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Enabling bidirectional real time interaction between biological and technical systems: Structural basics of a control oriented modeling of biology-technology-interfaces

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Abstract

Due to digitization, demographic change and a growing demand for sustainability, companies are facing great challenges. Latest research reveals the biological transformation of manufacturing as the next leap. Digital technologies enable the usage of sensitive biological materials for resource friendly production, gaining natural products and circular economy. Therefore, adaptive biology-technology interfaces are necessary in order to enable bidirectional real time information exchange between biological and technological systems, which is still a gap in research. We thus present conceptual basics of biology-technology-interface (BTI) engineering, discuss BTI examples for various industrial applications and introduce an interdisciplinary theoretical model for communication and process control across systems. We conclude with a summary and recommendations for future research.

Keywords: Sustainability, Digitization, Biotechnology

1. Introduction

Sustainability is inevitable for the future of manufacturing [1]. Companies currently face a variety of challenges, e.g. demographic change, individualization, digitization, assurance of continued resource availability and minimization of environmental impact. Although sustainability is playing an increased role in global politics and local business decisions since almost fifty years, little has changed. Global resource extraction has doubled in the past 30 years [2]. Under current circumstances a further doubling of resource consumption by 2050 is likely [3]. Many resources are already considered scarce today. Security of supply still largely determines regional prosperity. Simultaneously, climate change threatens large parts of the world as a result of drastically changing climatic and weather impacts. External costs for damage caused by air pollution account for roughly one trillion Euro p.a., only in Europe [4]. These examples show that previous strategies for the creation of a sustainable economy have barely succeeded. Assuming a need to preserve western standards of living, a suitable satisfaction of the (material) needs of future generations is required. This is, however, not possible with today's production techniques and process designs. In this context, recent studies reveal an increasing relevance of biological systems in future manufacturing environments not only in the process and medical industry, but as well in discrete parts manufacturing. While companies currently face great challenges in the context of the digital transformation, the biological transformation is viewed as the next technological leap. Byrne et al. thus predict an increasing “use and integration

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of biological and bioinspired principles, materials, functions, structures and resources for intelligent and sustainable manufacturing technologies and systems with the aim of achieving their full potential" [5]. Miehe et al. characterize the term biological transformation as the systematic application of the knowledge about biological processes leading to an increasing integration of production, information and biotechnology [6, 7]. Thereby, three development modes are differed (see figure 1) [6, 7].

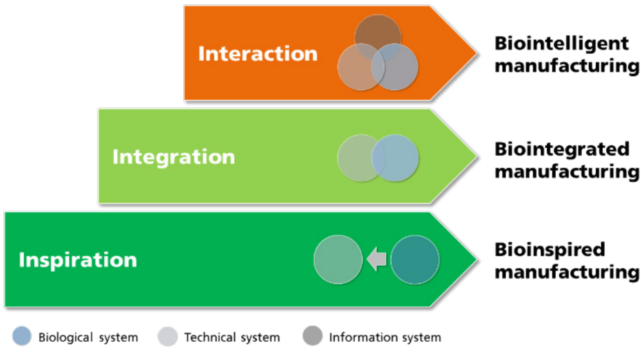

Fig. 1. Development modes of biological transformation according to Miehe et al. [6].

While the *inspiration* allows a translation of evolutionary biological phenomena into solely technical value creation systems (e.g. lightweight construction), functionalities (e.g. biomechanics), organizational solutions (e.g. swarm intelligence, neural networks), the knowledge of biology finds application in form of an actual *integration* of biological systems into production systems (e.g. substitution of chemical by biological processes). Practical examples of this mode are the functionalization of polymers, the recovery of bioplastics from CO_2 waste streams and the use of microorganisms for the recovery of rare earths from magnets. Not least, the comprehensive *interaction* of technical, informational and biological systems leads to the creation of completely new, self-sufficient production technologies and structures, so-called *biointelligent manufacturing systems*. A manufacturing system is considered to be biointelligent, if there is at least one biological component in the product or production process. In addition a real time exchange of information between biological and technical components is required, which in turn demands for online process control.

The vision drawn here by Miehe et al. is based on a pilot survey funded by the German government that included interviews with 123 highly renowned national and international experts as well as workshops with over 200 participants of various industries and backgrounds. Among others, the survey identified key technologies and future fields of action in order to shape the transformation. Artificial intelligence, 3D bioprinting, gene sequencing and editing, adaptive bioreactors and biorefineries as well as biosensors and –actuators were identified as the most promising technologies. With an increasing implementation of biological in technical systems, the demand for an appropriate design of biology-technology-interfaces (BTIs) rises. Consequently, the survey identified the realization of bidirectional, real-time informative connections between technical and biological systems as one of 10 decisive fields of future research in order to enable biointelligent value creation. Although the significance of adaptive biology-technology interfaces (BTIs) for the biological transformation remains unquestioned, its fundamental design currently depicts a gap in research. Hence, this paper discusses three basic questions of BTIs:

1. What types of BTIs exist?
2. What are fundamental aspects of a control oriented model?
3. What are areas of future research?

Therefore, the paper is to be understood as a first approach towards this highly substantial field of research in order to set the basis for further works in different application fields of BTIs. The results presented below are the outcome of a lose six months discussion of a highly interdisciplinary team of researchers including biologists, biotechnologists, industrial, process and control engineers as well as sociologists. The authors expect that the field of BTI will be of increasing importance to future research in the CIRP community, not only in the field of biomanufacturing and process engineering but in discrete manufacturing.

2. Basics and examples of BTIs

Although the interpretation of biological communication as sign processes and communication patterns dates back to the 1980s [8], basic scientific research in the field of BTI was first conducted extensively in the early 2000s within the German SFB 563 (bioorganic functional systems on solids) by the Max-Planck-Society [9]. Thereby, solid progress was made on the interface between living biological systems (cells or cell models) and anorganic solid state substrates (metals, semiconductors, insulators) aiming to enable a bio-functionalisation of solid surfaces, a detailed spectroscopic characterization of interactions between biosystems and their substrates, as well as an experimental realization of bioelectronic hybrid systems, e.g. living cells communicating with 'intelligent' substrates. From a basic research perspective the feasibility of various interface types between biology and solid state physics is thus verified. In contrast, a transfer of existing findings to applicable solutions for industries is required in order to realize biointelligent manufacturing systems, e.g. autonomous bioreactor-bioprinter systems. This especially applies to the creation of a real time exchange of information as well as appropriate online process control models.

Generally, the two most significant differentiation parameter of BTIs are type and level of interaction. For the former, various physical principles, e.g. electrical, chemical, mechanical or optical, may be used in order to achieve an interaction of technical components with cellular systems. Then again, the interaction with a technical system can be implemented with entire cells, organelles, individual biomolecules or even organisms (including humans). The exchange of information at the interface between biological and technical systems can be subdivided into sensory and actuarial components, whereby a control by means of actuators is possible both from the technical to the biological side and vice versa. The sensor system includes (physical, optical or spectrometric) metrological methods for recording state variables of biological or technical systems. Table 1 summarizes examples of BTIs at different levels and types of interaction.

Table 1. Examples of BTIs at different levels and types of interaction.

	Level of interaction	
Type of interaction	*Organism*	*Cell*
Electrical	Human-Brain-Interfaces	Neuron chips
Chemical	Bacterial cells in hydrogel	Protein receptors
Optical	Light control, emotion detection	Optogenetics, photoreceptors
Mechanical	Exosceleton feedback	Atom Force Microscopy

A common example of the utilization of biological cells via electrical signals are neuron chips or multi-electrode arrays, which connect neuronal signals with electrical circuits. Existing chips are used for both in vitro and in vivo applications [10, 11]. Due to the far greater sensitivity, sensor applications with neuron cells as the data-receiving component bear great potential for future application as they are likely to create completely new functions, e.g. smelling [6, 7, 12, 13]. Another example is the coupling of technical and biological systems via optical signals, i.e. optogenetics. Here, cells are specifically equipped with photoreceptors, so that cellular responses can be controlled and read out via light of different wavelengths [14-16]. While current examples of BTIs are developed in order to control biological systems via technology, a biointelligent manufacturing system requires a bidirectional real time information exchange between the systems in order involve the biological into the manufacturing system without harming its vitality. As a rare example of fully controlled systems that have been implemented in technical prototypes bioreactors equipped with integrated on-line sensors allowing constant control can be mentioned [17]. A multitude of research gaps remain in order to achieve applicability in manufacturing systems ranging across the development of basic control engineering models and regulatory principles [17], specific biological actuators, e.g. bacteriophages, as well as appropriate sensor technologies and integration, e.g. for online measurement. Other sensor related fields of research include the development of multivariate, bio-based, non-invasive and non-consuming sensor techniques and principles as well as softsensors with underlying process models and new concepts for biosensors [18, 19]. Even in the biological part of a BTI further research is needed. Especially the fields of synthetic biology and systems biology offer great potential for integrating biological molecules and components in technical systems in a targeted manner, to reduce their complexity and to make them manageable through a selection of functional components (semisynthetic systems) [20].

3. Theoretical basics at interdisciplinary level

In order to develop a generic model for bi-directional communication between different types of systems, a review of fundamental system theory approaches in life sciences, sociology and control engineering is required. Generic models of interactions between systems and their environment have a long history and are described by different authors [20-24]. How different systems (here: biological and technical) behave in close coupling has, however, received little attention in literature. In existing theory, technology has not been considered as autopoietic [22], which is likely to change in the era of machine learning and artificial intelligence. Biological, technical, social and mental systems are distinguished in general system theory in that they produce and reproduce themselves materially (biologically), follow algorithms (technically), operate meaningfully (socially) and think (mentally) [22]. In order to combine living and artificial systems in form of an intelligent interaction an intermediary function is needed. Biological systems are autopoietic, self-regulative, adaptive and variable – they follow the principle of ‘actio et reactio’ to keep the biological balance. In contrast, technical systems are static and allopoietic, their process regulation is developed by humans [22]. Neither the biological nor the technical system can act across logical contexts from within itself, observing their own behaviour in distinction to their environment. Intelligent interface behaviour, considering the interlinking of different contexts and logics, is solely observed in humans, yet. The adaptivity of humans is a quality that can be interpreted as a self-regulative network interaction on the interface of different systemic logics, namely biological, mental and social systems, each operating with reference to their environment [25]. The main task in systems design across biological and technical systems, is thus to equip the technical system with a BTI that provides correcting variables to support the technical system in developing towards self-regulation (adaptivity), just as the biological system does. To create appropriate conditions for the biological system on the other hand, the BTI must be able to recognize the outer and inner state of the highly variable biological system in the first place. To achieve a self-optimizing network interaction between both systems, they need the ability to act in relation to the (cross-) contextual sense of the industrial environment, too. Basic elements of BTIs thus are adaptive process control, sensors, actuators and network-based modelling of dynamical and highly variable systems.

4. Basics of control oriented modeling of BTI

Current approaches to the regulation of biological processes are non-linear model predictive regulations that are primarily applied in process engineering in order to identify optimal control values [26-28]. These models are, however, not adaptive. This function is, however, required, e.g. in order to advance bioreactor systems via cell-responsive automation or to converge single technical solutions (bioreactors, 3D printers, biosensors and actuators, self-learning algorithms) into Smart Biomanufacturing Devices (SBDs). These completely new decentralized, autonomous and organically adaptive

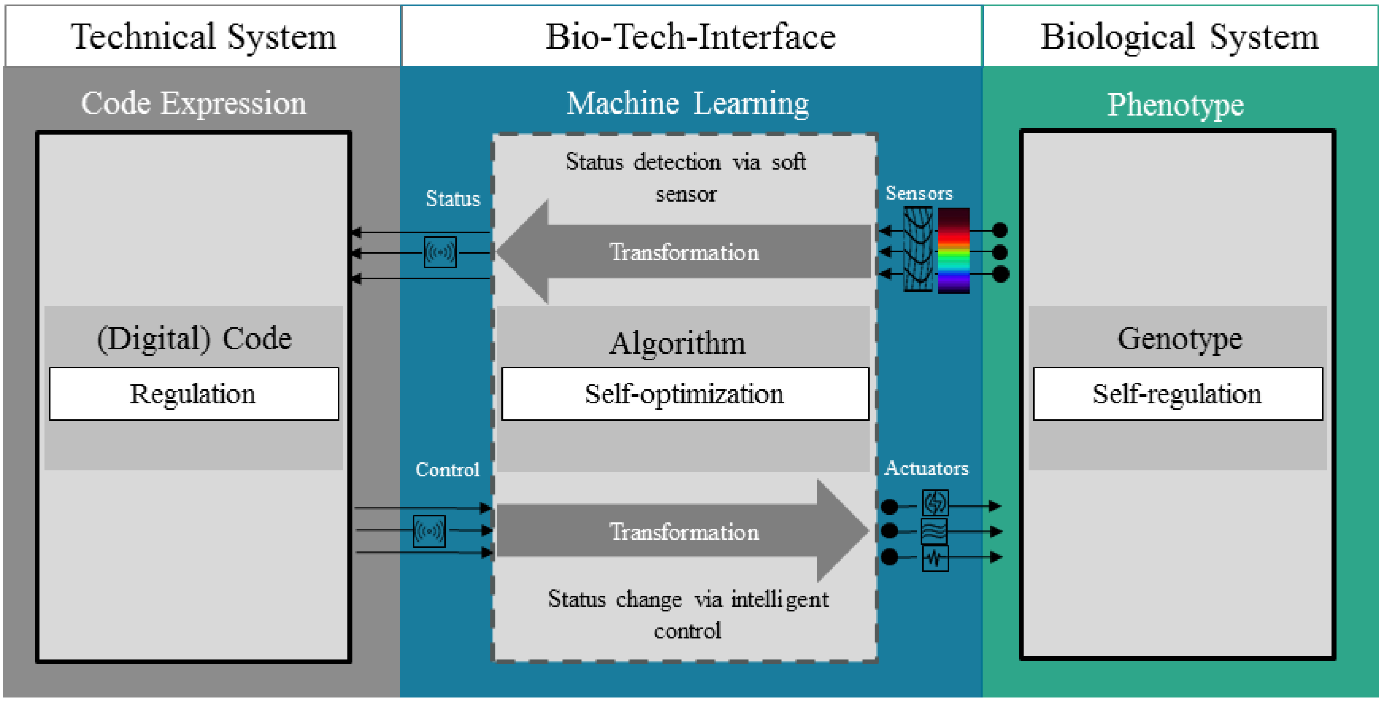

Fig. 2. General control oriented BTI model [own graphic].

manufacturing technologies are expected to enable distributed, personalized and scalable value creation.

Adaptive process control is thus indispensable for the direct coupling of biological and technical systems, since the behavior of biological systems can only be irritated from the outside, but not clearly predicted. Limited reproducibility and variability of results as well as the sole availability of indirect measurements pose additional difficulties of combining the two systems [31]. Today proper sensors for direct measurement simply do not exist. Furthermore, the analytical connections within biological systems have not yet been sufficiently explored nor can they be modeled appropriately. One way of predicting the behavior of living systems thus is through pattern recognition based on the systems structure, an approach well-known from the teaching of chaotic systems. In this context, trainable soft sensors represent a promising instrument as they are able to learn the recognition of the invisible inner state of a biological system through data from existing sensors, e.g. spatially resolved spectroscopy for material and condition monitoring [30].

Figure 2 illustrates an adaptive process control model between biological and technical systems in form of a BTI. The biological system could be an algae, producing different types of protein. Its proportion depends on the nutritional status and light irradiation. To achieve the production of a specific proportion of different protein, the corresponding supply of temperature, light and nutrition must be triggered via intelligent control on the basis of trained soft sensors or 2,5D-measurements. By the help of spectroscopic sensors the reaction of the algae is detected and possible nutrient deficiency could be stated. The BTI derives information from sensor data, transforms it into digital signals in order to control the technical system, which either provides the necessary inputs for controlling the biological systems or can use the information for parallel working processes. For the imaging of the dynamical variability of the biological system statistical modelling, known as “reservoir computing” [31, 32] and deep learning algorithms [33, 34] are downstreamed of the biochemical state recognition. The physical-mathematical models enable sensor simulation. On the basis of rugged and reliable state-descriptive models of biological objects, synthetic sensor data can be generated. Impinging the biological objects with surface defects, the availability of synthetic sensor data sets could be scaled to an unlimited amount. The specific challenge of biological objects is their optical correlation with light to visualize defects. With different methods of 2,5D-measurement a 3D-point-cloud can be received, which describes geometric surface characteristics of the biological object [35]. Through continuous feedback loops, production processes are maintained in optimal condition for the biological process by adapting their technical code expression. They do that by extending their range of biological behavior recognition and also by expanding their control capabilities. This demonstrates the biggest challenge for engineering science, the development of adaptivity in technology. The adaptability of biological systems generally serves to maintain the balance between necessary flexibility and stability ("edge of chaos"). For its transfer to technological systems, the soft sensor needs to get extended by self-learning ability in a polycontextural environment, driven by the logics of biology, technology and information to set the functionality of self-regulative balance in technical systems. Sensors, actuators, algorithms and a network-based modelling form the basis for the realization of a digital image for a biointelligent value creation system.

5. Summary and outlook

Due to digitization, demographic change and a growing demand for sustainability, manufacturing companies are forced to evolve their processes and technologies. The systematic application of the knowledge about biological processes, the so-called biological transformation, is viewed as a promising technological leap that will lead to an increasing integration of production, information and biotechnology. Whereas today's products are produced in complex value chains shipping resources and goods around the globe, the biological transformation will enable decentralized, autonomous, biointelligent value creation. Decisive for this novel form of manufacturing is the realization of appropriate bidirectional, real-time, informative connections between technical and biological systems.

In this paper, we thus presented fundamental elements of BTI engineering. Therefore, we briefly outlined conceptual basics, discussed the main features of BTI in terms of function, type and level of interaction based on existing literature and introduced an interdisciplinary theoretical model for communication and process control across systems. Several research fields, however, remain in order to extensively cross-link biological and technical manufacturing systems. Missing elements are in particular suitable sensors, actuators, algorithms and models for digital images of the biological system as well as their information-regulated interaction. BTI´s are likely to evolve for disruptive innovations through the interactions with biological elements and represent a basis for various industrial applications. Among others a closer cooperation between information and control engineering, biotechnology and manufacturing technology (e.g. robotics, microsystems technology, additive manufacturing) is required. As a limitation of the results it remains to be mentioned that in the future field of the development of fully interactive, bidirectional, real-time BTI not all developments are foreseeable, why the models presented here were kept as general as possible. Although major advances have already been made in biotechnology and information technology, basic research is necessary to make the vision a reality.

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