Biotechnology for tomorrow's world: Scenarios to guide directions for future innovation

List of authors:

Aleksandra Małyska, European Commission, corresponding author, aleksandra.malyska@wp.pl; +32472630841
Marc Cornelissen, BASF, Belgium
Amrit Kaur Nanda, 'Plants for the Future' European Technology Platform, Belgium
René Klein Lankhorst, Wageningen University & Research, Netherlands
Martin A.J. Parry, Lancaster University, UK
Vandasue Rodrigues Saltenis, Copenhagen Plant Science Centre (CPSC), Department of Plant and Environmental Sciences, University of Copenhagen, Denmark
Mathias Pribil, Copenhagen Plant Science Centre (CPSC), Department of Plant and Environmental Sciences, University of Copenhagen, Denmark.
Philippe Nacry, INRA, France
Dirk Inzé, Ghent University, Belgium
Alexandra Baekelandt, Ghent University, Belgium

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CropBooster-P https://www.cropbooster-p.eu/consortium.html
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Lancaster University https://www.lancaster.ac.uk/

Twitter accounts: @Plant_ETP; @Alexandra_Bkldt
ORCID-ID: 0000-0003-0816-7115

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Abstract

Depending on how the future will unfold, today's progress in biotechnology research has greater or lesser potential to be the basis of subsequent innovation. Tracking progress against indicators for different future scenarios would enable to focus, emphasize or de-emphasize discovery research timely and to maximize the chance for successful innovation. The COVID-19 crisis exemplifies that scenario indicators can offer time advantage to decisions on biotechnology research and innovation (R&I) investments, as well as to strategy development to minimize the spread of this type of disease. Tracking indicators that are specific for contrasting learning scenarios allows getting insights early in time when uncertainties pan out in a particular way, and can help the biotechnology field with its lengthy innovation timelines, high costs and uncertain future markets to develop most effectively. In this paper, we show how learning scenarios with a 2050 time horizon enable to recognize the implications of political and societal developments on the innovation potential of ongoing biotechnological research. We furthermore propose a model to further increase open innovation between academia and the biotechnology value chain to help fundamental research explore discovery fields that have a greater chance to be of value for applied research.

Developing scenarios for biotechnology in complex social systems

Biological science is expanding its knowledge frontiers at an ever-accelerating pace. The progressing insights into biological processes offer a broadening array of options to develop incremental and differential innovations across the medical, agricultural and industrial biotechnology sectors.

As timelines from understanding basic biological processes to the conception of an innovation and the development of a marketable product may range from ten to twenty-five years, a prime question for today's biotechnology discovery research is "innovation for what future world?" (Fig. 1).

To this end, we conducted in 2019 a first of its kind scenario analysis with a 2050 time horizon to understand the option space of agricultural biotechnology (https://www.cropbooster-p.eu/). Forty-five trends and twenty-two uncertainties dealing with the entire agricultural socio-economic system were reviewed to map the range of directions the future may take and to narrow down how agricultural biotechnology could best future-proof food, nutrition and health security. Trends ranged from consumer and demographics, farming and technology to politics, economy and societal developments while identified uncertainties were clustered around three themes: (1) needs for adaptation, (2) priorities in the value chain, and (3) the role of science (Fig. 2).

In order to identify towards which scenario today's world is heading, relevant indicators need to be developed [1,2]. For this, the critical developments or events that will be necessary for a scenario to arise need to be named, put in a chronological order through narratives, and checked for their informative value. Learning scenarios are reusable, and the scope of the indicators identified will depend on the diversity of expertise within the team exploiting the learning scenarios (Fig 3). Obvious examples of indicators are the developments around the legislation related to gene editing in the Bio-innovation and REJECTech scenario, personal data protection regulations in My choice scenario, while for instance the evolution of water availability in a particular country can be an indicator for Food emergency, as well as for Bio-innovation or REJECTech.

Steering focus in biotechnology discovery research with scenarios

The way the world will evolve will depend on a myriad of developments. Examples are the transition to renewable energy and decentralized storage, the global policy approach to enable the use of new genomic technologies, patients embracing new treatments, society buying into preventive medicine or demanding transparency about food properties, dietary shifts, development of new high-tech materials, shifts in lifestyle, and progress in robotics and artificial intelligence. Following such developments and extrapolating their long-term impact on the way we live, may inspire scientists to take a translational step and to open avenues of biotechnology discovery research that would provide the starting basis for R&I addressing future needs.

Biotechnology discovery research will undoubtedly be at the core of numerous innovations that will reach society by 2050. However, depending on how the future will unfold, today's progress in biotechnology research has a greater or lesser potential to be the basis of subsequent innovation. In addition, the lack of a widespread open innovation culture between industry and academia increases the risk of missing out on innovation that trend-wise is likely to meet industry or consumer demand.

For example, it is clear that the demand for climate change related biotechnology innovation will be high, and will be supported by policy makers [3, 4]. However, what the unmet needs will be for the different stakeholder groups is still unclear. Effects on cities, gardens, parks, lakes and crop fields linked to shifts and volatility in weather and the resulting new environmental conditions, including new pests and diseases, are not yet fully appreciated. Consequently, a translational step from innovation opportunity to required new knowledge is not obvious. Similarly, it is not clear how to incorporate innovation into products [5]. It may range from gene editing to novel knowledge-driven, societally accepted workflows that are not yet in place. The first activity, developing climate change knowhow, has a low risk of not being of relevance. The second, developing biotechnology innovation addressing climate change, is dependent on how policies develop across the globe, and therefore carries a higher risk [6]. For example, whereas it is conceivable in a "**Bio-innovation**" world that society may see a broad replacement of fossil-based synthetic materials by bio-based alternatives, such a development is less likely to occur in a "**REJECTech**" setting, as although the knowhow to do so would exist, the technical enablement would not be supported.

Another example relates to the exploitation of the microbiome. As microbes impact most, if not all, complex ecological systems, exploitation of biological knowhow is expected to offer innovation options in a broad range of biotechnology fields and be at the core of new markets and business models. These may include medicine, healthcare, food systems, industrial and household processes and materials, resource recycling and energy capture. For this to become reality, broad fundamental biotechnology discovery research on microbiomes needs to reach a tipping point, so that R&I for smaller and bigger opportunities across sectors becomes viable [7]. This necessitates a major public effort to advance pre-competitive knowhow and an enablement to a level sufficient for sector adoption within a reasonable risk perspective on a return of investment. A flagship approach in e.g. medicine building on ongoing big data efforts, such as in the human ‘100K genomes project’ [8], may serve as a vehicle to reach, in a five-year time span, the desired state of enablement and allow smaller initiatives to build on this cost-effectively. However, an entrepreneurial ecosystem is critical for this to happen, implying that such developments are more likely to occur under a “**Bio-innovation**” scenario or even in a “**Food emergency**” scenario, once society starts prioritizing access to food and health.

A third example refers to diet shifts toward alternative protein sources. Consumer choice is highly dependent on food properties such as taste, texture, palatability, color, convenience and price. Making alternative protein products competitive to meat would require, amongst other improvements, major advances in biological insights to upgrade food sources [9]. The challenge is to get specific on the carriers, e.g. algae, insects, crops, fermentation, etc., and the exact properties, so that the investments in biotechnology discovery have an effect. To do this successfully is not obvious as it is currently not clear which products and product properties will match future market demands. This brings us back to the importance of contrasting learning scenarios and the need to identify scenario-specific indicators to get insights early in time about how particular trends are panning out. These indicators may relate to e.g. yes/no decision points in policy development, or the timely establishment of critical enabling technologies or of sizeable consumer demands. Tracking progress of multiple (scenario-specific) indicators thus helps to steer focus in discovery research and o emphasize or de-emphasize timely to maximize the chance for successful innovation.

A current real-life example is the COVID-19 pandemic, an occurrence that was not foreseen because of which only relatively small and scattered efforts of research have been conducted prior to the pandemic. The current R&I race to develop a cure and vaccine against COVID-19 would have greatly benefitted from an advanced knowledge on coronaviruses, obtained through biotechnology discovery research

[10, 11]. Of course, in hindsight it is easy to highlight what should have been done. In practice, there are several million viruses in the world, over 200 of which are known to infect humans. Conducting extensive research on all these viruses in parallel would be too labor-intensive and unsustainable from an economical point of view. However, the current crisis reveals the advantage in time the use of scenario indicators can offer to international and local organizations dealing with public health. Such indicators might have flagged previous smaller outbreaks of other coronaviruses such as SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) in the last two decades. These outbreaks could then have been predictive for scenarios in which coronaviruses would become a major threat to human health, and could have triggered dedicated funding to advance specific biotechnological knowhow, as well as to develop strategies to minimize the spread of this type of disease. Major funding is currently being gathered to mitigate the consequences of the COVID-19 crisis, including $8 billion pledged by world leaders to support dedicated R&I [12]. However, today's continuing need to conduct significant biotechnology discovery research means that time, not necessarily funding *per se*, is a bottleneck. Along the same lines, developing scenarios today to understand how the future may unfold in the context of the COVID-19 pandemic, could help anticipate the long-term consequences of the actions that are being taken and could allow countries, states and communities to react to the crisis more effectively. In the context of the scenarios presented in Figure 3, the current pandemic emerges as a relevant indicator for the **Food emergency** scenario. A global economic crisis may put critical agricultural supply chains at risk, such that food security becomes an even greater issue in certain world regions.

Concluding Remarks

The above biotechnology examples demonstrate the risk of a low innovation output when the founding knowhow obtained from discovery research is not readily available and accessible in a useable format. The timely availability of founding knowhow may greatly improve by adopting the use of learning scenarios and the tracking of progress against indicators for these scenarios. To make such an approach effective, several outstanding issues need to be addressed first (Outstanding Questions)

We strongly believe that to improve the innovation output, the discussion should go beyond “financial instruments” and “creativity”. Rather, we would recommend to look at how the innovation ecosystem functions [13]: To maximize the utilization of advances in knowhow, the current working principles between academia, value chain players and society would benefit from extensive review. Biological science needs a continuous cross-stakeholder interaction to move more efficiently from discovery to innovation. To steer biotechnological R&I more efficiently, an open innovation governance concept to deal with pre-competitive and competitive big data information and activities is an absolute pre-requisite

We therefore propose to install virtual innovation workflows spanning academia and value chain players to address societal demands (Fig. 4). The idea is to set up dedicated ecosystem knowledge bases that serve, for example, the medical, agricultural or industrial biotechnology sectors or serve a broad innovation field such as the microbiome. These ecosystem knowledge bases should harbor harmonized and curated data in formats tailored to stakeholder use requirements. Such requirements can be defined for each of the biotechnology fields in a two-step process. First the generic workflow at handover points between academia and value chain players should be described, followed by the data and format requirements in this generic workflow, which would be necessary to start. These processes should ideally be described in both directions. In addition, users extracting information with their own software, if private, should commit to upload outcomes that are made anonymous, so that the next round of experimental questions can consider advanced information, and the knowledge base increases over time both in scope and in predictiveness.

To make this workable and sustainable, appropriate business models and governance concepts to deal with, among others, data ownership and intellectual property need to be developed, and dedicated data stewardship teams need to be installed. Setting this up will likely need several rounds of optimization to reach the best compromise between stakeholder interests. Yet, it is well positioned to improve the overall flow of innovation to the market and to offer the desired flexibility to deal with upcoming trends in an ever-changing world.

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***Disclaimer Statement**

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Figure 1. Innovation flow. *In the coming 15 years, the market will be served by R&D that is performed today. Different biotechnology sectors address changes in demand by repositioning and emphasizing what is in today's pipeline. New R&D and public research ideally address the demand of the future market. Scenario analysis is well suited to narrow down the most promising fields of investigation and to address the unmet needs of future markets. R: research; D: development.*

Figure 2. Trends and uncertainties. *Trends are considered developments going in a certain direction, while uncertainties can determine distinct outcomes with very different implications. Here the two most extreme ways that the uncertainties could play out are presented. Examples of specific uncertainties clustered around three more general themes are provided in the footnote.*
The exercise delivered four contrasting learning scenarios by detailing out specific aspects of possible future worlds and making them as concrete and vivid as possible. (Fig. 3). As the selected trends and uncertainties deal with society, environment, innovation and policy, the learning scenarios helped to characterize implications not only for the future of agriculture in Europe, which was the initial scope of the scenario building, but they can also serve to aid decisions on future research and innovation (R&I) investments in other fields of biotechnology globally.

Figure 3. Learning scenarios. *Four contrasting learning scenarios enable us to delineate the option space for the direction and context of future biotechnology.* ***Bio-innovation****: Biotechnology solutions are intensively used and sustainably provide*

sufficient high-quality food and large volume feedstock for a thriving bioeconomy; ***My choice****: Health and sustainability concerns drive all sectors to be diverse and transparent, meeting the needs and preferences of individuals, personalized medicine and nutrition are the norm;* ***REJECTech****: Consumers have little trust in politicians, scientists and big industry. Society is highly polarized and rejects biotechnology-derived products and services, despite dissatisfaction about missed opportunities, such as a broad adoption of the bioeconomy due to limited agricultural production;* ***Food emergency****: Due to severe environmental degradation, the world is struggling to fulfill basic food demand. In response to the crisis, global adoption of innovation, including biotechnology, occurs to mitigate impacts.*

Figure 4. Outline of a future "virtual innovation workflow" driven by biotechnology big data governance. *An example is given for agricultural innovation in Europe. To meaningfully contribute to the EU Green Deal, a rejuvenation of the agricultural ecosystem including academia, breeding and R&D companies, farm supply industry and farmers, is desirable. Required innovations should address environmental sustainability, impacts of increased weather volatility, climate change and associated pest and disease development, the European protein plan, development of more healthy and nutritious food, and an enablement of the bio-economy. It should offer a lever to improve farm economics structurally through product branding and traceability. The novelty of the proposed "virtual innovation workflow" is the bidirectional handover of outcomes and the holistic integration of data coming from plant, microbial, soil, agronomy, robotization, machine learning, modelling and weather/climate disciplines. Critical success factors are, amongst others, the alignment of key performance indicators of stakeholders, incentives to participate, an open innovation attitude, a common benchmark to measure progress, smartly located research field stations, dedicated data centers with a user-oriented data curation, harmonization, storage and display approach, and an agreeable data governance concept. A pipeline of consecutive innovations can be primed by raising, over time, the requirements to pass successfully the formal variety testing and registration process. Customer demand (not shown) is in this example translated to requirements for official variety testing trials that e.g. meet progressively increasing levels of sustainability.*

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Outstanding Questions

1. How to motivate all relevant stakeholders to develop jointly a common understanding of learning scenarios and their impact?
2. How to ensure that scenarios are timely updated to address specific developments over time, including aspects that were not covered during earlier scenario exercises?
3. How to organise the tracking of indicators and the dissemination of weaker and stronger signals that may indicate direction of change before any of the scenarios fully materializes?
4. How to improve the quality of scenario development and its utilization by the latest developments in digitalization and AI?

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Figure

Figure 1

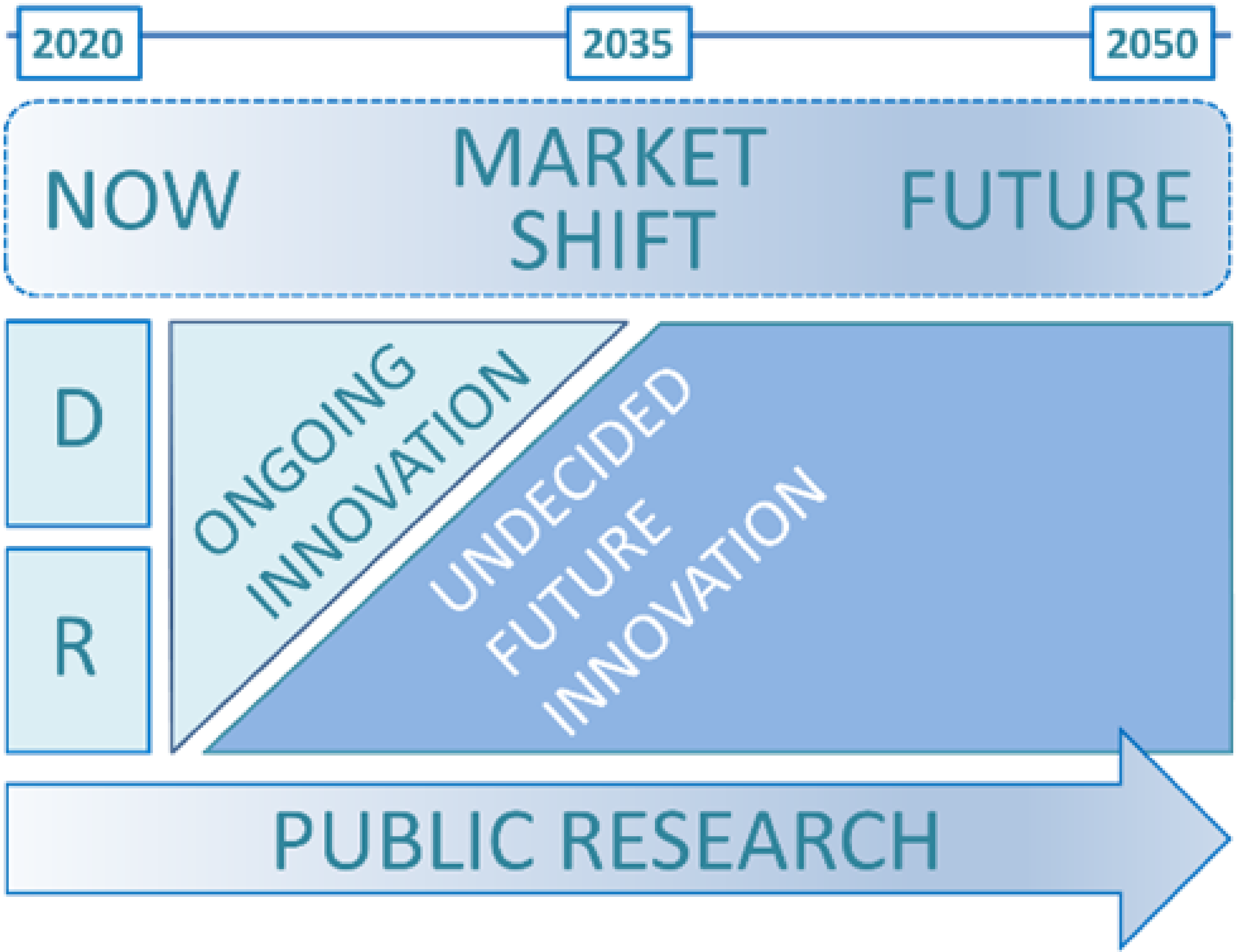
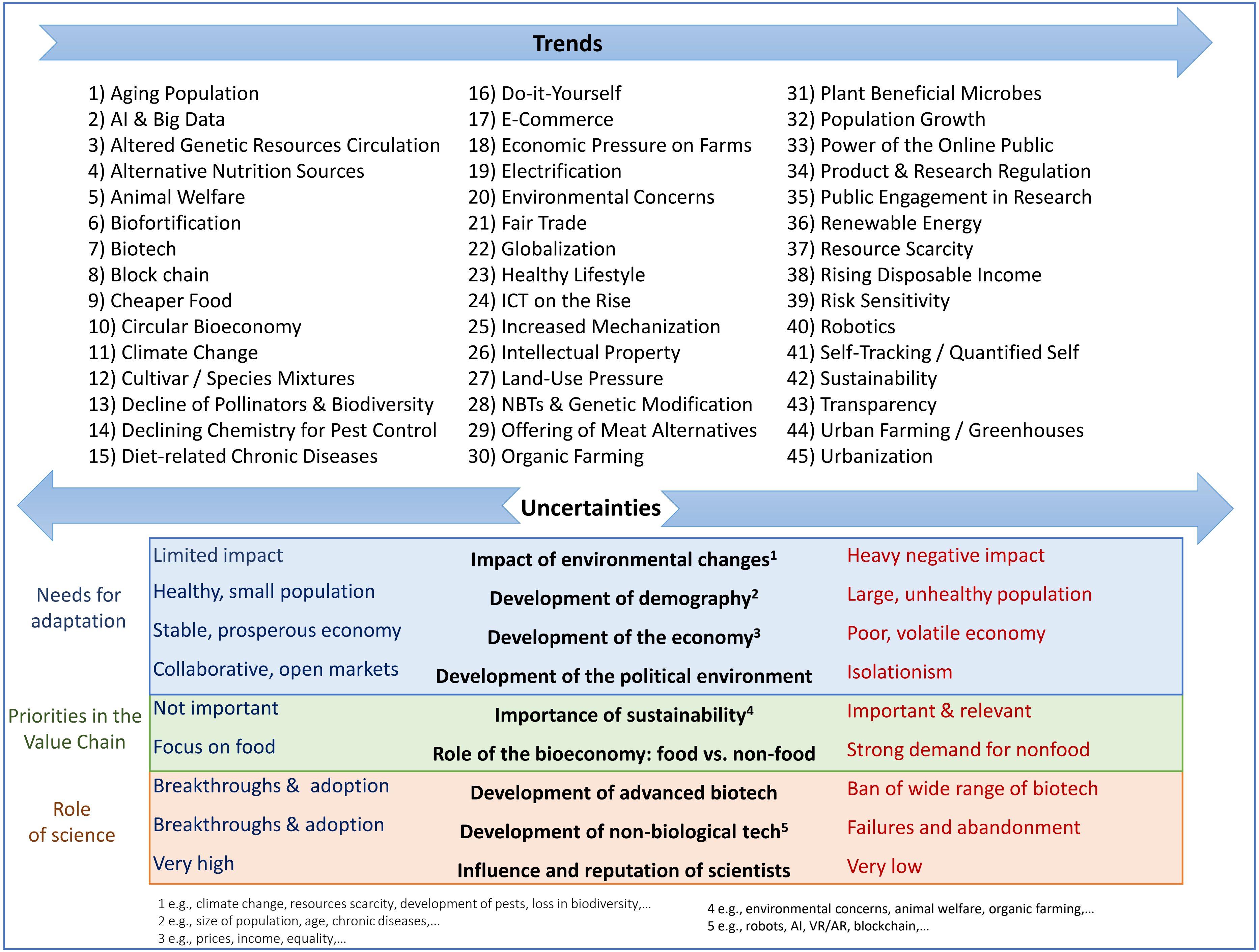
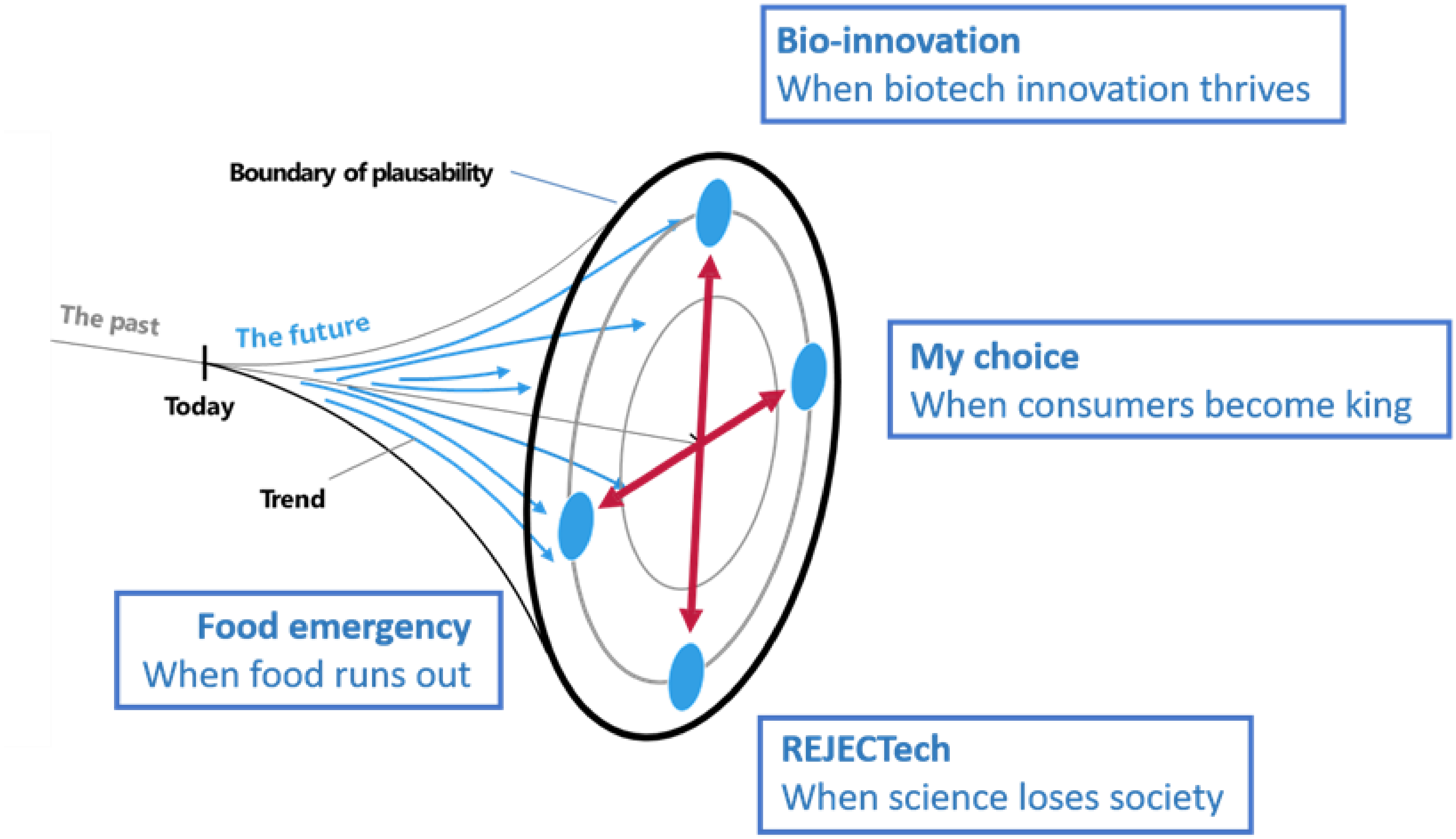


Figure 2



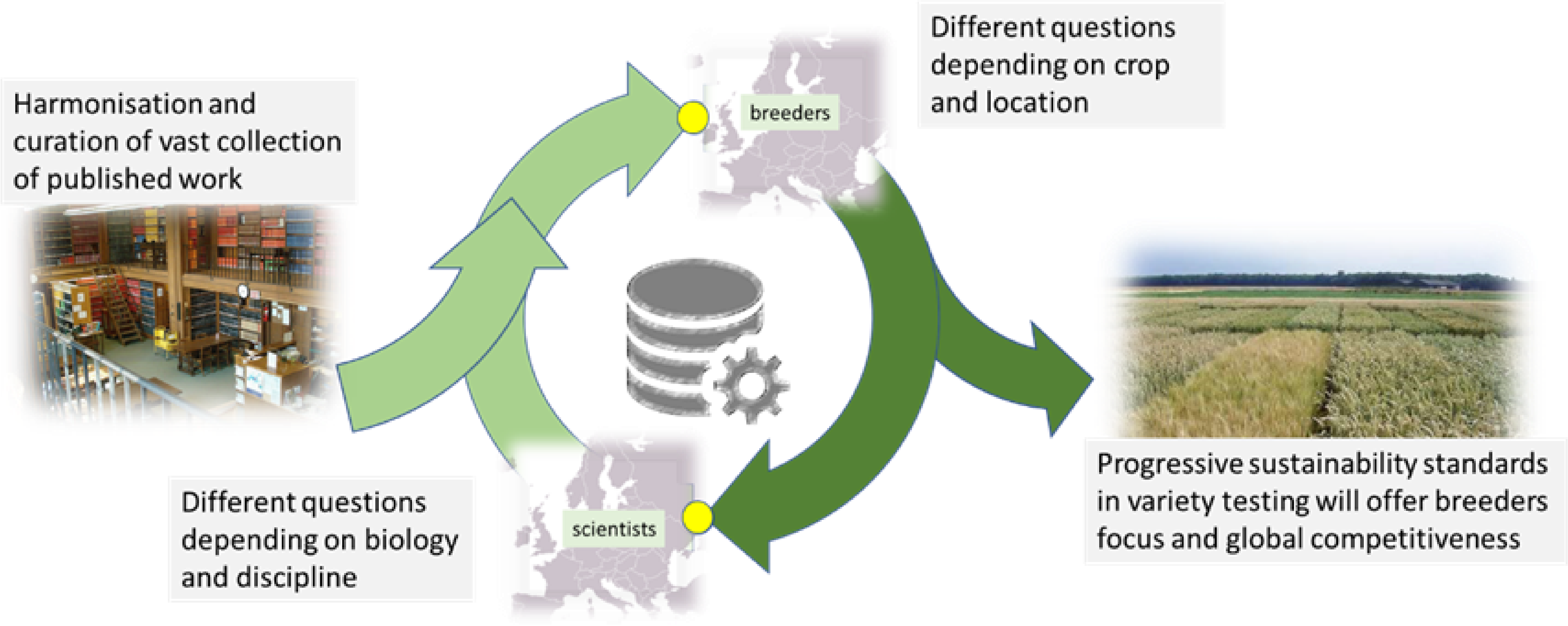
Trends
1) Aging Population
2) AI & Big Data
3) Altered Genetic Resources Circulation
4) Alternative Nutrition Sources
5) Animal Welfare
6) Biofortification
7) Biotech
8) Block chain
9) Cheaper Food
10) Circular Bioeconomy
11) Climate Change
12) Cultivar / Species Mixtures
13) Decline of Pollinators & Biodiversity
14) Declining Chemistry for Pest Control
15) Diet-related Chronic Diseases
16) Do-it-Yourself
17) E-Commerce
18) Economic Pressure on Farms
19) Electrification
20) Environmental Concerns
21) Fair Trade
22) Globalization
23) Healthy Lifestyle
24) ICT on the Rise
25) Increased Mechanization
26) Intellectual Property
27) Land-Use Pressure
28) NBTs & Genetic Modification
29) Offering of Meat Alternatives
30) Organic Farming
31) Plant Beneficial Microbes
32) Population Growth
33) Power of the Online Public
34) Product & Research Regulation
35) Public Engagement in Research
36) Renewable Energy
37) Resource Scarcity
38) Rising Disposable Income
39) Risk Sensitivity
40) Robotics
41) Self-Tracking / Quantified Self
42) Sustainability
43) Transparency
44) Urban Farming / Greenhouses
45) Urbanization
Uncertainties
Needs for adaptation
Limited impact
Impact of environmental changes[1]
Heavy negative impact
Healthy, small population
Development of demography[2]
Large, unhealthy population
Stable, prosperous economy
Development of the economy[3]
Poor, volatile economy
Collaborative, open markets
Development of the political environment
Isolationism
Priorities in the Value Chain
Not important
Importance of sustainability[4]
Important & relevant
Focus on food
Role of the bioeconomy: food vs. non-food
Strong demand for nonfood
Role of science
Breakthroughs & adoption
Development of advanced biotech
Ban of wide range of biotech
Breakthroughs & adoption
Development of non-biological tech[5]
Failures and abandonment
Very high
Influence and reputation of scientists
Very low
1 e.g., climate change, resources scarcity, development of pests, loss in biodiversity,…
2 e.g., size of population, age, chronic diseases,…
3 e.g., prices, income, equality,…
4 e.g., environmental concerns, animal welfare, organic farming,…
5 e.g., robots, AI, VR/AR, blockchain,…

Figure 3



Bio-innovation
When biotech innovation thrives
Boundary of plausability
The past
The future
Today
Trend
My choice
When consumers become king
Food emergency
When food runs out
REJECTech
When science loses society

Figure 4


Harmonisation and curation of vast collection of published work
Different questions depending on crop and location
breeders
scientists
Different questions depending on biology and discipline
Progressive sustainability standards in variety testing will offer breeders focus and global competitiveness