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The biological transformation of industrial manufacturing – Technologies, status and scenarios for a sustainable future of the German manufacturing industry

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ABSTRACT

The German manufacturing industry is forced to evolve its processes, techniques, and organizations due to increasing global competition and progressive sustainability requirements. In this context, the soaring possibilities of bio- and information technology have recently let few authors develop the vision of a biological transformation of manufacturing, a concept that to date has been barely concrete to politicians, scientists, and managers. In this paper, we present results of the first systematic assessment of the biological transformation of the German manufacturing industry. We chose a combination of the Delphi method and scenario planning in order to assess key technologies, determine the status quo of Germany and provide a forecast of potential developments. Thereupon, we identify ten fields of action for setting the course for a sustainable industrial value creation. We conclude with a summary and recommendations for decision makers in politics, industries and research.

1. Introduction

Industrial manufacturing is the heart of the German economy. Its manufactured goods account for over 80 % of exports of the country [1]. The manufacturing industry thus contributes essentially to the fact that Germany has had a positive current account for decades. With a world trade share of 11.5 % Germany recently displaced China and the USA from the sole lead as largest exporter of goods [1]. In addition, industry is the largest promoter of innovation in Germany, as 68 % of investments in research and development are made in and by manufacturing companies [2]. The significance of a strong industry became increasingly evident during the last financial crisis in the early 2000s which the German economy survived with comparatively little damage.

On the other hand, industrial value creation is responsible for great environmental damage and massive societal rejections. In the last 30 years global resource consumption doubled, resulting in an aggregated growth rate of 118 % [3]. A continuation of this trend eventually leads to another doubling until 2050 [4]. Due to the wasteful resource consumption of the past centuries since the first industrial revolution, many natural resources have already become scarce, e.g. silver, antimony [5]. A prosecution of this trend inevitably leads to an irresponsible exploitation of natural resources. Future generations will be deprived of the opportunity to independently decide on the distribution of natural, human and physical capital. Resource price increases or stoppage of supply poses major risks to industries. 40 % of middle class companies in Germany estimate a future downfall of the economy due to resource shortages [6]. The most prominent environment-related threat to traditional value creation is, however, climate change followed by manifold other environmentally related effects [7].

It thus becomes increasingly clear that the realization of a

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sustainable subsistence strategy is the fundamental challenge for today's societies. While the discussion (in modern times) dates back over 40 years [8], progress is limited due to system inherent effects such as leakage and rebound/backfire [9–11]. Both effects are well known to decision makers in politics and industry, efficiency increases, however, remain the universal remedy of many sustainability discussions and policies, while the consumption of goods is barely targeted. Although an increasing amount of studies present strategies for consumer behavior change, a global renunciation movement (sufficiency) appears quite unlikely [12–15]. After nearly half a century of intensive efforts and investments worth billions, we are now far from solving the sustainability problem. If realistically creating sustainable value means maintaining our standard of living while not depleting natural resources, current modes of production have to change massively.

In this context, various experts [16–18] view the biological transformation as the next technological leap. While the term bioeconomy has been discussed by many [19–21], only few authors have aimed to define the biological transformation. Patermann understands the biological transformation as the systematic application of knowledge about biology in order to incorporate new technologies [22]. From a manufacturing perspective, Byrne et al. predict an increasing "use and integration 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" [23]. Miehe et al. present an integrated concept by characterizing the biological transformation as the systematic application of the knowledge about biological processes leading to an increasing integration of production, information and biotechnology [24,25]. According to Miehe et al. the process of biological transformation can be distinguished into three development modes (see Fig. 1) [24,25]. First, 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). In a second mode, 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). Application examples of this mode are the use of microorganisms for the recovery of rare earths from magnets, the functionalization of polymers and the recovery of bioplastics from CO_2 waste streams. Third, 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 value-added system is considered to be biointelligent if there is at least one biological component in the product or production process. In addition an exchange of information between biological and technical components is made possible (in real time) via self-learning online process control and the existence of a digital twin. The essential levels of integration that form the basis for the process are the technical, the information and the biological level. Fig. 1 illustrates the process according to Miehe et al. [24,25].

In comparison to the bio- and circular economy, which rather represent visions of sustainable subsistence strategies, the biological transformation depicts a process of change that applies to the entire manufacturing industry.

In order to appropriately align strategic and scientific initiatives, the country and its industry however require a more detailed analysis of the potentials, demands and research gaps of the biological transformation. Therefore, the German government, represented by the BMBF, and the Fraunhofer Society set up a preliminary survey in late 2017 in order to address four primary research questions:

i What are key technologies of the biological transformation?
ii What is the current state of the German manufacturing industry in the context of the biological transformation?
iii What are potential developments of the German manufacturing industry in the context of the biological transformation?
iv How should the German government as well as Fraunhofer support the transition?

2. Objectives and methodical approach

The goal of the BIOTRAIN-project was thus to analyze the potentials and demands of a biological transformation of the German manufacturing industry until 2050 and to develop a research strategy for Fraunhofer with recommendations for public authorities. Hence, six Fraunhofer Institutes worked together with an advisory committee of 15 distinguished representatives of industrial players and research organizations focusing on four main aspects:

i The assessment of key technologies of the biological transformation,
ii the assessment of the current status of the German manufacturing industry in the context of the biological transformation,
iii the forecast of potential scenarios of development of the German manufacturing industry in the context of the biological transformation, and
iv the deduction of recommendations for future actions of the German

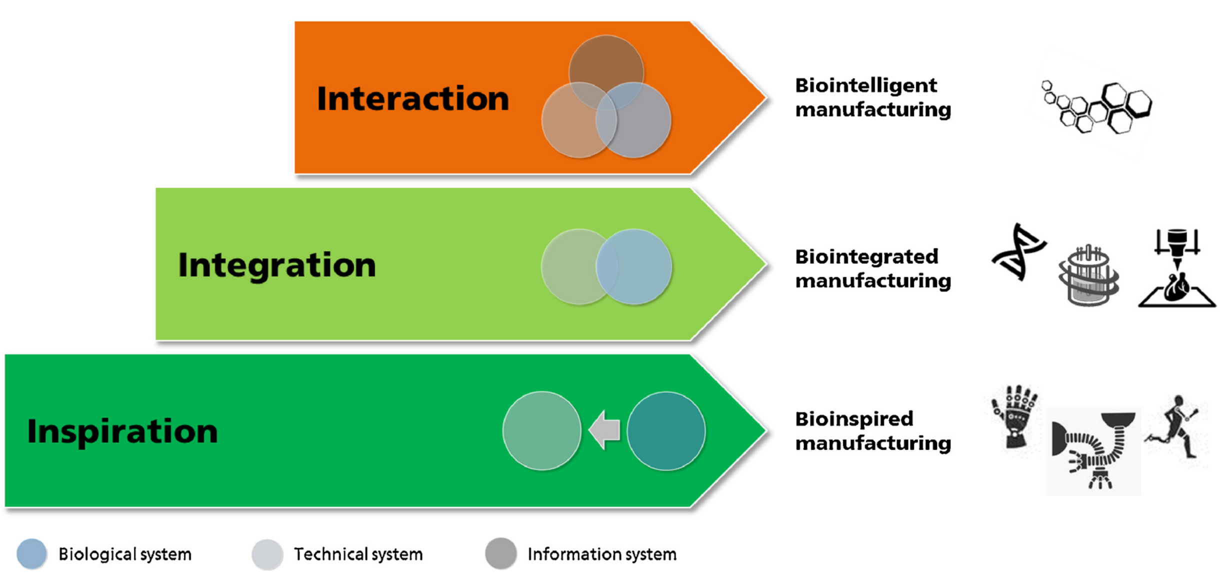

Fig. 1. Development modes of the biological transformation according to Miehe et al. [24,25].

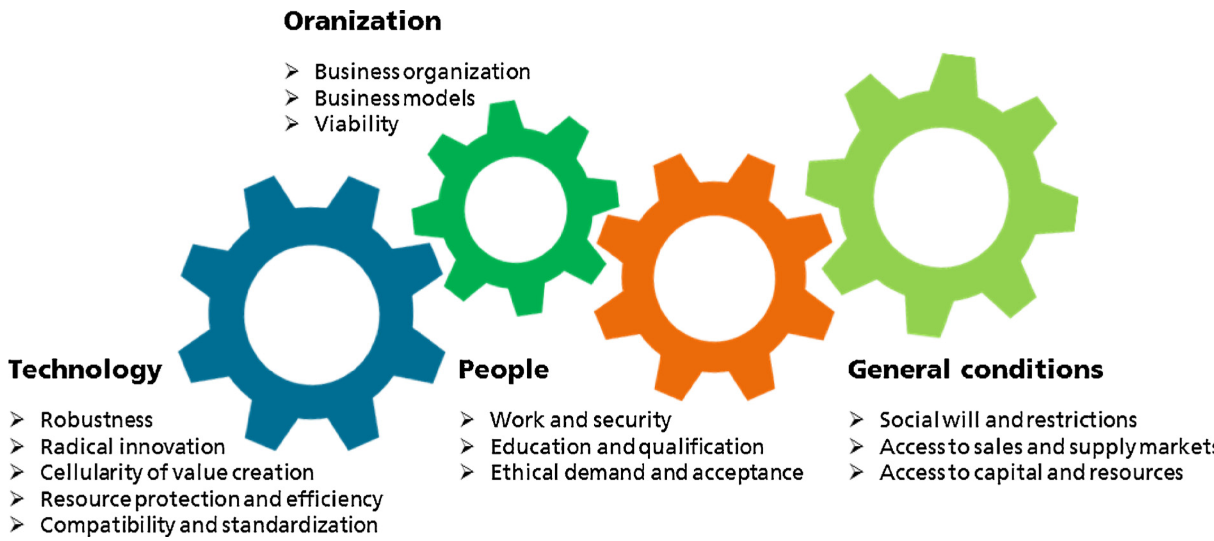

Fig. 2. Initial framework of the BIOTRAIN-project.

federal government as well as Fraunhofer.

In order to address these fundamental research modules, we combined the Delphi method and scenario planning. While the Delphi method was applied for a structured communication with a panel of experts based on an initial formulation of relevant hypothesis [26–29], scenario planning enabled a bundling of expert feedback and literature research results in form of three different development modes [30–37]. We thus divided the survey into seven steps:

1) During *instantiation* we formulated an initial definition of the biological transformation and identified major challenges of the German manufacturing industry via literature research. Thereupon, we developed an initial framework for the elaboration of a detailed questionnaire consisting of four perspectives (technology, organization, people, general conditions) and 14 focus topics. Fig. 2 illustrates the framework.
2) In a *first detailed analysis*, based on additional literature research, we then formulated 35 hypotheses regarding the strengths, weaknesses, opportunities and threads of the German manufacturing industry in the context of a biological transformation. Consequently, we developed a questionnaire consisting of 20–25 questions per focus topic (total: 330).
3) Within two months we executed a total of 123 national and international high-level *expert interviews* yielding in a wealth of results, among others the validation of the earlier formulated SWOT-hypotheses, a range of statements e.g. on possible future scenarios as well as examples for applications.
4) The mere quantity of results required *a second detailed analysis* in order to edit and structure the feedback as well as a complementary literature research in order to investigate the significance of expert opinions. Thereupon, the status quo of the German manufacturing industry was formulated (see section 3.2), while the conditioned interview results served as the basis for the development of a stakeholder workshop concept.
5) Within a period of one month, the results were presented to and validated by over 200 participants of different industries, private, public and political organization as well as NGOs in 10 *stakeholder workshops*. Thereby, the participants had to undertake a range predefined tasks, i.e. classifying hypotheses for future scenarios according to probability and time of occurrence as well as ranking technologies, challenges and potential fields of action regarding their significance to the manufacturing industry.
6) The following *aggregation* of the workshop results provided the basis for the formulation of three scenarios that depict the forecast of the biological transformation. The scenario 'extensive biological transformation' thereupon served as the reference for the vision that again served as the basis for the classification of fields of actions and recommendations for public authorities and Fraunhofer.
7) As the last step, the *dissemination* of the results of the BIOTRAIN-survey consisted of a conference in Berlin, Germany in June 2018 with roughly 85 participants as well as the publication of a popular science brochure that was linked to a website in order to provide detailed results of each project step (www.biotrain.info)[1] .

During the entire project, the advisory committee constantly reviewed intermediate results and rated its scientific and industrial relevance. Fig. 3 illustrates the methodical approach.

3. Results

According to the objectives, the results presented in this chapter are divided in four subsections.

3.1. Key technologies

Key technological areas of the biological transformation are bio, information, and machine engineering that are expected to increasingly converge. Although over 270 technology examples were collected during the project based on interviews, workshops and literature research, the quintessence was not a single enabling technology but the interdisciplinary cooperation between disciplines that will set the path for the biological transformation. While technologies are regarded as being available, its purposeful integration lacks behind. Nonetheless, eleven technological enablers are regarded as promising, although requiring either further basic or applied research in order to increase their technological maturity.

Further basic research is required for:

1) *Biosensors and neurorobotics*: Biosensors depict a basic ingredient of an interface of the biological, technical and informational systems. A biosensor is composed of a biological recognition element (e.g. enzyme, antibodies, DNA, receptors or whole cells / cell networks) and a physical sensor (transducer), which are in direct contact. A biosensor can be used to detect an analytical sample through a

[1] Currently German only.

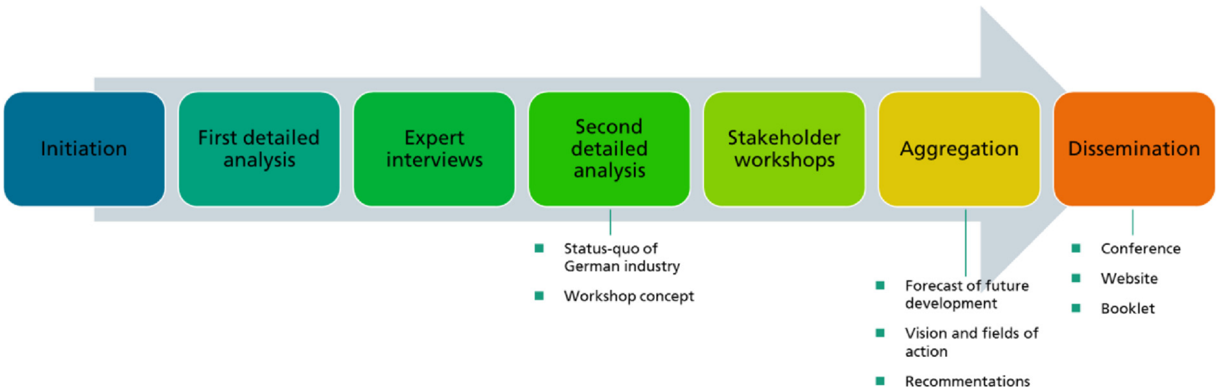

Fig. 3. Methodical approach of BIOTRAIN-project.

biological element and then generate a physical signal [38]. Major applications of these sensors are men-machine interfaces, which are among others increasingly relevant in prosthetics, virtual reality and future manufacturing environments. In this context, neurorobotics may significantly contribute to an improvement of the current state of the art by linking human nerve cells with technical components.

2) *Additive manufacturing of bio-based, bio-hybrid materials and electronic components*: Especially from an ecological point of view, compostable electronic components are of highest relevance for the biological transformation. Initial research results show success in the development of such components, in which e.g. semiconductors made of plant extracts or insulators of gelatin can be printed on biodegradable circuit boards (e.g. compostable plastic) with additive processes. Latest research reveals progress in the required technologies that enable 3D printing with often highly variable and inhomogeneous biomaterials [39]. Additive manufacturing of bio-based, biohybrid materials also covers all technologies that use the principles of tissue engineering to allow cells to grow in a controlled manner and to achieve a shape by means of their independent reproduction with technical aid (i.e. 3D bioprinting).
3) *Photobioreactors and switchable organisms:* Photobioreactors may decisively contribute to an increased functionality of products. Therefore, further development, especially with regard to efficiency criteria is required. As a basis for the cultivation of phototrophic organisms such as microalgae, cyanobacteria and purple bacteria products or energy sources can be obtained with the direct use of solar energy [40]. Additionally, phototrophism can also be used for the development of so-called switchable organisms that react due to light sensitivity [41,42]. Beyond that, programmable and controllable microorganisms are viewed as highly relevant for the biological transformation.
4) *Bio-based energy carriers*: Bio-based energy carriers, e.g. formic acid for hydrogen binding, could contribute to making energy supply more flexible. Intensified research on related technologies, including the integration of efficient microbiological, enzymatically catalyzed material transformations, is regarded as increasingly relevant. The same applies for enzymatic processing technology as shown by Miyazaki [43]. Of the innumerable naturally occurring enzymes some are already of industrial relevance, e.g. in the food industry. The majority, however, still plays a minor role.
5) *Bioleaching* is a microbial recycling technology that may significantly contribute to the closing of value chain loops [44]. Existing technologies in this field, however, massively lack in efficiency and reliability.
6) *Quantum computers* are not necessarily related to the biological transformation. Their sheer potential in e.g. managing large databases and factoring large numbers, however, depicts a possible future boost for biointelligent systems.

Further applied research is required for:

1) *Natural materials*: Some organic natural products will experience a renaissance through new manufacturing technologies such as 3D printing, fiber composite technology and compounding. Among others, these include lignin and chitin, whose occurence is enormous and will continue to increase [45]. Another current field of research with potentially massive impact is biodegradable plastics whose diffusion is still insufficient [46]. A combination of these two components, for example in the form of natural fiber-reinforced compounds with bioplastics, also has an expanded potential to find widespread applications in a timely manner.
2) *Bioinspired information technologies and man-machine-interfaces*: Information technologies such as distributed ledger, pattern and emotion recognition software, predictive analytics and learning algorithms (artificial intelligence) already represent focus areas of today's production research, while simultaneously bearing great potential for the biological transformation. This likewise applies to the coupling of man and machine. Examples of these technologies in the context of the biological transformation include adaptive exoskeletons that can physically relieve body movement in work processes [47]. These technologies are already close to dissemination.
3) *Biorefineries and adaptive bioreactors*: Biorefinery technologies are about to be transferred to industrial and large scale applications and may be used to provide bio-based or platform chemicals (e.g. ethylene, propene) or likewise for a more efficient generation of bio-based energy sources (e.g. methane, hydrogen) [48]. Both the plant-technical know-how of these refineries and the process development for the processing of the products still have to be raised to industry level in order to achieve sufficient process stability and far-reaching application possibilities.
4) *Microbial fuel and electrolysis cells* use living microorganisms that process organic substances as part of their energy metabolism to produce electricity or hydrogen. In conjunction with other bio (electro) chemical developments (e.g. bioelectrochemical power to gas, biological methanation) these technologies can, in addition to their contribution to the flexibilization of energy supply, form a basic technology for Smart Biomanufacturing Devices (SBD, see Section 3.3) [49]. Further applied research is as well required to enable adaptivity of bioreactors or fermenters [50]. Today's bioreactors are predominantly adjusted to a single process and not easily transferable to other processes, substrates (nutrients) or organisms. Latest sensor and actuator technologies as well as learning algorithms may, however, allow flexible adaptation of the process parameters to a larger selection of organisms and substrates which could significantly contribute to a flexible production of enzymes or other fermentation products (such as personalized pharmaceuticals).
5) *Interference with genetic material*: The redesign of DNA (gene editing)

Fig. 4. SWOT-matrix of current status of German manufacturing industry.

made possible by genetic engineering is in spite of its extremely high disruptive potential, e.g. in the medical sector, associated with risks for humans and the environment, a fact that applies to synthetic biology in general. From a sole technical perspective this technology represents a key ingredient of the biological transformation, e.g. in order to produce clean meat.

3.2. Current status of German industry

The below presented status quo of the German manufacturing industry is entirely based on the opinion of 123 experts that were questioned in regard to 35 predefined SWOT-hypotheses within 14 focus topics (see Section 2). Fig. 4 summarizes the results in form of a SWOT-matrix.

3.2.1. Strengths

The interviews revealed seven key strengths of the German manufacturing industry in the context of the biological transformation. First, German basic research in general is well positioned in an international comparison. Relevant fields of research in the context of the biological transformation such as bionics, biotechnology and bioeconomy have already lead to far-reaching innovations, e.g. lotus effect in surface coatings. In an international comparison, research in Germany is viewed as competitive in these fields. In addition to the existing research landscape, small and medium-sized enterprises (SMEs) form the basis for agility and the versatility of German industry. The existing SME landscape is globally renowned for its reliability, tradition, and quality. In addition, many large German corporations increasingly gain versatility by acquiring start-ups. Overall, the German ability to change its economy is rated at a good state.

In any case, the label "Made in Germany" is a recognized seal of quality worldwide. Products that are developed and manufactured in Germany or at least produced under German standards abroad are considered robust, functional, powerful and durable. This positive association strengthens the reputation of German goods abroad and forms one of the central foundations for Germany's success as an export nation in international trade. In addition, the label is more and more associated with sustainability. Another strength is seen in the country’s privileged position in international trade, as a comprehensive access to both sales and procurement markets depicts key strategic aspects of a company’s success. The perception of Germany in this context is strong due to its good foreign policy relations and its economic strength. Besides having access to various global trade agreements that ensure largely free trade, Germany has direct access to one of the world's largest domestic markets, the Schengen area. The German political and economic situation are viewed as comparatively stable overall due to a generally consolidated democracy, comprehensive social security, a de-escalative foreign policy and a stable currency. Moreover, the German government aims to maintain its production location in the long term by providing tailored supporting measures, which especially relieves industries in times of crisis. Other strengths are seen in standardization and occupational safety measures as well as environmental awareness and ethical standards. The introduction of novel value creation structures, new working conditions and work processes can only be achieved safely and efficiently by standardized guidelines. Germany occupies a strong international position in this field, as local standards are considered to be of extremely high quality and trustworthy worldwide. Hence, they often form the basis for international standards. Beyond that, Germany is viewed as a pioneer in environmental protection and sustainability. German companies occupy leading positions in environmental engineering worldwide. The nation’s society exhibits a comparatively high sensitivity for environment related issues, which in terms of sustainability may have a catalytic effect on certain topics of the biological transformation. Finally, the diversity and quality of the German education and training system is rated positively, as it offers a large number of disciplines as well as numerous forms of training, mostly free of charge. The ability of Germany to create demand-oriented new training and study programs is considered to be satisfactory. The training portfolio ranges from applied training in companies to a deep scientific studies at universities. All in all, interdisciplinary study programs and the dual education system form a sound foundation for an adaptable, multidisciplinary education, which is considered necessary for the success of the biological transformation.

3.2.2. Weaknesses

In contrast, the interviews revealed six key weaknesses of the German manufacturing industry that represent major barriers to the biological transformation. First, the German mentality is regarded as risk averse. Conservative attitudes are a widespread phenomena in large parts of society, business and politics leading to manifold impacts: restrictive legislations, little venture capital due to risk aversion of investors etc. Especially the latter is regarded as critical. Without a better and greater availability of venture capital, the conversion of many inventions to innovations will not succeed. Related to risk aversion, the

German society is regarded as extremely critical towards new and unknown technologies. The risks of innovations is often weighted higher than its opportunities. This fact especially applies to the biological transformation as it specifically seeks to connecting two particularly critical topics, namely bio and information technology. Especially in these fields regulations in Germany are viewed as comparatively strict, which impedes free action and rapid progress. Accordingly, the scientific freedom in genetic engineering is more limited than in comparable industrialized countries. Germany is exceeding the already strict EU rules and prohibiting, for example, research on embryos in the field of genetic engineering. As a result, the potential for innovation in Germany is severely hampered. This again leads to a low attractiveness of the location for leading experts and research institutions in the respective fields. High costs of German research and development depict another major obstacle of innovation as a result of high safety demands. German companies are thus often forced to acquire expensive technologies from abroad. German companies are predominantly viewed as hierarchically organized and highly static, a fact that depicts the exact opposite of a biological, decentralized and dynamic system, which represents the target state of the biological transformation. Furthermore, hierarchical structures are regarded to lead to a concentration of knowledge on individuals or groups. The ability of the German manufacturing industry to implement new technologies quickly is thus perceived as improvable. As a resource-poor country, Germany moreover is heavily dependent on imports from abroad. This applies to both energy and materials. A dependency, especially with regard to the energy supply, reduces the foreign policy scope of action of the federal government extremely and represents an obstacle to achieving political goals. In addition, the attractiveness of Germany as a business location is directly reduced by higher energy and raw material prices. Another weakness is seen in the limited development of digital systems and business models. In an international comparison, only a few internet-based start-ups from Germany have been able to establish themselves internationally. The German position in the field of digital business models is thus viewed in the lower third, which makes an improvement in this area imperative

3.2.3. Opportunities

The interviews revealed seven opportunities of the biological transformation to the German manufacturing industry. First, in order to maintain the attractiveness of the industrial location, the biological transformation is regarded as an outstanding chance. This especially applies to the fields of bio and information technology. In both fields Germany has recently lost ground against the USA and China. The biological transformation now offers an opportunity to catch up. Related to consolidation of the industrial location, the biological transformation is viewed to have an increasing impact on the labor market and on ways how work is done. Complex, self-optimizing systems can be monitored by well-trained specialists. The likelihood of new jobs being created is regarded as high. Contents and condition of work are as likely to change, as the emerging decentralized value added systems requires more responsibility and design possibilities in the hand of each individual employee. Digital and biological know-how will increasingly determine job market chances for employees. Another opportunity is seen in the regionalization and resource efficiency, as biointelligent technological innovations offer the potential to increase the efficiency of value creation and close loops. However, it remains open to what extend this optimum can ultimately be achieved. New organizational business models and biological structures are regarded to enable a higher degree of employee participation and more efficient work processes. Bioinspired structures, mechanisms and principles such as swarm intelligence create new competencies directly within a company. These can be adapted, collected and managed decentrally to the respective circumstances. Decentralized, networked or autonomous systems are considered to be extremely efficient and dynamically adaptable. Then again, the current dispersion of biotechnical systems in industrial value creation is considered to be expandable. It is assumed that these systems are going to diffuse strongly in the near future. A comprehensive standardization is viewed as a promising instrument in order to address the prevalent societal skepticism. In addition, the potential of process adaptability and robustness was highlighted. The biological transformation is viewed to create and promote more stable and multifunctional processes that deliver a higher performance. The speed and adaptability of the product development process may as well be improved. Stable, biointelligent system structures facilitate a more agile adaptability and performance of product development and production cycles. Not least, the biological transformation is viewed to offer great potential for radical innovation, as it aims to combine new ways of thinking and disciplines.

3.2.4. Threats

In contrast, the interviews revealed six threats of the biological transformation to the German manufacturing industry. First, legal regulations are regarded as a strong influencing factor for the success or failure of innovations. Especially radical innovations require a high degree of freedom. Restrictive legislations are thus viewed as a major obstacle. On the systems level they might lead to a decline of Germany's innovation potential. The degree of regulative limitations is determined by social will. Unclear added value e.g. due to bad marketing combined with unclear economic benefits and short-term thinking are thus viewed as major risk factors, as they might negatively influence social perception. The greatest threat of bioinspired, bio-based or biohybrid technologies is, however, seen in a possible loss of control over the processes and its results. While early standardization might pave the path to greater controllability, it poses a risk for the robustness of competing technical solutions and the existing innovation potential. A potential threat is also seen in new dangers at the workplace. The implementation of biological organisms into value creation may result in new and still largely unknown hazard potentials. Finally, Germany's dependence on resources poses a risk to the success of the biological transformation, as rising tariffs and restrictions on raw materials would have significant impact on the German economy. In addition, increasing protectionist tendencies within Europe as well as abroad are evident today (e.g. USA, China) and are viewed as a growing phenomena in the future.

3.3. Forecast

Future development in terms of penetration of markets was found to heavily depend on the application, promotion, and acceptance of the basic technologies as well as the available capital. The consensus that emerges from a social discourse decisively determines success, intensity, scope, and speed of the transformation process.

Scenario 1: Extensive biological transformation

The biological transformation quickly leads to comprehensive changes in industries. Germany becomes a pioneer to the biological transformation as it rapidly succeeds in the fusion of technology, biology and computer science. The initiated social discourse leads to a reduction of reservations against the basic technologies followed by a swift opening of markets and a dismantling of hampering regulations. The German government decides to intensify research funding in the current legislative period. Come 2030, the term biointelligent adding value is noticed worldwide as a synonym for sustainable manufacturing. Supported by quantum computers and self-learning algorithms the first decentralized, autonomous and organically adaptive Smart Biomanufacturing Devices (SBD) will enter the markets by 2040. The spreading decentralization of manufacturing leads to a steady regeneration of the ecosphere. While single sectors still require a centralized production, physical and mental relief opportunities such as exoskeletons reduce the average workload of employees with significant benefits to the health system. Come 2050, the better share of material and energy cycles are closed at the regional level, due to the further development and distribution of SBDs. Humans and machines co-exist in collaborative and symbiotic networks maintaining a high standard of prosperity and well-being. Self-learning algorithms are increasingly applied to develop solutions for remaining socio-ecological problems. The second half of the century marks the transition from a globally distributed supply economy towards a technology-based just-in-time economy that enables a fair, demand-oriented satisfaction of people's material needs while substantially relieving ecosystems globally. "Living" products and production systems are conquering markets, leading to steadily increasing, qualitative economic growth.

Scenario 2: Moderate biological transformation

The biological transformation leads to changes in industries, yet initially promoted by the USA and China that massively invest in artificial intelligence and biotechnology (especially genetic engineering). Germany misses the political momentum to intensify research funding in the current legislative period due to a lengthy political discussion and social skepticism. By the mid-2020ies the USA and China have not only accomplished technological leadership but have gained international sovereignty of the biological transformation of manufacturing leading to a less socio-ecologically oriented approach. Germany more and more acts a foreign-determined descendant in its former core competency, advanced manufacturing, leading politics to adapt the concept biointelligent value creation rather quickly in order to restore lost ground. As of 2030, the USA and China have made great progress due to groundbreaking innovations in biotechnology and artificial intelligence. However, it slowly becomes obvious that the advantages of the USA and China can no longer be regained. By 2040, German industries focus on niche markets, while core markets of the biological transformation are being dominated almost exclusively by the USA and China. The reputation of "Made in Germany" products and technologies gradually declines. Come 2050, little progress has been made in relieving the ecosystem from industrial damage due to the lack of a comprehensive concept and a pioneer willing to vouch for it.

Scenario 3: Marginal biological transformation

German politics fail to facilitate a comprehensive social discourse resulting in a denial of the biological transformation by the general public. While the application of self-learning algorithms, genetic engineering and biointelligent interface technologies are increasingly viewed as risky by the German population, the USA and China massively invest in their development. Despite noticeable economic downturns, framework conditions for enabling technologies remain restrictive. Due to massive public resistance, Germany more and more becomes an antagonist of the biological transformation. Come 2040, Germany has lost its position as technology leader in advanced manufacturing as well as its importance in international politics. Somehow, the nation manages to arrange itself with its subordinate role in world politics by 2050. The lack of alternatives and social consensus leads to the formation of another sustainable subsistence strategy: a nationwide demand economy focusing on the basic needs of its citizens.

3.4. Fields of action for future R&D

In order to structure the interview, workshop, and literature research results of over 250 potential research and development topics, we developed a framework of ten fields of actions. Thereby, we differ between challenges that can be solved by a single company (intra-organizational), require at least two partners from different disciplines (inter-organizational) or demand for a social dialogue and/or political decision (socio-political). Fig. 5 illustrates the framework according to Miehe et al. [24,25].

3.4.1. Bioinspired, bio-based, biohybrid materials

The development, fabrication and utilization of new materials offers great potential for the functionalization of products as well as the resource efficiency of both products and processes. Decisive for the fulfillment of the vision of a biointelligent adding value is an appropriate handling of material flows over their entire lifecycle as well as a possible subsequent use (re-fabrication) [51–53]. Significant potential for the use of biogenic and recycled materials was predicted by the involved experts, especially for industries with high material intensity, such as the construction industry or for the production of platform chemicals. Future activities should, therefore, focus on further exploring new uses of biogenic and recycled materials. Precise forecasting or even targeted activation of the degradation process of the materials as well as their adaptation to usage cycles are other ambitious goals that should be targeted by future research. In addition to the increased use of bio-based materials, their processing also bears great potential. The high functionality of organic molecules is already being used for self-organized structures such as DNA origami [54,55]. Intelligent composite materials, such as shape memory alloys and polymers, self-evolving structures or tissue engineering, combined with molecular control possibilities form the basis for nano-scale bio-based and functional structures [54,56]. Research in this field is regarded as the basis of disruptive developments in bioelectronics and biocomputing as well as sensor technologies. At present, applications are still lagging behind in their possibilities, with the exception of medicine and diagnostics [57]. Here further research and development activities are needed, which should be supported accordingly. 3D printing processes using biological material promise new approaches in the area of so-called tissue engineering or so-called 3D bioprinting (see section on manufacturing technologies). Another field of future research in the context of the biological transformation is smart materials, a term commonly referring to materials that can change their properties in response to external stimuli, such as temperature, pH, pressure or humidity. Such materials are already widely used as shape memory materials, chromogenic materials or piezoelectric materials [54]. However, biological materials or surfaces can be selectively accessed and activated through a wider range of stimuli. Self-X functions, such as self-induced reshaping or self-healing, could be realized. Then again, the integration of living biological organisms into material networks has predominantly been researched in biomedicine. However, the potential of organisms as actuators, sensors and controllers for advanced material functions is far from exhausted. Ultimately, this can be used to develop 'living materials', i.e. materials that have functionalities such as learning. As a step towards this, biological functionalization, which is already comprehensively addressed in research at the molecular level, must continue to add more complex functions, including the integration of living organisms. Great opportunities are seen in the emerging new gene modification technologies (e.g. CRISPR / Cas) that may set the basis for an efficient and targeted realization of complex functionalities in biomolecules.

3.4.2. Biology-technology-interfaces

An increased interaction between biological, informational and technical system, as envisioned by Miehe et al. [24,25], requires a variety of adaptive biology-technology-interfaces (BTIs). Basic scientific research in this field was conducted in the early 2000s within the German SFB 563 (bioorganic functional systems on solids) by the Max-Planck-Society leading to individual solutions, e.g. biointerfacing of diamond thin films with proteins or local biosensing using silicon based photonic nanostructures [58]. Generally, numerous physical principles, e.g. electrical, chemical, mechanical or optical, may be used in order to achieve an interaction of technical components with cellular systems. 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 [59,60]. 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 [61–63]. While current examples of BTIs generally are developed in order to control biological systems via technology, a

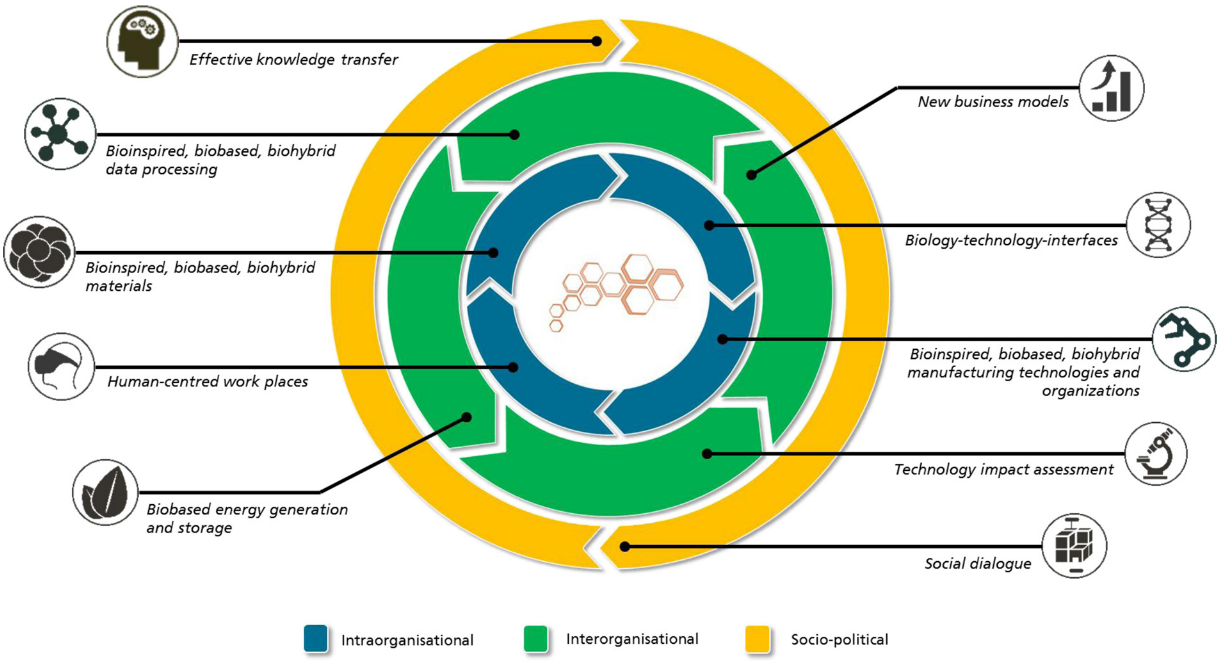

Fig. 5. Field of action framework (FAF) of biological transformation of industrial value creation according to Miehe et al. [24,25].

biointelligent manufacturing system requires a bidirectional real time information exchange between the systems. Although a few examples of fully controlled systems have been implemented in technical prototypes, e.g. bioreactors equipped with integrated on-line sensors allowing constant control [64], 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 [64], specific biological actuators, e.g. bacteriophages as well as appropriate sensor technologies and integration, e.g. for online measurement, there is more research necessary. 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 soft sensors with underlying process models and new concepts for biosensors [65,66]. 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) [67].

3.4.3. Bioinspired, bio-based, biohybrid manufacturing technologies and organizations

The development of new manufacturing technologies, processes and organizations represents the heart of the biological transformation of industrial value creation. Potentials in this field are manifold. Research for rather short-term improvements of existing manufacturing systems is required in the field of inspiration in order to create stable, quickly customizable and self-configurable production systems as well as organizational forms [68]. In this context, optimization solutions based on bioinspired algorithms will increasingly replace classical methods [69,70]. Basically, the goal is to significantly increase the resilience in production systems and processes, for example by self-adaptation, i.e. the ability of systems to adapt independently to changing requirements and conditions of an environment [71]. Prerequisites for this are robust sensors, actuators (see subsection BTIs) and computer techniques, which allow to continuously recognize and monitor relevant states of processes and production systems as well as the workpieces to be manufactured [72]. Further increases in productivity are expected due to an increase in the speeds of information acquisition and transmission as well as decreasing complexity (or failure criticality) [73]. Future research activities will not substitute but rather complement current developments, e.g. 'cyber-physical processes and systems', in order to increase productivity and product quality and to create new possibilities of process transparency and planning. Then again digital twins, prediction and algorithms based on natural processes play crucial roles (see subsection data processing) [74]. Currently, 'digital twins' are at an initial development phase [75–77]. In the context of the biological transformation, the digital twin, as an image of the planning information, is expected to adopt the function of a genotype to its respective component state, the phenotype. This 'manufacturing gene pool' is likely to expand by simulation results and to be optimized using bioinspired algorithm cycles, such as swarm intelligence and ant algorithms [78,79]. Analogies from biological systems can also be applied to business organizations [80,81]. One example is single-celled organisms that are able to form 'organization teams' when exploitable opportunities are identified in the immediate vicinity. Similar to unicellular organisms, organizational units will have to change their form agile and adaptively by adjusting their internal relationships, teams and members. At the same time, the structure of the unit remains consistent. If a unit begins to exceed the limit of the employees, new units are formed in analogy to the reproduction by division in unicellular organisms [23].

From a medium- and long-term perspective, integrational and interactional aspects are expected to dominate future research. This especially applies to the enhancement of additive manufacturing technologies capable of producing bio-based and biohybrid materials (incl. 3D/4D bioprinting), enabling promising new approaches in the area of tissue engineering [82]. In this way, different cells can be printed in spatially resolved forms, which can then develop into new, complex cell aggregates and tissues in a subsequent step [83,84]. To artificially produce organs is, however, not yet tangible. The use of 3D/4D bioprinting beyond biomedical applications depicts a massive potential to produce new, complex products and machinery. Hence, it is of great importance to further expand research in these fields [85,86]. Additional examples for research areas are the industrialization of biotechnological innovations, such as neuro cell sensors, the advancement of bioreactor systems via cell-responsive automation as well as the use of DNA origami to create molecular machines for the manufacturing of

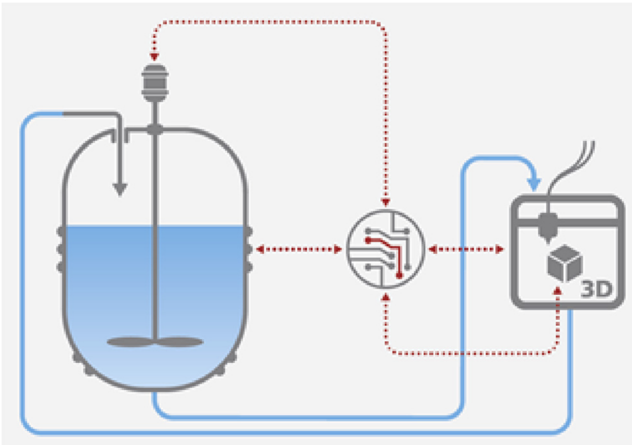

Fig. 6. Examplified SMD by combining an intelligent bioreactor, a bioprinter and real-time bidirectional information exchange via BTI.

nanoscale biohybrid products. Not least, the convergence of single solutions in Smart Biomanufacturing Devices (example see Fig. 6) is a major field of research in order to create completely new technologies that enable distributed, personalized and scalable value creation. For this purpose, a wide variety of existing individual technologies (additive manufacturing, bioprinting, biosynthesis, bioreactors, etc.) are to be purposefully combined in collaborative projects.

3.4.4. Human-centered work places

Jobs in today's manufacturing environments are strongly influenced by developments in information and communication technology. For more than thirty years now, this has led to a greatly accelerated, simultaneous change in the workplace, work content and working environment [87]. A large number of today's occupational profiles did not even exist a few decades ago. As humans and technologies are expected to increasingly interact at the work place, Gieseke predicts a rising need for further education measures as a task for employer, employees as well as public authorities [88]. Future workers are expected to become an active part of a more and more transformable factory as shown by Kucukoglu et al. [89]. The transformation of workplace design is thus of great interest to future research in order to improve both ergonomics and productivity [90]. Today’s research already increasingly focusses on men-machine-interactions leading to various new approaches in fields such as adaptive, anthropometrically and dermatologically compatible portable assistance systems. While existing anthropometrical wearables are heavy, slow single technologies, future biocompatible man-machine-interfaces will, besides person-specific intelligent assistance, allow quick adaptability and easy portability [91]. Therefore, significant research is needed in the detection and interpretation of human biosignals, in particular robust, non-invasive measurements of muscle and mental activities [92]. In addition, the development of technically assisted emotion and facial expressions is of central importance in future manufacturing environments. This as well applies to the optimization of the workplace with regard to the individual movement behavior of employees as well as the real-time evaluation of work movements [93]. This opens up new possibilities for the individual definition of break times and the optimization of movements with regard to ergonomics and process speed. Another field of research and development required in the context of the biological transformation is the appropriate handling of biomanufactured (half-finished) products, a challenge that employees are likely to increasingly face. Therefore the development of appropriate security and qualification measures is needed.

3.4.5. Bioinspired, bio-based, biohybrid data processing

Data processing is regarded as a key enabler of the biological transformation. The field bears a wide range of potential research areas ranging from bioinspired software (e.g. algorithms and communication mechanisms) [94–99] to visionary approaches of data storage and processing using biological structures (hardware) [100,101]. Information technologies are already the most important drivers in biological research and development today [102–104]. The complex diversity and enormous amounts of data required for understanding relationships in complex systems are challenges that can only be met by today’s IT-tools [105]. Although great advances in molecular biology have provided a profound understanding of how information from the genome is translated by chemical reactions, a full understanding of biological phenomena at the next level remains largely open. Obviously, information processing plays a crucial role in every biological system, appropriate theoretical models for the description of these information flows are however missing [106]. Then again, the increasing sensorization of production processes and products creates technological ‘ecosystems’ whose development and stability is to be controlled. A biointelligent system design uses the fundamental systemic principles of nature to design and control such equilibria [107]. Dynamic problems, changing constraints, erroneous or incomplete data sets, and insufficient computing power are new challenges in the development of data-driven solutions and in the design and control of large networks that need to be addressed. Smart bioinspired algorithms can provide solutions for effective and decentralized communication and control mechanisms in such technical ecosystems [108]. This field of research is currently dominated by the development of artificial Intelligence (AI), where research has so far focused on a few algorithms whose origins date back to the 1970s to the 1990s. These include neural networks, genetic algorithms, particle swarm, ant colonies etc. The latest algorithms which may provide superior solutions are still under-utilized in application areas [109]. Further fields of research and development are data storage, data structures and data security [110]. Due to the large amounts of data and complex links in biointelligent systems, these fields are of great practical importance. Bioinspired or bio-based hardware are molecule-based systems that are currently in their infancy theoretically capable of extremely high computing power and storage capacity [111,112]. Especially neural chips, DNA computing, programmable cell networks etc. are expected to lead to a variety of disruptive innovations. For politics and industry, there is a variety of design issues in the field of data processing, which are of increasing importance. The further expansion of the information technology infrastructure is regarded as a prerequisite for far-reaching information technology networking in industry. Data protection, data transparency and data processing standards are regulatory tasks that have to be completed faster and better in line with the progressing developments [113,114]. Not least, ethical issues need to be answered, such as how algorithm-based decisions are made and what responsibilities result.

3.4.6. Bioinspired, bio-based energy generation and storage

Adequate energy supply is an essential prerequisite for competitive industrial manufacturing. In the context of an inevitable de-carbonization of energy generation, both the relevance of renewable bio-based sources as well as the bioinspiration of energy systems are likely to increase. In many areas of energy supply, storage and conversion, bio-based or bioinspired technologies today are already being investigated and used. A prominent example are biorefineries that are often energy self-sufficient units receiving the required energy directly from the biomaterial being processed [115]. The substances produced, such as bio-based plastics, can also be energetically utilized after their material utilization phase. Biorefineries thus bear great potential to enable the fullest possible utilization of bio-based raw materials and to contribute to the regenerative provision of energy by means of liquid or gaseous organic energy carriers, so-called e-fuels or synfuels. As shortages supply of relevant resources for batteries are already foreseeable today, chemical energy sources should also be considered as an alternative energy source for applications in internal combustion engines.

Therefore, biotechnological methods play a key role, e.g. micro-algae for the synthesis of organic fuels or microbial electrolysis cells for regenerative hydrogen generation [116–118].

3.4.7. Technology impact assessment

As the biological transformation is to be understood as a path to sustainable value creation, proactive technology impact assessment has to be an integral part of research and development activities. While technologies grow more and more complex, decision makers in politics, research and industries require valid supporting measures of economical, ecological and social impact of future technologies. Although a variety of methods exist from an ecologic perspective, life cycle assessment (LCA) is widely accepted today as the standard approach for environmental impact assessment. The method however exhibits great deficits, e.g. data availability and quality, uncertainty, subjectivity, lack of standardization. Additionally, the biological transformation depicts a major challenge due to the lack of empirical values especially in the context of gene engineering technologies. Intensive further research is thus required in order to address existing social biases, control complex bioengineered systems, develop tailored approaches for holistic ex-ante risk assessment and mitigate rebound and leakage effects. Simultaneously, further standardization is required in order to avoid the assertion of subjective claims. Likewise, an increased application of AI-technologies for decision support appears promising.

3.4.8. New business models

Beside the technological convergence, the development of business models is regarded by experts as another prerequisite of the biological transformation. Therefore, digital business models have to be aligned with biointelligent products and systems. This especially applies to the vision of a technology based just-in-time economy, where a more decentralized adding value is probable (see Section 3.3). Therefore, new business model ratings have to be developed in order to account for more than just economic value. These to be developed models could be applied by legislators, e.g. for subsidization or taxation. A stronger prioritization of sustainability is viewed as essential for the success of the transformation. Research and development areas are the establishment of valuation and incentive approaches for a data-based, methodical development of business models with regard to economic and ecological aspects, the development of novel approaches to integrate consumers into value-added processes as well as the promotion of interdisciplinary projects in business model development and interdisciplinary education. In addition, the survey reveals the comparatively low start-up culture in Germany that has to be improved urgently, e.g. by providing adequate funding, bringing together inventors and investors at tailored platforms, reducing bureaucratic efforts.

3.4.9. Social dialogue

New technologies as envisioned by the biological transformation bear great potential for economic growth, public health and ecological sustainability [119]. Scientific progress is, however, strongly dependent on a social perception [120]. Since the development and introduction of new technology fields is usually associated with a controversial discussion about the risks and benefits, an intensified knowledge-based, transparent and open-led social discourse is needed in order to set the basis of trust for a far-reaching and sustainable development [119]. Current examples of discussion topics that involve a variety of social stakeholders are the application limits of artificial intelligence and the handling of generated data in a progressive digitization. The discourse is now less concerned with the technical feasibility, but is much more influenced by ethical issues such as the decision-making of artificially intelligent systems or their permissible autonomy degrees [117]. Potential fields of research and development in the context of the biological transformation are biologically engineered technologies and their impact on humans, nature and society, the definition of the role of scientists and managers as communicators in the social discourse as well as the establishment of secure dialogue formats for open, transdisciplinary discourses (e.g. e-governance). Transparency is very important when dealing with socially critical issues and, thus, has to be focused.

3.4.10. Effective knowledge transfer

Experts agree that interdisciplinary cooperation is the key enabler of the biological transformation. Future research and development thus has to bring together people from different disciplines in order to share their knowledge and approaches. Then again, the biological transformation can only succeed if it can develop a positive vision, a social momentum via public presence (media), opportunities for participation (discussion) as well as a targeted knowledge transfer (school, training, media). Therefore, a political strategy is needed in order to create appropriate early education in schools as well as appropriate study programs for generalists and specialists. A fundamental transformation of curricula and pedagogical concepts into more project-related work and interdisciplinary subjects networks seems promising in this context. In addition, an early sensitization of sustainable behavior is strongly required.

4. Summary and recommendations

The realization of a sustainable subsistence strategy is the fundamental challenge for today's societies. From a manufacturing perspective, current modes of production massively hamper the prospects of future generations to sustainably satisfy their material needs. However, according to experts, a sustainable value creation is possible through the biological transformation of manufacturing. It was for the first time systematically assessed for the German industry within the BIOTRAIN project presented in this paper. The goal of the project was to identify key technologies, to assess the current state of the German manufacturing industry, forecast potential scenarios of development and deduct recommendations for future actions of the German federal government as well as the Fraunhofer Society. Based on a combined approach of the Delphi method and scenario planning, we conducted 123 national and international high-level expert interviews, executed ten stakeholder workshops with over 200 participants and aggregated the results in form of a SWOT analysis of the German manufacturing industry. We derived a forecast of three possible scenarios (extensive, moderate and marginal biological transformation) as well as ten distinct fields of actions involving recommendations for public authorities and Fraunhofer. Further detailed information is provided on the project website (www.biotrain.info)[2] .

The status-quo analysis shows that German companies are currently in a promising position in many relevant areas. Germany's strengths in an international comparison, among others, include its strong basic and applied research as well as its very high standards in the field of environmental protection and sustainability. Major weakness are the aversion to potential risks and disruptive changes that lead to a relatively restrictive legislation as well as a comparatively low acceptance of new technologies. Regionalization and resource efficiency via circular economy are seen as main opportunities of the biological transformation. Significant risks are identified in potentially uncontrollable, complex production processes. Although the survey reveals eleven technological enablers that require further research, the quintessence of the project was not a single enabling technology, but the interdisciplinary cooperation between disciplines. While technologies seem to be available, their purposeful integration lacks behind. Consequently, the forecast predicts an increasing convergence of biological, technical and informational systems, that is likely to transform current linear production systems into decentralized Smart Biomanufacturing Devices if politics and industry take appropriate

[2] Currently in German only.

measures.

In order to become a pioneer and lead market of the biological transformation, a corresponding political framework is required. In a first step, this includes the establishment of an advisory board to the government and its ministries as well as the development of a political strategy. In order to increase public understanding the development of real life case studies is required. Possible focus topics are the development of biointelligent manufacturing and re-fabrication technologies, the design of human-centered workplaces, the advancement of processes via bioinspired algorithms, development and utilization of bio-based/biohybrid materials as well as the assessment of human-environment interactions in the context of biointelligent production. Another crucial aspect for policy making is the development of a tailored indicator system that enables the comparison of different countries, regions and sectors in the context of the biological transformation. From the companies' perspective, an open innovation culture is a prerequisite for a promising positioning for future innovations. Equally important is the recognition and evaluation of opportunities and risks. An interdisciplinary personnel structure, especially in research and development areas, is thus of increasing importance. At the strategic level, companies have to deal with new business models, production structures and recycling cycles that will emerge. Research needs to include the processing of bio-based multifunctional materials, the development of interfaces between biological and technical components as well as the biologically inspired data processing, and the necessary life cycle considerations. In the medium and long term, the establishment of appropriate research, development and education structures is of great importance, e.g. by appointing professors in the fields of biological transformation, creating attractive working conditions for free and interdisciplinary research and transforming curricula and pedagogical concepts in schools and universities into more project-related work and interdisciplinary subject networks

The Fraunhofer Society should aim at optimally supporting politics and industries in this transformation process. Therefore, a coordinating board moderating the internal and external stakeholder dialogue is needed in the near term. In order to facilitate and/or gain the position as a pioneering organization, Fraunhofer should discretely promote further leading-edge projects and clusters in relevant fields of the biological transformation

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