10 Biotechnological processes in the bioeconomy

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10.1 History and evolution of biotechnology

Biotechnology has been part of human life since ancient times, but it started to develop rapidly at the turn of the 20th and 21st centuries. The huge contemporary interest in biotechnology is a result of the unlimited potential of the benefits it brings in all areas, above all those related to such basic human needs as food, health and quality of life. Biotechnology also provides solutions to today's most pressing environmental problems, including alternatives to nearly depleted energy resources from fossil fuels, or the adaptation of primary production to ongoing climate change. Thanks to biological resources subjected to a variety of technologies, in other words biotechnology, our lives are much more comfortable and safe, and limits have been placed on our activities that are damaging to the environment. This illustrates that biotechnology is the actual foundation of the bioeconomy. But this did not just happen from one day to the next – people have been using living organisms for their own needs since ancient times, and, with the growth in knowledge, this has become increasingly common gradually leading to the current state of affairs today.

It is hard to point with absolute certainty to the "parents" of biotechnology, but there is no doubt that the first person to use the term was the Hungarian scientist and agricultural engineer dealing with animal husbandry and meat processing, Karl Ereky, who employed it in 1919, when he published a book entitled: *Biotechnology of meat, fat and milk production in an agricultural large-scale farm.*[1] Innovative at the time, Karl Ereky's vision is now being realised by thousands of companies and research institutions worldwide. Since the term biotechnology was first coined, its definition has been constantly evolving. In practical terms, the main purpose of biotechnology is to transfer its numerous benefits to human life. However, it should be remembered that, in addition to its beneficial applications, biotechnology may also give rise to products that can be dangerous or even fatal, such as those used in bioterrorism.

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Over the course of history, our needs have evolved, and so has biotechnology. Its development has fundamentally been based on observations and the application of these observations in various practical scenarios. Studying the development of biotechnology, it is possible to distinguish three main stages of development:

- ancient biotechnology,
- classical biotechnology,
- modern biotechnology.

It is remarkable that some ancient technologies are still being used today, but their effectiveness, efficiency and profitability continues to be systematically improved. The creation and evolution of some of the most important discoveries in the field of biotechnology are shown in Figure 10.1.

Solutions of **ancient biotechnology** were related primarily to basic human needs. This stage, above all, corresponds to the domestication of plants and animals as a result of problems with guaranteeing food from natural resources. This marked the beginning of the first human activity on our planet, one which remains fundamental to this day, namely agriculture. Once people had adopted appropriate species to cultivation and breeding in their own settlements, the problem of preservation and storage of food arose. People started, without knowing causes of phenomena, use of microorganisms for the processing of food. Cheeses started to be produced by adding rennet (an enzyme occurring

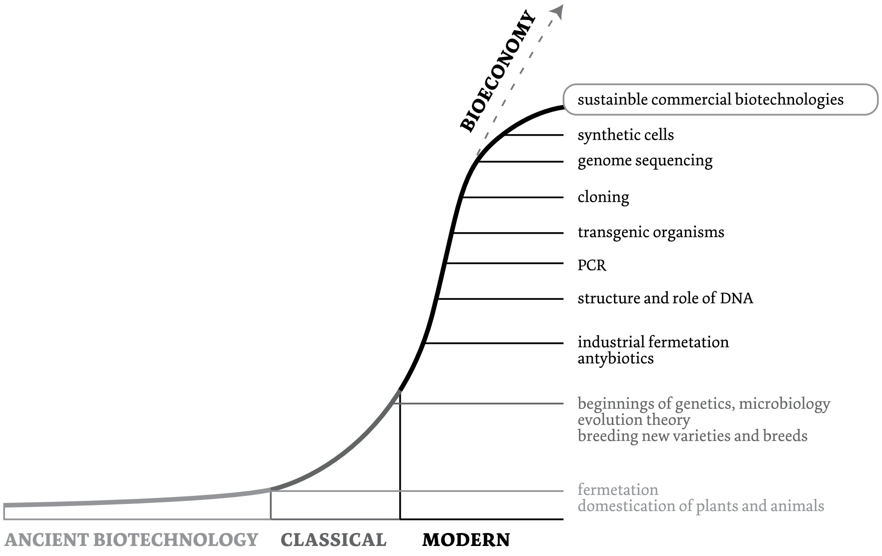


Figure 10.1 Categorisation and evolution of biotechnology.

Source: Own elaboration.

in the stomach of calves) to sour milk, which in turn is only possible when milk is exposed to microbes. The next breakthrough in food processing was in the use of yeast. To this day, they continue to be used in the production of basic products such as bread and fermented beverages. Another example of ancient biotechnology can be considered to be the first successful attempts to crossbreed animal species.[2]

The second phase in the evolution of biotechnology, referred to as the **classical stage**, only commenced around 1800. The 19th century can be considered to be a decisive period in the development of science, allowing us to understand the processes used in ancient biotechnology. This stage is inextricably linked to the genetics of organisms. The Czech scientist and monk, Gregor Johann Mendel (1822–1884), now recognised to be the father of genetics, was the first to present the laws of inheritance, when carrying out studies on *Pisum sativum*. He provided experimental proof that invisible internal units of information account for observable traits, and that these "factors" – later called genes – are passed from one generation to the next.[3] Mendel's work did not receive recognition among his contemporaries, however; it took another 34 years for it to be rediscovered by Hugo de Vries, Erich Von Tschermak and Carl Correns, who validated Mendel's theory. Another parallel breakthrough was the theory of evolution proposed by Charles Darwin (1809–1882), who claimed that all living species share the same origin. This opened the way for research into model organisms, the conclusions of which came to be more universally.[4] Biotechnology as we know it today would not exist also without the groundbreaking discoveries of Louis Pasteur (1822–1895), a pioneer in the field of microbiological research, who discovered the necessity of pasteurisation. Further discoveries, such as made by Robert Brown (nucleus in cells) and Fredrich Miescher (who identified the nuclein), became the basis of modern molecular biology. This related to the DNA as a genetic material and the role of DNA in the transfer of genetic information. In 1881, Robert Koch (1843–1910) described the first ever solid medium (potato slices) for the cultivation of bacteria. Walter Hesse (1846–1911), along with his wife Fanny, discovered agar and it was possible to commence intensive laboratory studies with microorganisms. These and other studies resulted in a description of chromosomes as an organised structure of DNA, protein present in cells, as well as a regulatory elements and nucleotide sequences in DNA and other phenomena in the field of genetics. At this time, the development of biological sciences reached an exponential phase. The principles of the genetics of inheritance were formulated, along with the theory of the gene, genotype and phenotype. At around the same time, Alexander Fleming (1881–1955) discovered antibiotics and observed that one microorganism can be used to kill another, thereby revolutionising the fight against infectious diseases.[5,6] At the same time as the development of genetics, numerous discoveries were being made in industrial biotechnology. Chaim Weizmann (1874–1952), considered to be the founding father of industrial fermentation, used a pure microbiological culture in an industrial process for the first time. He developed a process in which acetone, n-butanol and ethanol were produced as a result of bacterial fermentation. This development was related to the need to produce acetone used in explosive materials during World War I.[7]

The main, most dynamic development in biotechnology should, however, be considered to have taken place only in the mid-20th century, after the end of World War II. **Modern biotechnology** began with explanation of the secrets of DNA, as a genetic material, the presentation of the structural model of DNA – in other words, the double-helix model, the explanation of phenomena related to DNA replication of and their role in inheritance, the concept of the operon, the concept of cytoplasmic hybridisation and the production of monoclonal antibodies, which ultimately revolutionised diagnostics and opened the way for important scientific discoveries.[8,9] Modern biotechnology proper was born in the 1970s, when Paul Berg successfully spliced DNA molecules, and Herbert W. Boyer and Stanley N. Cohen then perfected this technology, transferring genetic material to bacterial cells so that it could be cloned. Intensive commercialisation of the newly established biotechnology industry followed in the 1980s, when the US Supreme Court gave its decision in the *Diamond v. Chakrabarty* case concerning the patenting of a genetically modified microorganism, a *Pseudomonas* bacterium capable of breaking down crude oil. Since then, it has been possible to patent a living organism. This was a breakthrough which allowed numerous biotechnological discoveries to be patented and led to research being transferred from scientific institutions to commercial companies, clearly accelerating the implementation of scientific discoveries in practice.[10] The turn of the millennium was a period of very intensive integration in the fundamental sciences, something which was of special significance for scientific progress and the commercialisation of research. In laboratories, work commenced on the synthesis, amplification and transformation of DNA. An adult animal was cloned (Dolly the sheep) and the human genome was sequenced. Advances in molecular techniques led to the need to analyse huge amounts of data, resulting in the creation and development of bioinformatics, and IT tools allowed results obtained by scientists to be collected and processed on a global scale. IT tools and networks can be considered to have enabled progress in biotechnology on a scale that would not have been possible before the era of computerisation.[11]

The now widely accepted definition of biotechnology is *The integration of natural sciences and engineering sciences in order to achieve the application of organisms, cells, parts thereof and molecular analogues for products and services* and refers to the interdisciplinary importance of this area of science.[12] In the 21st century, biotechnology has become such a broad area of science and industry, and of our daily lives, that the concept was developed of dividing it up into colours which are associated with the areas of its use.[13] This concept is called the “biotechnology rainbow”. Table 10.1 presents the identified branches of biotechnology and their description.

Taking account of the current state and diversity of the branches of biotechnology, it should now be considered to be one of the main strategic pillars

Table 10.1 Branches of biotechnology and areas which they concern divided up according to the rainbow code of biotechnology

Biotechnology colour	*Area of science and practices,* covers*, examples*
Red	**Medicine, pharmacy and health care** *diagnostics techniques and therapeutics* vaccines, antibiotics, biopharmaceuticals, pharmaceutical enzymes and metabolites, regenerative therapies, biocompatible implants
White	**Industry** *biological systems in industrial production and environmental protection* biocatalysis and bioprocesses, useful chemicals, enzymes as industrial catalysts, fuels/energy from renewable biomass
Green	**Agriculture** *improving production, implementation of methods of production which are more environmentally friendly* breeding technology, selection, design of transgenic crops, bioproducts (fertilisers, plant protection agents, stimulants)
Blue	**Water** *marine food, marine biodiversity as sources of new pharmaceuticals or industrial enzymes* aquaculture, food rich in omega-3 fatty acids, micro- and macroalgae; food additives, nutraceuticals, industrial enzymes
Gold	**Bioinformatics** *computational techniques allowing biological data* genomics, proteomics, metabolomics, interactome large-scale biological data processing; bionetwork, molecular interactions, protein functionally mapped
Grey	**Maintaining biodiversity and restoring ecosystems** *bioremediation, keeping a register of species present in ecosystems* phyto-, phyco- and bacterioremediation, gene banks, genetic analyses for the classification and cloning of endangered species
Yellow	**Food production** *fermentation, preservation, functionalisation and new food sources* wine, cheese, beer production, sourcing, insects, algae as food, artificial food
Brown	**Arid, saline soils** *management of resources under arid or saline conditions* improved seeds, GMO varieties for dry areas, post-harvest soils conservation, saline agriculture
Violet	**Legal, ethical and philosophical aspects of biotechnology** *patenting; legalisation and legal regulation; protection of intellectual property rights; use of animals in scientific research*
Dark	**Bioterrorism, biological weapons, warfare** *use of toxins of biological origin or microorganisms as weapons, use of microorganisms and toxins to cause disease and death*

of the global bioeconomy. In Europe, as early as 2020, the European Commission had noted that "*The next era of industry will be one where the physical, digital and biological worlds are coming together*." Such a combination is possible above all thanks to primary production, which includes green biotechnology and white industrial biotechnology. All the other branches of biotechnology complement this combination in the area of knowledge and/or practice. Development of the bioeconomy, which, according to its definition, "*promotes the production of renewable biological resources and their conversion into vital products and bioenergy for achieving [...] societal challenges [...] in the domains of food security, employment and competitiveness, climate change, sustainable management of natural resources and dependence on non-renewable natural resources*"[14,15] would be impossible without the progress which biotechnology has provided our society with, and especially its basic areas of activity in the green and white bands of the biotechnology rainbow.

10.2 Agriculture and green biotechnology

Modern biotechnology has a lot to offer agriculture, and green biotechnology is the best way of making agriculture sustainable and ensuring global food security and safety. When trying to define agricultural biotechnology, we can use the definition proposed by US Department of Agriculture: *Agricultural biotechnology is a range of tools, including traditional breeding techniques, that alter living organisms, or parts of organisms, to make or modify products; improve plants or animals; or develop microorganisms for specific agricultural uses.*[16]

10.2.1 Plant biotechnology

People have caused changes in the world of plants since the advent of agriculture, thus allowing development of human population. Civilisations could not exist without agriculture, and agriculture could not sustain the civilised world without continuously improved crop varieties. From this point of view, it becomes clear that plant breeding, which can now be described as plant biotechnology, is one of the main foundations of civilisation and is also of fundamental importance for the modern bioeconomy.

At the current stage of development of civilisation, it can no longer be denied that transgenic breeding is an inevitability of plant biotechnology, but conventional techniques are still very important. The oldest of these methods continues to be plant breeding based on observed variation by the selection of plants based on natural variants appearing in nature or within traditional varieties. Another technique is crossbreeding (hybridisation), which allowed significant progress to be made in obtaining desired traits. The crossbreeding of plants with appropriate traits and selecting offspring with the desired combination of traits as a result of specific gene combinations inherited from parent individuals is the basic technique that has been used since Mendel's discoveries were accepted. It is, however, a technique which takes significantly longer to achieve the desired outcome compared to molecular techniques and which is limited due to possibility of the genome variation, over which the creators of new varieties do not in principle have any influence because of genetic correlations between different traits, which may be due to genes with pleiotropic effects, to physical linkage between genes in the chromosomes, or to population genetic structure.[17] Currently, the conclusion reached by the scientific community is that, in order to meet the needs of the human population, it is necessary to use the most modern molecular methods which allow monitoring of the dynamics of genome recombination and the breeding of varieties gene by gene.

Genetically modified (GM) plants, which are also called transgenic or genetically engineered plants, are defined as plants having been produced using transgenic methods. According to the European Union (EU), genetically modified organisms (GMOs) are defined as *any organism, except humans, carrying an altered genetic material that does not occur naturally through natural selection or mating*. Plant biotechnology is based on changes aimed at: improving agricultural properties, increasing the yield of plants and quality of food obtained from them (improvement in nutritional value), improving post-harvest durability and mitigating environmental pollution. This is achieved, for example, by increasing their resistance to abiotic stress like drought, salinity or high/low temperatures; increasing tolerance to herbicides, insects and viruses resistance, improving growth rate, changes in the composition of the crop such as increased content of protein, fats/oils, and carotenoids or reduction of sugar content – which is important for food production sector, or plant-based remediation processes (e.g. removing heavy metals from the soil) – which are important for environment protection.[18]

The first GM plants were planted in fields in 1994. This was a variety of GM more rot-resistant tomato called FlavrSavr (Calgen Inc.). Although the commercialisation of this transgenic variety was unsuccessful just two years later (1996), the area under GM plants had already reached 1.66 million ha[19] (Brookes and Barfoot, 2013) and, in 2022, GM crops were being grown over an area of 202.2 million hectares. In the early 21st century, the global market for GM crops was dominated by such plants as: soybean, maize and cotton. The first GM soybean was used in the USA in 1996 by Monsanto. As early as 2022, the herbicide-resistant soybean GM accounted for 73.7% of its crops area. The first GM maize resistant to herbicide was commercialised in 1996, also by Monsanto. In the same year, GM maize with gen of crystal toxins (Cry) from the entomopathogenic *Bacillus thuringiensis* (Bt) bacteria was also introduced to the market. Bt GM maize has revolutionised pest control in many countries and opened the door to other Bt GM species. By 2022, maize was the second-most common GM crop (after soybean, excluding plants which are not grown for human consumption, such as cotton), with 66.2 mln hectares all over the world. GM plants cultivation has been growing dynamically, especially in the USA, Brazil and Argentina.[20] The size and scope of GM crops in the 11 leading countries worldwide in 2022 are shown in Figure 10.2.

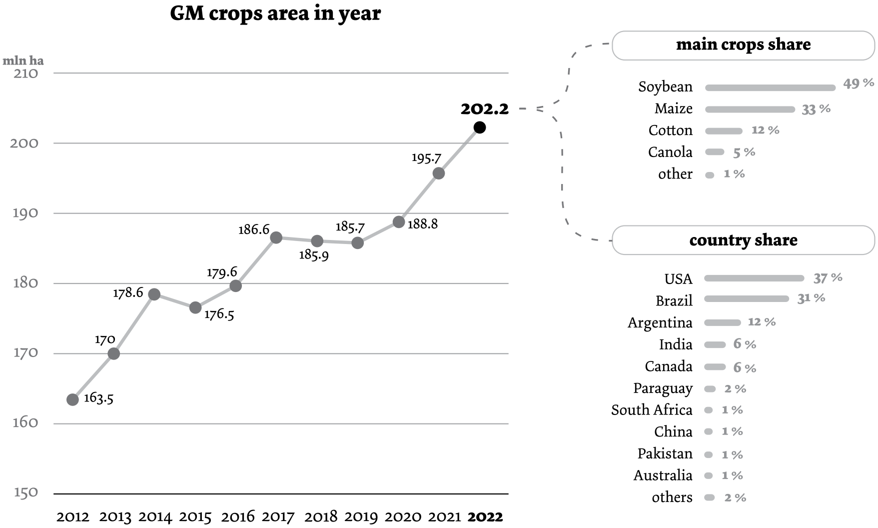


Figure 10.2 Development in GM crops since 2012 and 2022.

Source: Own elaboration, based on: https://gm.agbioinvestor.com.

Currently, the list of GM includes plants such as: soybean (mainly herbicide-tolerant, insect-resistant or with altered oil profile), maize (mainly insect-resistant and/or herbicide-tolerant), cotton (insect-resistant or herbicide-tolerant), herbicide-tolerant oilseed rape (canola) and alfalfa, rice (pest-resistant, enriched with beta-carotene) and also non-browning apples, eggplant (insect-resistant), papaya (ringspot virus-resistant), pineapple (increased levels of carotenoids and inhibited flowering), potato (reduced black spot bruising, levels of free asparagine and sugars or virus-resistant), squash (virus-resistant) and herbicide-tolerant sugarbeet,[21] tobacco and some others. The only GM crop grown in the EU Single Market is maize (in Spain and Portugal, and in small areas of Slovakia and the Czech Republic). It should be underlined that the most recent scientific research indicates that GM crops have a significant impact on the global bioeconomy. The positive impact on yields is particularly noticeable in developing countries. Data analyses conducted have confirmed that, without GM crops, the world would need an additional 3.4% of arable land to maintain global agricultural production, which is particularly important in the context of land scarcity and the bioeconomy's need to grow plants providing biomass for energy or industrial purposes. Scientists emphasise that bans on GM crops are limiting the global benefits of the adoption of GM to one-third of its potential, and that developing countries would benefit most from the lifting of those bans.[22] Besides the direct production of GM crops for food and industrial purposes, another important sector of modern plant biotechnology has become exploiting their potential as biological factories, that is as bioreactors for the molecular farming of recombinant macromolecules, such as blood proteins, vaccines and antibodies and raw materials for cosmetics. The first reports of the production of mammalian proteins in plants appeared at the end of the 1980s and, since then, the concept of "molecular farming" has been slowly gaining ground in the global bioeconomy. The concept of molecular farming or "biofarming" was introduced by Fischer et al.,[23] describing "the production of recombinant proteins in plants".

Other plant biotechnologies which are important to the modern bioeconomy also include soilless growing systems, such as *in vitro* farming, hydroponics, aquaponics, aeroponics and vertical farming. Since its discovery by Gottlieb Haberlandt (1854–1945) at the start of the 20th century, *in vitro* plant culture has, above all, been used for micropropagation, in other words, vegetative propagation with the aid of tissue cultures. Micropropagation has several advantages compared to traditional vegetative propagation methods, including the preservation of genotype composition, rapid multiplication of shoots or roots, production of material free of viruses and/or other contaminants, and easier collection, storage, and transportation. Culture of apical meristems, the induction of axillary and adventitious shoots and regeneration by somatic embryogenesis and organogenesis are common micropropagation techniques allowing stable and homogeneous material to be obtained on a large scale. Due to the numerous advantages of micropropagation and *in vitro* plant tissue culture it is also an efficient and cost-effective technique for the biosynthesis, biotransformation or bioconversion of compounds of plant origin (used in biofarming already described above).[24] Hydroponic techniques, such as deep water culture (plant seeds are sown in an inert medium floating on a deep tank of circulating water or nutrient solution, where roots develop in search of food) and nutrient film techniques (nutrient solution delivered continuously in a shallow, recirculating stream through an inclined growth tray where the roots are minimally submerged, which improves aeration of the root zone and has a positive impact on plant development), are very efficient in terms of water use, but are quite costly in terms of equipment, energy and space. Aquaponic systems are characterised by the simultaneous cultivation of both fish (aquaculture) and plants (hydroponics). They use the conversion of fish waste into food for plants by naturally occurring microbiota, followed by recultivation and recirculation of the water consumed by plants (see Chapter 8). These systems are highly efficient from the point of view of consumption of water and nutrients, though they do require constant monitoring and adaptation of the nutrient composition due to the nutritional requirements of fish, bacteria of the system microbiota and plants.[25] Aeroponic methods consist of providing nutrients in the form of aerosol droplets (10–100 μm) using various atomisation techniques. Their indisputable advantage is to offer the highest water efficiency of all soilless cultivation methods and excellent root zone aeration. In this case, the disadvantages are sophisticated instrumentation, susceptibility to power outages, or suboptimal nutrient formulations.[26] Vertical farming involves plant cultivation in vertically stacked irrigation systems, using artificial or natural light. The main cultivation methods in vertical farming are hydroponics or

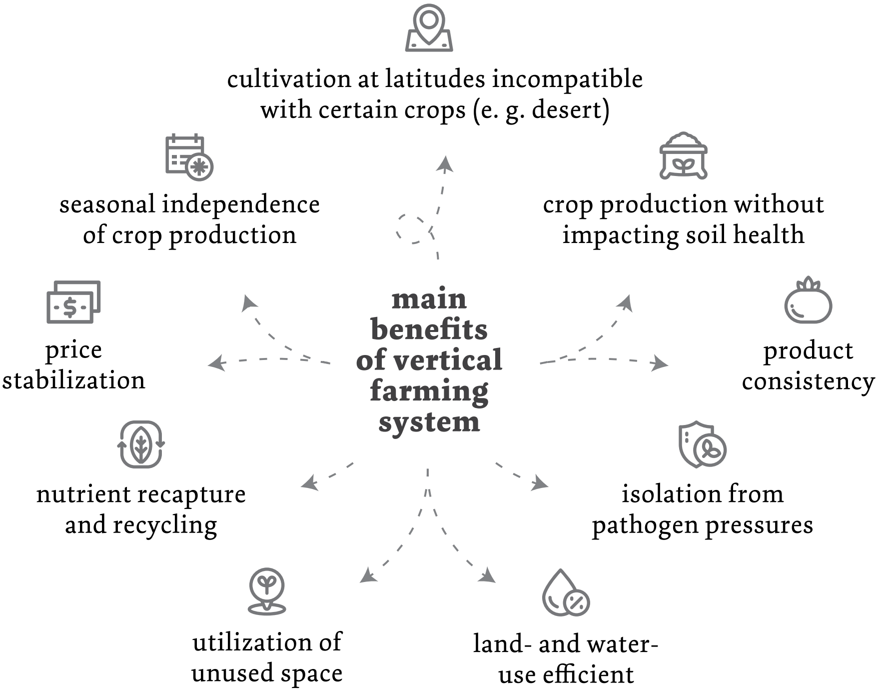


Figure 10.3 Advantages of vertical farming.

Source: Own elaboration.

aeroponics already discussed above. Vertical systems have been developed in response to the need for urban food production (urban farming), and policy to reduce the share of transport in food-supply chains.[27] Significant advantages of vertical farming are shown in Figure 10.3.

The potential benefits and value that vertical farming brings to the bioeconomy are undeniable and closely related to sustainable development goals. Market research suggests that the vertical farming sector is expected to grow by over 20% annually in the years to come to reach an estimated value of $9.96 billion by 2025.[28]

10.2.2 Animal biotechnology

Animal products, such as meat, milk, eggs and fish, are important components of the human diet, which is why, for many years, breeders have been trying in traditional ways to improve breeds of animals (mainly through crossbreeding) to obtain the best results. Crossbreeding combines two sexually compatible species, creating a new valuable variety with the desired characteristics of the parents. Examples include new breeds of animals with more meat, giving more milk with high fat content, laying more eggs. A scientific breakthrough in the field came when the first GM mouse was bred. Since then, GM mice have been an indispensable part of medical research, serving as also human disease models.[29] Although this does not have a direct impact on the bioeconomy, it is helping to change the perception of the value of GM animals for the quality of our lives. Currently, most GM animals are used in red biotechnology related to medicine – not only for model-based research but also for the production of substances important in the therapy of human diseases (e.g. insulin, medicinal proteins). There are also GM animals with potential for use in xenotransplantation. Breeding GM animals is a big step forward in animal biotechnology, but too many unknowns mean that widespread commercialisation of these animals will not occur in the coming years. In 2015, the United States Food and Drug Administration (US FDA) gave its first approval to sell AquAdvantage GM salmon to consumers which was modified for a faster growth rate. In 2020, the US FDA also approved the use of genetically modified GalSafe GM pigs in both food and medical products. These GM pigs can be used to produce medicines, provide organs and tissues for human transplants, and produce meat that is safe to eat for people with meat allergies.[30] It must be emphasised that more than 95% of animals used for meat and dairy in the United States eat GM crops, but GM foods do not affect the health and safety of animals[31] and these animals are not classified as GM.

10.2.3 Bioproducts

The increased interest in "healthy food" has led many agri-food research and biocontrol technologies to search for natural substances and microorganisms that promote the growth of crop plants or can be used in biological plant protection and weed control. Currently, numerous initiatives are being undertaken to reduce the use of chemicals while limiting the negative side effects of their use in agriculture. In the years to come, both agricultural science and practice will have to devote a lot of attention and effort to the development and implementation of integrated crop protection methods. With regard to the agro market, in many countries we can find preparations originating from a living organism or its products (biologically based agents) which can be used as biopesticides and biofertilisers, as well as selected cultures of microorganisms for soil remediation and composting.

The term *biological control* was first used by Harry Scott Smith in 1919. It relies on predation, parasitism, herbivory or other natural mechanisms, but typically also involves an active human management role. There are three basic strategies for biological pest control: classical (importation), where a natural enemy of a pest is introduced in the hope of achieving control; inductive (augmentation), in which a large population of natural enemies are administered for quick pest control; and inoculative (conservation), in which measures are taken to maintain natural enemies through regular reestablishment.[32] According to the United States Environmental Protection Agency,[33] the major classes of biopesticides are:

- biochemical pesticides – naturally occurring substances that control pests by non-toxic mechanisms: include substances that interfere with mating, such as insect sex pheromones, as well as various scented plant extracts that attract insect pests to traps (examples in Table 10.2),
- microbial pesticides – consisting of a microorganism (bacteria, fungi) and viruses as the active ingredient; each specific to the target pests (e.g. entomopathogenic fungi, *B. thuringiensis* producing *Cry* toxic proteins) (examples in Table 10.2),
- Plant-Incorporated-Protectants (PIPs) – pesticidal substances that plants produce from genetic material that has been added to the plant (e.g. Bt maize).

Biopesticides are inherently less toxic than conventional pesticides. They are often very specific, effective in very small quantities, compatible with other control agents and leave little or no residue. However, they have lower potency than synthetic pesticides. Biological plant protection is still not used extensively due to high competition from chemical plant protection product, variable effectiveness depending on environmental conditions, plant species or variety, and the relatively small number of registered biopreparations. Successfully implementing a biological control programme requires an understanding of the pests, natural enemies, the environment, and the interactions of all factors. Despite difficulties in adoption, biological control and Integrated Pest Management (IPM) can provide benefits that contribute to building a sustainable environment and increasing profitability by reducing management overhead.

Macroorganisms form a separate group of biological plant protection agents. The effective protection against pests using their natural enemies (referred to as macroorganisms despite their rather microscopic dimensions) was first reported in England in 1927. At the time, a *Encarsia formosa* wasp parasitising the greenhouse whitefly was used in tomato cultivation. In 1960, a predator of spider mites – the *Phytoseiulus persimilis* predatory mite – was discovered in Germany on orchids imported from Chile. A technology to breed them was developed quite quickly. To this day, these two historic examples remain methods of biological protection used in pest control with the use of "macroorganisms". Currently, beneficials mites and Trichogramma wasps (parasitoids of lepidopteran eggs, such as European corn borers) are of practical importance globally. Another interesting group of macroorganisms are insecticidal nematodes. In practice, two genera of nematodes, Steinernema and Heterorhabditis, are used in bioinsecticides. These are soil nematodes which look for host insects and enter them through natural openings in the body. Once inside the haemocoel, the nematodes release *Xenorhabdus* and *Photorhabdus* bacteria, with which they live in a mutualistic relationship. The bacteria multiply and secrete a range of toxins and hydrolytic enzymes that are responsible for the death of the insects within 24 to 48 hours. Steinernema and Heterorhabditis have a very wide range of hosts among pests of economic importance and are environmentally safe.[36]

Table 10.2 Commercially important examples of plant compounds, microorganisms and viruses used as biopesticides and their applications[34,35]

Group	*Example*	*Mode of action*
biochemical insecticides – plant compounds	azadirachtin	insect growth regulator, interfering with the development in preimaginal stages; inhibits the formation and secretion of ecdysone, has an effect on the hormonal level, causing morphogenetic disorders, leading to the formation of what are referred to as "permanent" larvae; has a repellent effect resulting from a gustatory, olfactory and neurophysiological effect, causes a significant decrease in the egg-laying activity and the viability of eggs; also limits the growth of fungi
	pyrethrins	in contact rapidly attacks the nervous system of insects; pests lose the ability to coordinate movements and gradually become paralysed, short-term toxicity, synergising ingredients are usually added to commercially available preparations, which increases the effectiveness thus blocking the system responsible for detoxification
microbial insecticides –bacteria	*Bacillus thuringiensis*	pathogenicity is determined by the action of Cry and Cyt crystalline toxins, which cause structural loosening and perforation of guts, leading to the digestive system or general paralysis, pests stops feeding and dies, these toxins also disturb the functioning of the nervous system through changes in ion exchange
	Lysinibacillus (Bacillus) sphaericus	binary toxin protein: bina + binb bound to specific receptors of the intestinal epithelium of the stomach and midgut, causing perforation, which leads to disruption of the osmotic balance, cell lysis, and ultimately death of the insect
	Serratia entomophila	bacterium releases toxins after ingestion by the insect, resulting in the cessation of food intake, emptying of the intestine and retention of digestive enzymes in the stomach, infected larvae take on a characteristic amber colour
microbial insecticides –fungi	*Beauveria bassiana* *Isaria fumosorosea* *Metarhizium anisopliae*	infections caused by all species of entomopathogenic fungi follow a typical course for a fungal disease initiated by adhesion, spore germination and mycelial overgrowth through the cuticle into the haemocoel, which results in the death of the host

(*Continued*)

Table 10.2 (Continued)

Group	*Example*	*Mode of action*
microbial fungicides –fungi	*Trichoderma* spp.	limit the development of other fungi (including phytopathogenic fungi) through hyperparasitism, competition and antibiosis
virus insecticides	*Cydia pomonella* granulosis Virus (CpGV)	once the virus is in the host cell, its nucleic acid takes control of the cell's metabolic system and virus particles start to replicate, leading to cell death

The control of pests is not the only possible positive impact on obtained yields. For several decades now, one particularly intensive area research has been stimulation of plant growth and immunity. Plants never exist in isolation – they always interact with environmental components. The plant-microbiome or phytomicrobiome plays a crucial role in plant health and yield by modulating the production of phytohormones, improving root development, increasing the availability nutrients and resistance against pests and mitigating biotic and abiotic stresses. Rhizosphere fungal and bacterial communities that have a beneficial effect on plants are called Plant Growth-Promoting Microbes (if fungi PGPFs, if rhizobacteria PGPRs). Bacteria can fix nitrogen (symbiotic and free-living N2 fixers), convert insoluble soil phosphorus into plant-available forms through various mechanisms of solubilisation and mineralisation, as well as solubilise potassium, oxidise sulphur, or solubilise or chelate micronutrients and facilitate the production of siderophores enhancing iron update – thus acting as biofertilisers. Also root mycorrhizal fungi play a special role because they can form symbiotic relationships with ~80% of land plant species. The best-studied plants–fungi symbiosis refers to obligate, arbuscular mycorrhizal fungi (AMF) of the Glomeromycota phylum. These fungi contribute to nutrient mobilisation, increasing the uptake of minerals (i.e. P, N, S, Cu and Zn) and water by host plants. Generally biofertilisers can be defined as preparations containing living microorganisms (single strains or consortia) that promote plant growth by increasing the availability and acquisition of nutrients. Microbial fertilisers are considered key elements of sustainable agriculture, having a long-term impact on soil fertility.[37] Another group of such preparations based on raw materials of natural origin, which can be amino acids, protein hydrolysates, humic substances, macro or microalgae, chitosan and other biopolymers are called plant biostimulators. Biostimulators are used in very small quantities and improve plant growth by stimulating direct or indirect release of phytohormones.[38]

The wide range of bioproducts discussed meets all the requirements for sustainable agricultural means of production and allows modern requirements of the bioeconomy to be fulfilled in the area of primary production. The application of bioproducts can prevent the excessive use of synthetic chemical means of production. Of course, bioproducts implemented in practice should be tested and meet all safety requirements while complying with the applicable standards for all substances or organisms introduced into the environment. Bioproducts are already an important part of integrated and ecological plant production! One very optimistic piece of information is, that based on research conducted on the pesticides market, it is expected that biological protection will become the main method of crop protection by 2030, and the share of biopesticides in the global market for plant protection agents will be over 50%. Other bioproducts, namely biofertilisers and biostimulants, are also an important sector in innovative means of production, and the development of this sector will be even more dynamic due to the less restrictive process of registration for this type of substance. Sustainable, integrated or ecological plant production, including biological protection, natural fertilisation and biostimulation of crop plants, is the only way forward for global agriculture, which will have to meet the challenges facing the global bioeconomy.

10.3 White biotechnology

The next branch of biotechnology essential to the bioeconomy, termed white biotechnology, stands at the confluence of nature and industry. White biotechnology refers to the use of living cells and enzymes to synthesise products that are traditionally produced through industrial methods. This covers a range of products from biofuels and chemicals to bioplastics. White biotechnology offers a greener alternative to conventional manufacturing processes. By utilising renewable raw materials and minimising waste through biotransformation processes, white biotechnology aligns industrial production with environmental responsibility and often results in reduced energy consumption and increased efficiency, what make it economically viable. The advancement of white biotechnology is critical to expanding the bioeconomy and the circular economy. At the heart of this sector of biotechnology lie the microscopic powerhouses – bacteria, fungi, and yeast with unique metabolic capabilities – that drive the synthesis of a multitude of products, have positioned themselves as indispensable assets in this sector (Figure 10.4). Figure 10.4 shows the systematic conversion of diverse input feedstocks, such as agricultural-derived sugars, various gases, and lignocellulosic biomass, into an assortment of chemical products with the central role of biotransformation mechanisms, including fermentation processes utilising microorganisms, along with cell-free systems. The resulting products are a spectrum of industrially significant compounds ranging from basic organic acids to complex molecules like diols, alcohols, diamines, as well as isoprene, terpenes, hydrocarbons, and a variety of other organic compounds.

Bacteria (unicellular prokaryotic microorganisms) are versatile in biotechnological applications.[39] The most renowned, *Escherichia coli*, has been genetically engineered in countless ways to produce biofuels, pharmaceuticals, and even specialty chemicals. Beyond *E. coli*, other species from the *Bacillus* and *Corynebacterium* genus have become useful in enzyme production and amino acid synthesis, respectively. Also fungi, especially filamentous, are famous for

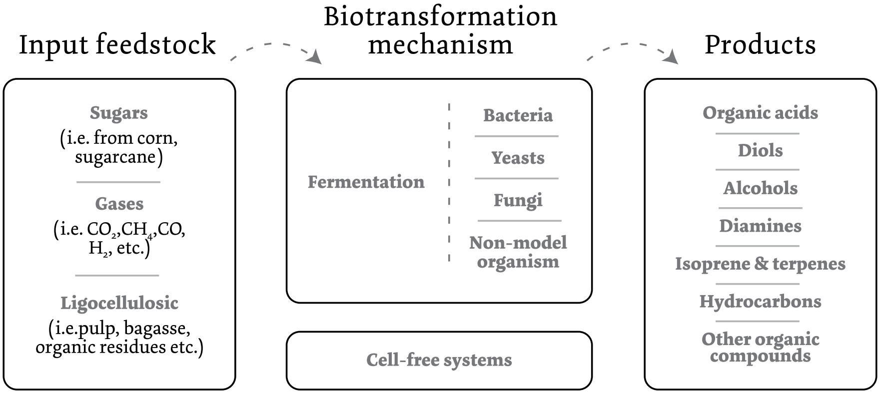


Figure 10.4 Comprehensive overview of white biotechnology processes.

Source: Own elaboration based on: IDTechEx, https://www.idtechex.com.

their ability to produce a plethora of enzymes and molecules, and unique to this group antibiotics. Their inherent capability to degrade complex substrates has led to their widespread use in food, paper and textiles productions. *Aspergillus niger*, for instance, is a chief producer of citric acid – an additive ubiquitously found in foods and beverages. *Saccharomyces cerevisiae* yeast, having been used for millennia in bread-making and alcohol fermentation, in modern industrial biotechnology, its applications have been expanded. GM yeasts are now instrumental in producing bio-based chemicals. The power of these microorganisms lies not just in their ability to reproduce rapidly or their flexibility to genetic manipulation but also, and predominantly, in their vast and diverse metabolic pathways. The relevance of this metabolic versatility is profound. Different industries have distinct requirements. The pharmaceutical industry might require a specific chiral compound; the biofuel sector might need efficient conversion of biomass to ethanol, and the food industry could be after a specific flavouring agent. With metabolic engineering, yeasts can be tailored to fit these niche requirements, optimising the desired pathway to enhance yield, purity or efficiency. Furthermore, the metabolic diversity serves as a treasure trove for discovering novel compounds. Synthetic biology, a burgeoning field, takes research beyond mere tinkering with existing metabolic pathways; it aspires to design and construct entirely new biological systems. By rewriting the genetic code, introducing synthetic DNA, or even creating minimalistic genomes tailored for specific tasks, synthetic biology can generate micro-factories with unprecedented capabilities often achieve unparalleled production yields.

Every biological process, from digestion to DNA replication, hinges on enzymes. These proteins have a unique ability: they can speed up chemical reactions without themselves being consumed. This catalytic power is attributed to their intricate structure, particularly an active site that binds specific molecules, or substrates, and aids in their transformation. Their action is akin to fitting a key into a lock, where only the right key (substrate) fits perfectly, ensuring high specificity and reduced unwanted side reactions. It is essential to note that these enzymes are often produced by microbes, a core facet of white biotechnology, through either natural strains or GMOs. The industrial application of enzymes is vast and varied.[40] Proteases have become mainstays in laundry detergents. They break down protein-based stains (e.g. blood, grass), allowing for effective cleaning even at lower temperatures. Lipases and amylases are used to target fat and starch stains, respectively. A groundbreaking application of lipases is in the chiral synthesis of biopharmaceuticals. In non-aqueous solvents, lipases can selectively act on specific isomers, enabling the synthesis of chiral compounds vital for drug development. This specificity is crucial because different isomers, or enantiomers, of a drug molecule can have vastly different therapeutic effects. The textile industry employs enzymes in processes like desizing and biopolishing. Cellulases are used to give denim its faded look without the use of harsh chemicals or abrasive stones. Enzymes play vital roles in food processing: amylases are used in baking to break down starches, improving the texture of bread; in the brewing industry they help in breaking down grains to release fermentable sugars; rennet, a mixture containing chymosin, is traditionally used in cheese production to coagulate milk. Enzymes also find a wide range of applications in the paper industry, biofuel production, waste treatment and pharmaceutical manufacturing. Enzyme engineering, using techniques like directed evolution or rational design, can modify structures to improve stability, specificity, or activity. For instance, an enzyme that is naturally sensitive to heat can be engineered to function optimally in the high-temperature conditions of an industrial process. Immobilisation techniques have also revolutionised enzyme technology. By attaching enzymes to solid supports or entrapping them in gels or matrices, they can be reused multiple times, enhancing process efficiency and reducing costs. Immobilised enzymes also offer easier product separation and enable continuous processing.

10.3.1 Bio-based chemicals

Organic acids, notably citric, lactic, and acetic acids, have been traditionally sourced from chemical processes. However, microbial fermentation offers a greener and often more efficient alternative. For instance, *A. niger* is employed to ferment sugars into citric acid, a critical industrial chemical with applications ranging from food and beverages to pharmaceuticals. Similarly, many strains of *Lactobacillaceae* are able to convert carbohydrates into lactic acid, which can be used as a food preservative but more notably as a precursor for bioplastics – polylactides. Amino acids, the building blocks of proteins, have also seen a shift towards microbial production. Lysine and glutamic acid, vital for human nutrition and widely used in the food industry, are now predominantly produced by fermenting specific strains of *Corynebacterium glutamicum*. The advantages include higher yields, reduced costs, and enhanced purity compared to chemical syntheses or extraction from protein hydrolysates. Vitamins, essential micronutrients, have also benefited from biotechnological interventions. For instance, Vitamin B2 (riboflavin) production was conventionally based on chemical synthesis. Today, fermentative production using microbes like *Ashbya gossypii, B. subtilis*, and *Candida* spp. has become a leading method due to its efficiency and reduced environmental footprint.

The pharmaceutical industry is constantly seeking new and effective compounds, with natural sources frequently serving as primary candidates. However, direct extraction of these compounds from plants or animals can be resource-intensive, expensive, and occasionally raise ethical concerns. Biotechnology offers a solution by facilitating the microbial synthesis of these crucial compounds. Penicillin, the pioneer antibiotic, provided an early example of this. While originally extracted from the fungus *Penicillium*, advances in biotechnology have optimised strains for enhanced production levels. Another striking example is the production of artemisinin, an antimalarial drug. Traditionally, this has been sourced from the sweet wormwood plant. Through synthetic biology, a yeast strain was engineered to produce artemisinic acid, a precursor to artemisinin, ensuring a consistent and scalable supply. Furthermore, microbes can be harnessed to produce precursors for synthesising complex drugs, reducing the steps and resources required in traditional chemical synthesis. With combination of theoretical modelling and artificial intelligence this approach not only ensures a more sustainable and scalable production method but can also lead to derivatives of the original molecule, potentially yielding drugs with enhanced efficacy or reduced side effects.

10.3.2 Biofuels and bioenergy

The ever-growing demand for energy, coupled with the detrimental environmental impacts of fossil fuels, has driven the global quest for alternative, sustainable energy sources.[41] Biofuels and bioenergy stand at the forefront of this pursuit, offering renewable energy options derived from biological materials. First-generation biofuels are derived from sugars, starches and vegetable oils. These feedstocks are usually food crops like corn, sugarcane and soybean. The biofuels produced include ethanol (from fermented sugars and starches) and biodiesel (from vegetable oils and animal fats). While they provide a cleaner-burning alternative to fossil fuels, the primary criticism of first-generation biofuels lies in the competition with food supply. Using agricultural crops for energy production raises concerns about food security and potential implications for food prices. Nevertheless, bioethanol and biodiesel, as sustainable alternatives to fossil fuels, play important roles in the evolution of renewable energy sources for transportation. Bioethanol is an alcohol primarily derived from the fermentation of sugars present in crops like sugarcane, corn and beet. When used as a fuel, it can be blended with gasoline to produce a mix suitable for vehicle engines. The use of bioethanol offers several advantages. First, it is renewable, being derived from plants that can be cultivated annually. Second, it has a cleaner combustion profile, leading to reduced greenhouse gas emissions compared to pure gasoline. Biodiesel, on the other hand, is derived from vegetable oils, animal fats or even used cooking oil. It can replace or be blended with conventional diesel fuel. The transesterification process converts these oils and fats into biodiesel and glycerin. Biodiesel offers a reduction in carbon emissions and is biodegradable, reducing environmental risks in cases of spills. Moreover, it provides an avenue for recycling used cooking oils. Like bioethanol, the sustainability of biodiesel depends on its feedstock, pushing research towards non-food sources like algae or waste materials. Second-generation biofuels, on the other hand, are produced from non-food biomass sources. This includes agricultural residues (like straw and husks), forest residues, and specially cultivated energy crops. These materials are primarily composed of lignocellulosic fibres, which, being tougher to break down, can be converted to biofuels like cellulosic ethanol. The advantage here is the reduction in competition with food crops and, often, a better overall carbon footprint due to the full utilisation of plant materials. There are many examples of the second-generation energy sources; however, two are notably the most promising – algal biofuels and biomethane. Algae, given their rapid growth rate and high oil content, are emerging as a promising feedstock for biofuel production. Algal biofuels do not compete with arable land meant for food crops. Moreover, algae can be cultivated in various environments, including saline water, reducing the strain on freshwater resources. Once harvested, the lipids from the algae are extracted and converted into biodiesel, while the remaining biomass can be used for other applications, further maximising resource utilisation. Biogas primarily consists of methane and carbon dioxide and is produced through the anaerobic digestion of organic materials. This includes any organic waste available. Once produced, biogas can be used directly for heating or electricity generation. Biomethane is the purified form of biogas, where the carbon dioxide and other impurities are removed, resulting in a higher methane concentration. It possesses similar characteristics to natural gas and can be injected into the gas grid or used as a transport fuel. In essence, biofuels and bioenergy offer promising alternatives to our reliance on fossil fuels. As research continues and technologies mature, it is expected that biofuels and bioenergy will play an even more significant role in our global energy landscape.

10.3.3 Biomaterials and biopolymers

As our understanding of biological systems advances and intertwines with materials science, a new epoch of materials – biomaterials and biopolymers – emerges.[42] These materials, either derived from nature or inspired by it, not only promise reduced environmental impact but also boast properties that can be tailored for specific applications, from packaging to advanced healthcare. The global concern about plastic waste, especially its persistence in the environment, has accelerated research into biodegradable polymers. Unlike conventional plastics derived from petrochemical sources, biodegradable polymers break down into harmless components under natural conditions, alleviating concerns about long-term environmental contamination. Polyhydroxyalkanoates (PHAs) and polylactic acid (PLA) are prime examples. PHAs are produced by bacteria under nutrient-limited conditions and are fully biodegradable. Depending on the bacterial strain and cultivation conditions, PHAs can have properties ranging from being elastomeric to highly crystalline, making them suitable for a variety of applications. PLA, derived from the fermentation of plant sugars to lactic acid, is another leading biopolymer. It is processed in a similar way to petrochemical-based plastics, but, upon disposal, it can be composted, breaking down into its monomers, a naturally occurring compound – lactic acid. The allure of these materials is not just their biodegradability but also their origin: renewable resources, often agricultural by-products or waste, ensuring a lower carbon footprint than their petrochemical counterparts.[43]

10.3.4 Bioprocess engineering

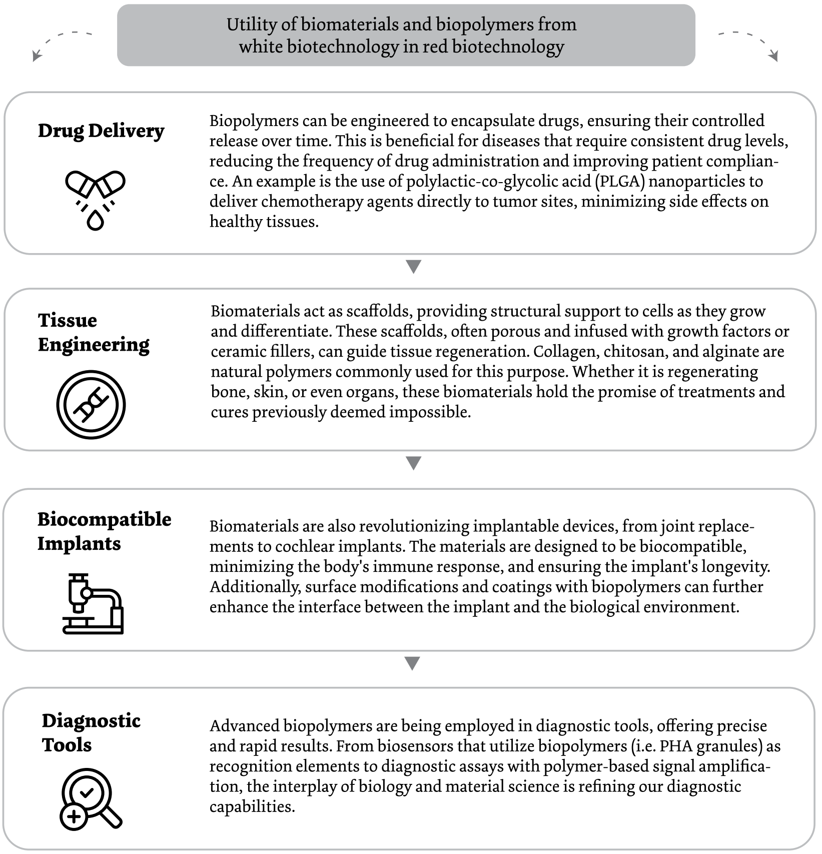
Bioprocess engineering that encompasses the principles and practices required to translate the discoveries of life sciences into tangible products, especially through the use of living cells or their components constitutes an important aspect in white biotechnology.[44] Central to this field is the ability to harness biological systems for the production of goods spanning from biofuels to therapeutics. Key aspects include designing and optimising fermentation processes, bioreactor configurations and downstream processing techniques. Table 10.3 presents the types of fermentation used in biotechnology.

Case study

The use of white biotechnology in an application related to red biotechnology – functional materials for medical applications

Despite the division of biotechnology, all its colour branches create a complementary network. Many technologies of a given branch find applications in others, resulting in the great impact that has biotechnology on and the contribution it makes to the sustainable development of the bioeconomy and other areas of our lives. A case study is provided as an example of the flow between branches of biotechnology.

Within the medical realm, the utility of biomaterials and biopolymers exceeds mere biodegradability. The convergence of biotechnology and materials science is generating materials with functionalities tailored for sophisticated medical applications. Figure 10.5 summarises the use of white biotechnology-derived biomaterials in drug delivery, tissue engineering, biocompatible implants, and diagnostic tools. It emphasises their role in controlled drug release, scaffold-based tissue regeneration, enhanced compatibility of medical implants and the advancement of diagnostic technologies.



Utility of biomaterials and biopolymers from white biotechnology in red biotechnology

Drug Delivery

Biopolymers can be engineered to encapsulate drugs, ensuring their controlled release over time. This is beneficial for diseases that require consistent drug levels, reducing the frequency of drug administration and improving patient compliance. An example is the use of polylactic-co-glycolic acid (PLGA) nanoparticles to deliver chemotherapy agents directly to tumor sites, minimizing side effects on healthy tissues.

Tissue Engineering

Biomaterials act as scaffolds, providing structural support to cells as they grow and differentiate. These scaffolds, often porous and infused with growth factors or ceramic fillers, can guide tissue regeneration. Collagen, chitosan, and alginate are natural polymers commonly used for this purpose. Whether it is regenerating bone, skin, or even organs, these biomaterials hold the promise of treatments and cures previously deemed impossible.

Biocompatible Implants

Biomaterials are also revolutionizing implantable devices, from joint replacements to cochlear implants. The materials are designed to be biocompatible, minimizing the body's immune response, and ensuring the implant's longevity. Additionally, surface modifications and coatings with biopolymers can further enhance the interface between the implant and the biological environment.

Diagnostic Tools

Advanced biopolymers are being employed in diagnostic tools, offering precise and rapid results. From biosensors that utilize biopolymers (i.e. PHA granules) as recognition elements to diagnostic assays with polymer-based signal amplification, the interplay of biology and material science is refining our diagnostic capabilities.

Figure 10.5 Applications of biomaterials and biopolymers in red biotechnology.

Source: Own elaboration.

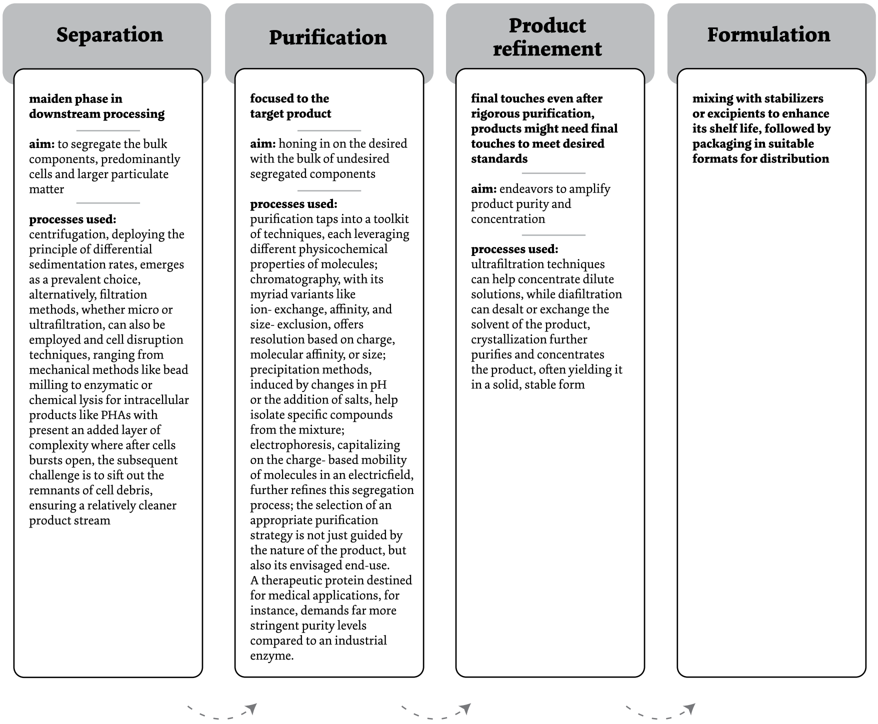
Bioreactors stand as the core elements in bioprocessing, serving as meticulously designed chambers wherein biological reactions unfold under carefully modulated conditions. These essential vessels, conceptualised to foster life, are moulded based on factors such as the organism in focus, the targeted end-product, and the anticipated operational scale. The basic variants of bioreactors are: stirred-tank bioreactors, airlift bioreactors, packed-bed bioreactors and fluidised-bed bioreactors. Stirred-tank bioreactors are the workhorses of both microbial and mammalian cell culture processes. Their inherent design incorporates impellers that facilitate thorough mixing, ensuring that nutrients, oxygen, and the cultured cells are uniformly dispersed throughout the liquid medium. Such an even distribution promotes consistent growth conditions, enabling reproducible outcomes. The versatility of these bioreactors, combined

Table 10.3 Characteristics of fermentation processes used in white biotechnology

Type of fermentation	*Characteristic*
Batch	Begins with the introduction of all essential nutrients into the bioreactor. From this point, the fermentation progresses autonomously without any subsequent input or extraction of materials until its conclusion. This approach is particularly appropriate for the production of biomass or for products that emerge during growth-associated phases. Nonetheless, it has intrinsic limitations. Over time, there is a tangible risk of nutrients being exhausted and the accumulation of waste, which might inhibit the fermentation process.
Fed-batch	Adopts a more controlled approach, involves the periodic or slow and steady addition of nutrients to the bioreactor. This strategic supplementation ensures that microbial growth and productivity are sustained over a prolonged period. By preventing the complete exhaustion of nutrients and averting excessive waste accumulation, fed-batch processes can enhance the yield of the target product. This mode is especially efficacious for the production of compounds that are synthesised during non-growth linked phases.
Continuous	Perpetual introduction of fresh medium into the bioreactor. In tandem, an equivalent volume of the spent medium – laden with products, residual cells, and unused substrates – is systematically evacuated. This continuous exchange stabilises the operational conditions within the bioreactor, ensuring a consistent cell density and a steady rate of product formation. When scalability and uniformity in production are paramount, especially for growth-associated products, continuous fermentation emerges as the method of choice.

with the ease of scalability, renders them a preferred choice for many industrial applications. Airlift bioreactors are distinguished by their reliance on air to facilitate mixing and oxygenation, and are tailored for cultures that demand gentler handling. The absence of mechanical agitators means there is reduced shear stress, making them particularly apt for cultivating fragile cells, including certain microalgae and plant cells. Given their design, these bioreactors are often used for large-scale biomass production, especially when dealing with photosynthetic organisms that benefit from light exposure. At the core of packed-bed bioreactors lies a fixed bed, densely packed with immobilised cells or enzymes. As the culture medium meanders through this packed matrix, it interacts intimately with the immobilised biological entities, leading to efficient conversion processes. One of the hallmarks of packed-bed bioreactors is their resilience, especially when the production environment contains compounds that are detrimental to the cells. The immobilised cells, protected in their fixed state, often showcase enhanced resistance to toxicants, ensuring uninterrupted production. In dynamic fluidised-bed bioreactors, cells find themselves anchored to minuscule carrier particles. When the culture medium is introduced with an upward thrust, these particles (along with the attached cells) get fluidised, creating an environment that blends the merits of both stirred-tank and packed-bed bioreactors. The resulting setup encourages excellent mixing and elevated rates of mass transfer. Moreover, the constant movement minimises cell clumping and fosters a uniform exposure to nutrients and oxygen.

At the culmination of fermentation or any bio-based production process, the sought-after product often finds itself submerged in a diverse milieu of cells, residual substrates, and a spectrum of metabolites. The journey of retrieving and refining this product from this intricate web is encapsulated in the downstream-processing realm as illustrated in Figure 10.6, where stages of bioproduct processing such as separation, where cells and larger particulate matter are isolated; purification, focusing on the extraction of desired molecular components; product refinement ensuring the product meets rigorous quality standards; formulation describes the integration of stabilisers and packaging, crucial for the product's shelf life and distribution readiness are presented.



Separation

maiden phase in downstream processing

aim: to segregate the bulk components, predominantly cells and larger particulate matter

processes used: centrifugation, deploying the principle of differential sedimentation rates, emerges as a prevalent choice, alternatively, filtration methods, whether micro or ultrafiltration, can also be employed and cell disruption techniques, ranging from mechanical methods like bead milling to enzymatic or chemical lysis for intracellular products like PHAs with present an added layer of complexity where after cells bursts open, the subsequent challenge is to sift out the remnants of cell debris, ensuring a relatively cleaner product stream

Purification

focused to the target product

aim: honing in on the desired with the bulk of undesired segregated components

processes used: purification taps into a toolkit of techniques, each leveraging different physicochemical properties of molecules; chromatography, with its myriad variants like ion- exchange, affinity, and size- exclusion, offers resolution based on charge, molecular affinity, or size; precipitation methods, induced by changes in pH or the addition of salts, help isolate specific compounds from the mixture; electrophoresis, capitalizing on the charge- based mobility of molecules in an electricfield, further refines this segregation process; the selection of an appropriate purification strategy is not just guided by the nature of the product, but also its envisaged end-use. A therapeutic protein destined for medical applications, for instance, demands far more stringent purity levels compared to an industrial enzyme.

Product refinement

final touches even after rigorous purification, products might need final touches to meet desired standards

aim: endeavors to amplify product purity and concentration

processes used: ultrafiltration techniques can help concentrate dilute solutions, while diafiltration can desalt or exchange the solvent of the product, crystallization further purifies and concentrates the product, often yielding it in a solid, stable form

Formulation

mixing with stabilizers or excipients to enhance its shelf life, followed by packaging in suitable formats for distribution

Figure 10.6 Stages of bioproduct processing.

Source: Own elaboration.

10.3.5 Biorefineries – the future of sustainable production

In a world biorefineries emerge as the cornerstones of sustainable production, bridging the gap between renewable resources and our ever-growing demands for energy, materials, and chemicals.[45] They represent not just an industrial facility, but a paradigm shift, echoing the holistic principles of traditional refineries but with an emphasis on green, renewable sources. Just as petroleum refineries process crude oil into a plethora of valuable products ranging from gasoline to plastics, a biorefinery processes biological raw materials, primarily biomass, into a variety of bio-based products and bioenergy. The core principle underscoring biorefineries is their multi-product approach: extracting maximum value by converting biomass components into a spectrum of marketable products, be it biofuels, biochemicals, or biomaterials. Their use of biomass – a renewable and often locally available resource – reduces dependency on fossil raw materials, curbing greenhouse gas emissions in the process. Biomass is a complex assembly of carbohydrates (such as cellulose and hemicellulose), lignin, proteins, and lipids. The skill of the biorefinery revolves around deconstructing this intricate network into valuable products. For instance, cellulose and hemicellulose can be degraded into fermentable sugars via hydrolysis. These sugars then act as primary feedstocks for the microbial fermentation of bioethanol or other bio-based compounds. Lignin, which is frequently viewed as a residue in many bioconversion routines, is gaining attention for its potential in producing valuable products like bioplastics, resins and carbon fibres. Additionally, abundant lipids and oils in sources like algae or seeds are processed into biodiesel or other significant chemicals using methods such as transesterification. The hallmark of an efficient biorefinery is its integrated approach, where the aim is to harness every fragment of the biomass. This philosophy echoes nature's zero-waste principle, ensuring that what might be deemed 'waste' in one process becomes 'feedstock' in another. For instance, the residual biomass post biofuel production, often rich in proteins, can be channelled as animal feed. The lignin, once stripped of its polysaccharides, can be valorised into myriad products or even combusted to generate energy that can power the biorefinery, closing the loop in the process. This integrated, circular approach underscores the efficiency of biorefineries, ensuring economic viability. Whether it is through genetically modified organisms tailored to enhance bioconversion efficiency or novel catalysts that speed up reactions, the world of biorefineries is ever-evolving, ever-optimising. By reimagining the way we produce, by replacing the finite with the renewable, and by integrating processes to extract maximal value with minimal waste, biorefineries embody the synergy of nature and technology.

Case study

Circular biorefinery – transforming cellulosic sugars to bio-based products

In an era where sustainability and resource efficiency are paramount, the conceptualisation of a biorefinery that not only produces a primary product but also channels its by-products into further value-added outputs is revolutionary. The following case study delves into a unique biorefinery model that champions the principles of the circular bioeconomy, using cellulosic sugars as a cornerstone. This biorefinery model demonstrates a circular bioeconomy approach. Utilising sugars from cellulose, it produces a biopolymer and efficiently uses all by-products, including spent medium and post-catalysis solvents, for further value-added production. By closing the loop, this model offers a blueprint for future biorefineries, underscoring the principles of sustainability, innovation, and efficiency (Figure 10.7).

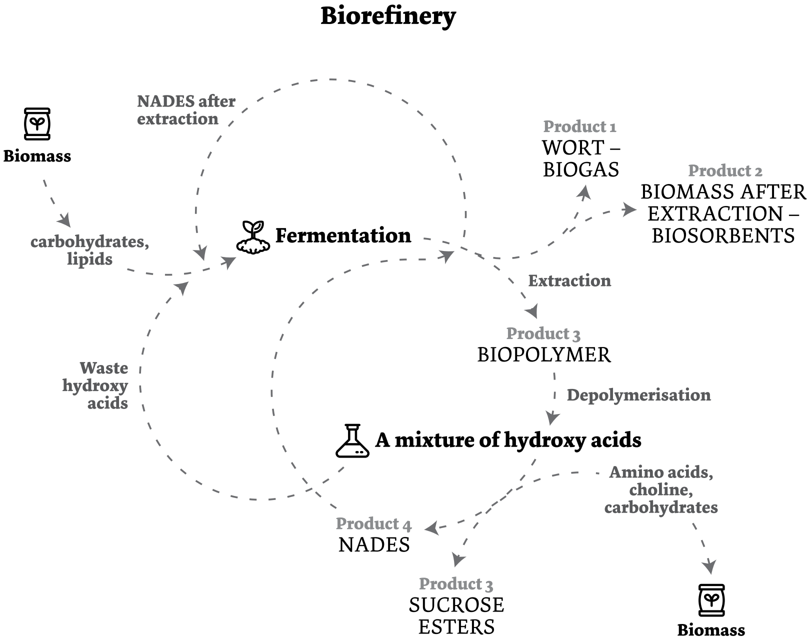


Figure 10.7 Biorefinery process diagram: circular economy from plant inputs to reusable products.

Source: Own elaboration.

Description of phases

Phase 1: Production of biopolymer and fertilisers

Input: Sugars derived from the biodegradation of cellulose, an abundant bioresource. Process: Fermentative production of Polyhydroxyalkanoates (PHA). *Outputs*: primary product – PHA, a biopolymer with myriad applications ranging from medical to environmental solutions due to its biodegradability and biocompatibility; by-products – Post-fermentation spent medium and bacterial biomass after extraction of PHA. Both serve as valuable organic fertilisers, rich in nutrients and minerals.

Phase 2: Valorisation of the biopolymer
Direct utilisation: PHA, in its polymer form, can be directly utilised in various applications. For instance, its biocompatibility makes it a coveted material for medical applications, from sutures to drug delivery systems. Depolymerisation: PHA can be further processed to break it down into its constituent monomers, specifically 3-hydroxyacids. *Synthesis of green solvents*: The derived 3-hydroxyacids can be integrated with other biomolecules, like choline chloride, to fabricate Deep Eutectic Solvents (DESs). These solvents, known for their eco-friendliness, serve as potent mediums for catalysis.

Phase 3: Creation of platform chemicals
Input: Sugars from cellulose, identical to the input in Phase 1. *Process*: Utilising DES as the catalytic medium, the sugars undergo transformations. *Outputs*: Formation of platform chemicals like hydroxymethylfurfural (HMF), which is fundamental in the synthesis of a multitude of high-value chemicals and biofuels.

Phase 4: Closing the loop
The post-catalysis spent DES, instead of being discarded as waste, is directed back into the fermentative production of PHA. This looping back exemplifies a sustainable approach, ensuring minimal wastage and maximum resource efficiency.

10.3.6 Challenges and future prospects

White biotechnology presents a promise for a sustainable future, intertwining biology's know-how with industrial processes to proffer eco-friendly solutions. However, while its potential is vast, the pathway to its extensive adoption is riddled with challenges. Scaling up biotechnological processes from the lab to industrial production is more intricate than merely expanding equipment size. The inherent complexity of biological systems means that they, unlike traditional chemical processes, rely on living organisms whose behaviour can fluctuate based on various factors, leading to inconsistent product yields and quality. Furthermore, aerobic operations necessitate efficient oxygen transfer, a task that becomes progressively challenging as the size of the reactor grows, with the central aim being to distribute oxygen uniformly without inflicting damage on cells due to excessive shear forces. Additionally, the exothermic nature of biological processes means that as they scale up, the effective dissipation of generated heat to maintain ideal temperatures becomes crucial. Moreover, ensuring the reproducibility of results, whether across different batches or during continuous operations, is vital for commercial success, but this too presents challenges given the variable nature of biological systems. Navigating the confluence of biology and industry presents an intriguing yet complex terrain, with economic considerations playing a main role in its widespread integration. Biotechnological ventures, particularly pioneering ones, demand hefty initial investments encompassing research and development, acquisition of specialised machinery, and onboarding of skilled staff. While biomass frequently emerges as an economical raw material choice, logistical hurdles associated with its aggregation, preservation, and preliminary processing can escalate costs. In the marketplace, products birthed from white biotechnology struggle against counterparts stemming from traditional methodologies. Ensuring cost-competitiveness, even when supplemented by ecological advantages, remains a formidable challenge. Furthermore, the trajectory of bioproduct production and market introduction, especially those leveraging genetically modified organisms, can be significantly influenced – either obstructed or expedited – by prevailing local regulations and policy frameworks.

Amid the rise of challenges, solutions also flourish, with the dynamic domain of white biotechnology continuously evolving, driven by both needs and innovative strides. Advances in synthetic biology now empower researchers to devise and assemble novel biological components, mechanisms and systems, presenting avenues to refine organisms for industrial applications in ways that transcend the bounds of classical genetic engineering. Moreover, grappling with the multifaceted nature of biological systems has instigated a paradigm shift towards a more encompassing systems biology perspective. Here, the emphasis is on decoding entire systems rather than isolated elements, a venture greatly facilitated by computational modelling. Concurrently, there is an ascending momentum behind the valorisation of industrial and agricultural residues, turning these potential waste streams into prized commodities. Such activities not only offer cost-effective feedstock alternatives but also present resolutions to waste management problems. Building on our earlier case study, the development of integrated biorefineries – producing multiple outputs from a single input – highlights the principles of maximum resource utilisation, increased process efficiency and economic viability. Moving away from broad-based solutions, the industry is now trending towards tailored approaches, specifically designed based on regional resource availability, market demands and regulatory frameworks.

10.4 Summary

This chapter has discussed selected achievements of global green and white biotechnology, which have had an unprecedented impact on the bioeconomy. It should be recognised that, without the biotechnological processes developed from the period of ancient biotechnology, through the era of classical biotechnology, and, above all into the times of its most intensive development, that is the age of modern biotechnology, the bioeconomy would not be able to be a global development strategy. The bioeconomy is currently rapidly and positively evolving towards respecting the needs and ecological limitations of the planet and drawing on the achievements of all areas of the biotechnology rainbow taking account of socio-economic and political changes, is thus becoming a new economic paradigm. It should be added that a new, exceptional perspective has now opened up for the development of biotechnology and the bioeconomy. This development has entered the phase of exponential growth, based on artificial intelligence (AI).[46] AI already plays a significant role in activities of such importance as machine learning, Big Data analytics, knowledge discovery and data mining, biomedical ontologies, knowledge-based reasoning, natural language processing, decision support and reasoning under uncertainty, temporal and spatial representation and inference, and methodological aspects of explainable AI. Specialists point to the fact that, in the not-so-distant future, the role of humans will only be to plan development so that it is beneficial for people and our planet.

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