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Prospects of Synthetic Biology in the Actualization of Green Chemistry and Environmental Solutions

Emmanuel Chimeh Ezeako [a], Yemiode Bernard Itam [a,b], Gloria Oluchukwu Osuagwu [c], Chisom Roseline Ogbodo [a], Okpanachi Nuhu Oyibo [a], Amarachi Njoku Olokor [a], Cynthia Doowuese Aondover [a], Nnamdi Ginikachukwu Amuzie [a], Silas Arubi Ijaja [a], Humphrey Sam Samuel [d], Fidelis Nnaemeka Chukwuma [a], Malachy Chigozie Odo [a,e], Ekene John Nweze [a] and Chibuzo Valentine Nwokafor [f*]

[a] *Department of Biochemistry, University of Nigeria, Nsukka, Nsukka, 410001, Enugu, Nigeria.*
[b] *Department of Biochemistry, Faculty of Basic Medical Sciences, University of Calabar, Calabar, Nigeria.*
[c] *Department of Applied Biochemistry, Nnamdi Azikwe University, Awka, Anambra State, Nigeria.*
[d] *Department of Chemical Sciences Federal University Wukari, Taraba State, Nigeria.*
[e] *Department of Biomedical Science, University of Wolverhampton, England, United Kingdom.*
[f] *Department of Microbiology, University of the West of Scotland, Glasgow, United Kingdom.*

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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**Corresponding author: E-mail: chibuzonwokafor@gmail.com;*

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ABSTRACT

Synthetic biology (SynBio) is an emerging field of endeavor that uses modular and replaceable biological parts or devices in standard chassis, or whole organisms to generate intended and programmed outputs that can be quantified and optimized until they meet the desired efficiency. As a result, SynBio is becoming increasingly popular for addressing critical global challenges such as the bioremediation of recalcitrant organic and inorganic pollutants in the environments and the reduction in emission of toxic waste from industrial processes. Although synthetic chemistry and the chemical industry have greatly enhanced the quality of life of the human race, they have also caused significant detrimental effects in terms of pollution, toxic waste emissions, and public health endangerment. SynBio technology has now found application in the bioremediation of polluted environments and to actualize previously unfeasible industrial outcomes and green chemistry. This study elucidates the innovative applications of SynBio concepts in the bioremediation of polluted environments, the actualization of eco-friendly industrial operations, and the realization of green chemistry principles. We also explore SynBio-based strategies for minimizing toxic waste emission and energy consumption, while simultaneously enhancing the production of value-added industrial products from renewable feedstocks, industrial wastes, and greenhouse gasses. Several ethical and safety concerns and regulatory framework required to ensure the responsible application of SynBio technology were also reviewed. By unearthing the propitious potential of SynBio in biotechnology, sustainable development, and green chemistry, this study aims to afford insights into the future directions of SynBio technology and its potential impact on various sectors, from industry to environment.

Keywords: Synbiology; renewable feedstocks; green chemistry; bioremediation; sustainable development; genetic engineering; gene editing.

1. INTRODUCTION

SynBiology or Synthetic biology (SynBio) is a discipline of biology that employs engineering ideas to design and construct new biological systems with predefined functions [1,2]. Essentially, SynBio encompasses the design of novel approaches for programming predictable cellular modalities and depends immensely on the growing wealth of knowledge and expanding research efforts in genomics, computer sciences, biomedical and chemical engineering, and even mathematics [3,4,5]. It entails using genetic engineering, computer modeling, and other methodologies to create biological components and systems for a variety of applications, including industrial microbial processes, environmental microbiology, and green chemistry [5]. System biology is founded on genetic engineering and has been utilized for decades to edit and manipulate the genetic materials of living organisms. Conversely, toggling a step further, SynBio technology alongside modifying existing systems seeks to construct novel and more efficient cellular systems from scratch that do not exist in nature. In connection with this, SynBio is viewed as a "bottom-up" strategy of cell engineering that entails the assemblage of smaller functional parts to build large cellular systems that can produce intended outcomes [2,5].

Globally, large portions of land and water resources are already contaminated due to industrial activities, such as mineral mining, polymer synthesis, transportation, and agriculture [6,7,8]. As a way to curb this menace, innovative methods of minimizing waste emission, handling tainted waste, and restoring damaged areas are now developed through the application of synthetic biology [2,8,9,10].

Furthermore, before concerns about the environment, human health, and safety came to prominence, the manufacturing and distribution of chemicals had a relatively easy economy [2]. In the past, feedstock expenditures, energy requirements, and product marketability were among the main economic issues at play [11]. However, expenditures now include expenses related to waste disposal, end-of-pipe waste treatment, liability, and regulatory compliance [6]. Auspiciously, green chemistry is proposed to eliminate or significantly reduce the additional costs associated with meeting the environmental and safety requirements of conventional chemical synthesis by doing away with or drastically reducing the use of toxic or hazardous feedstocks and catalysts as well as abrogating the production of dangerous intermediates and byproducts [7]. Consequently, the tenets of green chemistry are being adopted and propagated in various life domains, including medicines, material sciences, agriculture, biotechnology, and environmental sciences [8]. Also, biodegradable products harnessed from renewable feedstock such as lignocellulosic waste, and agricultural and industrial bioproducts are now used to substitute petroleum-based products, hence mitigating their environmental implications. In the same vein, chemical reactions in the production chain are being controlled and monitored by smart devices, such as biosensors, microfluidic chips, and nanomaterials [9]. In addition, industrial processes continue to adopt more eco-friendly solvents and ionic liquids, including supercritical fluids, deep eutectic solvents, or switchable solvents for the dissolution or extraction of materials [10]. The sustainable synthesis and utility of novel enzymes to catalyze reactions that would otherwise require hazardous chemicals and extreme conditions is one striking innovation afforded by SynBio technology [11].

The application of SynBio-based technology in industrial operations is proposed to hold promise in curbing environmental pollution [12,13]. For instance, only recently have bacteria designed using SynBio techniques been deployed to tackle dangerous and recalcitrant heavy metals like mercury and arsenic that elicit deleterious immune reactions [13]. Nowadays, engineered microorganisms that can degrade resistant environmental toxins have found applications in various product and manufacturing sectors. We can now engineer organisms capable of degrading everyday wastes, such as plastics, pharmaceuticals, hydrocarbons, pesticides, and personal care products that predominate in water bodies, air, and polluted soils [14]. In the same vein, SynBio-enhanced biosensors have now emerged and are being deployed to monitor and detect the presence of hazardous substances in the environment; keeping their toxic effects on humans and the environment in check [12]. SynBio technology has found massive utility in the management of industrial sites and the restoration of polluted areas [15]. Interestingly, several environmental merits and assurance have been realized by the adoption of SynBio in addressing certain quintessential global concerns, and it is projected to create a sustainable future (Fig. 1). However, some key ethical considerations, safety protocols, and regulatory frameworks must be instituted and constantly reviewed to ensure the responsible application of SynBio technology. The present study reviews the prospects of SynBio technology in the actualization of green chemistry and environmental solutions.

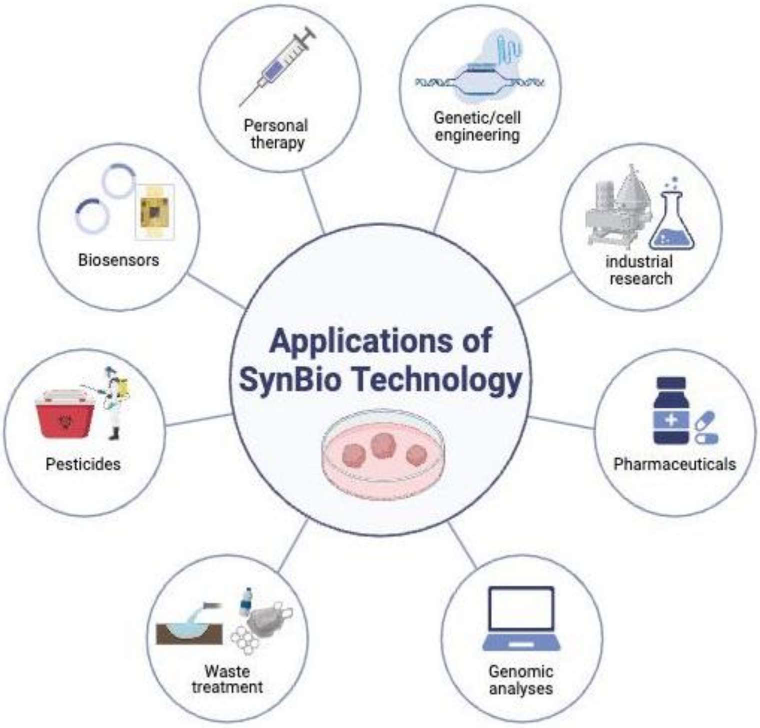

Fig. 1. SynBio technology; the new directions for sustainable future

1.1 Challenges and Innovations in Environmental Microbiology

Environmental microbiology investigates the dynamic interactions that exist between microorganisms and their ecological niche and utilizes available data to solve several environmental problems. In recent times, as the world currently witnesses the impact of the evolution of novel and more aggressive forms of infectious agents in the environment, new recalcitrant compounds have also been discovered in surface and ground waters that previously served as our potable water sources [12]. Perhaps, this could be due to the increasing strains placed on water resources, as society grows. For example, groundwater is currently being pumped out faster than it can replenish itself in some regions of the United States [16]. With rising waste discharges containing chemical and biological contaminants finding their way into our water resources, it is evident that environmental microbiologists face significant challenges in this regard. These challenges also arise in polluted soils. Land resources are becoming increasingly scarce as the world population grows, and settlements are encroaching on contaminated places such as agricultural fields with years of pesticide use, landfills, and mine tailings sites. The use of molecular genetics and biotechnology tools has considerably improved these subjects in both circumstances. With the worldwide population rise, the development and assessment of new ways of detecting and eradicating germs and pathogens in food and water supply, as well as the air that humans breathe, has become vital to public health. Additionally, pathogens and pollutants detection capacity of modern-day technologies have immensely improved and expanded. Sequel to this, the use of risk assessment to determine the need for control where it is most effective, as well as community education to lessen the dangers associated with living near polluted sites, is becoming increasingly worthwhile. However, despite the horizon and advancement of research efforts, microbial communities remain poorly understood and challenges in replicating complex ecosystems remain an impending factor [17]. Nevertheless, the application of SynBio techniques in environmental microbiology is laying the foundations for more precise genetic engineering, allowing for the introduction of artificial or optimized metabolic pathways into certain microbial strains aiming at bioremediation [2]. Possibly, the addition of SynBio-based functions to microbiological organisms is projected to enhance bioremediation, nutrient recycling, and ecosystem restoration as discussed later on.

2. FABRICS OF GREEN CHEMISTRY

Green chemistry entails the integration of chemical innovations, expertise, and practicality to reduce or eliminate the use of harmful substances in the design, production, and use of chemical entities along the production chain. The concept of green chemistry is centered on resource conservation, pollution reduction, health, safety, and sustainable environment promotion [18]. As an emerging and multifaceted concept, green chemistry accentuates safe and efficient chemical synthesis, the deployment of alternative solvents, and biocatalysts, and the realization of clean and renewable energy. Green chemistry is targeted at eliminating the detrimental effects of hazardous industrial products or by-products on the environment, and curbing the recently increased mortality and mortality accompanying industrialization [19]. Green chemistry lessens the harmful environmental effects of chemical production processes, contributing to the development of a more sustainable industrial landscape [20]. The 12 principles of green chemistry (Fig. 2) can also be successfully applied to organic synthesis, where hazardous solvents are typically used: maximum atom economy (avoidance of wastes and by-products, especially when using solvent-less techniques, i.e. dry media), safer and innocuous chemical synthesis routes void of harmful chemical substances, use of renewable precursors (biomass replacing fossil fuels), small amounts of catalysts (innocuous and preferably solids to be renewable), safer chemicals and solvents (water, ionic liquids) and biodegradable materials. Ionic liquids have attracted considerable attention as alternative reaction media for a wide range of chemical transformations, because of their low vapor pressure, good solvating characteristics, considerable thermal stability, and easily adjustable physical (e.g. melting point, vapor pressure, or viscosity) and chemical properties (e.g. polarities, basicity, and acidity, basicity). By adhering to green chemistry principles, it is now possible to implement energy-efficient processes that minimize waste production, promote matter and energy economy, employ safer solvents and renewable chemicals, produce less hazardous materials, and execute smart catalysis with fewer byproducts or derivatives under biodegradable process design [21].

Fig. 2. The 12 principles of green chemistry

2.1 Renewable Resources

Chemistry is required for the creation of most products utilized in daily life, such as fuels, transportation devices, construction materials, food products, pharmaceuticals, personal care products, and communication accessories. Given the breadth of this sector and its expansion requirements to ensure development and technological progress that can satisfy the demands of the growing global population, the time has come for a new chemical era in which the environmental impact of chemical products is minimized in terms of hazards, carbon footprint, life cycle, and resource sustainability. Despite recent reports of global warming and depletion of fossil fuel reserves, international efforts to promote the production of carbon-neutral end products and reduce CO_2 emissions following the Kyoto Protocol have not been fully realized. Scientific investigations continue to focus on identifying and developing innovative solutions for the substitution of petroleum-based resources with renewable alternatives [22]. The use of biomass as readily available and internationally scalable feedstock has come into the limelight for the chemical industry and is upheld as a promising alternative to the usage of carbon resources. Green chemistry promotes the utility of renewable feedstock utility, such as biomass and plant-based resources, as opposed to non-renewable resources, to produce sustainable products [22]. Biomass utilization to produce energy, chemicals, and industrial commodities is a significant step toward the realization of sustainable product development. Biomass includes all macromolecular feedstocks derived from agricultural proceeds, forestry products, and their residues. Synthetic biology has enabled the sustainable synthesis of aromatic terpenes, green synthesis of sitagliptin [23] and chemical alternatives for agarwood perfume (sesquiterpenoids) [24] using renewable resources. Green synthesis of sitagliptin is ecologically friendly and emits substantially less waste than the first-generation approach and significantly removes watery waste streams [25].

The use of renewable feedstocks, particularly biomass, is a critical component of green chemistry. Using biomass for chemical processes cannot be regarded as an end in itself until all other green chemistry principles are meticulously applied. Hence, the principles of green chemistry are required to guide the entire biomass utility process. The core principles of green chemistry, which entail the efficiency of reactions, atom economy, moderated resource consumption, waste prevention, and increased safety of manufacturing processes and end products, all apply at all stages of biomass utility, from biomass generation and conversion to ultimate utilization of biobased products.

2.2 Atom Economy

Atom Economy entails the design of chemical reactions that consumes all starting materials and emits the least amount of toxic waste. The primary objective of the atom economy is to optimize the incorporation of starting ingredients into the ultimate result of any given industrial process. If maximum integration cannot be accomplished, then the levels of side products should preferably be minute and ecologically innocuous. Conversely, the reaction yield is solely concerned with the amount of the desired product that is recovered compared to the theoretical amount of the product. Along with the desired output, the atom economy considers all consumed reagents and undesired byproducts. Substitutions and eliminations, for example, account for the majority of uneconomical classical reactions in which intrinsic wastes are unavoidable. There is a fundamental difference between how a reaction yield and an atom economy yield are calculated [23].

2.3 Biocatalysis

Green chemistry emphasizes the deployment of biological catalysts to speed up chemical reactions to greatly reduce the amount of energy and resources consumed during the production of industrial products. In general, a bio-based economy entails multidisciplinary research efforts at the interface of biotechnology and chemical engineering, with an emphasis on the creation of environment-friendly chemo- and bio-catalytic modalities for the conversion of waste biomass into biochemicals, biofuels, and other bio-based products. In this regard, biocatalysis has a lot to offer. They are biodegradable and derived from renewable biomass. In addition, biocatalyst-based production processes generate less waste and use less energy than conventional ones because they operate in milder conditions [22]. Biocatalysis is a sustainable and green technology based on the ideas and measurements of sustainable development and green chemistry.

The tremendous break-even made in molecular biology and biotechnology over the last 20 years is primarily responsible for this progress [23]. Through the use of protein engineering, it is now possible to create completely new biocatalytic reactions that were not previously known to exist in nature as well as to optimize already existing enzymes. Enzymatic transformations that meet predetermined parameters are now developed with great ease, leading to inherently sustainable processes [24]. Consequently, this approach has been deployed effectively in the industrial production of active pharmaceutical compounds and other value-added industrial products [25]. Other biocatalysis engineering techniques, such as medium, substrate, and reactor engineering, are now applied in addition to protein engineering to increase the productivity, economy, and sustainability of biocatalytic reactions [26]. Moreover, enzyme stability is enhanced even more through immobilization, allowing for repeated use and improved performance as well as commercial viability. As a result, biocatalysis is being used extensively in the manufacturing of several valuable industrial chemical commodities, including active pharmaceutical ingredients [27]. For example, amidases, transaminases, and lipases, which catalyze amide bonds hydrolysis, synthesis of amines, and fats breakdown, respectively, are essential in the pharmaceutical industry [99]. Of note, biocatalysts such as alcohol dehydrogenases and nitrile hydratases are highly utilized in the production of fine chemicals (e.g., acrylamide, agrochemicals, fragrances, and flavors) due to their sustainability, selectivity, and amenability [100]. Besides, proteases and tyrosinase are extensively deployed in detergent making and the cosmetic industries to remove dead skin cells, regulate melanin production and reduce hyperpigmentation [101]. The food industry utilizes key enzymes such as amylases, lactase, and pectinases for wine brewing, production of dairy products like yogurt and cheese, and juice making, respectively [102]. Also, cellulases and hemicellulases are very important enzymes in biofuel production from lignocellulosic biomass

[103]. The *de novo* synthesis of these enzymes using SynBio technologies continue to open new frontiers in biotechnology and industrial operations. Moreover, it has been projected that the developing biobased economy associated with biocatalysis will further encourage its wider adoption in the future [28].

2.4 Designs for Degradation

The concept of design for degradation is targeted at creating chemical products that are easily degraded after use and pose no potential threat to the ecosystem [12]. In the realm of green chemistry, chemicals ought to be made in such a way that, after serving their purpose, they should be able to break down into innocuous byproducts and disappear from the environment. Unintentional hazards associated with the manufacture and use of chemicals pose terrible effects on human health and induce deplorable environmental damage. The lack of integrated thinking during the production and distribution of chemicals has frequently resulted in the manifestation of these adverse impacts on the environment [29]. Traditional industrial processes have not been able to adequately account for the pre- and post-market conditions of industrial products. Too many negative consequences are found after products and chemicals are dispersed throughout our environment, despite the robust testing systems [30]. In solving these problems, the first step is to ascertain the "molecular itinerary" of a product, which entails factoring and forecasting who, what, where, when, and why of an industrial product along its trajectory from production to degradation. This can be likened to a travel agency offering a comprehensive schedule for an extended, multi-city journey. When all the points on the itinerary tract are well considered, everyone is content, healthy, and makes it home safely, with unfavorable events either avoided or significantly reduced. These efforts are the core objectives of green chemistry [31].

2.5 Safer Solvents

Green chemistry promotes the use of non-flammable and non-toxic solvents that pose the least detrimental effect on the environment [21]. Solvents are widely understood to pose severe hazards to the environment. Also, one of the primary goals of green chemistry is to reduce solvent consumption. Furthermore, selecting the appropriate solvent can considerably improve the sustainability of a chemical production process. The use of so-called green solvents, such as supercritical fluids and ionic liquids, has also been extensively researched [32]. Notably, simple alcohols, Ionic liquids, and bio-based solvents, including d-limonene and cyrene are extensively used as green solvents in the chemical and pharmaceutical industries [104]. Notably, twelve (12) requirements for the conformity of green solvent have been proposed, viz; availability, price, recyclability, grade, synthesis, toxicity, biodegradability, performance, stability, flammability, storage, and renewability [33]. Nonetheless, the majority of solvent technologies that lead to increased sustainability are derived from the use of well-established and workable solvents. It is also clear that increases in business performance are necessary for the effective adoption of environmentally friendly procedures. Process chemists and engineers must work closely together to select the right solvents, use the fewest solvent classes possible in each step, steer clear of azeotropes and emulsions, optimize reflux or near-reflux conditions for high-temperature extended reactions, and, lastly, maximize solvent recovery and distillation in the process [34]. Similarly, close cooperation between chemical engineers and process chemists is necessary, as the latter are typically more skilled in azeotrope production, distillation, and process optimization [35]. In addition, several risk control techniques can be employed along the various chemical steps involved in the fabrication process to reduce environmental risks. The use of different precursor molecules, catalysts, solvents, and reagents, as well as alternating target product production, real-time process monitoring, and short-duration synthesis has aided the realization of green chemistry in industrial operations.

3. APPLICATION OF SYNBIO IN ENVIRONMENTAL MICROBIOLOGY

SynBio has been applied in environmental microbiology operations to produce biotreated systems capable of mitigating the levels of toxic recalcitrant organic pollutants, heavy metals, and other environmental contaminants in the environment. For example, breakthroughs in SynBio have allowed the development of engineered bacteria that can consume recalcitrant non-biodegradable waste such as plastic waste [36]. Synthetic microbes with optimized efficiency in sensing, degrading, and reporting toxic pollutants in the environment are now been designed. Also, the development of SynBio-based biosensors with customized abilities is now not only used as herbicides and pesticides but also applied to sites containing heavy metals or other environmental contaminants that need remediation [37]. SynBio enjoys enormous industrial applications for the implementation of the concept of green chemistry. The application of SynBio principles has enabled the fabrication of enzymatic modalities for the realization of renewable and environmental-friendly bio-products such as bioplastics and biofuels, renewing hopes for the actualization of clean energy and sustainable environment at the heart of industrialization [38,39].

3.1 Merits of SynBio in Environmental Microbiology

Recently, SynBio has shown great potential in re-engineering microorganisms with enhanced functionalities for performing more efficient biodegradation and bioremediation processes, resulting in more sustainable environments [40]. SynBio technology has improved the degradation of resistant compounds in polluted soil by optimizing the biodegradation capabilities of bacteria via genome manipulation [12]. Presently, microbial consortiums can be modified using SynBio-based technologies for improved biodegradation. A microbial consortium refers to a group of microorganisms working together to undertake a single complex metabolic activity. The design of synthetic microbial consortia with improved biodegradation and bioremediation outcomes is another huge accomplishment brought on by SynBio technology [41]. These microbial consortia are capable of degrading a broad range of pollutants in wastewater and other industrial effluents [40]. The metabolic functions of these synthetic microbes are engineered to exhibit excellent degrading abilities on certain environmental pollutants [14].

Environmental monitoring and biosensing have also seen massive improvement via the application of SynBio technology. In the last few years, SynBio-based engineered microorganisms have been introduced into the environment to screen and detect harmful compounds or adverse environmental conditions and today is seen as a powerful environmental monitoring and assessment tool [40]. Sequel to this, researchers now design microbial agents capable of detecting certain pollutants occurring in the environment. These microorganisms produce fluorescent proteins in response to target toxic substances and thus monitor the concentrations of these noxious chemicals in the environment (whether air, soil, or water) within certain limits [42].

3.2 SynBio-Based Bioremediation

Synthetic biology has numerous potentials and is being put to good use more and more in industrial microbial operations, particularly in bioremediation [12]. The deployment of engineered bacteria to degrade hazardous materials in the environment and restore the ecosystem is thought to be an efficient approach to bioremediation. These bioremediation efforts have been hugely successful via SynBio-based development of microbial entities capable of digesting environmental recalcitrant pollutants, including polycyclic aromatic hydrocarbons (PAHs), and Per- and polyfluoroalkyl substances (PFAS) as shown in Fig. 3 [43,44,45]. Currently, researchers are now able to construct key microbial biochemical pathways that effectively target the degradation of certain waste or pollutants, which fuels the pathways as substrates, and in some cases results in the synthesis of value-added products [12]. Also, toxic and environmental recalcitrant heavy metals, such as cadmium, mercury, lead, arsenic, and copper, which are capable of inflicting devastating adverse effects on human health as well as on the environment are now monitored and sequestered from the environment via SynBio techniques. In this regard, certain microorganisms have been engineered as biosensors capable of selectively detecting heavy metals in contaminated areas more rapidly and efficiently, as well as binding and removing these noxious compounds from the affected area [46].

Conventional bioremediation methods are impeded by several drawbacks. They require more time, remove or assimilate fewer pollutants, disrupt natural ecosystems by covering more land for extended periods, and cause unpleasant odors in the surrounding area [47,2]. For the greatest outcomes, scientists are therefore keen to find novel bioremediation strategies [48]. Application of synthetic biology has been shown to enhance bioremediation processes (Fig. 4). In this regard, [49] described synthetic biology as a boosting strategy in bioremediation. It has been demonstrated that this approach captures the metabolic and catabolic complexity while utilizing the synthetic capacity of the microbial population [50]. Basically, information required to develop synthetic microbial models for bioremediation are obtained by mining genes from appropriate databases [51]. Computer logic can then be used to determine how microbial cells interact with compounds that are resistant to their effects [52]. Combining these strategies can help develop microbes into novel and fascinating biological forms utilizing their innate metabolic ability [47].

Generally, the identification and removal of hazardous and recalcitrant heavy metals in the environment has been a key challenge to environmental scientists and this continues to pose a threat and has prompted the need to propose novel approaches to deal with this menace [53]. In a bid to address these problems, a study deployed SynBio-based genetic circuits and reporter functionalities to ensure higher sensitivity, greater effectiveness with various types of contaminated materials, and cost-efficiency. A detection range of 100 nM-1 μM and 100 nM-10 μM for P. fluorescens and E. coli, respectively was recorded. Another study by [54] used a pmerRBPmerlux genetic circuit to detect mercury in soil samples, in which the rate of release of mercury into the water from the soil was speed-up by using a rhamnolipid biosurfactant and a bioluminescent immobilized E. coli MC106 cell, which contained the genetic circuit. Progressively, [55] developed a cell-free

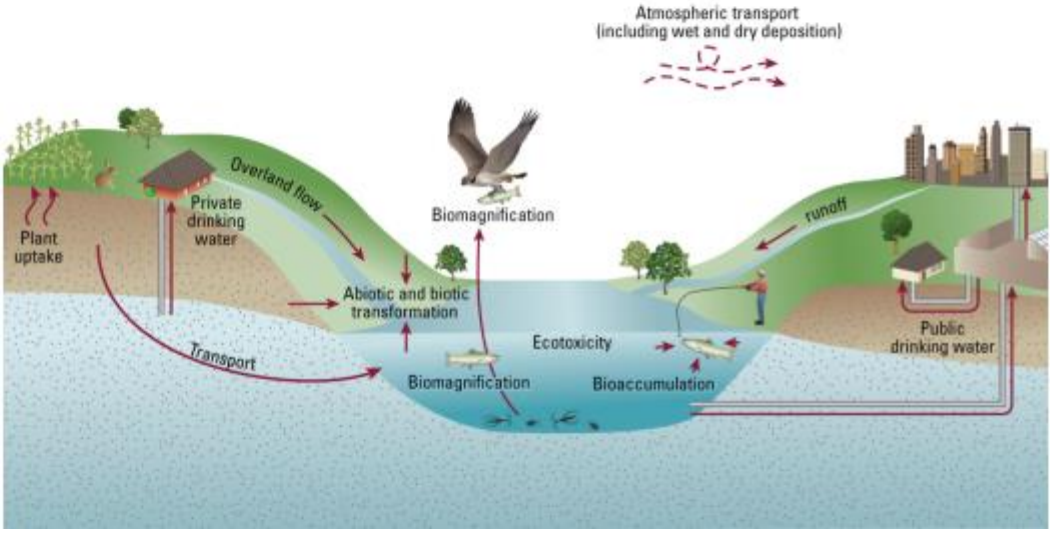

Fig. 3. Per-And Polyfluoroalkyl Substances from the Environment [45]

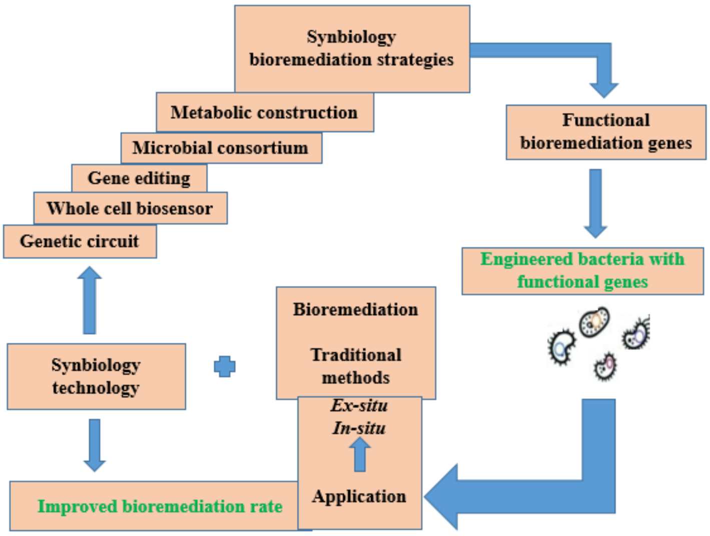

Fig. 4. SynBio-based strategies for improved bioremediation

system using an evolved mutant of ArsR that enabled efficient, sensitive detection of Arsenic with a limit of 3.65 µg/L which is within the limit given by WHO. In a study carried out by [56] to establish the most effective biosensor combination, thirty whole-cell cadmium biosensors were constructed using WCB KT-5-R with P. putida KT2440 as the host, and a gene circuit comprising mCherry and CadR. To boost the efficiency, a positive feedback amplification module and a larger reporter gene dose were introduced. From their result, whole-cell biosensors (WCBs) with the T7RNAP amplification module, p2T7RNAPmut-68, demonstrated great specificity and enhanced cadmium tolerance with a detection limit of 0.01 [57] engineered E. coli Rosetta that was able to express ribB and OprF with promoter PcusC and Pt7, respectively that could produce porin and detect Cu2+ to generate riboflavin. This modified strain's cell membrane permeability was increased, and the concentration of riboflavin generated (1.45-3.56 M) was correlated positively with Cu2+ levels (0-0.5 mM). Furthermore, increased production of riboflavin was observed upon activation of PcusC in the presence of Cu2+ in water. This strain was then employed in microbial fuel cell (MFC)-based biosensors. Resultantly, the liberation of riboflavin into the extracellular matrix by the OprF-encoded porin enhanced MFC voltage generation. A linear correlation was also recorded between Cu2+ at concentrations ranges of 0.1-0.5 mM and MFC biosensor voltage generation (248-407 mV), indicative of the suitability of this system in Cu2+ monitoring in drinking water [57].

3.3 Biosensors

Biosensors are analytical tools that translate electrical signals from a biological reaction [58]. There are several varieties of biosensors, such as enzyme-based, thermal, tissue-based, DNA, piezoelectric, immunosensors, and immunosensors. Biosensors are essentially required to have high specificity, be reusable, and be unaffected by physical conditions like pH and temperature [59]. Essentially, transcription-factor-based (TFB), RNA-based (RNAB), and two-component biosensors (TCBs) are examples of genetically encoded biosensors [60,61,62]. The TCB is composed of a transmembrane sensor histidine kinase (SK), which measures extracellular levels of a given metabolite, alongside an SK cognate cytoplasmic response regulator (RR), and an RR cognate promoter [63]. Specific metabolite concentrations within cells are detected by TFBs and RNABs [64]. Therefore, the variations in the spatial distribution of the metabolites that are identified dictate how these biosensors should be used.

3.3.1 Biosensor fabrication

The biosensor output and performance are optimized by using different engineering strategies to fine-tune the biosensor components (promoters, RBS, and operator) [65]. Additionally, biosensor specificity is being modified using RNA and protein domain swapping strategies [66]. The designed biosensors usually respond to the extracellular or intracellular level of a single specific compound by generating visible signals, such as bioluminescence or cell growth [67]. Hence, coupled with the desired biosensors and the diverse mutagenesis strategies, the intended genotype can be tested via high-throughput screening of the measurable phenotype. By doing this, TCBs can detect changes in the extracellular concentration of a target chemical substance and can be used in directed evolution [68]. Directed evolution is a valuable tool used for manipulating the structure and functions of protein by exploring natural evolution, but on an abridged duration. It allows for rapid selection of variants of biomolecules with more suitable properties required for a particular application [69,70]. Intracellular substances can be detected by TFBs and RNABs. Notably, the spatial distribution of the substances identified should determine which biosensor type is applied [71]. However, currently, the biggest constraint to this technique is to precisely and effectively construct these biosensors [59]. The primary source of time and labor expenditures associated with trial-and-error methods for producing the intended biosensors is the optimization of TF, SK, RR, and riboswitch expression levels and structures [72]. To address this issue, deep learning, and machine learning-based artificial intelligence technologies are starting to be included in the biosensor design process, greatly enhancing the accuracy and productivity of the final product [73]. [59] opined that because biosensor design does not yet have a unified large data-collecting method for artificial intelligence model training, it is premature to use artificial intelligence in biosensor design.

3.3.2 Coupling biosensors with omics technologies

Furthermore, it has been reported that biosensors could function more efficiently when combined with high-throughput omics technologies, ultimately affording a systems-level view of the organisms, macromolecules, and metabolites of study [74]. Data obtained from -omics studies could be leveraged to restore microbial activities and ecological functions, as well as discover molecular switches in microbial populations, such as genes linked to greenhouse gas production. The deployment of -omics technologies in microbial population studies has been very operative in establishing ecological hypotheses. It is insufficient to solely provide all-inclusive information regarding certain cause-and-effect conditions [75]. On the other hand, a reductionist approach that investigates the distinct impacts of individual microbial cells and their liberated biomolecules on environmental outcomes could be achieved using biosensors [76]. Biosensors can generate additional temporal and spatial clues on the activities of certain members of a given microbial community, the environmental determinants that stimulate cellular behaviors, and the impacts of the local environment on the bioavailability of biomolecules [77].

3.3.3 SynBio-Enhanced biosensors applications

SynBio technology has enabled the fabrication of improved biosensors used in environmental monitoring, which in turn has facilitated the production of clean water, void of heavy metal toxicity. A recent submission documented the discovery of a genetic circuit in bacteria that, in response to traces of heavy metal exposure (such as arsenic), produced chromophoric proteins. Investigators are now able to create biological systems that can react to and identify dangerous ubiquitous substances that are difficult to control, such as pesticides and herbicides, thanks to SynBio concepts [78]. Generally, advances in biosensor development have had significant impacts on the implementation of environmental monitoring, clean energy, medical diagnostics, improved agriculture, and food safety, in recent years. Recently, investigators and medical associations have switched focus toward using low-cost biosensors to test food and water pollutants, manage human biological processes, determine precise health diagnoses, and other applications [79]. Researchers and medical practitioners require safe and cost-effective methods of conducting research, guaranteeing public safety, and providing personalized health care to patients. Biosensors application is one of such approaches that can be simply implemented [80]. Biomedical diagnostic research is becoming increasingly important in the modern medical profession. The applications of biosensors include infectious disease screening and early diagnosis, chronic illness therapy, health management, and well-being monitoring. Improved biosensor technological capabilities enable disease detection and tracking of the body's reaction to therapy [81].

Basically, a biosensor comprises three modules, viz; the sensitive biological element, which attaches to the target molecule, the transducer, which converts the interaction into a measurable signal; and the signal processor, which presents the result in an easy-to-read manner. Usually, DNA circuit diagrams, which show details on the genes in each module, the regulation of gene expression, and the interactions between module components, are used to illustrate biosensors. Biosensor input and output relationships usually have a sigmoidal form. A sensor's dynamic range is the difference between its maximum input before saturation and the threshold environmental input required for activation, also known as the limit of detection. The recent influx of novel synthetic biology modules has significantly expanded the spectrum of detectable inputs, the intricacy and functionalities of processing modules, and the range of conditions where outputs can be identified. Thus, there is an opportunity to develop biosensors that address fundamental questions in fields such as environmental engineering, biogeochemistry, geobiology, and ecosystem ecology. Although a few early tools were utilized in environmental samples [82,83], these resources have not been widely accessible to the Earth and environmental science communities.

Furthermore, advanced biosensors provide an opportunity to investigate unresolved environmental research inquiries. This includes detecting biogenic substances at micro concentrations, observing organisms' interactions, monitoring how environmental cues influences cell-cell signaling, quantifying variations in horizontal gene transfer (HGT) in the changing environments, and recording information in cells while preserving spatial and temporal heterogeneity in the natural environment. Biosensors, which continuously capture information at the micron scale, offer unique opportunities for studying ecosystems from a microbial perspective. Moreover, the evolving innovations of SynBio technology have pulled through the development of an avalanche of improved biosensors. These encompass the creation of more sophisticated genetic circuits and approaches for fine-tuning circuit components for environmental applications. SynBio principles have made feasible the development of in-vitro and in-vivo biosensors [84]. Originally, biosensors were developed by programming easily modifiable and rapidly growing bacteria strains. However, while these bacteria laid the foundation of biosensor creations, the recent growing initiative to broaden the horizon of reliable and programmable microbial strains via SynBio concepts remains the mainstay of modern biotechnology [85]. Biosensors derived from environmental microbes could prove valuable in reporting new types of information within more realistic settings. For instance, enabling biosensors to report on their own experiences in situ within environmental matrices. Recent innovations in cell-free biosensors have facilitated the creation of fast and easily deployable sensors capable of monitoring macroscale spatial and temporal heterogeneity at field sites. This is analogous to point-of-care diagnostics commonly used in biomedical applications.

3.4 Advances of SynBio in Harnessing Environmental Sustainability

Despite the significant improvement in the standard of living synthetic chemistry and the chemical industry have offered humans, they have also posed tremendous negative impacts on human health and the environment in terms of toxic waste, and pollution, and represent serious threats to public health [30]. The growing awareness and rising need for a clean environment geared in part by global warming and environmental sustainability have driven the emerging concept of green chemistry, which is the act of designing synthetic processes and products in ways that generate the least toxic compounds as well as reduces the requirements of energy and natural resources [86] nature has contributed immensely to the actualization of this goal. Several years of evolution have resulted in an extremely diversified assortment of natural products and their associated enzymatic processes [87]. Synbiologists are taking advantage of the wealth of possibilities nature affords to design chemicals and synthetic processes in more renewable forms to mitigate pollution at all phases of production, which is the mainstay of the goal of green chemistry [88]. There are many advantages that biosynthetic technologies have over industrial chemical synthesis. Naturally, enzymes catalyze their specific reactions most efficiently and frequently under certain optimized conditions, including normal temperatures and pressures, neutral pH, and aqueous solutions, and allow for the simultaneous operation of a variety of enzymes within the same medium, such as organelles or cells [89]. This concept has enhanced the creation of multiple-step synthetic pathways for the in vivo production of complex compounds from less expensive and renewable feedstock (Fig. 5).

The SynBio-based fabrication of microbial ‘living factories’ that could produce valuable chemicals that were formerly unfeasible in nature or initially feasible only via very expensive routes is one notable impact of synthetic biology in the chemical industry [1]. For instance, the bioplastic monomers 1,3-propanediol and styrene are readily synthesized using biosynthetic pathways and engineered microbial biocatalysts fabricated *de novo* [38]. Synbiologist deploy retrobiosynthetic strategy to design and fabricate novel metabolic pathways akin to retrosynthetic schemes deployed by organic chemists for the synthesis of certain target molecules [38]. The concept of engineering retrobiosynthetic pathway has prompted the engineering of newer routes that displaces the limitations of nature's biosynthetic capabilities [44]. SynBio also aid in the actualization of green chemistry by enhancing the exploration of the natural diversity of enzymes to construct enzymatic cascades that catalyze the conversion of renewable substrates to specific products of interest [41].

Engineered organisms can produce a wide range of key compounds from renewable resources, waste, and potentially harmful substances such as carbon dioxide.

3.5 Potential Impacts of SynBio on the Environment and Society

The possible impacts of SynBio on the human community and its environment are broad and complicated. Although SynBio renders clear-cut potential to address several sustainable development goals as well as provide solutions to deal with environmental and societal bottlenecks, it also raises crucial social and ethical concerns [90]. The design and deployment of synthetic microbes or biomacromolecules into the environment can result in alteration in the normal composition of ecosystems which could ultimately be detrimental to human health. The high possibility of spreading genetically modified microbes into natural populations, which could sprout unintended repercussions, poses great concerns among policymakers [91]. There are also several social and ethical concerns associated with SynBio as pertain to the main beneficiaries of the technology and risk bearers. Therefore, it is necessary to consider a case-by-case basis to achieve a balanced compensation for beneficial attributes of SynBio technologies as well as considering possible detrimental outcomes for vulnerable groups [92]. Hence, it would be appropriate to design and implement regulatory frameworks regarding the application of SynBio technologies.

3.6 Sustainability, Biotechnology, and Global Solutions

Synthetic biology operates as a revolutionizing field that combines engineering, biotechnology, and biology principles to fabricate novel biosystems or redesign existing ones. SynBio applications are consistent with key concepts like the circular economy, biotechnology innovations, and resilience to global challenges, affording improved modalities for actualizing sustainability goals, resource efficiency, and global health [105]. Notably, SynBio is projected to aid the circular economy as it facilitates the production of bio-based materials and industrial procedures that upholds the tenets of green chemistry, resources recycling of and minimizes waste emission [106]. For example, the use of synthetic microbes to remove plastic waste from the environment and the valorization of agricultural residues for the production of biodegradable products [36]. This paradigm shift from unsustainable production to a regenerative and closed-loop process with reduced dependence on fossil fuels and its environmental impact is the future direction of environmental microbiology and industrial processes.

In addition, advances in SynBio techniques have been instrumental in engineering and biotechnological innovations via its capacity to create highly efficient and intended biological systems. Microbial factories and engineered biocatalysts are utilized to improve the sustainability of industrial processes, lower energy demands and waste emission [107]. They offer solutions to issues such as climate change, food security, and energy sustainability [108]. Moreover, synthetic cells are recruited to capture carbon dioxide from the atmosphere or convert it into useful byproducts. Besides, the progressive global transition to cleaner energy and adoption to biofuels and alternative industrial products [109].

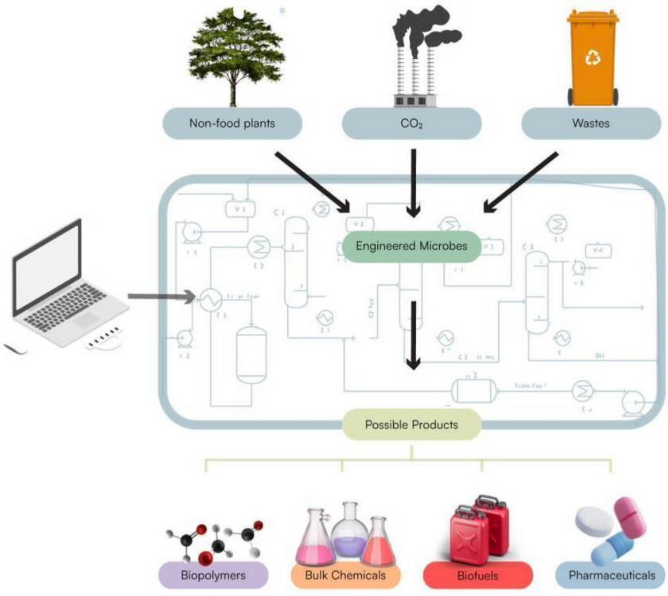

Fig. 5. A schematic of the possible contribution of SynBio to green chemistry

4. FUTURE DIRECTIONS OF SYNBIO TECHNOLOGY ON MODERN SCIENCE

Several SynBio applications such as genome reduction, orthogonal biosystems, genome editing, and DNA synthesis have pilot key advancements in modern biology in terms of genetic manipulations for industrial applications.

4.1 Genome Reduction

Genome reduction is the purposeful minimizing of an organism's genetic material, removing non-essential genes to generate streamlined, minimum genomes. This technique has notable significance in synthetic biology applications since it enables researchers to create organisms with improved metabolic pathways, decreased complexity, and greater stability [2]. Such shortened genomes provide a solid foundation for creating microbes with specific, customized capabilities, whether for industrial production, medicinal uses, or environmental interventions. Naturally developed organisms have complex genomes that allow them to thrive in their environments. However, the complexity of genomes frequently hinders their comprehensive elucidation and limits their biotechnology exploration [110]. Minimal genomes, on the other hand, show decreased complexity, which improves engineerability, greater biosynthetic capacity by removing extraneous genetic components, and less resistance to thorough characterization (Fig. 5) [111,112].

4.2 Orthogonal Biosynthesis

Orthogonal biosystems toggles further introducing completely new-fangled biosystems that vary from the native operations of living organisms. These biological pathways function sufficiently, deploying alternative sets of substrates, such as synthetic amino acids or novel genetic transcripts engineered to function side by side with natural systems [3]. The concepts of orthogonality avail a valuable tool for diversifying the biochemical operations and capabilities of cells, facilitating the synthesis of new and improved gene products, essential biopolymers as well as designing synthetic lifeforms with altered biochemistry [4]. Orthogonal biosynthesis has broadened scientific horizons and interpretations of natural phenomena and open doors for the fabrication of novel modalities for biotechnological innovations [112].

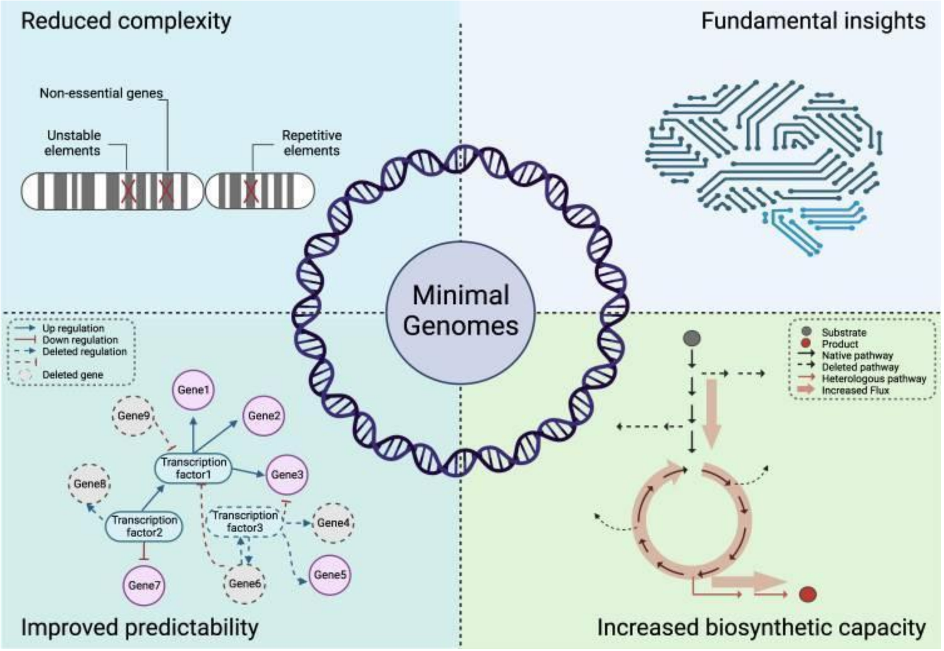

Fig. 6. Applications of synthetic and synthetic-minimal genomes

Genome reduction allows for better engineering and elucidation of genome biology, decreasing genome complexity by deleting non-essential genes and enhancing genome stability by removing repetitive regions. The predictability of rational design is enhanced with reduced complexity in metabolic and regulatory networks. Redundant genes and gene products are also eliminated to upscale biosynthetic capacity. In addition, new-to-nature genomic constructs for high-throughput analysis are also tested [2].

4.3 Genome Editing

In addition, advances in genome editing, such as the utilization of novel gene editing paradigms such as the CRISPR-Cas9 system hold huge transformative potentials in genetic engineering and represent an efficient tool for the precise alteration and manipulation of DNA sequences within living organisms. This gene editing tool has food applications across several fields of endeavors, including sustainable agriculture, green chemistry and bioremediation [113,114]. Ultimately, precision and ease in genome editing have enhanced investigations in biotechnology, medicine, and agriculture and herald a new era of genomic manipulations. In addition, *de novo* synthesis of DNA sequences at high scale and accuracy has enabled the development of the entire genome of living organisms, design of complex genetic circuitries, and artificial genetic constructs that when inserted into a target organism could endow them with certain properties of biotechnological importance [115].

4.4 Safety Concerns and Ethical Issues

Among the drawbacks of SynBio are its safety profile and that of any of its end-products. The major safety concerns focus on the possibility of accidental escape into nature by these artificial microbes, which could cause harm to human health or have negative environmental impacts [93]. A case of reference is the recent COVID-19 outbreak that claimed many lives [94]. Therefore, learning from experience with such heinous threats, many ethical issues and safety concerns have been raised about the application of SynBio technologies. For policymakers, the danger that artificial cells or their products will be abused and weaponized, in addition to the fear that artificial pathogens could mutate and become invasive or harmful, then spawn diseases affecting public health or even distorting ecosystems are the major hindrances to the full adoption of this innovation [95]. Therefore, many experts have come up with the view that safety measures and standards governing artificial microorganisms should be continuously reviewed at each stage of their progress to ensure they are not harmfully deployed. Moreover, the fear that some of these synthetic organisms might cause unexpected threats to human health or the environment in the future has also caused many researchers' ethical concerns [96]. In fact, the ethical considerations and moral implications of creating life in the lab are also worrisome [97]. As a result, several regulatory frameworks have already been developed with the aid of which it will be possible to monitor global conformity with respect for ethical values when designing and using synthetic cells [97,98].

5. CONCLUSION

Synthetic biology holds tremendous prospects in the actualization of green chemistry and bioremediation of polluted environments and offers a remarkable shift towards the materialization of sustainable and environmentally responsible technologies. This has been possible due to the ability of this emerging technology to design and engineer biological systems with high precision, availing tools to curtail the environmental footprint of chemical processes and products itinerary. The principles of green chemistry emphasize mainly on the significant reduction in the use and emission of hazardous substances in the production pipeline and the use of renewable resources as feedstocks in industrial operations. SynBio has been instrumental in the realization of green chemistry by virtue of its role in the design of greener Son industrial protocols, development of bio-based substitutes to petroleum-based products, manufacturing biodegradable materials, and substantial decline in energy utility and waste emission during production.

Furthermore, the application of synthetic biology technologies has led to the fabrication of novel synthetic organisms that could effectively drive bioremediation processes, carbon capturing, and the biodegradation of recalcitrant pollutants. This has proposed the innovative potential of SynBio technology in tackling the environmental challenges caused by pollution, climate change, and depletion of natural resources. Also, the actualization of the circular economy, where waste emission is drastically curtailed and natural resources are conserved are greatly encouraged in industries that deploys synthetic biology in green synthesis and operations. Thus, the future directions for the realization of green chemistry and environmental solutions from industry to environment is the responsible application of SynBio technologies in most of its operational pipeline. SynBio promises to tremendously transform and reshape industrial operations, optimize resource utility, and contribute immensely to environmental sustainability across the globe. However, the technology is faced with several ethical and regulatory bottlenecks, which have chiefly limited its applications and implementations. Nevertheless, focusing on the prospects of this technology, such as the deployment of artificial intelligence and non-genetic biomolecular entities to optimize and design synthetic systems comes with many expectations.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ball P. Synthetic biology: engineering nature to make materials. MRS Bulletin. 2018;43:477-484. DOI:10.1557/mrs.2018.191
2. Xu X, Meier F, Blount BA, et al. Trimming the genomic fat: minimising and re-functionalising genomes using synthetic biology. Nat Commun. 2023;14:1984. Available:https://doi.org/10.1038/s41467-023-37748-7.
3. Mohler K, Moen JM, Rogulina S, Rinehart J. System-wide optimization of an orthogonal translation system with enhanced biological tolerance. Mol Syst Biol. 2023;19(8). Available:https://doi.org/10.15252/msb.202110591.
4. Wang X, Liang Q, Luo Y, Ye J, Yin Yu Y, Chen F. Engineering the next generation of theranostic biomaterials with synthetic biology. Bioact Mater. 2024;32:514-529. Available:https://doi.org/10.1016/j.bioactmat.2023.10.018.
5. Maerkl SJ. Bottom-up construction of complex biomolecular systems with cell-free synthetic biology. Front Bioeng Biotechnol. 2020;8:213. Available:https://doi.org/10.3389/fbioe.2020.00213.
6. Jiménez-Díaz V, Pedroza-Rodríguez AM, Ramos-Monroy O, Castillo-Carvajal LC. Synthetic Biology: A New Era in Hydrocarbon Bioremediation. Processes. 2022;10(4):712. Available:https://doi.org/10.3390/pr10040712
7. Kumar M, Seth A, Singh AK, Rajput MS, Sikandar M. Remediation strategies for heavy metals contaminated ecosystem: A review. Environmental and Sustainability Indicators. 2021;12: 100155. DOI:10.1016/j.indic.2021.100155
8. Moloantoa KM, Khetsha ZP, van Heerden E, Castillo JC, Cason ED. Nitrate Water Contamination from Industrial Activities and Complete Denitrification as a Remediation Option. Water. 2022;14(5): 799. Available:https://doi.org/10.3390/w14050799
9. Toma P, Frittelli M, Apergis N. The economic sustainability of optimizing feedstock imports with environmental constraints. Socio-Economic Planning Sciences. 2023;87:101581. Available:https://doi.org/10.1016/j.seps.2023.101581
10. Siddiqua A, Hahladakis JN, Al-Attiya WAK. An overview of the environmental pollution and health effects associated with waste landfilling and open dumping. Environmental Science and Pollution Research. 2022;29:58514-58536. Available:https://doi.org/10.1007/s11356-022-21578-z
11. Kharissova OV, Kharisov BI, Oliva González CM, Méndez YP, López I. Greener synthesis of chemical compounds and materials. R Soc Open Sci. 2019 ;6(11):191378. Available:https://doi.org/10.1098/rsos.191378
12. Salem SS. A mini review on green nanotechnology and its development in biological effects. Arch Microbiol. 2023;205: 128. Available:https://doi.org/10.1007/s00203-023-03467-2
13. Aziz T, Ullah A, Ali A, Shabeer M, Shah MN, Haq F, Khan FU. Manufactures of bio-degradable and bio-based polymers for

bio-materials in the pharmaceutical field. J Appl Polym Sci. 2022;139(29). Available:https://doi.org/10.1002/app.52624

14. Almohasin JA, Balag J, Miral VG, Moreno RV, Tongco LJ, Lopez ECR. Green Solvents for Liquid–Liquid Extraction: Recent Advances and Future Trends. Eng Proc. 2023;56(1):174.
Available:https://doi.org/10.3390/ASEC2023-16278
15. Ferreira-Leitão VS, Cammarota MC, Gonçalves Aguieiras EC, Vasconcelos de Sá LR, Fernandez-Lafuente R, Freire DMG. The Protagonism of Biocatalysis in Green Chemistry and Its Environmental Benefits. Catalysts. 2017;7(1):9.
Available:https://doi.org/10.3390/catal7010009
16. Bala S, Garg D, Thirumalesh BV, Sharma M, Sridhar K, Inbaraj BS, Tripathi M. Recent Strategies for Bioremediation of Emerging Pollutants: A Review for a Green and Sustainable Environment. Toxics. 2022;10(8):484-895.
17. Somayaji A, Sarkar S, Balasubramaniam S, Raval R. Synthetic biology techniques to tackle heavy metal pollution and poisoning. Synth Syst Biotechnol. 2022;7(3):841 -846.
Available:https://doi.org/10.1016/j.synbio.2022.04.007
18. Cao Z, Yan W, Ding M, Yuan Y. Construction of microbial consortia for microbial degradation of complex compounds. Front Bioeng Biotechnol. 2022;10:1-14.
19. Aminian-Dehkordi J, Rahimi S, Golzar-Ahmadi M, Singh A, Lopez J, Ledesma-Amaro R, Mijakovic I. Synthetic biology tools for environmental protection. Biotechnol Adv. 2023;68:108239.
20. Liu Y, Feng J, Pan H, Zhang X, Zhang Y. Genetically engineered bacterium: Principles, practices, and prospects. Front Microbiol. 2022;13:1-15.
21. Widder S, Allen R, Pfeiffer T, et al. Challenges in microbial ecology: building predictive understanding of community function and dynamics. ISME J. 2016;10:2557-2568.
Available:https://doi.org/10.1038/ismej.2016.45
22. de Marco BA, Rechelo BS, Tótoli EG, Kogawa AC, Salgado HRN. Evolution of green chemistry and its multidimensional impacts: A review. Saudi Pharm J. 2019; 27(1):1-8.
https://doi.org/10.1016/j.jsps.2018.07.011
23. Mani V, Park S, Kim JA, Lee SI, Lee K. Metabolic Perturbation and Synthetic Biology Strategies for Plant Terpenoid Production—An Updated Overview. Plants. 2021; 10(10):2179.
Available:https://doi.org/10.3390/plants10102179
24. Gutiérrez S, Overmans S, Wellman GB, Vasilios VG, Oviedo C, Gede M, et al. A green alternative to fragrant agarwood sesquiterpenoid production. bioRxiv; 2023.
Available:https://doi.org/10.1101/2023.10.06.561217.
25. Hansen KB, Hsiao Y, Xu F, Rivera N, Clausen A, Kubryk M, Krska S, Rosner T, Simmons B, Balsells J, Ikemoto N, Sun Y, Spindler F, Malan C, Grabowski EJ, Armstrong JD 3rd. Highly efficient asymmetric synthesis of sitagliptin. J Am Chem Soc. 2009 ;131(25):8798-804.
DOI: 10.1021/ja902462q.
Sheldon RA, Woodley JM. Role of Biocatalysis in Sustainable Chemistry. Chem Rev. 2017;118(2):801-838.
Available:https://doi.org/10.1021/acs.chemrev.7b00203
Li C, Zhang R, Wang J, Wilson LM, Yan Y. Protein Engineering for Improving and Diversifying Natural Product Biosynthesis. Trends Biotechnol. 2020;38(7):729-744.
Available:https://doi.org/10.1016/j.tibtech.2019.12.008
France SP, Lewis RD, Martinez CA. The evolving nature of biocatalysis in pharmaceutical research and development. J Chem Theory Comput. 2023;3(3):715-735.
Available:https://doi.org/10.1021/jacsau.2c00712
26. Woodley JM. New Frontiers in Biocatalysis for Sustainable Synthesis. Curr Opin Green Sustainable Chem; 2019.
Available:https://doi.org/10.1016/j.cogsc.2019.08.006
27. Sheldon RA, Basso A, Brady D. New frontiers in enzyme immobilisation: robust biocatalysts for a circular bio-based economy. Chem Soc Rev. 2021;50(10): 5850–5862.
Available:https://doi.org/10.1039/d1cs00015
28. Lokko Y, Heijde M, Schebesta K, Scholtès P, Van Montagu M, Giacca M.

Biotechnology and the bioeconomy—Towards inclusive and sustainable industrial development. New Biotechnol. 2018;40:5–10.
Available:https://doi.org/10.1016/j.nbt.2017.06.005

29. Ostad-Ali-Askari K. Management of risk substances and sustainable development. Appl Water Sci. 2022;12:65.
Available:https://doi.org/10.1007/s13201-021-01562-7
30. Naidu R, Biswas B, Willett IR, Cribb J, Kumar Singh B, Paul Nathanail C, et al. Chemical pollution: A growing peril and potential catastrophic risk to humanity. Environ Int. 2021;156:106616.
Available:https://doi.org/10.1016/j.envint.2021.106616
31. Anastas N, Miller GW. A Farewell to Harms: The Audacity to Design Safer Products. Toxicol Sci. 2018;161(2):211-213.
Available:https://doi.org/10.1093/toxsci/kfx288
32. Carpentieri S, Soltanipour F, Ferrari G, Pataro G, Donsì F. Emerging Green Techniques for the Extraction of Antioxidants from Agri-Food By-Products as Promising Ingredients for the Food Industry. Antioxidants. 2021;10:1417.
Available:https://doi.org/10.3390/antiox10091417
33. Armenta S, Esteve-Turrillas EA, Garrigues S, de la Guardia M. Alternative green solvents in sample preparation. Green Anal Chem. 2022;1:100007.
Available:https://doi.org/10.1016/j.greeac.2022.100007
34. Valentini F, Vaccaro L. Azeotropes as Powerful Tool for Waste Minimization in Industry and Chemical Processes. Molecules. 2020;25(22):5264.
Available:https://doi.org/10.3390/molecules25225264
35. Kianinia M, Abdoli SM. The Design and Optimization of Extractive Distillation for Separating the Acetone/n-Heptane Binary Azeotrope Mixture. ACS Omega. 2021; 6(34):22447–22453.
Available:https://doi.org/10.1021/acsomega.1c03513
36. Xiang L, Li G, Wen L, Su C, Liu Y, Tang H, Dai J. Biodegradation of aromatic pollutants meets synthetic biology. Synth Syst Biotechnol. 2021;6(3):153-162.
37. Hara TO, Singh B. Electrochemical biosensors for detection of pesticides and heavy metal toxicants in water: recent trends and progress. ACS ES&T Water. 2021;1(3):462–478.
38. Nielsen DR, Moon TS. From promise to practice. The role of synthetic biology in green chemistry. EMBO Rep. 2013;14 (12):1034-1338.
39. Osman AI, Elgarahy AM, Eltaweil AS, et al. Biofuel production, hydrogen production and water remediation by photocatalysis, biocatalysis and electrocatalysis. Environ Chem Lett. 2023;21:1315–1379.
Available:https://doi.org/10.1007/s10311-023-01581-7
40. Rafeeq H, Afsheen N, Rafique S, Arshad A, Intisar M, Hussain A, Bilal M, Iqbal HMN. Genetically engineered microorganisms for environmental remediation. Chemosphere. 2023;310: 136751.
41. Adamu KS, Bichi YH, Nasiru AY, Babangida AM, Umar MM, Usman G, Muhammad R. Review: Synthetic Microbial Consortia in Bioremediation and Biodegradation. Int J Res Innov Appl Sci. 2023;8(7):232.
Available:https://doi.org/10.51584/IJRIAS
42. Chaudhary P, Xu M, Ahamad L, Chaudhary A, Kumar G, Adeleke BS, Verma KK, Hu DM, Širić I, Kumar P, Popescu SM, Abou FS. Application of synthetic consortia for improvement of soil fertility, pollution remediation, and agricultural productivity: a review. Agronomy. 2023;13:643-653.
43. Tran KM, Lee HM, Thai TD, Shen J, Eyun SI, Na D. Synthetically engineered microbial scavengers for enhanced bioremediation. J Hazard Mater. 2021;419: 126516.
Available:https://doi.org/10.1016/j.jhazmat.2021.126516
44. Young NA, Lambert RL, Buch AM, Dahl CL, Harris JD, Barnhart MD, Sitko JC, Steel JJ. A synthetic biology approach using engineered bacteria to detect perfluoroalkyl substance (PFAS) contamination in water. Mil Med. 2021; 186(Supplement_1):801–807.
Available:https://doi.org/10.1093/milmed/usaa367
45. Samuel HS, Okibe G, Undie DA, Ochepo E. Carbon-Based Adsorbent for Remediation of Per-And Polyfluoroalkyl Substances from Industrial Wastewater. Appl J Environ Eng Sci. 2024;10(2): 85-98.

Available:https://doi.org/10.48422/IMIST.PRSM/ajees-v10i2.48765

46. Thai TD, Lim W, Na D. Synthetic bacteria for the detection and bioremediation of heavy metals. Front Bioeng Biotechnol. 2023;11:1178680. Available:https://doi.org/10.3389/fbioe.2023.1178680
47. Dangi AK, Sharma B, Hill RT, Shukla P. Bioremediation through microbes: systems biology and metabolic engineering approach. Crit Rev Biotechnol. 2019;39(1): 79–98. Available:https://doi.org/10.1080/07388551.2018.1500997
48. Jaiswal S, Shukla P. Alternative Strategies for Microbial Remediation of Pollutants via Synthetic Biology. Front Microbiol. 2020; 11:808. Available:https://doi.org/10.3389/fmicb.2020.00808
49. Dvořák P, Nikel PI, Damborský J, de Lorenzo V. Bioremediation 3.0: engineering pollutant-removing bacteria in the times of systemic biology. Biotechnol Adv. 2017;35:845–866. Available:https://doi.org/10.1016/j.biotechadv.2017.08.001
50. Jacquiod S, Demanèche S, Franqueville L, Ausec L, Xu Z, Delmont TO, et al. Characterization of new bacterial catabolic genes and mobile genetic elements by high throughput genetic screening of a soil metagenomic library. J Biotechnol. 2014; 190:18–29. Available:https://doi.org/10.1016/j.jbiotec.2014.03.036
51. Fajardo C, Costa G, Nande M, Botías P, García-Cantalejo J, Martín M. Pb, Cd, and Zn soil contamination: monitoring functional and structural impacts on the microbiome. Appl Soil Ecol. 2019;135:56–64.
52. Kim B, Kim WJ, Kim DI, Lee SY. Applications of genome-scale metabolic network model in metabolic engineering. J Ind Microbiol Biotechnol. 2015;42:339–348. Available:https://doi.org/10.1007/s10295-014-1554-9
53. Vardhan KH, Kumar PS, Panda RC. A review on heavy metal pollution, toxicity and remedial measures: Current trends and future perspectives. J Mol Liq. 2019; 290:111197. Available:https://doi.org/10.1016/j.molliq.2019.111197
54. Petänen T, Virta M, Karp M, Romantschuk M. Construction and use of broad host range mercury and arsenite sensor plasmids in the soil bacterium Pseudomonas fluorescens OS8. Microb Ecol. 2001;41(4):360–368. Available:https://doi.org/10.1007/s002480000095
55. Wang L, Song J, Zhang W. Tianjin Biosecurity Guidelines for codes of conduct for scientists: Promoting responsible sciences and strengthening biosecurity governance. J Biosaf Biosecur. 2021;3(2):82-83.
56. Jia X, Liu T, Ma Y, Wu K. Construction of cadmium whole-cell biosensors and circuit amplification. Appl Microbiol Biotechnol. 2021;105(13):5689-5699. Available:https://doi.org/10.1007/s00253-021-11403-x
57. Zhou T, Li R, Zhang S, Zhao S, Sharma M, Kulshrestha S, et al. A copper-specific microbial fuel cell biosensor based on riboflavin biosynthesis of engineered Escherichia coli. Biotechnol Bioeng. 2021; 118(1):210-222. Available:https://doi.org/10.1002/bit.27563
58. Mehrotra P. Biosensors and their applications - A review. J Oral Biol Craniofac Res. 2016;6(2):153-159. Available:https://doi.org/10.1016/j.jobcr.2015.12.002
59. Mao Y, Huang C, Zhou X, Han R, Deng Y, Zhou S. Genetically Encoded Biosensor Engineering for Application in Directed Evolution. J Microbiol Biotechnol. 2023; 33(10):1257-1267. Available:https://doi.org/10.4014/jmb.2304.04031
60. Mahr R, Frunzke J. Transcription factor-based biosensors in biotechnology: current state and future prospects. Appl Microbiol Biotechnol. 2016;100(1):79-90. Available:https://doi.org/10.1007/s00253-015-7090-3
61. Mitchler MM, Garcia JM, Montero NE, Williams GJ. Transcription factor-based biosensors: a molecular-guided approach for natural product engineering. Curr Opin Biotechnol. 2021; 69:172-181. Available:https://doi.org/10.1016/j.copbio.2021.01.008
62. Jeon Y, Lee Y, Kim K, Jang G, Yoon Y. Transcription Factor-Based Biosensors for Detecting Pathogens. Biosensors (Basel). 2022;12(7):470.

Available:https://doi.org/10.3390/bios12070470

63. Ishii E, Eguchi Y. Diversity in Sensing and Signaling of Bacterial Sensor Histidine Kinases. Biomolecules. 2021;11(10):1524. Available:https://doi.org/10.3390/biom11101524
64. Mo GC, Ross B, Hertel F, Manna P, Yang X, Greenwald E, Booth C, Plummer AM, Tenner B, Chen Z, Wang Y, Kennedy EJ, Cole PA, Fleming KG, Palmer A, Jimenez R, Xiao J, Dedecker P, Zhang J. Genetically encoded biosensors for visualizing live-cell biochemical activity at super-resolution. Nat Methods. 2017;14(4): 427-434. Available:https://doi.org/10.1038/nmeth.4221
65. Ding N, Zhou S, Deng Y. Transcription-factor-based biosensor engineering for applications in synthetic biology. ACS Synth Biol. 2021;10:911–922. Available:https://doi.org/10.1021/acssynbio.0c00252
66. Lim HG, Jang S, Jang S, Seo SW, Jung GY. Design and optimization of genetically encoded biosensors for high-throughput screening of chemicals. Curr Opin Biotechnol. 2018;54:18–25. Available:https://doi.org/10.1016/j.copbio.2018.01.011
67. Zhou S, Alper HS, Zhou J, Deng Y. Intracellular biosensor-based dynamic regulation to manipulate gene expression at the spatiotemporal level. Crit Rev Biotechnol. 2022;43:646–663. Available:https://doi.org/10.1080/07388551.2022.2040415
68. Yang J, Kim B, Kim GY, et al. Synthetic biology for evolutionary engineering: from perturbation of genotype to acquisition of desired phenotype. Biotechnol Biofuels. 2019;12:113. Available:https://doi.org/10.1186/s13068-019-1460-5
69. Sellés Vidal L, Isalan M, Heap JT, Ledesma-Amaro R. A primer to directed evolution: current methodologies and future directions. RSC Chem Biol. 2023; 4(4):271-291. Available:https://doi.org/10.1039/d2cb00231k
70. Yu W, Xu X, Jin K, Liu Y, Li J, Du G, Lv X, Liu L. Genetically encoded biosensors for microbial synthetic biology: from conceptual frameworks to practical applications. Biotechnol Adv. 2023;62: 108077. Available:https://doi.org/10.1016/j.biotechadv.2022.108077
71. Tellechea-Luzardo J, Stiebritz MT, Carbonell P. Transcription factor-based biosensors for screening and dynamic regulation. Front Bioeng Biotechnol. 2023; 11:1118702. Available:https://doi.org/10.3389/fbioe.2023.1118702
72. Hernández-Ortega EP, van der Meulen S, Kuijpers LJ, Kok J. Riboswitch RSthiT as a Molecular Tool in Lactococcus lactis. Appl Environ Microbiol. 2022;88(4). Available:https://doi.org/10.1128/AEM.01764-21
73. Mowbray M, Savage T, Wu C, Song Z, Cho BA, Del Rio-Chanona EA, Zhang D. Machine learning for biochemical engineering: A review. Biochem Eng J. 2021;172:108054. Available:https://doi.org/10.1016/j.bej.2021.108054
74. Kaczmarek JA, Prather KLJ. Effective use of biosensors for high-throughput library screening for metabolite production. J Ind Microbiol Biotechnol. 2021;48(9-10). Available:https://doi.org/10.1093/jimb/kuab049
75. Li M, Wen J. Recent progress in the application of omics technologies in the study of bio-mining microorganisms from extreme environments. Microb Cell Fact. 2021;20(1):178. Available:https://doi.org/10.1186/s12934-021-01671-7
76. Tiquia-Arashiro S, Li X, Pokhrel K, Kassem A, Abbas L, Coutinho O, Kasperek D, Najaf H, Opara S. Applications of Fourier Transform-Infrared spectroscopy in microbial cell biology and environmental microbiology: advances, challenges, and future perspectives. Front Microbiol. 2023; 14:1304081. Available:https://doi.org/10.3389/fmicb.2023.1304081
77. Tan C, Kalhoro MT, Faqir Y, Ma J, Osei MD, Khaliq G. Climate-resilient microbial biotechnology: a perspective on sustainable agriculture. Sustainability. 2022;14:5574-5583.
78. Adamala KP, Martin-Alarcon DA, Guthrie-Honea KR, Boyden ES. Engineering genetic circuit interactions within and

between synthetic minimal cells. Nat Chem. 2017;9(5):431-439.

79. Mohammad ZH, Ahmad F, Ibrahim SA. Application of nanotechnology in different aspects of the food industry. Discov Food. 2022;2:12.
Available:https://doi.org/10.1007/s44187-022-00013-9
80. Bhatia D, Paul S, Acharjee T, Ramachairy SS. Biosensors and their widespread impact on human health. Sensors Int. 2024;5:100257.
81. Haleem A, Javaid M, Singh RP, Suman R, Rab S. Biosensors applications in the medical field: A brief review. Sensors Int. 2021;2:100100.
Available:https://doi.org/10.1016/j.sintl.2021.100100
82. DeAngelis KM, Firestone MK, Lindow SE. Sensitive whole-cell biosensor suitable for detecting a variety of N-acyl homoserine lactones in intact rhizosphere microbial communities. Appl Environ Microbiol. 2007;73:3724–3727.
Available:https://doi.org/10.1128/AEM.02187-06
83. DeAngelis KM, Ji P, Firestone MK, Lindow SE. Two novel bacterial biosensors for detection of nitrate availability in the rhizosphere. Appl Environ Microbiol. 2005;71:8537–8547.
Available:https://doi.org/10.1128/AEM.71.12.8537-8547.2005
84. Wang X, Zhu K, Chen D, Wang J, Wang X, Xu A, et al. Monitoring arsenic using genetically encoded biosensors *In vitro*: The role of evolved regulatory genes. Ecotoxicol Environ Saf. 2021;207:111273.
Available:https://doi.org/10.1016/j.ecoenv.2020.111273
85. Hicks M, Bachmann TT, Wang B. Synthetic Biology Enables Programmable Cell-Based Biosensors. ChemPhysChem. 2020;21(2):132-144.
Available:https://doi.org/10.1002/cphc.201900739
86. Kabeyi MJB. Biogas Production and Applications in the Sustainable Energy Transition. J Energy. 2022;2022:1-43.
Available:https://doi.org/10.1155/2022/8750221
87. Noda-Garcia L, Tawfik DS. Enzyme evolution in natural products biosynthesis: target- or diversity-oriented? Curr Opin Chem Biol. 2020;59:147–154.
Available:https://doi.org/10.1016/j.cbpa.2020.05.011
88. Ncube A, Mtetwa S, Bukhari M, Fiorentino G, Passaro R. Circular Economy and Green Chemistry: The Need for Radical Innovative Approaches in the Design for New Products. Energies. 2023;16:1752.
Available:https://doi.org/10.3390/en16041752
89. Adesina O, Anzai IA, Avalos JL, Barstow B. Embracing biological solutions to the sustainable energy challenge. Chemistry. 2017;2(1):20–51.
90. Gupta A, Gupta R, Singh RL. Microbes and environment. Principles and Applications of Environmental Biotechnology for a Sustainable Future. 2016;15:43–84.
91. Briški F, Vuković DM. Environmental microbiology. Phys Sci Rev. 2017;2(11):1-12.
92. Anderson J, Strelkowa N, Stan GB, Douglas T, Savulescu J, Barahona M, Papachristodoulou A. Engineering and ethical perspectives in synthetic biology. EMBO Rep. 2012;13(7):584-590.
93. Brennan AM. Development of synthetic biotics as treatment for human diseases. Synth Biol (Oxford). 2022;7(1).
Available:https://doi.org/10.1093/synbio/ysac001
94. Li J, Zhao H, Zheng L, An W. Advances in Synthetic Biology and Biosafety Governance. Front Bioeng Biotechnol. 2021;9:598087.
Available:https://doi.org/10.3389/fbioe.2021.598087
95. Bedau MA, Triant M. Social and Ethical Implications of Creating Artificial Cells. In: Sandler RL, editor. Ethics and Emerging Technologies. Palgrave Macmillan. 2014; 377–387.
Available:https://doi.org/10.1057/9781137349088_37
96. Wang F, Zhang W. Synthetic biology: Recent progress, biosafety and biosecurity concerns, and possible solutions. J Biosaf Biosecur. 2019;1(1):22-30.
97. Douglas T, Savulescu J. Synthetic biology and the ethics of knowledge. J Med Ethics. 2010;36(11):687-693.
98. Jefferson C, Lentzos F, Marris C. Synthetic biology and biosecurity: challenging the

"myths". Front Public Health. 2014;2:115-121

99. Meghwanshi GK, Kaur N, Verma S, Dabi NK, Vashishtha A, Charan PD, Purohit P, Bhandari HS, Bhojak N, Kumar BR. Enzymes for pharmaceutical and therapeutic applications. Biotechnol Appl Biochem. 2020;67(4):586-601.
    Available:https://doi.org/10.1002/bab.191.
100. Wiltschi B, Cernava T, Dennig A, Galindo Casas M, Geier M, Gruber S, Wriessnegger T. Enzymes revolutionize the bioproduction of value-added compounds: From enzyme discovery to special applications. Biotechnol Adv. 2020;40:107520.
    DOI:10.1016/j.biotechadv.2020.107520.
101. Pillaiyar T, Manickam M, Namasivayam V. Skin whitening agents: medicinal chemistry perspective of tyrosinase inhibitors. J Enzyme Inhib Med Chem. 2017;32(1):403-425.
    Available:https://doi.org/10.1080/14756366.2016.1256882.
102. Raveendran S, Parameswaran B, Ummalyma SB, Abraham A, Mathew AK, Madhavan A, Rebello S, Pandey A. Applications of microbial enzymes in food industry. Food Technol Biotechnol. 2018;56(1):16-30.
    Available:https://doi.org/10.17113/ftb.56.01.18.5491.
103. Benatti ALT, Polizeli MLTM. Lignocellulolytic biocatalysts: the main players involved in multiple biotechnological processes for biomass valorization. Microorganisms. 2023;11(1):162.
    Available:https://doi.org/10.3390/microorganisms11010162.
104. Jemli S, Ayadi-Zouari D, Hlima HB, Bejar S. Biocatalysts: application and engineering for industrial purposes. Crit Rev Biotechnol. 2016;36(2):246-58.
    DOI: 10.3109/07388551.2014.950550.
105. Garner KL. Principles of synthetic biology. Essays Biochem. 2021;65(5):791-811.
    Available:https://doi.org/10.1042/EBC20200059.
106. Ncube A, Mtetwa S, Bukhari M, Fiorentino G, Passaro R. Circular economy and green chemistry: the need for radical innovative approaches in the design for new products. Energies. 2023;16(4):1752.
    Available:https://doi.org/10.3390/en16041752.
107. Qumsani AT. The contribution of microorganisms to sustainable development: towards a green future through synthetic biology and systems biology. J Umm Al-Qura Univ Appl Sci; 2024.
    Available:https://doi.org/10.1007/s43994-024-00180-8.
108. Malkawi HI, Kapiel TYS. Microbial biotechnology: a key tool for addressing climate change and food insecurity. Eur J Biol Biotechnol. 2024;5(2):1-15.
    Available:https://doi.org/10.24018/ejbio.2024.5.2.503.
109. Almomani F, Abdelbar A, Ghanimeh S. A review of the recent advancement of bioconversion of carbon dioxide to added value products: a state of the art. Sustainability. 2023;15(13):10438.
    Available:https://doi.org/10.3390/su151310438.
110. Chen XR, Cui YZ, Li BZ, Yuan YJ. Genome engineering on size reduction and complexity simplification: a review. J Adv Res. 2024;60:159-171.
    Available:https://doi.org/10.1016/j.jare.2023.07.006.
111. Choe D, Cho S, Kim SC, Cho BK. Minimal genome: worthwhile or worthless efforts toward being smaller? Biotechnol J. 2015;11(2).
    DOI:10.1002/biot.201400838.
112. Laohakunakorn N, Grasemann L, Lavickova B, Michielin G, Shahein A, Swank Z, Ansori AN, Antonius Y, Susilo RJ, Hayaza S, Kharisma VD, Parikesit AA, Zainul R, Jakhmola V, Saklani T, Rebezov M, Ullah ME, Maksimiuk N, Derkho M, Burkov P. Application of CRISPR-Cas9 genome editing technology in various fields: a review. Narra J. 2023;3(2).
    Available:https://doi.org/10.52225/narra.v3i2.184.
113. Chaudhari M, Solanki K. Role of CRISPR-Cas technique in bioremediation of pesticides. Int J Curr Microbiol Appl Sci. 2023;12(8):82-93.
114. Khanna K, Ohri P, Bhardwaj R. Nanotechnology and CRISPR/Cas9 system for sustainable agriculture. Environ Sci Pollut Res Int. 2023;30(56):118049-118064.

DOI:10.1007/s11356-023-26482-8. Epub 2023 Mar 27. PMID: 36973619.

115. Hughes RA, Ellington AD. Synthetic DNA synthesis and assembly: putting the synthetic in synthetic biology. Cold Spring Harb Perspect Biol. 2017;9(1). Available:https://doi.org/10.1101/cshperspect.a023812.

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