Carbin Fibre Reinforced Plastics (CFRP). *International Journal of Advanced Manufacturing Technology* 90(2017):457–472.

[249] Wang J, Chen G, Huang S, Zhang H, Chen Q, Zhang C, Du Z (2022) Multi-Scale Modeling And Simulation For Multi-Pass Processing of Ta-2.5W Alloy. *Internat-Journal of Mechanical Sciences* 218:107069.

[250] Wang P, Wang J, Fang FZ (2021) Study On Mechanisms Of Photon-Induced Material Removal On Silicon At Atomic And Close-To-Atomic Scale. *Nanomanufacturing and Metrology* 4:216–225.

[251] Wang S, Urban MW (2020) Self-Healing Polymers. *Springer Nature reviews Materials* 5:562–583.

[252] Wang Y, Xue P, Cao M, Yu T, Lane ST, Zhao H (2021) Directed Evolution: Methodologies And Applications. *Chemical Reviews* 121(20):12384–12444.

[253] Warnck M, Binder M, Edelmann G, Früchtl M, Taha I (2022) Condition Monitoring Of Multi-Material Lightweight Components Through A Sensitive Outer Skin Using Fiber-Bragg-Grating Sensors. *Procedia CIRP* 110:311–316.

[254] Warwick K (2007) Cyborgs. in Callahan D, Singer P, Chadwick R, (Eds.) *Encyclopedia of Applied Ethics*, Academic Press, . ISBN 9780122270659.

[255] Warwick K (2014) The Cyborg Revolution. in Coenen C, (Ed.) *NanoEthics*, Springer; 2014. https://doi.org/10.1007/s11569-014-02. ISSN 1871-4757.

[256] Warwick K, Hutt B, Gasson M, Goodhew I. (2005) An Attempt To Extend Human Sensory Capabilities By Means Of Implant Technology. Proceedings IEEE International Conference on Systems, Man and Cybernetics, Hawaii: 1663–1668.

[257] Wasilewski T, Gębicki J, Kamysz W (2017) Bioelectronic Nose: Current Status And Perspectives. *Biosensors and Bioelectronics* 87:480–494.

[258] Wegener K, Bleicher F, Heisel U, Hoffmeister H-W, Möhring H-C (2021) Noise And Vibrations In Machine Tools. *CIRP Annals* 70(2):611–634.

[259] Wegener K, Gittler T, Weiss L (2018) Dawn of New Machining Concepts: Compensated, Intelligent, Bioinspired. *Procedia CIRP* 77:1–17.

[260] Wegener K, Spierings AB, Teti R, Caggiano A, Knüttel D, Staub A (2021) A Conceptual Vision For A Bio-Intelligent Manufacturing Cell For Selective Laser Melting. *CIRP Journal of Manufacturing Science and Technology* 34:61–83.

[261] Wegener K, Weiss L, Mayr J, Gittler T. (2022) Konnektivität von Maschinen, Lernen und Intelligenz. In 4. Innovationsforum Zerspanung 2022 Tuttlingen 2022

[262] Wells LJ, Camelio (2013) A Bio-Inspired Approach For Self-Correcting Compliant Assembly Systems. *J Manufacturing Systems* 32:464–472.

[263] Wenz F, Schmidt I, Leichner A, Lichti T, Baumann S, Andrae H, Eberl S (2021) Designing Shape Morphing Behavior through Local Programming of Mechanical Metamaterials. *Advanced Materials* 33:2008617.

[264] Wheatcroft D, Price TD (2013) Learning And Signal Copying Facilitate Communication Among Bird Species. *Proceedings of the Royal Society B: Biological Sciences* 280(1757):20123070.

[265] Willett FR (2021) A High-Performance Handwriting BCI. in Guger C, Allison BZ, Gunduz A, (Eds.) *Brain-Computer Interface Research: A State-Of-The-Art Summary 10. SpringerBriefs in Electrical and Computer Engineering*, Springer Intern, Publishing, Cham, 105–109.

[266] Willett FR, Avansino DT, Hochberg LR, Henderson JM, Shenoy KV (2021) High-Performance Brain-To-Text Communication Via Handwriting. *Nature* 593 (7858):249–254.

[267] Williams DJ, Thomas RJ, Hourd PC, Chandra A, Ractliffe E, Liu Y, Rayment EA, Archer JR (2012) Precision Manufacturing Foor Clinical-Quality Regenerative Medicines. *Philosophical Transactions of The Royal Society A* 370:3924–3949.

[268] Willocx M, Ayali A, Duflou J (2020) Where And How To Find Bio-Inspiration? A Comparison Of Search Approaches For Bio-Inspired Design. *CIRP Journal of Manufacturing Science and Technology* 31:61–67.

[269] Winters J (2003) Communicating by Brain Waves. *Psychology Today* . Retrieved on 17.08.2022.

[270] Woods DD, Hollnagel E (2006) *Joint Cognitive Systems*, CRC Press Taylor and Francis. ISBN 10: 0-8493-3933-2.

[271] Wool RP (2008) Self-healing Materials: A Review. *Soft Matter* 4:400–418.

[272] Xia D, Johnson L, López G (2012) Anisotropic Wetting Surfaces with One-Dimensional and Directional Structures: Fabrication Approaches, Wetting Properties and Potential Applications. *Advanced Materials* 24:1287–1302.

[273] Yang C, Qin W, Lai S, Wang J, Zhang Y, Jiao F, Ren L, Zhuang T, Chang Z (2011) Bioleaching Of A Low Grade Nickel–Copper–Cobalt Sulfide Ore. *Hydrometallurgy* 106:32–37.

[274] Yang JC, Mun J, Kwon SY, Park S, Bao Z, Park S (2019) Electronic Skin: Recent Progress And Future Prospects For Skin-Attachable Devices For Health Monitoring, Robotics, And Prosthetics. *Advanced Materials* 31:1904765.

[275] Yang F, Huang Y, Li Y, Li Y (2021) Large-Area Flexible Organic Solar Cells. *npj Flexible Electronics – Nature* 5(1):1–12.

[276] Yang X, Ma J, Shi Y, Sun Y, Yang J (2017) Crashworthiness Investigation Of The Bio-Inspired Bi-Directionally Corrugated Core Sandwich Panel Under Quasi-Static Crushing Load. *Materials and Design* 135:275–290.

[277] Yao Y, Wang Q, Wang H, Zhang B, Zhao C, Wang Z, Xu Z, Wu Y, Huang W, Qian PY, Zhang XX (2013) Bio-Assembled Nanocomposites In Conch Shells Exhibit Giant Electret Hysteresis. *Advanced Materials* 25(5):711–718.

[278] Ye Z, Kobe AC, Sanga T, Aparicio C (2020) Unraveling Dominant Surface Physicochemistry To Build Antimicrobial Peptide Coatings With Supramolecular Amphiphiles. *Nanoscale* 12. 20767-20767.

[279] Yuan S, Shaoying L, Jihong Z, Yunlong T (2021) Additive Manufacturing Of Polymeric Composites From Material Processing To Structural Design. *Composites Part B: Engineering* 219:108903.

[280] Zhang P, Li G (2016) Advances in healing-on-Demand Polymers And Polymer Composites. *Progress in Polymer Science* 57:32–63.

[281] Zhang W, Wang D, Han B (2020) *Self-healing Concrete-Based composites. Self-Healing Composite Materials*, Elsevier Inc, . https://doi.org/10.1016/B978-0-12-817354-1.00015-6.

[282] Zhao J, Jiang Z, Dobrzański LA, Lee CS, Yu F (2005) Recent Development in Micromanufacturing of Metallic Materials. *Materials* 13:4046.

[283] Zheng Y, Bai H, Huang Z, Tian X, Nie FQ, Zhao Y, Zhai J, Jiang L (2010) Directional Water Collection On Wetted Spider Silk. *Nature* 463:640–643.

[284] Ziervogel F, Boxberger L, Bucht A, Drossel W-G (2021) Expansion of the Fused Filament Fabrication (FFF) Process Through Wire Embedding, Automated Cutting, and Electrical Contacting. *IEEE Access* 9:43036–43049.

[285] Zimmermann N, Büchi T, Mayr J, Wegener K. (2022) Self-Optimizing Thermal Error Compensation Models With Adaptive Inputs Using Group-LASSO for ARX-Models. 50th SME North American Manufacturing Research Conference (NAMRC 50, 2022).