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Value Chains for Industrial Biotechnology in the Bioeconomy-Innovation System Analysis

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Abstract: Industrial Biotechnology (IB) is considered as a key technology with a strong potential to generate new growth, spur innovation, increase productivity, and tackle environmental and climate challenges. Industrial Biotechnology is applied in many segments of the bioeconomy ranging from chemicals, biofuels, bioenergy, bio-based plastics, and other biomaterials. However, the segments differ profoundly regarding volume, price, type, and amount of needed feedstock, market condition, societal contributions as well as maturity, etc. This article aims to analyse a set of five different value chains in the technological innovation system (TIS) framework in order to derive adequate policy conclusions. Hereby, we focus on quite distinctive value chains to take into account the high heterogeneity of biotechnological applications. The analysis points out that policy maker have to take into account the fundamental differences in the innovation systems and to implement differentiated innovation policy to address system weaknesses. In particular, market formation is often the key bottleneck innovation systems, but different policy instruments for various application segments needed.

Keywords: bioeconomy; industrial biotechnology; technological innovation systems; innovation policy

1. Introduction

Industrial Biotechnology (IB) is considered as a key technology with a strong potential to generate new growth, spur innovation, increase productivity, and tackle environmental and climate challenges. It enables new applications and to transform existing markets [1]. The European Commission identified Industrial biotechnology as one of the key enabling technologies (KETs) in the EU and established significant respective funding mechanisms such as the Leadership in Enabling and Industrial Technologies (LEIT) actions in Horizon 2020. Moreover, IB is a key source of innovation in the concept of the bioeconomy. This concept relates to the transformation from a fossil-based towards a renewable resources based economy in order to contribute to societal goals such as mitigating climate change, lowering resource use, increasing food security, generating economic growth, and securing jobs [2]. Significant efforts to foster R&D activities in IB in particular under the umbrella of the concept of the bioeconomy already exist. Examples are the funding of biotechnology projects under the context of societal challenges in Horizon 2020, the establishment of the Public-Private-Partnership or the encouragement of specialization strategies in the context of the European Structural Investment Funds (ESIF). Additionally, in more and more EU member countries, bioeconomy strategies have been elaborated and are in the process of being implemented [3].

As the framework conditions have changed since the first bioeconomy strategies were adopted a few years ago, the goals associated with the bioeconomy have been further developed. The substitution of fossil raw materials has lost some of its importance because of the low price of crude oil. By contrast, the potential contribution to the achievement of climate and environmental protection goals, as well as the United Nations' Sustainable Development Goals has gained in importance and legitimacy for promoting the bioeconomy [4–6].

In the same vein, a number of market actors shifted their focus from feedstock-intensive products, which aim to substitute fossil resources in large quantity, towards high-value, low volume products with only small fractions of biomass input [7–9]. Industrial Biotechnology is applied in segments ranging from specialty chemicals, biofuels, bioenergy, bio-based plastics, other biomaterials, biolubricants, biosurfactants, etc. However, the value chains differ significantly from each other regarding different aspects, regarding volume/price, potential advantage, product characteristics, maturity, and sector [10].

There has evolved a rapidly increasing bunch of literature about drivers and barriers for the bioeconomy, which usually considers industrial biotechnology as an important technology for the transformation process. Some of those contributions explicitly take up a system of innovation perspective [4,11,12]. During the emergence of the innovation system (IS) approach, biotechnology has been a key subject of investigation, however with a focus on health biotechnology [13]. Those studies point out that government policies have to address many dimensions of the system of innovation. Not only tools for science and technology policy have become more important, but also other stages of the innovation cycle, such as education, collaboration between academia and industry, creation of business venture, establishment of technological platforms, or the creation and development of clusters encompassing scientific and educational institutions as well as manufacturing companies [14].

Recently, a significant amount of current contributions assesses the bioeconomy [8,11,12]. Some contributions have a rather broad focus and point out key policy issues on the general level of bio-based products, mostly pointing out missing coherence and stability of policy as well as missing demand side incentives [4,8]. However, those analyses can hardly assess and may overlook the issue that potential highly differentiated policy approaches are useful for the different segments.

Moreover, there are rather many analyses that address innovation and policy for biofuels and bioenergy [11,12,15–19]. These contributions point out the high impact of demand-side policies, such as quotas or monetary incentives for technology diffusion. Instead, material uses of biomass, which are less affected by demand side policies, are more seldom analyzed. There are some studies focusing on certain innovation aspects of future development of some type of materials [20,21]. However, the challenge to provide more information about the segments on materials uses lies in the wide variety of applications and value chains. The focus on high volume value chains may have a significant impact to sustainable development and (re-) industrialization in mature and emerging companies than high-value added niches could ever do. Moreover, the need of policy support is often clear articulable with high investments and needed and a certain community lobbying together. However, it is rather a consensus among stakeholders that, in particular industrialized EU-countries with limited natural resources, can be competitive mainly in high value-added segments with high requirements regarding technological competencies.

These considerations imply that current research provide to little information about specific characteristics of certain value chains of the bioeconomy in comparison, so that issues across value chains, but also policy relevant specifics can be identified. Therefore, this contribution aims to analyze a set of different value chains from an innovation system perspective in order to derive adequate policy conclusions. We use the technological innovation system (TIS) approach, because it focuses on novel technologies, as well as the institutional and organizational changes required for emerging technological fields to progress [22]. We chose distinctive value chains for the TIS analysis to take into account the high heterogeneity of biotechnological applications.

The selected value chains are lignocellulosic ethanol, bio-based plastics, enzymes, biotechnologically produced flavors and fragrances (F&F) and the production of biopharmaceuticals. Regarding the latter, the focus lies on the production stage, as this refers to processes related to industrial biotechnology, while health biotechnology that is applied in the R&D process for new therapeutics is not considered here. Moreover, there are some overlaps between the value chains; in particular, enzymes are often used in other biotechnological value chains. However, we focus on the

R&D and production of enzymes as well as the whole bunch of end products to make a more clear-cut distinction between the five segments.

This portfolio, but not necessarily every single value chain it contains, cover aspects such as drop-in vs. new functionalities, volume and types of feedstocks needed, horizontal or vertical integration of IB in value chains, and low-volume, high-price products vs. high-volume, low-price products. For all value chains further, technological innovations are of key importance, segments with slow further technological progress such as bioenergy were excluded. Moreover, for all value chains a high potential for innovation and for significant economic impact can be assessed.

The article is structured as follows: Section 2 presents the main features of the TIS framework as well as the methods and data sources. Section 3 presents first the differences between biotechnology innovations in various segments, and then presents different innovations systems in biotechnology. In Section 4, the differences between the innovation systems and its implications for policy are discussed. Finally, Section 5 presents the conclusions of the study.

2. Methods

To analyze the different biotechnology innovation segments, we use the technological innovation system (TIS) approach. The TIS approach has been used very frequently for the analysis of new technological fields, as it provides a holistic and dynamic perspective on the evolution of technological fields. Usually, the focus lies on the drivers and barriers that influence the innovation and diffusion process in order to derive policy interventions needed to overcome the hurdles, e.g., [22–25]. Therefore, different functions of an innovation system are analyzed. The specific functions in TIS studies vary somewhat in prior studies. In the present article, we use resource mobilization, market formation, influence on the direction of search, entrepreneurial experimentation, legitimation, and knowledge development and diffusion. Table 1 summarizes these six functions.

Table 1. Functions of a technological innovation system (TIS).

Function	Definition
F.1 Knowledge development and formation:	This function contains the depth of the knowledge base of the TIS and how well that knowledge is diffused and combined in the system
F.2 Entrepreneurial activity	Entrepreneurs act as risk takers, which perform the innovative commercial experiments, seeing and exploiting business opportunities
F.3 Market formation	The factors that stimulate the emergence of markets for new products. These include articulation of demand from customers, institutional change, and changes in price and performance of the products
F4. Guidance of the search	This function represents the selection process that is necessary to facilitate a convergence in technology development, involving policy targets and expectations about technological options.
F5. Resource mobilisation	The TIS's ability to mobilize social capital (e.g., through education, entrepreneurship etc.), financial capital (e.g., venture capital, government investment in long-term R&D) and complementary assets (e.g., complementary products, services)
F6. Creation of legitimacy	The social acceptance of the technology and the actors and compliance with relevant institutions. Legitimacy is formed through conscious actions by various actors who may form advocacy coalitions in order for the new TIS to acquire political strength this process may often be complicated by competition (and lobbying) from adversaries defending existing technologies and regimes.

We combine different methods and data sources to analyze the functions. Main sources for the analysis are intensive literature research and document analysis (i.e., trend reports, market reports, sector studies etc.), combined with expert interviews and a workshop for each innovation system. In all of these five workshops, experts from large companies, small firms as well as from research or network associations took part. The workshops were conducted in standardized set-up in order to derive a comparable assessment of the TIS.

Moreover, with this standardized setting we address the main challenge for the analysis is that these innovation paths have been, to a very different extent, subject of existing analysis from a socioeconomic or innovation policy perspective. While lignocellulosic ethanol and bio-based plastics have been analyzed in some studies from an innovation perspective, there is rarely innovation for the others.

In contrast to existing TIS studies, we do not focus one or two innovation system, but analyze five systems. That innovation system may differ from each other is of course very well in the nature of the innovation system literature as the knowledge base, technological characteristics, inputs and demand differs between sectors and technologies [26]. However, in the literature seldom more than two innovation systems have been analyzed in comparison. For example, Reference [27] analyzes the interaction and competition between different technological innovation systems for renewable energy technologies. However, according to our knowledge, implications for differentiated set of policy making to foster different technological innovation system on a core technology have not been addressed in the literature.

In the TIS literature, two different approaches exist [25]: One analyses TIS structures, which comprise actors, interactions, institutions, and infrastructures, while the other examines those TIS functions considered mandatory for an innovation's success. Regarding the latter, some TIS analysis have pointed a set of drivers and barriers across the IS functions, as often policy weaknesses etc. do not only effect one function [4,12]. In this contribution, we focus on the functions approach and perform the analysis at two levels. We present the main characteristics, strength and weaknesses for each function in each TIS. Moreover, we summarize the main issues across functions by distinguishing between two types of value chains.

Of course, the TIS are not completely isolated from each other, but synergies and conflicts between them arise. While the technological basis is often very similar, innovative pathways with very different end-use applications may compete for the same financial resources, particularly in the form of public R&D support, or human capital [4].

3. Results

In the following, we first discuss the cross-sectional characteristics of industrial biotechnology by pointing out potential differences between applications, ending with a detailed characterization of the five value chains in the focus of this article. Then, we present key results of the TIS analysis by distinguishing two types of innovation systems, first for lignocellulosic ethanol and bio-based plastics as value chains with rather high volume. Moreover, ethanol and some bio-based plastics are pure drop-ins. These are products with identical or similar technical properties to their fossil counterparts. Second, we present the other innovation paths characterized by rather low volume and high value, as well as often different functionalities compared to fossil-based alternatives. This differentiation is useful, because major policy-relevant issues arise because of the volume and drop-in character. However, within the analysis we further distinguish for both strands regarding differences between the value chains, especially regarding maturity and further demand characteristics.

3.1. Cross-Sectional Characteristics of Biotechnology

Biotechnology is usually considered as a cross-sectional technology with many applications and strong spillover effects between them [28]. However, it has to be taken into account that these segments differ highly from each other in several aspects.

Firstly, bio-based products differ significantly between those segments that contain high volume, low price products and low volume products, high price products. High-value added products usually require high skills expertise and existing industry expertise and networks. Instead, mass products often require high biomass resources and low production costs.

Secondly, market conditions and institutions may differ profoundly between the sectors, e.g., regarding the dominance of large incumbent firms, the importance of dynamic SMEs, business-to-business vs. business-to-consumer relationship, price vs. quality competition, concurrence to fossil-based products. Regarding the later, as described above, some bio-based products are drop-ins, with identical or similar technical properties to their fossil counterparts, Drop-ins do not face high market uncertainties, can be partly build on existing infrastructure and existing technological knowledge for the conventional product and do not lead to switching costs for users [29]. In contrast, non-drop-ins have significant different functionalities and may require new infrastructure or knowledge on the user side.

Thirdly, while biotechnology is expected to contribute strongly to societal challenges, the related missions differ between the segments. This may imply certain requirements for the characteristics and performance that differ between the implications, e.g., reducing CO_2-emissions, substitution of high quantities of resources, safety and health effect, efficiency. Hence, technological challenges as well as factors for diffusion may differ. Moreover, the trend to mission-oriented policies in the EU and many countries lead to different institutional settings between the segments. For example, health applications of biotechnology are expected to contribute to health, demographic change and wellbeing and is subject to different R&D&I funding systems and programs compared to biotechnology solutions for industry with potential to address climate change. A related perspective is that there are different transition paths for bio-based innovations with different impacts. Dietz et al. [30] differentiate between four paths: "(1) substitution of fossil fuels with bio-based raw materials; (2) productivity increase in bio-based primary sectors; (3) increasing efficiency in biomass utilization; and (4) value creation and addition through the application of biological principles and processes separate from large-scale biomass production." These transformation pathways can be driven by different supply and demand dynamics [30].

Fourthly, biotechnology innovation activities differ in their maturity. In some value chains, biotechnology products are established since few decades, such as biopharmaceuticals, enzymes for food and feed, biolubricants. Instead, in other segments, biotechnological solutions are just emerging and no experiences for production exist (e.g., certain biotechnological bulk chemicals). Hence, learning and scale effects have not been realized yet [4].

Fifthly, while there are independencies between the segments in resource use and technological processes, rather little spillover effects between application sectors arise. As [31] already stated in the late 1990s "[...] the distinction broadly holds that biotechnology firms depend on existing companies in their own sector of application for their market and for the joint development of their products. Links have tended to run vertically downstream to user industries for each sector rather than between sectors, with little technological interdependence between sectors". Therefore, biotechnology differs e.g., compared to ICT, with the latter generating strong network effects. Consequently, innovation and diffusion of biotechnology evolves more independently between the sectors and evolving in separated innovation systems.

Due to the differences in technological, institutional, and market characteristics, as well as the potential contributions to societal goals and consequently being the subject of relating initiatives, the potential drivers, barriers, and consequences differ significantly between the value chains.

In order to analyze the consequences of these differences for the innovation process, we analyze the respective innovation system for the five mentioned value chains. Table 2 summarizes key differences between these TIS.

3.2. Innovation System Analysis for High Volume, Biomass-Intensive Segments

The development of high volume, biomass-intensive segments contributes potentially to sustainable development by substituting fossil resources with more sustainable production based on biomass. Due to their volumes, they would have significant potential for reducing GHG emissions. Moreover, by increasingly using-food feedstocks such as lignocellulose, negative social implications such as concurrence to food production may be avoided.

Table 2. Characteristics of five IB innovation segments.

Segment	Delineation/Description	Volume and Price	Quantity of Feed-Stock	Maturity Stage	Potential Advantage	Drop-In Character
Ligno- cellulosic ethanol	Lignocellulosic ethanol for fuels (road and air transport) from non-food biomass	Very high volume, low price	Very high	Early commercialisation phase	Substitution of fossil fuel with non-food-biomass, potentially reducing GHG emissions	Yes
Bio-based plastics	Biotechnologically produced* polymers based on biomass (biodegradables and non-biodegradables) for different applications	High volume, rather low price	High	Niche market with considerable market growth	Substitution of fossil resources with biomass, different performance for some products, potentially reducing GHG emissions	Drop-ins and drop-ins are equally presented in the market
Enzymes	Enzymes are proteins that act as macromolecular biocatalysts, either in living cells or in isolated form.	Low volume, high price	Very low	Established markets, but new application opportunities	Potential higher resource efficiency compared to the use of chemical catalysts	Enzymes are non-drop-ins, some end-products are drop-ins
Production of Bio-pharmaceuticals	Production technology and processes for biotechnologically produced biologics; boundary of analysis at the production stage	Very low volume, high price	Low	Significant market size and dynamics for biopharmaceuticals	Provision of novel therapeutics	No

3.2.1. Continuous Knowledge Development, but Bottlenecks in Upscaling

Regarding knowledge development, almost since decades R&D projects have been carried on different technologies readiness scales levels supported by European national R&D programmes. Technologies for the production of lignocellulosic ethanol and bio-based plastics have made subsequent progress, such as the engineering microorganisms for bioconversion, ability to use a higher variety of feedstocks, etc. [5,32]. While an increasing number of R&D projects achieves higher maturity, the transfer of innovations from R&D settings to commercial applications in Europe is gaining importance. Scaling up production to pilot, demonstration or even commercial scale has turned out to be a major difficulty for biotechnological processes [19,33]. Thereby, there is lack of skilled people in scale-up, as there is only limited number of personnel with necessary experiences from lab to production.

3.2.2. Market Activities of Firms

In trend, large firms dominate in production activities. Small firms are only active with smaller scale production sites in niche markets. Currently, the majority of the lignocellulosic ethanol production facilities in Europe are at pilot and demonstration scale, being operated with the purpose to test and validate the technology and to prove its economic viability. At the end of 2018, in the EU only two cellulosic ethanol plants with commercial scale in the EU exist with SEKAB plant in Sweden [34] and the plant of Beta Renewables in Crescentino formerly, which has been recently bought up by the Italian chemical firm Versalis [35]. New dynamics may evolve by the Swiss company Clariant, which currently builds a plant Romania and out licensed one to Slovakia [36]. Overall, the number of firms active in commercial production is rather low, as some small and large firm left the market, such as Amyris or DuPont.

Regarding bio-based plastics, the actor landscape of bio-based plastics is diverse. There are few suppliers of bio-based plastics such as large chemical firms like BASF, Nature Works that is owned by PTT Global Chemical and Cargill, Corbion or Braskem. Moreover, there are some specialized firms in bio-based plastics such as Novamont, NatureWorks, FkuR Kunststoff, Innovia Films, Biomer, or BIOTEC. In downstream sectors, there is a rather high number of converters of bio-based plastics to final products based on biopolymers [37].

The main challenge for actors in both value chains is to achieve cost-competitiveness to fossil-based products in mass production. The current low oil price is hampering especially the demand for those bio-based products that heavily depend on feedstock prices (e.g., drop-in chemicals, biofuels).

3.2.3. Legitimacy Challenges and Market Formation Support

As market competitiveness is missing, guidance of search of biotechnology has been influenced by specific policy initiatives regarding the bioeconomy. Beginning in the early 2000s, the bioeconomy has been accorded a high political significance on an international level. End of 2018, almost fifty countries had already published strategies to support the development of a bioeconomy [38]. While the various strategies differ between each other, biotechnology is often acknowledged for a key in role in this concept [39].

However, ambitious visions have mostly not been followed up with concrete actions for market formation. Because of missing cost competitiveness compared to fossil fuels, the ethanol market is mainly driven by the obligation of the Renewable Energy Directive. According to the Renewable Energy Directive (RED) from 2009 [10], incentives for advanced biofuels such as lignocellulosic ethanol are small. There is no obligatory mandate specified for this kind of biofuel, only an indicative target of 0.5 percent of total fuels. Moreover, there is a double counting system for advanced biofuels, meaning that advanced biofuels count twice to fulfil the mandated quota for biofuels. There have intensive discussions about the recast of the RED from 2021-2030. A final compromise text among the EU institutions was agreed in June 2018 [40]. It foresees that advanced fuels must be supplied at a minimum of 0.2% of transport energy in 2022, 1% in 2025 and increasing to at least 3.5% by 2030 [41]. Instead, for bio-based plastics, globally there are still hardly any policies in place, which support product diffusion. There have been discussion about suitable policy instruments [42–44], however they have not put into practice yet.

Hereby, a key driver for stronger promotion for bio-based bulk products is its legitimacy, which depends among others on its social impact as well on its contribution towards sustainability. While some assessments are optimistic that CO_2 emissions will be reduced [45], an expansion of the market and production will lead to an increasing demand of feedstock [37,46]. The increased industrial use of biomass may have negative impacts for food security and increase agricultural intensification, which is associated with negative impacts on ecosystem services and biodiversity through monocultures and high pesticide use [46].

Hence, the overall impact of bio-based bulk products on sustainability is ambiguous and future environmental performance remains highly uncertain. This accounts also for non-food biomass value chains as changes in direct and indirect land-use are per se unclear. The difficulty is to assess all dimensions of sustainability through all stages of the value chain of bio-based products, from biomass production to end-use. The lack of a widely accepted mechanism to assess and confirm sustainability is still an important barrier [47]. This is crucial as sustainability performance may turn out as a decisive point in the development. For bio-based plastics, there are also positive signs that a significant number of large brands strategically entered the bio-based plastics value chain to improve their reputation concerning sustainability. These firms may demand high product volumes and their activities is a signaling function for others.

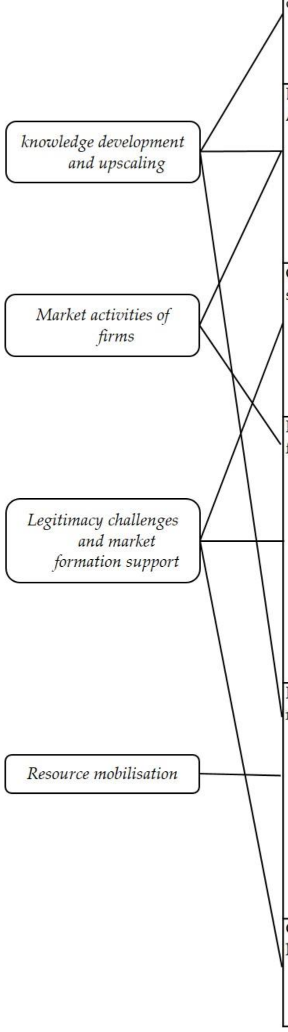
However, both bio-based products do not only compete against cheaper fossil-based products, but other alternative concepts evolve to address the related societal needs exists, such as electric mobility for transport, or CO_2 based polymers. Moreover, there are increasing initiatives to reduce plastics use to avoid littering, instead of just changing the resource basis for plastics.

Another market related barrier is the persistency effects towards existing buyer behavior. For some value chains, there is no compatibility to existing routines or infrastructures. In the case of bio-based plastics, this may refer to missing compatibility to recycling systems. In the case of new facilities for lignocellulosic ethanol, long-term contracts would be needed, but they are unusual in the fuels business.

3.2.4. Resource Mobilization

Consequently, from the view of potential investors, the perspectives are uncertain and consequently there is a lack of funding possibilities for pilot and demonstration activities. Potentially, there are high synergies between the two regarded segments in the context of biorefinery [48]. First, a direct conversion of ethanol to chemical intermediate products as a building block for bio-based plastics is possible. A second possibility would be the integrative development of distinct products for biofuels and bio-based plastics based on the same raw materials. However, according to experts such a concept is rather unlikely in the near-term future. This is because the development for both markets is highly challenging and resource intensive. The penetration of these markets complicates logistics as well as marketing and sales without providing long-term security are assessed as even more risky from investor's perspective.

Figure 1 summarizes the strength and weaknesses of both value chains.



Function	Lignocellulosic ethanol	Bio-based plastics
Knowledge development	+ Long-term research efforts	+ Long-term research efforts + Established networks between academia, applied research and some parts of industry - Missing technological performance of some key materials
Entrepreneurial Activities	0 Various changes of players in the field - Gap between the demonstration phase and the commercial growth phase - Market exit by some companies - Start-up scene disappeared	+ Some companies with strong activities to build up innovation eco system + Specialized bio-based plastic firms and incumbents from chemical industry - Low number of polymer producers + Significant number of user firms, including brand-owners
Guidance of search processes	+ Aim to achieve higher sustainability via 2nd generation feedstock - low oil price reduces activities of private and public actors to search for alternative solution to fossil-based products	0 Guidance changes over time from biodegrability to use of renewable resources to avoidance of plastics - Incentives and goals lacking for bio-based plastics - Low oil price reduces activities of private and public actors to search for alternative solution to fossil-based products
Market formation	+ Markets for biofuels established - Missing cost competitiveness to fossil fuels and 1 gen biofuels - Policy instruments only slightly favouring 2nd generation biofuels - Alternative mobility concepts on the rise - No long-term contracts common	+ Markets for drop-in bio-based plastics established + Strategies of brand-owner companies as gatekeeper for the demand side + Rather high general acceptance - Cost disadvantage for bio-based plastics - Low consumer awareness and little willingness to pay - No recycling systems for bio-based plastics - Infrastructure of user firms sometimes not compatible for using bio-based plastics
Resource mobilisation	+ Access to research funding and investment in scaling up technology through pilot demonstration facilities - High investment needs combined with uncertain market development limit investments; - Limited number of professionals for scaling up of production	- High investment needs combined with uncertain market development limit investments - Shortages in financing of commercial plants - Limited number of professionals for scaling up of production
Creation of legitimacy	- Reservations touse of biomass for energy purposes 0 Sustainability of 2nd biofuel as key driver, but performance yet unclear	- Lack of dominant design - General concerns regarding plastic use - Sustainability performance of bio-based plastics mixed

Figure 1. Functional assessment of selected high volume, low value biotechnological innovation systems; + relates to strengths; − to weaknesses; 0 to key functional characteristics without clear directional impact.

3.3. Innovation System Analysis for High-Value Added Value Chains

High-value added segments are often attractive for industrialized countries. Those countries possess competitive advantages in knowledge accumulation and established quality standards, which may outweigh missing cost competitiveness. In addition, bio-based products in high value applications provide often-unique characteristics and may provide benefit for health, sustainability, or lifestyle needs.

3.3.1. Knowledge Development and Entrepreneurial Activities

As for the innovation systems referred above, for flavors and fragrances, enzymes and production of biopharmaceuticals continuous advances in knowledge development have been and new products of applications have been developed. The future potential is not limited to incremental advances, as for all three value chains advanced technologies, such as advanced metabolic engineering, systems, and synthetic biology have high potential for increasing the cost efficiency and environmental performance of production processes.

Concerning industry structure, in all three IS large firms dominate in those rather established industries, while smaller innovative firms focus on niches or certain activities, such as R&D development or services. This is mentionable as usual advantages for large firms such as required large production sites or scale effects only exist to a limited degree in those IS. Nevertheless, market access and relatively large investments are still needed, favoring larger firms. For example, in the biopharmaceutical market, large established multinational pharmaceutical companies have forcefully shifted their focus onto large molecule drugs (biologics) in the last decade. This applies for R&D as well as subsequent manufacturing. Companies focused on product development still own a major share of the production capacity for biopharmaceuticals [49]. However, manufacturing of biopharmaceuticals is a much more complex process than producing traditional small-molecule pharmaceuticals [50]. Therefore, in parallel, these multinationals have become increasingly dependent on CMOs and dedicated biotechnology firms (DBFs) in order to acquire the necessary additional capabilities, as the internal capabilities of even the most powerful pharmaceutical firms are not sufficient to develop, manufacture, and market these new and innovative technologies by themselves [50].

In the F&F industry, biotechnology requires additional competencies from biotechnology providers. The top 10 F&F firms are all active in the field of biotechnology [51]. They either built up in-house development competencies in biotechnology, have acquired biotechnology companies, or cooperate with biotechnology firms, particular in the case of synthetic biology. Several synthetic biology firms (e.g., Amyris, Evolva, and Gingko Bioworks) have recently turned their focus to flavours and fragrances. There have been several partnerships between large F&F and synthetic biology firms and first joint products have been already commercialized [52,53]. However, despite the single partnerships, networks across the EU between the actor's form academia and industry are still rather weak. Moreover, it appears unlikely that the industry structure will change enormously and the top F&F will lose significant importance, as their competencies regarding controlling the supply chain and knowing customer trends remain highly relevant [52].

3.3.2. Market Growth and Regulation

The value chains face positive market dynamism especially with increasing demand for special food applications and biopharmaceuticals. Consequently, the enzymes industry benefits of the dynamism of those application markets. Moreover, in the case of enzymes and biopharmaceutical, the biotechnology markets are well established and no direct chemical substitutes for the biotechnological products exist, as they can only be produced by biotechnological methods and provide unique product properties. Hence, there is no direct cost competition or requirements of the customers to achieve established performance parameters derived from chemical processes. However, this does not mean that the high R&D and production costs can be easily passed on the consumer. The end products produced with enzymes have to compete with functional similar chemical products and the high prices limit market expansion. In the same vein, stakeholders regard the high production costs for biopharmaceuticals as the key bottleneck for the expansion of biopharmaceuticals.

Overall, the regulatory market environment has a significant impact on IB growth opportunities and innovation incentives in the value chains. Relevant regulations and the implemented or proposed regulatory instruments differ highly between value chains. In difference to the large volume products not regulation that are closely connected to demand-side policies in terms of feed-in-tariffs or quotas of usage are relevant, but regulation concerning product characteristics matters. The latter cannot be assessed as being generally positive or negative for IB. The IS in focus of this section rather benefit form policy regulation and can be considered as "protected niches". This is particularly the case for flavors. The key potential value of the biotechnological production of flavors from natural raw materials by microbial or enzymatic methods compared to chemical synthesis is that in many cases that the respective flavor can be labeled as "natural" in the US and Europe [53]. No specification regarding the exclusion of certain biotech methods (e.g., use of genetically modified organisms) are used. Consumers in general prefer products with "natural" flavors and are more interested in products that contain "natural" rather than chemically synthesized flavors [54].

The production of biopharmaceuticals and in the case of enzymes the pharmaceutical and food production, are highly regulated segments with complex product and process specifications. While related burdens increase costs to compliance and may lengthen time to market, they are hardly assessed as general hindrances at least for large firms and have some advantage features for EU firms. In particular, for production biopharmaceuticals they enhance competiveness of European actors. Although lower-end biopharmaceuticals and biosimilars are manufactured increasingly in Asian countries, highly industrialized countries–despite their higher labor costs–still have a competitive advantage in the manufacturing of high-value biopharmaceuticals. This is due to the complexity of the production process, and the regulatory requirement to comply with the highest quality standards in Good Manufacturing Practice. Currently, no finished biopharmaceutical produced in China is allowed to be exported to the EU or the US because of lack of compliance with authorization requirements [55].

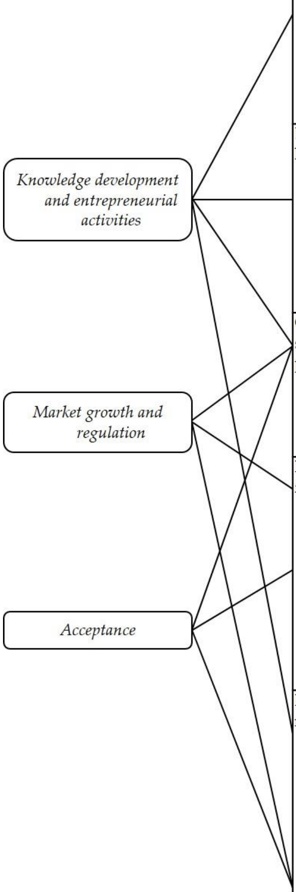
On the downside, markets are often fragmented in many small volume products, in particular for fragrances. In a significant amount of cases, it is not economically viable to engage in costly activities for a substitution of existing synthesized or plant-derived natural products by biotechnologically produced products. This is a key limitation for resource mobilization in those innovation systems.

3.3.3. Acceptance

A key driver for legitimacy is the acceptance for biotechnology. In particular, health applications of biotechnology such as biopharmaceuticals are rather well accepted. Generally, the l public attitude towards IB products is assumed to be mostly positive, but may differ substantially depending on the target group, product segment, application, technologies used, or benefits perceived. In particular, there is some skepticism towards some advanced technologies in applications "near the human body", e.g., for F&F and enzymes in personal care, textiles, and food. This is because it may evoke negative perceptions in parts of the public and certain consumer groups. Hence, the presently positive perception of enzymes and even regulations may change in the future. Issues of concern may be for example the use of genetically modified production organisms and genetically engineered enzymes, in particular for applications such as food. In such a scenario, the use of enzymes would be limited to certain segments.

In addition, the impact on environment and sustainability may be key drivers for certain enzyme segments (e.g., for bio-based chemicals, textiles) as well as F&F reducing energy and environmental pollution compared to fossil-based products. However, sustainability measurement is, in particular, challenging for the large set of heterogeneous small volume products. This hinders the introduction of adequate potential policy instruments to foster such innovations.

Figure 2 summarizes the strength and weaknesses of both value chains.



Function	Production of Biopharmaceuticals	Enzymes	F&F
Knowledge development	+ Strong in-house knowledge of large firms; + Advantages of EU actors in fulfilment of high quality standards - Limited knowledge in providing new forms of treatment	+ Long-term accumulation of know-how by leading companies 0 Still high number of non-discovered natural enzymes and applications	+ All leading F&F firms developing or acquiring biotech know-how - Low connection of F&F to other sectors - Low knowledge for scaling up
Entrepreneurial Activities	0 Highly capitalized international pharma companies and specialized contract manufacturing firms active; - High investments needed; - High entry barriers for newcomers	0 Dominance of few firms - High entry barriers for production	+ Entrance of biotech firms as developers 0 Dominance of traditional F&F firms in production and sales
Guidance of search processes	+ Production of therapeutics that provide positive health effects; + Higher production efficiency as important possibility to lower costs for health care provision	+ Higher resource efficiency	0 Natural claim for biotechnologically produced F&F based on natural resources; + Potential advantageous sustainability performance
Market formation	+ Strong market growth of biopharmaceuticals - Uncertainty in market evolution for biosimilars	+ Mostly established market + Strong demand in some end-user markets 0 Strong dependence on development in end-user markets; - Weak dynamic in some potential applicant markets (e.g. biofuels)	+ Biotechnological production of flavours from natural raw materials can be labelled as "natural" in the US and Europe - Large existing product portfolio of chemical synthesized F&F - Acceptance of F&F produced with synthetic biology uncertain
Resource mobilisation	+ Companies with significant resources and capabilities to invest - Investment needs combined with uncertain market development exceed too risky for many firms - CMOs only in some segments with high investments	+ Some companies with significant resources and capabilities to invest; - Rather low investment in potential new applications	- As markets are fragmented in many small volume products, it is not always economically viable to mobilize resources
Creation of legitimacy	+ Biotechnology for medicine well accepted; - High costs can turn into a risk of acceptance	+ Potential high resource efficiency - Concerns using GM organism for production	- Potential concerns that products using GM organism are regarded as natural products

Figure 2. Functional assessment of selected low volume, high value biotechnological innovation systems; + relates to strengths, − to weaknesses, 0 to key functional characteristics without clear directional impact.

4. Discussion and Policy Options

The strength and weaknesses of the innovation systems help to identify and justify policy options, by either leveraging the strengths of the innovation or addressing weaknesses of the innovation system. This focus on structural deficiencies or advantages implies a broader justification of the use of policy instruments as compared to market failure-based policies. However, in the innovation system approach policymakers are part of the system itself are unable to design the system in a top-down way. Hence, policies are adaptive and incremental and policy has rather a coordinating function by supporting and linking actors.

Overall, the analyses in this contribution based on the innovation system approach indicates that there are similar challenges between the value chains, but also specific challenges exist, which may call for additional or modified policy instruments.

For all value chains, further advances in knowledge development is key prerequisite for further diffusion [48,56]. While there have been important advances in the past, without significant developments efficiency or performance is insufficient to achieve cost competitive to fossil-based products. Hence, the continuation of innovation funding is of key importance for all IB innovation systems. While established and emerging advanced life science technologies remain core competencies, significant progress may be expected from the integration with other technologies, such as environmentally benign chemical processes and with digital technologies and bioinformatics [57]. The specific technological challenges are partly similar and overlapping between the IS, to some degree specific challenges such as pre-treatment for lignocellulosic for ethanol exist. However, the limitations of R&D policy also have to be pointed out. First, R&D resources could not be identified as the key bottleneck in the various value chain. Second, in most of the value chains large multinational firms dominate the actor landscape, and R&D funding to increase activities in certain topics can only incentivize those firms to a limited to degree.

As IB is entering more mature stages the need to address the various barriers to commercialize IB products and processes becomes even more pressing, such as upscaling, improving production efficiency, and building-up market intelligence. Existing efforts to overcome these barriers have to be continued, such as continuously supporting the collaboration between academia and industry, fostering the start-up scene, including financing and venture capital. Thereby, the development of teams with commercialization-relevant expertise (e.g., scaling up, market intelligence) should be improved by actively bringing different experts (researchers, investors, and intermediaries) closer together. Moreover, specific skills for scaling-up processes from lab to production as well as business skills for commercialization are needed increasingly. While this can be addressed in the longer term by amending curricula accordingly, short-term options are attracting such experts to IB from related industrial branches, e.g., the pharmaceutical or chemical industry. In addition, for bio-based plastics and lignocellulosic ethanol biomass supply is highly relevant. However, as the overall potential of sustainable provision appears to be a limiting factor, resource mobilization is a crucial issue.

Market formation is the key challenge for all value chains, however rather low synergies between the markets regarding penetration arise. The markets differ in terms of customers and adequate business models. There are almost no firms that are active in more than one of the five IS, although strong technological or production synergies between some of the value chains exist. Adequate policy instruments differ between the innovation systems as market characteristics (e.g., variety of products, price and quality competition) customers (business vs. consumer vs. public) and regulation highly differs between the segments. The high-value added segments are subject to product regulation in terms of labeling of certain methods or resource basis or requirements regarding purity. However, discussions and current regulations regarding biofuels and bio-based plastics mainly relate to demand side support in terms of quotas or monetary support, as the products are not cost competitive. However, while there are often requests for stronger demand side policies or more friendly regulation towards novel technology, the ambivalent legitimacy regarding sustainability and partly limited acceptance has to be taken into account

Attitudes and acceptance differ substantially depending on stakeholder group, application, and technologies. Particularly sensitive areas are the potentially negative environmental impacts, distribution of socio-economic benefits and burdens of IB, and skepticism towards advanced technologies in certain applications. As the analysis shows the acceptance of the high-volume products relate rather to environmental and social implication, while for the high-value niches, more concerns regarding the use of advanced technology concepts exist.

Of course, there is no easy way out of these legitimacy issues. On the one hand, short-term pushes such as for biofuels in the last decade with unclear impact or a potential consumer misleading regulation advantage as in the case of the flavors, may be counterproductive in the long-term. On the other hand, without the realization of learning and scale effects the full performance of those applications may not be realized. Current options include increasing efforts to improve the sustainability footprint of bio-based products via technological and logistical advances, but also the continuous elaboration of common visions and goals of the bioeconomy and biotechnology. Therefore, constructive stakeholder dialogues and public participation should be continued in order to develop a commonly shared future vision for IB and to address value chain specific concerns. It should be ensured that these involvement processes may have the consequence that certain areas may no longer be funded publicly, that regulations may have to be amended, that presently neglected R&D topics may become more important, and that sufficiency concepts could be taken into consideration. In combination with such stakeholder processes, R&D&I strategies may be tailored in a way that they are guided by societal issues, such as the UN Sustainable Development Goals [58]. In addition, that co-evolution of science and technology developments with market regulations are of critical importance. The challenge is to align R&D policy with regulatory activities, both with respect to timeline and areas incentivized. Regulations should also be seen as instruments for establishing trust and credibility in IB by balancing incentives for R&D and industry with, potentially differing, interests of the public and consumers.

5. Conclusions

For the realization of the potential of biotechnology, further innovation and diffusion in value chains are needed. Only a broad portfolio of biotechnology applications is robust and flexible enough to cope with unfavorable or changing external factors and frame conditions, allowing the full exploitation of the enabling character of IB for a bioeconomy and a circular economy that can contribute to mastering the grand challenges.

This article contributes to addressing the question of how biotechnology innovations evolve in different systems and applications. From a technological point of view, there are direct synergies or at least very similar challenges that may be brought together in further strategies and innovation programmes. However, the innovation systems partly differ profoundly. Policy makers have to be aware of the broad spectrum of the industrial biotechnology and should implement a differentiated innovation policy mix to address system weaknesses. While biotechnology profits from the initiative towards the bioeconomy, overall strategies may overlook the specifics for the various applications. This applies particular for market formation, which is a key bottleneck for many biotechnology value chains. Here, different ways of functioning systems have to be found, which may require, in some cases, dedicated support measures, but smart product regulation in other cases.

The article tried to point out some key differences between technologies and implications for policymaking. A clear limitation of the research is that the different innovation systems are compared independently, while synergies because of technological interrelatedness to each other may occur. Moreover, they also compete for partly con-strained markets, resources, and policy support. In order to provide a more comprehensive picture, e.g., regarding the future emergence of the transition to the bioeconomy those interrelations have to be analyzed more in detail.

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References

1. Commission of the European Communities. *Current Situation of Key Enabling Technologies in Europe: Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions*; European Commission: Brussels, Belgium, 2009.
2. Bugge, M.; Hansen, T.; Klitkou, A. What Is the Bioeconomy? A Review of the Literature. *Sustainability* **2016**, *8*, 691. [CrossRef]
3. JRC, BBI JU and IEA Bioenergy. *Joint Survey on Bioeconomy Policy Developments in Different Countries: Background, Methods Used and Recommendations for Future Editions*; European Commission: Brussels, Belgium, 2018; pp. 1–30.

4. Purkus, A.; Hagemann, N.; Bedtke, N.; Gawel, E. Towards a sustainable innovation system for the German wood-based bioeconomy: Implications for policy design. *J. Clean. Prod.* **2018**, *172*, 3955–3968. [CrossRef]
5. Hüsing, B.; Kulicke, M.; Wydra, S.; Stahlecker, T.; Aichinger, H.; Meyer, N. *Evaluation der "Nationalen Forschungsstrategie BioÖkonomie 2030": Wirksamkeit der Initiativen des BMBF—Erfolg der geförderten Vorhaben—Empfehlungen zur strategischen Weiterentwicklung—Abschlussbericht*. 2017. Available online: https://www.isi.fraunhofer.de/content/dam/isi/dokumente/cct/2017/Evaluation_NFSB_Abschlussbericht.pdf (accessed on 12 October 2018).
6. Schütte, G. What kind of innovation policy does the bioeconomy need? *New Biotechnol.* **2018**, *40*, 82–86. [CrossRef]
7. Scheiterle, L.; Ulmer, A.; Birner, R.; Pyka, A. From commodity-based value chains to biomass-based value webs: The case of sugarcane in Brazil's bioeconomy. *J. Clean. Prod.* **2018**, *172*, 3851–3863. [CrossRef]
8. OECD. *The Next Production Revolution: Implications for Governments and Business*; OECD Publishing: Paris, France, 2017.
9. Jiménez-Sánchez, G.; Philp, J. Genomics and the bioeconomy: Opportunities to meet global challenges. In *Genomics and Society*; Elsevier: Amsterdam, The Netherlands, 2016; pp. 207–238.
10. European Commission. *Directive 2009/28/EC of the European Parliament and of the Council of 23 April 2009 on the Promotion of the Use of Energy from Renewable Sources and Amending and Subsequently Repealing*; Directives 2001/77/EC and 2003/30/EC; European Commission: Brussels, Belgium, 2009.
11. Giurca, A.; Späth, P. A forest-based bioeconomy for Germany? Strengths, weaknesses and policy options for lignocellulosic biorefineries. *J. Clean. Prod.* **2017**, *153*, 51–62. [CrossRef]
12. Hellsmark, H.; Mossberg, J.; Söderholm, P.; Frishammar, J. Innovation system strengths and weaknesses in progressing sustainable technology: The case of Swedish biorefinery development. *J. Clean. Prod.* **2016**, *131*, 702–715. [CrossRef]
13. Leimbach, T.; Wydra, S. Friendly or hostile take over: The growing linkage of innovation and industry policies and instruments. In *Innovation System Revisited*; Fraunhofer, I., Ed.; Fraunhofer Verlag: Stuttgart, Germany, 2012.
14. Göransson, B.; Pålsson, C.M. *Biotechnology and Innovation Systems: The Role of Public Policy*; Edward Elgar Publishing: Cheltenham, UK, 2011.
15. Suurs, R.A.A.; Hekkert, M.P. Cumulative causation in the formation of a technological innovation system: The case of biofuels in the Netherlands. *Technol. Forecast. Soc. Change* **2009**, *76*, 1003–1020. [CrossRef]
16. Costantini, V.; Crespi, F.; Martini, C.; Pennacchio, L. Demand-pull and technology-push public support for eco-innovation: The case of the biofuels sector. *Res. Policy* **2015**, *44*, 577–595. [CrossRef]
17. Eggert, H.; Greaker, M. Promoting Second Generation Biofuels: Does the First Generation Pave the Road? *Energies* **2014**, *7*, 4430–4445. [CrossRef]
18. Huenteler, J.; Anadon, L.D.; Lee, H.; Santen, N. *Commercializing Second-Generation Biofuels*; Harvard College: Cambridge, MA, USA, 2014.
19. Koekoek, P. *Biofuels: The Next Generation: How Innovation Can Brighten Europe's Energy Future*; Science Business Publishing Ltd.: Brussels, Belgium, 2011.
20. Lettner, M.; Schöggl, J.-P.; Stern, T. Factors influencing the market diffusion of bio-based plastics: Results of four comparative scenario analyses. *J. Clean. Prod.* **2017**, *157*, 289–298. [CrossRef]
21. Schwark, F. Influence factors for scenario analysis for new environmental technologies—The case for biopolymer technology. *J. Clean. Prod.* **2009**, *17*, 644–652. [CrossRef]
22. Bergek, A.; Jacobsson, S.; Carlsson, B.; Lindmark, S.; Rickne, A. Analyzing the functional dynamics of technological innovation systems: A scheme of analysis. *Res. Policy* **2008**, *37*, 407–429. [CrossRef]
23. Markard, J.; Raven, R.; Truffer, B. Sustainability transitions: An emerging field of research and its prospects. *Res. Policy* **2012**, *41*, 955–967. [CrossRef]
24. Jacobsson, S.; Bergek, A. Innovation system analyses and sustainability transitions: Contributions and suggestions for research. *Environ. Innov. Soc. Trans.* **2011**, *1*, 41–57. [CrossRef]
25. Wieczorek, A.J.; Hekkert, M.P. Systemic instruments for systemic innovation problems: A framework for policy makers and innovation scholars. *Sci. Public Policy* **2012**, *39*, 74–87. [CrossRef]
26. Malerba, F. Sectoral systems of innovation and production. *Res. Policy* **2002**, *31*, 247–264. [CrossRef]

27. Dreher, C.; Kovač, M.; Schwäbe, C. Competing technological innovation systems as a challenge for new mission orientation-insights from the German Energiewende. *Int. J. Foresight Innov. Policy* **2016**, *11*, 43–72. [CrossRef]
28. Tylecote, A. Biotechnology as a new techno-economic paradigm that will help drive the world economy and mitigate climate change. *Res. Policy* **2019**, *48*, 858–868. [CrossRef]
29. De Almeida Oroski, F.; Alves, F.C.; Bomtempo, J.V. Practitioner's Section Bioplastics Tipping Point: Drop-in or non-drop-in? *J. Bus. Chem.* **2014**, *11*, 43–50.
30. Dietz, T.; Börner, J.; Förster, J.; von Braun, J. Governance of the Bioeconomy: A Global Comparative Study of National Bioeconomy Strategies. *Sustainability* **2018**, *10*, 3190. [CrossRef]
31. Swann, G.; Prevezer, M.; Stout, D. *The Dynamics of Industrial Clustering: International Comparisons in Computing and Biotechnology*; Oxford University Press: Oxford, UK, 1998.
32. Taylor, R.; Nattrass, L.; Alberts, G.; Robson, P.; Chudziak, C.; Bauen, A.; Im Libelli; Lotti, G.; Prussi, M.; Nistri, R. *From the Sugar Platform to Biofuels and Biochemicals: Final Report for the European Commission Directorate-General Energy*. 2015. Available online: https://ec.europa.eu/energy/sites/ener/files/documents/EC%20Sugar%20Platform%20final%20report.pdf (accessed on 11 October 2018).
33. Warner, M. What Makes Scale-Up of Industrial Biotechnology so Difficult? 2015. Available online: http://www.biofuelsdigest.com/bdigest/2015/12/02/what-makes-scale-up-of-industrial-biotechnology-so-difficult/ (accessed on 14 March 2019).
34. Alberts, G.; Chudziak, C.; Bauen, A. *Ramp up of Lignocellulosic Ethanol in Europe to 2030: E4tech (UK) Ltd for the Co-Sponsors of the 6th International Conference on Lignocellulosic Ethanol*. 2017. Available online: http://www.e4tech.com/wp-content/uploads/2017/10/E4tech_ICLE_Final_Report_Dec17.pdf (accessed on 13 January 2019).
35. Voegele, E. Versalis Buys Biochemtex, Beta Renewables. Available online: http://www.ethanolproducer.com/articles/15638/versalis-buys-biochemtex-beta-renewables (accessed on 26 February 2019).
36. Tag: Clariant. Available online: https://www.biofuelsdigest.com/bdigest/tag/clariant/ (accessed on 26 February 2019).
37. Van den Oever, M.; Molenveld, K.; van der Zee, M.; Bos, H. *Bio-Based and Biodegradable Plastics: Facts and Figures: Focus on Food Packaging in the Netherlands*; Wageningen Food & Biobased Research: Wageningen, The Netherlands, 2017.
38. German Bioeconomy Council. *Bioeconomy Policy (Part III)—Update Report of National Strategies around the World*; European Commission: Brussels, Belgium, 2018.
39. Meyer, R. Bioeconomy strategies: Contexts, visions, guiding implementation principles and resulting debates. *Sustainability* **2017**, *9*, 1031. [CrossRef]
40. International Council on Clean Transportation. *Final Recast Renewable Energy Directive for 2021–2030 in the European Union*; International Council on Clean Transportation: Berlin, Germany, 2018.
41. Council of the European Union. *Proposal for a Directive of the European Parliament and of the Council on the Promotion of the Use of Energy from Renewable Sources—Analysis of the Final Compromise Text with a View to Agreement: Interinstitutional File: 2016/0382 (COD)*; Council of the European Union: Brussels, Belgium, 2018.
42. BIO-TIC. *Overcoming Hurdles for Innovation in Industrial Biotechnology, Non-Technological Roadmap*. Available online: www.industrialbiotech-europe.eu/wp-content/uploads/2015/09/Non-technological-Roadmap.pdf (accessed on 12 December 2018).
43. Commission Expert Group for Bio-Based Products. *Working Group on Evaluation of the Implementation of the Lead Market Initiative for Bio-Based Products' Priority Recommendations*. Available online: https://ec.europa.eu/docsroom/documents/13269/attachments/1 (accessed on 14 November 2018).
44. Philp, J. OECD Policies for Bioplastics in the Context of a Bioeconomy, 2013. *Ind. Biotechnol.* **2014**, *10*, 19–21. [CrossRef]
45. Daystar, J.S.; Treasure, T.; Gonzalez, R.; Reeb, C.; Venditti, R.; Kelley, S. The NREL biochemical and thermochemical ethanol conversion processes: Financial and environmental analysis comparison. *BioResources* **2015**, *10*, 5096–5116. [CrossRef]
46. Detzel, A.; Kauertz, B.; Derreza-Greeven, C. *Study of the Environmental Impacts of Packagings Made of Biodegradable Plastics*; Federal Environment Agency: Dessau, Germany, 2013.
47. OECD. *Future Prospects for Industrial Biotechnology*; OECD Publishing: Paris, France, 2011.

48. Philp, J. The bioeconomy, the challenge of the century for policy makers. *New Biotechnol.* **2018**, *40*, 11–19. [CrossRef]
49. Seymour, P.; Ecker, D.M. Global Biomanufacturing Trends, Capacity, and Technology Drivers: Industry Biomanufacturing Capacity Overview. Available online: https://www.americanpharmaceuticalreview.com/Featured-Articles/188840-Global-Biomanufacturing-Trends-Capacity-and-Technology-Drivers-Industry-Biomanufacturing-Capacity-Overview/ (accessed on 26 February 2019).
50. Gennari, A.; Loesch, M.; Santagostino, A. The Evolving Biopharma Contract-Manufacturing Market. Pharmaceutical Manufacturing. Available online: https://www.pharmamanufacturing.com/articles/2017/the-evolving-biopharma-contract-manufacturing-market/ (accessed on 26 February 2019).
51. Wydra, S.; Hüsing, B.; Piret Fischer; Angela Jäger; Djerdj Horvat. *PROGRESS: Priorities for Addressing Opportunities and Gaps of Industrial: Deliverable D 6.4 Brochure*. Project Number: 723687. Available online: www.progress-bio.eu (accessed on 11 January 2019).
52. Brenna, E.; Parmeggiani, F. Biotechnological Production of Flavors. *Ind. Biotechnol. Prod. Process.* **2017**, 271–308. [CrossRef]
53. Waltz, E. Engineers of scent. *Nat. Biotechnol.* **2015**, *33*, 329–332. [CrossRef]
54. Hayden, E.C. Synthetic-biology firms shift focus. *Nature* **2014**, *505*, 598. [CrossRef]
55. Qing XIA, V.; Yang, L.C.; Langer, E.S. China Biopharma—Is a Wave of GMP Exports in Our Future? Available online: https://www.pharmafocusasia.com/strategy/china-biopharma-gmp-exports (accessed on 26 February 2019).
56. Dupont-Inglis, J.; Borg, A. Destination bioeconomy–The path towards a smarter, more sustainable future. *New Biotechnol.* **2018**, *40*, 140–143. [CrossRef] [PubMed]
57. Delebecque, C.J.; Philp, J. Education and training for industrial biotechnology and engineering biology. *Eng. Biol.* **2018**, *3*, 6–9. [CrossRef]
58. Heimann, T. Bioeconomy and Sustainable Development Goals (SDGs): Does the bioeconomy support the achievement of the SDGs? *Earth's Future* **2018**. [CrossRef]