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Editorial Introduction

Kashyap Kumar Dubey* and Krishna Ravi Srinivas**

Welcome to the third issue of Volume 25! The response to the last issue, the Special Issue on 'Bioeconomy for the Common Good' was excellent!

Bioeconomy is an emerging cutting-edge economic sector that usages of biological resources and processes to provide goods and services in a sustainable manner. Industry 4.0 has been recognized as a key component in the age of sustainable development for the bioeconomy. The adoption and implementation of Industry 4.0 in the bioeconomy area in the context of Asia is a major challenge.

As we are in Fourth Industrial Revolution, or Industry 4.0, a confluence of technologies such as artificial intelligence (AI), the Internet of Things (IoT), and robotics are reshaping the landscape of biotechnology industries. Yet, amidst this digital resurgence, another transformative force is also gaining momentum i.e., the bioeconomy. This emerging paradigm, which leverages biological resources to meet societal needs across various sectors, is not merely a complementary element but a crucial pillar for sustainable growth in the age of Industry 4.0.

The bioeconomy represents an economic system based on the sustainable production and conversion of renewable biological resources into a range of value-added products, including food, feed, bio-based products, and bioenergy. It encompasses a diverse array of sectors, from agriculture, forestry, and fisheries to biotechnology, bio-based industries, and beyond. While the digital innovations of Industry 4.0 are revolutionizing manufacturing, supply chains, and services, the bioeconomy offers a complementary pathway to address pressing challenges related to resource scarcity, environmental degradation, and climate change.

The Bioeconomy of India has risen from USD 70.2 billion to USD 100 billion in 2022 and India is set to achieve the target of USD 150 billionBioeconomy in 2025. The growing market of bio-based products will reach USD 270-300 Billion by the year 2030 (India Bioeconomy Report, 2022).

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One of the most compelling synergies between Industry 4.0 and the bioeconomy lies in the realm of sustainable production and consumption. Upcoming technologies like AI, machine learning, and IoT can optimize resource usage, zero waste, and enhance the efficiency of bio-based processes. For instance, precision agriculture systems equipped with sensors, drones, and data analytics can enable precise monitoring and management of crops, which will enhance yields and lower environmental impact. Similarly, biorefinery processes utilize advanced biotechnologies processes and operations to convert agricultural residues, underutilized biomass, and algae into biofuels, biochemicals, and biomaterials efficiently with a low carbon footprint. Moreover, the integration of digital technologies and biological sciences is unlocking unprecedented opportunities for innovation and diversification across the bioeconomy value chain. Meanwhile, bioinformatics tools and computational models facilitate the rapid screening, optimization, and scale-up of bio-processes, accelerating the development and commercialization of bio-based solutions. Bioeconomy is fostering cross-sectoral collaboration and knowledge exchange between the digital and biological innovation ecosystems is essential to co-create integrated solutions, scale innovations, and unlock new market opportunities.

Ecosystem in India with respect to Bioeconomy

According to Indian Bioeconomy Report 2023, the Bt cotton production for the year 2022 has showcased a consistent economic output of approximately USD 28 million daily within the BioAgri sector. In 2022, the Bioeconomy in the Diagnostic Sector has improved by 1.5-fold from 2018, contributing to the yearly output of USD 10.8 billion. The Biopharma vaccine market adds up to USD 1.16 billion monthly to the Bioeconomy with an annual production of about 2 billion doses. Accompanying the Biopharma vaccine, Biopharma Therapeutics also showcases its strong contribution with an annual value of USD 6.8 billion in the bioeconomy. Since enzymes play a crucial role in bioindustries, such as poultry, and aqua, they have contributed around USD 17 billion. India's ethanol production has doubled since 2020 and contributes up to USD 26 billion.

Indian bioeconomy has contributed more than USD 11 billion to the national GDP. India's bioeconomy has shown an impressive rise of 29 percent in the year 2022 with USD 137 billion. Biotech startups have also shown a remarkable surge of 23 per cent making a cumulative count of 6,755 biotech startups. Startups are categorized into various activities such as healthcare, manufacturing chemicals and products thereof, business services, trading, agriculture, and research and development.

The incorporation of artificial intelligence (AI) into the pharmaceutical business holds enormous promise for crafting a brighter future in healthcare and beyond. People turned to online platforms for their healthcare needs as a result of the COVID-19 epidemic, which has hastened the use of e-pharma services. AI can reveal previously overlooked patterns and insights in healthcare data from sources such as clinical trials, drug formulations, and feedback from medical equipment or patient apps. The ability of AI to analyze such huge amounts of data allows academics and healthcare practitioners to make more educated judgments, discover new correlations, and potentially locate novel treatments or approaches that would have gone unreported otherwise.

Despite advances in AI in different fields, there is still potential for advancement in the use of AI and machine learning in medical sales and healthcare professionals in India. Still, a large number of companies are at the beginners level of AI execution. The core agenda of the top AI companies in India includes providing cost-cutting solutions for healthcare, cutting down drug development costs, and making a hands-free interaction with people. AI will undoubtedly assist medical professionals in comprehending diseases better and faster.

In this Special Issue on 'Biotechnology for Bioeconomy', there are five articles. These five articles have covered a wide canvass related to Bioeconomy. The article by Pramod Khandekar and Prasanta Kumar Ghosh, 'Bioeconomy: Different Countries, Different Strategies, Multiple Benefits', gives an excellent account of the driving factors and components of bioeconomy in different countries that may have a determining impact on the development of the regions and on the kinds of technologies and industries coming up in the short, medium and long terms. The authors have also argued for the setting-up of the global forums on a precautionary principle for an undisputed sound resolution, in light of the elements of ethics and social acceptance issues, including rights to choose and legal provisions. The second article, 'Utility of Bioenzymes for Sustainable Food Systems', by Radhika Hedaoo, explores the utility of bio enzymes in food production and processing and in improving food quality, nutritional value, and safety and its role in the environmental impact. The author also traces the latest technological developments and innovations in the food industry and argues that bioenzymes would enable food industry to become sustainable, accessible, and move towards becoming carbon neutral. In the third article, 'Sustainable Biofuels and Carbon Footprints', the authors, Arpit Srivastava, Piyush Kant Rai and Kamlesh Choure, have discussed the significance of biofuel, the energy demand and supply statistics and how biofuels are going to play a very important role in uplifting the global bioeconomy. The authors have also pointed out the concern regarding the carbon footprint of biofuels. In the fourth article, authors Punit Kumar and Archana, have discussed the role of Industry 4.0 in biotechnology to produce environmentally sustainable biotechnology products. The fifth and final article, 'Significance of Technology Transfer Offices in Strengthening Technology Transfer Ecosystem and Translation of Life Sciences Innovation into Commercialization for Rapid Industrial Growth: Indian Perspectives', by Shiv Kant Shukla and Susmita Shukla explores the role and importance of Technology Transfer Offices (TTOs) by illustrating some of the successful institutions and models. The authors have also highlighted the need for having a larger network of professional TTOs, harmonised policy for managing IP and technology and a robust tech-transfer system which will help all the stakeholders leading to creation of a large number of start-ups, job-creations and, overall, in building the robust innovation and tech-transfer ecosystem for industrial growth.

Future Prospects

Industry 4.0 offers a unique opportunity to reimagine, reinvent, and reshape our bio-based economies. However, it needs strategic investment, and collaborative action across sectors, disciplines, and borders. Together, we can harness the power of the bioeconomy and Industry 4.0 to build a more sustainable, inclusive, and prosperous future for all.

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Bioeconomy: Different Countries, Different Strategies, Multiple Benefits

Pramod Khandekar* and Prasanta Kumar Ghosh**

Abstract: The steering and operative aspects and components of bioeconomy in different countries that may have a determining impact on the development of the regions and on the kinds of technologies and industries coming up in the short, medium and long terms have been discussed. The flavour of bioeconomy directions and their drivers as conceived in different regions have been touched upon in monetary terms over the future years, based on available data and information. The emphasis for future development in the biotech sectors for pushing up bioeconomy is different in different regions. The stress on mastering biotechnological capabilities is also dissimilar. The developments in bioeconomy plans and programmes in the European Union, UK, USA, China, India, Japan, Brazil, ASEAN countries, South Korea and Russia have been profiled. Australian plans and programmes in synthetic biology have been included. Harnessing bioeconomy is anticipated to enable more recycling of wastes and promotion of environmental sustainability. Advancement of bioeconomy is anticipated to elevate the health, longevity and living standards of people. Contributions to global GDP are anticipated to be substantial from bioeconomy activities; the horizons of more effective newer biotechnologies are appearing fast in certain bioeconomy countries. Advancement in wealth creation by developing products involving the manipulation of genes, cell lines, and natural life forms has strong societal acceptance issues. The elements of ethics and social acceptance issues, including rights to choose and legal provisions, need to be worked upon through united global forums on a precautionary principle for an undisputed sound resolution.
Keywords: Bioeconomy, Green economic activities, Paris Agreement, Sustainable development goals, Synthetic biology

Introduction

Bioeconomy refers to economic activities emanating through plans, actions, and activities involving extensive use of biotechnology for the production of biomass, energy and a wide range of other goods and services, especially in the areas of agriculture, healthcare, chemicals and energy production and distribution sectors. The activities also include multiple efficient recycling methods of materials generated through human activities. Green economic activities are promoted to resist the damaging effects and

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consequences of climate change emanating from human activities. Green economic activities imply and express occupation and income-driven by investment into economic activities that promote reduced carbon emissions and pollution, prevent loss of biodiversity, and increase resource usage efficiency. Bioeconomy is not yet a fixed concept all over the world but is accepted to be an economy, driven by knowledge-based production methods that involve utilisation of biological resources and biological principles to sustainably deliver goods and services over multiple economic sectors. The concept of bioeconomy revolves around harnessing the potential of renewable biological resources derived from both land and sea, including crops, forests, marine life, animals, and microorganisms. These resources are leveraged to create essential commodities such as food, materials, and energy. Moreover, the bioeconomy taps into the largely untapped reservoir of value within vast quantities of biological waste and residual materials. Its primary objective is to foster sustainable development and promote circular practices. Specifically, it embraces the core principles of the circular economy, which encompass reusing, repairing, and recycling materials, thus reducing overall waste generation and its environmental impact.[1,2] Countries are making use of bioeconomy in their territories emphasising strategies that provide more cutting-edge advantages to them. Strategies taken by countries are linked to their biotechnological development and progress. Consequently, there are observable distinct differences in strategies and action plans among countries as biotechnological progress and capabilities are at different levels of advancement.

Certain identified pathways towards the monitoring of sustainable bioeconomy include economic aspects linked to the GDP, investment, increase in trade and services, employment generation and job creation etc.; socioeconomic aspects linked to R&D spending and intellectual property generation, income inequality rationalisation, food security, health security, energy security, gender equity in employment, education and training of citizens etc.; and environmental aspects hovering around sustainable use of natural resources, biodiversity conservation, reduction in the emission of greenhouse gasses, etc. Bioscience-related strategies include the use of both conventional and modern biotechnological inventions and discoveries.

The ill effects of climate change from human activities have started becoming vivid in many parts of the world. Climate change refers to a change in the pattern of climate, which is traceable and ascribable directly or indirectly to human activities. There has been much increase in the greenhouse gasses in the atmosphere from human activities, resulting in the trapping of heat and an increase in the overall temperature of the global climate. If, therefore, mammoth actions are not initiated fast by the people, the future of human existence would get from bad to worse. The threat from climate change is real and therefore, to take actions to move towards environment-friendly economy is not only a necessary but a core responsibility. Sustainable bioeconomy activities and strategies include actions towards the reversal of ill-effects of climate change.

It was being increasingly realised after the discovery of recombinant DNA technology(r DNA) by Herbert Boyer and Stanley Cohen in 1973 and thereafter that the new science of manipulating the genes, and broadly more understanding in the whole span of genomics in all life forms shall enable the human kind to produce multiple substances of human use in more greener ways. The first industrial use of r DNA based technology usage was with the manufacture of human insulin. Recombinant DNA-based human insulin was prepared for the first time in Genentech, USA by David Goeddel and his team by expressing the A and B chains of insulin in Escherichia coli, isolating the pure peptides and chemically combining the two chains, followed by purification to get authentic human insulin. The technology was procured by Elli Lily, USA from Genentech, and the first commercial human insulin was authorised by the USFDA for use (Quianzon and Cheikh 2012). This landmark invention ushered the beginning of the use of r DNA-based technology worldwide. Multinational companies(MNCs) got immensely interested to invest in genomics for it was realised that understanding, identification and manipulation of genes and profound greater knowledge in genomics were going to be the future for multiple industries, including pharmaceuticals; agriculture, including food, feed and fodder industry; industrial products such as enzymes, detergents, biodegradable plastics, fibers etc.; and environment management issues. Dominant MNCs, especially in the pharmaceutical sector; agribusiness including horticulture and animal sciences; and chemical sector, started to invest in molecular technologies and genomics thereafter (Enríquez 1998).

There were, however, apprehensions and skepticisms about the risks emanating from the use of r DNA-based technologies, and therefore laws and rules were established in every country to use the technologies under precautionary principles. The use of recombinant DNA (rDNA) technology for economic benefits began in 1973 when Herbert Boyer and Stanley Cohen discovered that genetic material could be transferred directly to organisms through non-sexual methods. Safety concerns arose, leading to the Asilomar Conference in 1975. The conference emphasised the need for regulations, transparency, and precautionary principles in research involving rDNA technology and genetically modified organisms (GMOs). In response to the conference's recommendations, India introduced Environment Protection

Laws in 1986 and Rules in 1989 to address environmental safety and human and animal health concerns related to rDNA-based technologies. Additionally, the United Nations established an Ad Hoc Working Group on Biological Diversity in 1988. This led to the Cartagena Protocol of Biosafety in 2000, emphasizing the precautionary principle for the transboundary movement and use of genetically modified substances, ensuring safety for the environment and human health. India is a signatory to the Protocol, which is followed by all signatory countries, while non-signatory countries assess the safety of genetically modified substances within their own territories using their own laws and protocols. For the transboundary movement of living genetically modified organisms (LMOs), a global treaty was established.3 Interestingly, most developed countries, including the USA, Canada, countries in the European Union, Russia, Japan, Australia and South Korea; developing countries such as China and India; and small countries like Cuba had invested heavily in modern biotechnology, which resulted in the emergence of multiple benefits in the invention and emergence of new products and processes in medicines, agriculture including animal husbandry and fisheries sector, and bio-industrial products. Europe had shown apprehensions about the use of genetically modified seeds, and European farmers remained behind in the use of LMOs from their own production. Research in molecular biology resulted in the invention and advancement of 'omic' technologies (Dai and Shen 2022) besides advancement in nanotechnologies (Ghosh 2000). It started to become clear that multiple techniques of recombinant DNA technology could also be used not only to produce goods and services in a greener way but also to reverse several ill effects of the deteriorating global climate.

In the meantime, intense human activities resulted in adverse global climate change, making the environment from bad to worse over the years, particularly due to the increase in emission of green gasses because of excessive use of fossil fuels loss in biodiversity resulting from excessive over- exploitation of living resources and deforestation endeavour; overexploitation of ground water resources resulting in loss of land productivity and the manifestation of food security issues; accumulation of non-biodegradable wastes; and several other adversities. Such changes drew the attention of the global community, and concerns were being voiced to take remedial actions against such deteriorating climate changes.

Over a period of time, the need for remedial measures for preventing the deterioration of global climate was being explored by a number of countries, and a new economic paradigm was founded on the use and recycling of biological resources by making use of the advances of modern biology and biotechnology besides other congruent technological inputs. The new paradigm evolved from the initial use of the term 'biotechonomy' in 1997 by Juan Enríquez and Rodrigo Martinez at the American Association for the Advancement of Science (AAAS) Genomics Seminar.[4] The term has also been used later as 'biobased economy' and 'bioeconomy'. Presently, the term is widely used as 'bioeconomy' by most of the policy makers, all over the world. Bioeconomy covers the whole activities, including biobased non-food goods as well as food and feed.[5]

Methodology of the study

The information and data sources included in the paper are based on retrieving data sets from scientific, technological and economic information available on the internet at the web pages of different governments, scientific and technological institutions, and other trustworthy sources. Google search engine was used for collecting data. The authors have extensive hands-on training and practical experience in multiple aspects of biological sciences and technologies. They were involved in the planning, development, execution and review of biotech projects in many areas in India.

Aims of Bioeconomy

The need for ensuring food, energy and health security for people all over the world within a more sustainable natural environment in the midst of a rising global population requires sustainable plans, policies, activities and actions that can intercept, tackle and resolve these burning issues. Activities within the ambit of bioeconomy are aimed at addressing these. The environment is already over-exploited by multiple human activities and has derogated considerably as a consequence, requiring reversal and repair. The projects and tasks pursued under bioeconomy by countries as a new vision of development are to essentially achieve sustainable development goals (SDGs) and commitments under the global climate treaty, popularly known as the Paris Agreement. The Paris Agreement (PA)[6] is a treaty on climate change, which was adopted by 196 countries at the UN Climate Change Conference in Paris, France, on 12th December 2015. Through this treaty, efforts would be made to limit global warming to 1.5°C by the end of this century. Different countries have different strategies towards working for SDGs.

While pursuing bioeconomy for societal benefits, another lately developed term, namely circular economy, is often used. They both focus on sustainability and the efficient use of resources, but they have different primary areas of emphasis. Bioeconomy is like making the best use of nature's gifts, like plants and animals, to create valuable things while taking care of the environment. It's about using biological resources wisely. While, circular economy, on the other hand, is like a big recycling and waste-reduction program for everything we use, not just biological things. It's about using, reusing, and recycling as much as possible to cut down on waste and pollution. While they are related in their focus on sustainability, the key difference is that the bioeconomy specifically deals with biological resources, whereas the circular economy is a broader approach that encompasses all types of resources in a sustainable way.

Technological Advancements in Bioeconomy Efficiency

Technological advancements have significantly boosted the efficiency of the bioeconomy. By adopting highly mechanised production systems, selecting efficient cultivars and planting materials, and employing fertilizers alongside effective water management, global agricultural yields for crops, vegetables, fibers, and biomass have seen remarkable growth. The use of biofertilizers and biopesticides has reduced the reliance on chemical alternatives. Breeding technologies have increased meat, milk, and animal fiber production, while mechanisation in poultry has led to higher egg and poultry meat output. In the fisheries sector, conventional technological inputs have improved productivity. Bio-catalysis technologies find applications in various fields, offering innovative solutions. Extensive documentation technologies enable tracking saleable bio products back to their source, ensuring transparency and safety. With the advent of rDNA, genomics, proteomics, and genome editing technologies, human capabilities to modify and produce organisms with enhanced genetic traits have grown exponentially. Bioinformatics, fast computation, and artificial intelligence have accelerated research. Bioreactors, ultracentrifuges, chromatographic systems, and analytical techniques contribute to efficient resource utilisation.

The integration of these technologies falls under the umbrella of synthetic biology technologies (SBTs). SBTs empower the redesigning of organisms at the genetic level, creating opportunities to produce drugs, chemicals, fuels, and materials. They can also aid in bioremediation and the development of efficient planting cultivars. However, these technologies are capital and technology-intensive and require stringent environmental biosafety considerations. To harness the potential of these technologies for sustainable bioeconomy, countries must carefully assess risks and gains in each project. Integration of modern technologies is essential to improve the efficiency of using renewable biological resources. Public awareness and trust are crucial, and ethical and legal frameworks should ensure the safe and effective utilisation of these advancements in the bioeconomy.

Elements of Bioeconomy Framework in Different Countries

In a study report by the Food and Agriculture Organisation (FAO) of the United Nations of 2018, an analysis was made by measuring the contribution of bioeconomy in selected countries, chosen from six continents, namely Germany and the Netherlands from Europe; Malaysia from Asia; Argentina from South America; USA from North America; South Africa from Africa; and Australia.[7] The study analysed how different countries were measuring the contribution of bioeconomy to their overall country objectives of economy. It was revealed that while these countries had adopted bioeconomy as a new vision of development, the set of sectors and subsectors of activities under bioeconomy were widely different, and the technological expertise and inputs required for pursuing and promoting those activities were also widely divergent. For example, in Europe, while Germany had included into their bioeconomy, exhaustive activities comprising agriculture, automobile and engineering, chemicals including bioplastics (biodegradable plastics and materials based on polyhydroxybutyrate or polyhydroxyalkanoates), biofuels and bioenergy, biorefining, construction and building industry, consumer goods including cosmetics and cleaning products, feed, fisheries, food and beverage industry, forestry, knowledge and innovation, pharmaceutical industry, paper and pulp industry, and textiles; the Netherlands had not included many of these activities. Argentina and South Africa included a couple of activities under bioeconomy but did not monitor or measure their progress periodically. The USA had included only a few activities such as agriculture, chemicals including bioplastics, biorefining, forestry, and textiles under their activities.

It was evident from the report that different countries had included different sets of sectors and subsectors under bioeconomy, where widely different kinds of technological expertise and inputs are required and used. Consequently, there could be no one method of evaluation of each country's bioeconomy efforts. Further, every country had not created periodic evaluation infrastructure for its bioeconomy activities, which exists in some countries only. This would hinder taking corrective policy from time to time in countries that do not have the reviewing and assessment infrastructure. There is a need to create measurable environmental, economic and social objectives in every country promoting a bioeconomy strategy for development.

A serious bioeconomy framework requires periodic monitoring, measurement and reporting of the gains in economic parameters such as contributions to national gross domestic product (GDP), employment generation and job creation, increase in trade and services and new investments; socio-economic parameters such as conduct of R&D and generation of intellectual property rights (IPRs), income increase of people and reduction in poverty, food and health as well as energy security, increased infrastructure development, increased education and training of people in skills, gender inequality rationalisation and growing inequality among people in different countries; and improvement in the environment hovering around sustainable use of natural resources, reduction in the emission of greenhouse gasses, conservation of biodiversity etc.

Technological advancements in biosciences are linked with industrial applications as means of industrialisation in bioeconomy. Leader countries in biosciences such as the USA, EU, Japan, Canada China, India, Australia, Israel and Cuba, followed by several Asian countries like Malaysia, Thailand, Vietnam, Indonesia and Singapore; South American countries like Brazil, Mexico and Argentina among others, and South Africa, Kenya, Egypt and Nigeria among the African countries are the regions that have made considerable progress. Taking into consideration the factors such as the current GDP at Nominal values (GDP measured as aggregate output using current prices in a year) as well as GDP at PPP values (GDP converted to international US dollars using purchasing power parity rates); the population of the country; and the levels of modern biotechnological developments, the authors had chosen to elaborate the bioeconomy plans and programs in European Union, UK, USA, China, India, Japan, Brazil, ASEAN countries, South Korea and Russia. Australian plans and programmes in synthetic biology have been included.

The elements of micro and macro development goals for different countries in the context of promoting bioeconomy cannot be the same. In a Global Bioeconomy Summit (GBS) held in 2015 in Berlin (El-Chichakli *et al*. 2016), the experts concluded that to rationalise the needs of different countries, multiple policy initiatives need to be evolved and pursued for improving the quality of air, water and soil, and to use the biological resources on a sustainable basis at each region. The elements of policy initiatives and their implementation strategies would, however, be different, and have to be evolved, taking into consideration the regional factors and expertise. Five unifying generic cornerstones were identified in the GBS as sustainable development goals through bioeconomy which were (1) intensifying international collaborations between governments and public and private researchers for optimizing use and sharing of resources; (2) ways to measure the development and contributions to sustainable development goals in priority factors such as food security; (3) bioeconomy initiatives to be linked more closely with SDGs 2030 agenda[8] which is essentially an agenda and a plan of action for people, planet and prosperity) with provisions of follow up with Paris Agreement (a legally binding international treaty on climate change) and Aichi Biodiversity Agreement[9] (the agreement had identified 20 specific targets to address and mitigate biodiversity loss across the globe); (4) in the context of possessing the relevant knowledge, skills and competence required for developing a bioeconomy for sustainable use of biological materials in different regions and parts of the world, the experts and educators need to define these elements and assist in preparing road maps requiring interdisciplinary approach, based on which government could build international teaching, learning and exchange programs for imparting and sharing skills; (5) research and development support programmes are needed, based on which global programmes in a few break-through projects could be developed. The need for such programmes in specific areas such as new and novel food systems, development of bio-principled cities, sustainable aquaculture, biorefinaries, artificial photosynthesis, citizen and consumer participation and global governance were identified.

Bioeconomy Requires Attention to Unique Social and Technological Issues

Economic growth is commonly measured in terms of the increase in the aggregated market value of additional goods and services produced, using estimates such as contributions to GDP. In any country, the rewards of economic growth should be rationally distributed for its sustainability. Elevation of GDP through bioeconomy needs to be treated in the same manner as are economic gains resulting from other economic contributors.

Of all the factors responsible for economic growth, the development and deployment of highly improvised technology, and blossoming of the full potential of talented and skilled human capital are the most contributing factors.

Advancement in wealth creation by developing products involving manipulation of genes, cell lines, and natural life forms have strong societal acceptance issues. Invention and regulation seem to be inversely related. If there is relaxation in the conduct of experiments using human subjects or the development of products for human use, where safety and ethical issues are compromised, and where risk capitals are easily available from funding sources for research, and further where the laws are not strong, their innovations and inventions may proceed at higher speed, but may also bring about catastrophic results. Presently, genome editing work is going on in several laboratories. The first work (Alonso and Savulescu 2021) was started by He Jiankui, a Chinese scientist, in 2018, and He gene-edited embryos in-vitro in 2018 and transplanted the edited embryos to the donor mother, which resulted in the birth of twin baby girls, who are doing fine, according to a news.[10] He Jiankui used CRISPR technology for the editing work to produce HIV resistant babies. He Jiankui was sent to prison for 3 years as the work was considered unethical, and He did not have approval from any ethical committee or agency.

Heritable human genome editing followed by using such modified embryos cannot be used for reproduction in any country. Such an act is illegal and is punishable by law in some countries. In India, human genome editing for reproductive cloning is banned by the National Guidelines for Stem Cell Research.[11] There are, however, no enforceable laws to deal with the offenders.

Research in heritable human genome editing is, however, carried out (Baylis *et al*. 2020) in many countries. Gene editing in plants and animals is, however, authorised and carried out in many countries, which is done to improve crops in agriculture, and in animals, including in the fisheries sector, to obtain better animals and fish; the USA has been the most advanced in carrying out Gene editing in multiple life forms, followed by many other countries including China, Argentina, Brazil, Mexico, India and some smaller countries like Bangladesh. Europe had not been adopting these technologies in many countries for multiplying transgenic life forms in open environment but had been using such substances produced elsewhere. Recently, the UK passed their Genetic Technology (Precision Breeding) Act,[12] which indicated that changes are in the air for adopting these technologies gradually in Europe.

However, Germ line editing work on humans is under debate and is vexed. Gene editing techniques are being pursued in the research stage for mono gene editing in somatic human cells as a curative therapy for a number of diseases. US FDA has prepared recommendations[13] for developing human gene therapy products incorporating genome editing (GE) of human somatic cells in different research setups. FDA considers the use of CRISPR/Cas9 gene editing in humans to be gene therapy.

Like gene editing technologies, which are presently in high risks category of technologies and cannot be used without exhaustive research, some other technologies such as artificial intelligence (AI) products and technologies, have great risks if blindly used. AI products and technologies are based on the integration of sound science and sound data through complex algorithms and need to be upgraded continuously. As such products and technologies may not always be based on current knowledge, errors can come. Therefore, while AI-based products and technologies can be useful, their use in many situations, such as advice for human therapy and other areas of bioeconomy should be made judiciously, and ethical rules should be in place.

The elements of ethics, social acceptance issues, including rights to choose and the necessary legal provisions need to be worked upon in several areas of research contemplating genome editing, use of AI etc., through united global forums on a precautionary principle for undisputed resolution.

Selected Region and Country-Specific Bioeconomy Programmes and Activities

European Union (EU)

There are 44 countries in Europe of which presently 27 countries, namely Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden are the European Union (EU) countries.[14] The UK was a part of the EU, but left the EU on 31 January 2020. Switzerland is not an EU.

The EU GDP[15] was US$16.6 trillion (nominal; 2022) and US$24.05 trillion (PPP; 2022) with a population of 447.7 million as of January 2020. The GDP by sectors were agriculture: 1.5 per cent, industry: 24.5 per cent, services: 70.7 per cent and others 3.3 per cent, as per2016 data. The EU economy is the joint economy of the member states and is the third largest economy in the world in nominal terms, after the United States and China.

The EU Bioeconomy strategy was adopted and launched[16] on February 13, 2012. The EU history of evolving into strategies in bioeconomy is fascinating. The European Commission (EC) had been actively involved in framing and managing the Biotechnology and Life Sciences programmes of the EU since 1982. Over the years, the activities increased. The transformations were to create research groups, with the objective of exploiting the research results through the industry to benefit the society. The early Life Science programmes had gone through the conceptualization and implementation of policy frameworks to create solid foundations in European research in biotechnology. The concept of the "Cell Factory" followed by key action plans elaborated in the 5th Framework Programme (1998-2002), was an important milestone reached. Germany created for the first time its "Bioökonomierat", which was a Bioeconomy Council to advise its Chancellor and the Government in 2009, and in 2010 published its Bioeconomy Strategy. Later, more European countries started planning in life sciences technologies. Eventually, in 2012, a strategy on Bioeconomy was adopted for the whole of the EU, and the EU matured up to the present time, planning more systematically for the future (Patermann and Aguilar 2018).

The EU activities are enshrouded among all sectors and systems that rely on biological resources, which include animals, plants, microorganisms plus organic wastes; land and marine ecosystems; agriculture, forestry, fisheries and aquaculture; and all industrial sectors using biological resources and processes for producing food, feed, fodder, bio-based products, energy and services. The EU defined bioeconomy to include[17] the use of renewable biological resources from land and sea. The biological resources emanate from crops, animals, fish, microorganisms, and forests to produce food, materials and energy. The EU strategy addressed intensifying and magnifying production of the needed materials and substances through renewable biological resources and their conversion into vital industrial products and bio-energy. The intent of the EU Bioeconomy strategy is to accomplish five main objectives namely (1) to ensure food and nutrition security; (2) to manage natural resources on a sustainable basis;(3) to reduce dependence on non-renewable, un-sustainable resources secured locally or obtained through imports;(4) to mitigate and adapt to climate change; and (5) to strengthen competitiveness while creating jobs. Multiple kinds of technological inputs, including conventional and modern biotechnological methods, nanotechnology, artificial intelligence, bioinformatics etc., are included in the EU Bioeconomy strategy. The turnover value of EU bioeconomy was estimated at Euro 2.3 trillion in 2015 and the activities supported nearly 8.2 per cent of the EU workforce (Ronzon and M'Barek 2018) which provides a flavour of the economic importance of bioeconomy in the EU.

The present EU bioeconomy strategies are based on four key priorities,[18] which include (a) strengthening and scaling up of the bio-based sectors; (b) increased investments and development of new markets are promoted ; (c) deployment of local bioeconomy projects rapidly across the whole of Europe; and (d) understanding the ecological boundaries of the bioeconomy.

A study conducted on the contribution of bioeconomy services to GDP and employment generation in the EU Member countries (Ronzon *et al.*

2022) over 2008-2017 indicated that during the more recent years in 2015-2017, the EU economic growth was stronger in bioeconomy services than the total EU economy, indicating the increased importance of this sector. Bioeconomy services accounted for between 5 per cent to 8.6 per cent of the EU GDP and 10.2 per cent to 16.9 per cent of the EU labour force.

UK

The United Kingdom (UK), with a population of 67 million as of June 2021 has a GDP of US $3.159 trillion (nominal; 2023) and USD$3.847 trillion (PPP; 2023). The GDP economy is contributed by agriculture: 0.7 per cent, industry: 20.2 per cent, and services: 79.2 per cent as per 2017 estimate. The UK economy is a highly developed social market economy and is the 6th largest national economy in the world, as measured by nominal GDP value.[19]

The UK has been benefiting from its highly developed bioscience base. The future strategies[20] are to ensure that the UK move towards paths of pulling out from their reliance on finite fossil resources whilst increasing productivity across their habitats. High-end bioeconomy harnesses the power of bioscience and biotechnology, as the technologies address challenges in food, human and animal health, chemicals, materials, energy and fuel production, and environmental deteriorations. The potential benefits include the use of processes and technologies that ensure low green gas emissions. It has been reported that the UK bioeconomy in 2014 contributed to £220 billion of output across the UK economy, supporting 5.2 million jobs.

The Government, industry and the research community have been working together to realize a visible transformation in their bioeconomy. For future developments in bioeconomy, the country has set out 4 high-level goals, which include (a) capitalizing the world-class R&D in biosciences, (b) maximizing productivity, using existing renewable biological resources(c) delivering measurable benefits with the aim of creating new jobs, increasing productivity and increasing the size of the impact of the bioeconomy to £440 billion by 2030, and (d) creating the right national and international market conditions to enable innovative bio-based products and services to thrive, raising public interest, increasing skills in the workplace and sales to the market.

These goals are aimed at activities in bioeconomy that include designing and producing new forms of clean energy and new routes to high-value industrial chemicals; turning out and fabricating smarter, cheaper materials such as bio-based plastics and composites for everyday items as part of a more circular, low-carbon economy; decreasing and minimising plastic waste and pollution by developing a new generation of advanced and environmentally sustainable, biobased, biodegradable plastics and packaging materials, and ensuring pollution from microplastics; coming up with sustainable, healthy, affordable and nutritious foods; improving the productivity, sustainability and resilience of agriculture and forestry in UK; and inventing and producing newer medicines of the future while also manufacturing the existing ones more efficiently.

USA

USA[21] has a population of 334.6 million as of January 2022 with a GDP of US$26.854 trillion (nominal; 2023) and US$26.854 trillion (PPP; 2023). USA GDP is contributed by agriculture: 0.9 per cent; industry: 18.9 per cent; and services: 80.2 per cent as per 2017 estimate. The USA is a highly developed mixed economy. The USA economy by nominal GDP is the largest economy by nominal GDP in the world, and the second-largest by purchasing power parity (PPP), behind China.

In the USA, three regulatory authorities, namely the U.S. Environmental Protection Agency (EPA), U.S. Food and Drug Administration (FDA), and U.S. Department of Agriculture (USDA) are involved to steward the country to make use of products and services derived from biotechnology emanating from plants, animals and microorganisms. These authorities are empowered by the US White House who approve the federal regulatory policies for ensuring the safety of biotechnology products.[22] In recent times, the USA has been the most productive country, coming out with multiple innovative technologies involving biosciences such as the m RNA vaccines, CAR-T Cell technology, CRISPR Cas 9 technology and others in medicines; GMOs and LMOs in agriculture; renewable biomass sources for energy; and biochemicals/ chemicals etc.

The Congressional Research Service (CRS) of the USA has defined bioeconomy as “the share of the economy based on products, services, and processes derived from biological resources (e.g., plants and microorganisms)”[23] This definition is a bit narrower than what is understood by the term in many other countries.

Bioeconomy is fructified and materialized through multiple applications where manufacturing is the bio-engine. In the USA, the country had enacted its CHPS and Science Act and the Executive Order (EO) 14081, Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe and Secure American Biotechnology to promote bioeconomy. The CHIPS Act, signed into law on August 9, 2022, is designed to boost competitiveness, innovation, and national security in the USA. It would catalyze investments in multiple sectors through R&D and commercialization in biotechnology and bio manufacturing, artificial intelligence, clean energy, quantum computing, nanotechnology, semiconductor manufacturing capacity, and create new regional high-tech hubs to create a highly skilled workforce with an investment of USD 280 billion over a period of time.[24] The intent of the Executive Order is to promote the advancement of economic activity derived through biotechnology and biomanufacturing in the country to promote and encourage innovative solutions across health, energy, food security, agriculture, the supply chain, and climate change to bring in robust national and economic security.[25]

The USA has identified three major factors that must be cogently addressed to enhance the country in maintaining its competitive edge and maximize the benefits from biotechnology.[26] These factors are to enable (1) the manufacturing capacity and the skills of the US workforce in biotechnology need to advance in a manner that both in manufacture and in new product development, the country maintains its leadership position, and therefore, the necessary policy should be place and funds must be allocated;(2)the regulatory review and approval process for new cross-cutting bio products must advance faster as delays can hinder or even stop the initiatives and commercialization process;(3) an integrated and overarching bioeconomy strategy must be in place, which needs to be updated regularly to help guide the Federal Agencies to take actions for developing and transferring such powerful biotechnologies towards social and economic advancements. The emphasis and urges are to implement a long-term vision document and action plans for advancing the country in biomanufacturing to support the US bioeconomy.

The major recommendations of the government are (a) to create strong biomanufacturing infrastructure hubs through coordination among several relevant government agencies and universities in a time-bound manner; (b) to establish a sound and strong but fast, Regulatory Approval Process; and (c) to establish a new data-based strategy for bioeconomy by preparing a long-term strategy document for bioeconomy through multiple identified offices and establishments such as the National Science and Technology Council(NSTC); Director, Office of Science and Technology Policy (OSTP) of the White House; the Secretary of Commerce; and the Bureau of Economic Analysis(BEA). NSTC coordinates science and technology policy for the Federal research and development enterprises. OSTP works by providing advice to the President and the Executive Office of the President on matters related to science and technology. BEA is an independent, principal federal statistical agency that is devoted to promoting a better understanding of the U.S. economy.

The present US bioeconomy is estimated[27] to be valued at over USD 950 billion, and account for more than five per cent of the US GDP. This economy is predicted to grow globally to over USD 30 trillion over the next two decades.

China

China[28] has a population of 1411.7 million as of December 2022.The GDP of China is US$19.373 trillion (nominal; 2023 est.) and US$33.014 trillion (PPP; 2023 est.). The GDP by sector is Agriculture: 7.9 per cent;

Industry: 40.5 per cent; and Services: 51.6 per cent(2017 estimate). The Chinese economy is considered as an upper middle-income developing mixed socialist market economy. China advances through its strategic five-year plans incorporating firm industrial policies for growth. China is presently the world's second-largest economy by nominal GDP. But when measured by the purchasing power parity (PPP), it is the largest global economy.

China unveiled[29,30] a new plan to promote their bioeconomy activities during the country's 14th Five-Year Plan period (2021-25) in May 2022. The plan was to protect and intensify the use biological resources for the development of novel and useful goods and services in the areas of medicine, healthcare, agriculture, forestry, energy, environmental protection, materials and other linked sectors to promote bioeconomy and the action plans would show results by 2025. The document prepared for this purpose and the actions proposed is thought to boost meeting rising domestic demand for healthcare to improve the quality of lives, foster high-quality economic development, prevent and control biosecurity risks and modernize China's system and capacity for governance in bioeconomy during the period. In the bioeconomy sector, four areas and industrial activities shall be in sharp focus for development, which would be health care, bio-agriculture, biofuel and bio-informatics. While pursuing bioeconomy projects, China will promote low-carbon growth technologies and would enhance their technological capabilities to effectively face future epidemics. Through bioeconomy action plan, the country will explore biomass to help boost sustainable development and resource conservation. It will reinforce prevention, control and treatment of animal and plant diseases, besides human disease. Projects would also be pursued using novel techniques in bio-based breeding, the use of biofertilisers and biopesticides in agriculture to produce healthier foods.

The action plan shall push the proportion of bioeconomy to the country's GDP sizably, witnessing a significant increase in the number of enterprises engaged in the bioeconomy. Thereafter, bioeconomy in China shall steadily grow, and by 2035, China aims to be at the forefront of bioeconomy activities in the global context. The above '14th Five-Year Plan for Bioeconomy Development' (2021-2025) was critically evaluated (Zhang *et al*. 2022) by an academic group, and it was concluded that China's bioeconomy development plan, encompassing three pathways to improve bioeconomy through technological innovation, industrialization and policy supports were relevant, timely and valuable. It was revealed that China had the meantime, invested US$3.8 billion over the period of 2008–2020 in biotechnology R&D, and its biotechnology industry had contributed RMB two trillion to China's bioeconomy by 2011, maintaining a growth of about 20 per cent annually in value terms, from 2013 to 2015. The new 14th Five-Year Plan period (2021-25) initiative is therefore anticipated to make a major contribution to Chinese bioeconomy, and to their GDP.

India

India, with a population of 1417.2 million as of 2022, has a GDP ofUS$3.737 trillion (nominal; 2023 est.) and US$13.033 trillion (PPP; 2023 est.) and is ranked as the 5th largest economy (nominal; 2023) and 3rd largest (PPP; 2023) in the world. Indian GDP contributions from bioeconomy were through (a) agriculture: 18.8 per cent; (b) industry: 28.2 per cent; and (c) services sector: 53 per cent(FY 2021-22 estimate). The Indian economy has transitioned from a mixed-planned economy to a mixed middle-income developing social market economy. The services sector is the fastest-growing sector. Agriculture sector provides more than 40 per cent of the labour force, while the service sector provides over 30 per cent, and the rest is provided by the industry sector.[31]

Indian bioeconomy has been defined[32] as "an economy where the basic building blocks for matter, chemicals and energy are derived from renewable biological resources." In a Report[33] released in 2022, the Indian bioeconomy was valued at US$70.2 billion in 2020, which moved up to US$ 80.12 billion by the end of 2021, registering a monetary growth of 14.1 per cent. The bioeconomy segments comprised of biopharma; COVID Economy (consisting of COVID-19 Vaccines and COVID-19 testing and diagnostics); bio-agriculture; bio-industrial segment; and bio-IT and Research services. The sectors and subsectors of industrial activities included in bioeconomy in India are those where modern biotechnology techniques are hovering around the use of r DNA technologies, where studies are involved and undertaken in the genetic materials of living substances, and useful products and services are evolved. One guiding star in the fast progress of bioeconomy in India was due to government involvement and government promotion of this sector by creating in place laws, rules and procedures for handling r DNA technologies by the Indian Ministry of Environment Forests & Climate Change (MOEF&CC) and the Department of Biotechnology (DBT). The proactive actions of the government enabled rapid development of r DNA-based technologies in all the sectors and subsectors, and especially in pharmaceuticals. In bio-agriculture, major contributions came from the use of Bt-cotton technology. Much more contributions could have come in bio agriculture from the use of LMOs. However, the myopic views of non-science based opinion makers and their opposition to the introduction and use of LMOs in food, feed and fodder sector prevented the use of other such products in India. This resulted in loss of opportunities by the Indian farmers, and loss in the accrual of the potentially acquirable benefits was put at stake. Indian bioeconomy constituted about 2.6 per cent share of the GDP of the country in 2021. It is predicted that the bioeconomy of India may touch US$ 150 billion by 2025 and US$ 300 billion by 2030.

Japan

Japan[34] is a country with a highly developed economy. The economy of the country is ranked as the 3rd largest in the world by nominal GDP, and 4th largest by purchasing power parity (PPP). Japan had a population of 124.49 million as of 1 March 2023 estimate. The GDP of the country is US$4.4 trillion (nominal; 2023 est.) and US$6.4 trillion (PPP; 2023 estimate). The GDP is contributed by agriculture: 1.1 per cent; industry: 30.1 per cent and services: 68.7 per cent(2017 estimate). Labor force employment is agriculture: 3 per cent; industry: 25 per cent; and services: 72 per cent (FY 2018 estimate).

The Japanese government from their Ministry of Economic, Trade and Industry Division planned in 2017, formulating their new national policy in the field of biotechnology to boost their bioeconomy blueprint. The elements of planning included (a) practicing smart eco-friendly agriculture, using techniques of modern biotechnology to increase food production, (b) producing new functional materials for sustainable growth, using living cells,(c)reducing dependency on fossil fuel and producing energy through biofuels, (d) emphasising on factors leading to good health and increased longevity by using biotech food-based healthcare and medical care, and (e) developing new industrial sector and new markets, creating bioeconomy via smart living cell- based innovation.[35] The New Energy and Industrial Technology Development Organization (NEITDO), Japan estimated in 2019 the size of bio-industry market size of Japan to be of 3.6 trillion yen(USD 32 billion), and included in the basket, biotech products and services emanating from recombinant DNA products. The estimate would swell if conventional biotech products and services are also included.

In 2019, the government of Japan funded nearly 6.2 billion yen (USD 56 million) to promote bio-manufacturing technologies. Japan government had formulated their bioeconomy strategy to advance the biotechnology sector to reach 92 trillion yen (USD 837 billion) by 2030, encompassing development in(a)bio pharmacy, regenerative medicines, cell therapy, and gene therapy to reach 3.3 trillion yen(USD 30 billion); (b) life-style related health care improvement technologies to reach a value of 33 trillion yen) USD 300 billion); c) high-performance biomaterials and bio plastics valued at 53.3 trillion yen (USD 485 billion) ; (d) sustainable primary production systems in bioeconomy valued at 1.7 trillion (USD 15.5 billion); and (e) large scale wood-based construction valued at 1 trillion yen (USD 9 billion).[36] Attaining a market size of 92 trillion yen by 2030 would require creating highly skilled bio-communities and promoting policies that attract early investments and hard work of nearly a decade. Japanese government started taking steps as early as 2017 for this purpose. They had also partnered a global biotechnology summit in 2020 to keep the speed of development vibrant[37] in their country.

Brazil

There are presently 33 countries in Latin America and the Caribbean, and another 15 dependencies or other territories,[38] of which population wise as well as area wise Brazil is the largest. While many of these countries have moved to improve their GDP through activities linked with bioeconomy, Brazil has the largest GDP among all countries in the region.[39] The other two large countries in this region, namely Argentina and Mexico, are also poised for improving economy and using modern biological processes, while many other Latin America and the Caribbean countries are also doing so. Genetically modified cotton, maize, soybean, sugarcane, flex etc., are being cultivated in several countries in this region. However, the basic biotechnologies and the genetically modified planting materials are often inducted from other developed nations, and the local seeds are transformed by back-crossing. The biotechnological base is not yet at the most advanced levels. In a research-based study (Mungaray-Moctezuma 2015) the characteristics of technology and human capital needed in order to evolve towards a knowledge-based economy, where the importance of institutions for their development and the necessary human capital from the perspective of bioeconomy were studied for Argentina, Costa Rica and Mexico. It was revealed that Argentina has greater potential to compete in an economy that is sustained in the creation and dissemination of knowledge, while in Mexico there are pressing needs for improving its institutional structure and skills in human resources so as to enable them to adopt knowledge-based bioeconomy pathways. Agriculture and biodiversity are important components for development in every agro-based economies. Appropriate plans and programmes in these areas can boost bioeconomy in these regions.

South America[40] is home to 434 million people (as of July 2022), which is about 6 per cent of the world population. The GDP is US$4.04 trillion (nominal; 2023 estimate) and US$8.2 trillion (PPP; 2023 estimate). South American economy, measured by nominal GDP (2023), is 4th in the world and 5th by PPP GDP (2023). Agriculture, animal husbandry, mining, industry, oil and natural gas, and tourism are the main components of their economy. The continent could not keep pace with current global developments. The education system and the institutional structure as well as the developmental infrastructure, have remained behind; the colonial past has had a negative influence towards faster modernisation.

In this review, the bioeconomy of Brazil has only been discussed in more detail. Among the Latin American and the connected Southern Hemisphere countries, the economy of Brazil is the largest. Brazilian economy[41] is a middle-income developing mixed economy. Brazil has a population of 215 million (2022), with a GDP of US$2.081 trillion (nominal; 2023 estimate) and US$4.020 trillion (PPP; 2023 estimate). The GDP economy of the country is country when compared with the global GDP is 10th on a nominal basis (2023) and 8th on a PPP basis(2023).The service sector GDP represents over 60 per cent, followed by industry, over 15 per cent , and the agriculture sector at about 6 per cent(2020 estimate).

Brazil is globally an established economic giant[42] in mining, agriculture, and manufacturing, and has a rapidly growing service sector. Presently, Brazil is getting more interested in bioeconomy, and aims to promote (Maximo *et al*. 2022) sustainable development in areas of expertise of the country, using biotechnological processes and innovations utilising renewable raw materials, which are forest and agriculture-based, to substitute the use of fossil-based materials. In Brazil, their bioeconomy periphery is majorly bound by the application of biotechnological knowledge to renewable biological resources emanating from agriculture and the forest sector. Forests and the forest sector form an important part of Brazilian economy. Brazil has the second-largest forest area in the world. The pulp and paper industry of Brazil is significant, and for this sector forests play an important role. Latex rubber and timber are other significant forest-based products. Forests also enable the production of many other value added products in Brazil such as nano-crystalline nano-size cellulose, wood-based textile fibers, lignin-based products, and chemical derivatives from tall oil.

Brazilian policies and programmes in bioeconomy dates back to the 6th German-Brazilian dialogue in science, research and innovations,[43] held on November 8, 2017 at Sao Paulo, where Brazilian strategies, policies and programmes were cogently conceived and framed out of discussions with multiple stakeholders. It was realized that success in bioeconomy was primarily based on and linked with innovations, especially in biotechnology. The aims were to add value to primary production, use of bio-wastes gainfully, reduce dependence on fossil fuel by replacing fossil fuel based energy with bioenergy production systems. Brazilian government evolved their bioeconomy strategy involving agribusiness, tropical agriculture research, natural biodiversity usage, including forests and biofuel production, while empowering the academic sector and evolving structured new bio business sector. The Brazilian government strategy and their industry were to focus research and innovation in (a) bio control and biotechnological processes in in a sustainable manner for managing agricultural pests, (b) biomass processing, (c) developing proficiency in renewable green chemistry, (d) environmental biotechnologies applied to the recovery of degraded and contaminated lands and processing of bio-wastes for value addition, and (e) development and scale-up of biotechnological processes. Brazilian efforts in bioeconomy also included intent to collaborate with multiple biotechnology-rich countries so as to induct knowledge and expertise therefrom for the country.

A researched based study (Machado *et al*. 2021) on the macroeconomic aspects of Brazilian economy derived from biomass (bioeconomy) through a Computable General Equilibrium model revealed that by 2030, the amount of chemicals and energy production through fossils versus biomass for the country, based on sugarcane, soy and forest crops may result in almost irrelevant negative impacts on GDP and in small increases in unemployment rate, when compared to business as usual, as the reference scenario. It was further revealed that if there was an increase in efficiency regarding land use in the livestock and agriculture sectors, then such effects might be reversed. However, if there was not enough rise in the efficiency and productivity from the learnt innovative technologies, then the biobased costs of products could be higher, and it might be necessary to provide subsidies to encourage the use of these technologies. These results clearly point towards intense attention and activities in R &D to develop technologies that contribute to improve efficiencies. However, the country has already turned towards efforts to magnify their GDP through bioeconomy activities, and a study report has claimed[44] that by 2050, the bioeconomy of Brazil can generate US$ 284 billion in revenue per annum, and that it has been flagged that a list of solutions that would increase yield in agriculture and would also reduce the emission of greenhouse gasses.

Brazil has another significant responsibility in the global context, which emanates from the issues linked with their Amazon rainforests. It is estimated that the rainforest contributes[45] about $8.2 billion a year to the economy of the country from products including rubber and timber. But the Amazon forest is often hit by fires that irreversibly clear thousands of miles of rainforests, thereby worsening the carbon capture capacities of Mother Earth, and causing potential environmental damage. Added to this, if the rainforest is over exploited by human activities, there could be much increase in the worsening of the environment. Corrective actions (Brouwer *et al*. 2022) in this context on a global platform need to be intensified to maintain the good health of the Amazon rainforests.

The ASEAN Countries

The ASEAN Member States are Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam.The ASEAN States account for about 7 per cent of global GDP and is home to nearly 0.7 billion people. It accounts for 9 per cent of global GDP growth during the past 10 years (2012-2022).[46] They visualise as a single market and production base, which is characterised by the free flow of goods and services, capital, investments and labour. Agriculture provides a maximum number of employments to the member countries, which employs more than 8.2 per cent of the region's labour force and generates over USD 2.3 trillion in sales annually (Wang *et al*. 2022). Critical studies on the transition of bioeconomy through agriculture, forestry, agribusiness and other certain sectors that produce and use bio-based raw materials make good economic sense. There is a strong need to develop improved and efficient technologies that ensure improved efficiencies. Long-term national and regional strategy and action plan for such activities need to be framed and systematically pushed. There is yet no unified strategic document for the ASEAN countries to identify the technological gaps and barriers as also the best practices to be adopted for the region to address the challenges faced by the governments and the policymakers, the researchers and practitioners, including the industry for a successful bioeconomy for the region. In the renewable energy area, the ASEAN countries have plans[47] to achieve 23 per cent share in the total primary energy supply from renewables by 2025. Each country has different plans and programme.[48] As of 2019, the capacities for generating energy from renewable sources was the highest in Vietnam and lowest in Singapore. The Government of Vietnam in 2015 announced.[49] their first-ever national development strategy for energy, from renewable sources and has plans to reach 32 per cent of their primary supply of electricity from such sources by 2030.

The impact of resources emanating from the agricultural and forestry sectors for sustainable development aiming at achieving improved bio-economy in ASEAN countries has caught attention of many intellectual groups. In one recent study (Phuoc Huu Vo and Thanh Quang Ngo 2021) from Vietnam, it was shown that the agricultural resources such as agricultural land both irrigated as well as rain fed, agricultural practices, forest resources, forest area and forest rent((round wood harvest times the product of regional prices and a regional rental rate), and fishing economic activities including fishing industry (activities concerned with catching, culturing, processing, preserving, storing, transporting, marketing or selling fish or fish products from sea and land waters)have a positive association with the transition towards bio-economy in ASEAN countries. The primary renewable production systems like conventional agriculture, the use of forests and forest products for human benefits, fisheries and aquaculture shall be affected by global climate change, and therefore, there would be a need to develop new technologies and strategies to keep the production from these primary production systems efficient and more productive. This would be possible by inducting modern biotechnological systems into conventional practices. There is presently a lack of development in modern biological technologies in the ASEAN region. Future researchers may develop road maps for the development of modern biotechnologies to assist the policymakers to come up with strategies and action plans that benefit the region.

South Korea

South Korea with a population of about 51.3 million in 2021, had a GDP of US$2.76 billion in 2022. The per capita GDP was US$33591(nominal) in 2022 and US$ 53574(PPP) during the same period. South Korea is the 4th largest economy in Asia and 12th in the world. South Korea is a highly developed mixed economy. Their agricultural sector is only 2.2 per cent of the GDP; the latter is dominated by industry (39.3 per cent of GDP) and the services sector (58.3 per cent). Only 4.4 per cent of the labor is employed by the agriculture sector.[50] The term 'bioeconomy' is understood in South Korea to mean the economic sectors related to the biosciences, medical biotechnology and the health sector. Bioenergy, green chemistry and bio-electronics have also been attributed to bioeconomy.[51]

South Korea has a great interest in bioeconomy. The term 'bioeconomy' is understood in South Korea to mean the economic sectors related to the biosciences, medical biotechnology and the health sector. Bioenergy, green chemistry and bio-electronics have also been attributed to bioeconomy.

As early as in 2006, South Korea prepared a document entitled " Bio-Vision 2016" and adopted it as the "2nd Framework plan for Promotion of Biotechnology" with clear targets for the biotech industry with a view to develop their bioeconomy. The document aims to develop a prosperous bioeconomy in the country and to provide healthy life to its citizens. In 2008, the South Korean government published a document with "Low Carbon, Green Growth strategy. For promoting bio-industries, their Ministry of Trade, Industry and Industry in 2012 came out with a document on "Strategy for promotion of industrial biotechnology"[52] South Korean Government continues to support and promote bioeconomy activities. On July 14, 2020, the government announced to invest KRW of 114 trillion (USD 94.5 billion) over a period of time on Green Technologies, comprising green renewable energy, housing (energy saving buildings), mobility through electric cars, and industry, and the initiatives are anticipated to create 1.9 million new jobs by 2025.[53]

The bioeconomy of South Korea is presently leaning towards the medical care industry (Wei *et al*. 2022). The Government has made sizable investments to promote the sector. The sector has made commendable progress and in manufacturing recombinant DNA-based therapeutic proteins of high value, biosimilar molecules and stem cell therapy as well as high-class medical devices, such as molecular diagnostics and equipment with global competitiveness. It is anticipated that the country shall also take up massive projects utilising modern biotechnologies in the field of agriculture, the environment, oceans, energy, and the bioelectronics industries, where the present emphasis would need to be strengthened.

Russia

Russia[54] with a population of 147 .1 million as of late 2021 census has a GDP of US$2.063 trillion (nominal; 2023 estimate) and US$4.989 trillion (PPP; 2023 estimate). Russian GDP economy is driven by agriculture: 5.6 per cent;industry: 26.6 per cent; and services: 67.8 per cent(2022 estimate). Labour employments is 9.4 per cent in agriculture; 27.6 per cent in industry, and 63 per cent in the services sector (2016 estimate).

Russian government launched their programme called BIO-2020 strategy[55] in 2012 with an investment of US$18 million. Efficient development of biotechnology to bring the country to a globally leading position in areas including biomedicine, bio-pharmaceuticals, agro biotechnology, food, environmental biotechnology, marine biotechnology, forests, industrial sector and bio energies, with the aim of creating a globally competitive bioeconomy sector in Russia was the plan. The span of the programme was 2012-2020. Several government departments, including ministries, government agencies and academic institutions, were involved in the plan. Bioeconomy was to contribute to 1 per cent of the Russian GDP by 2020, and 3 per cent by 2030.[56] The President of Russia, in his address to the Federal Assembly on January 15, 2020 had emphasized the need for a circular economy as a part of the Russian bioeconomy as their development priorities.[57] Wastes generated by the industry would have to be mitigated by them. This calls for the development of new and sustainable technologies.

The BIO 2020 programmes seemed to have been conceived essentially as the programmes with a beginning; the money allocated appears to be too small for such massive plans and projects. In an academic analysis in 2021, it was revealed that the forecast made in 2012 through BIO 2020 did not materialize (Boyarov *et al*. 2021). While business interest is gradually emerging in pursuing the bioeconomy sector, newer strategies need to be adopted with more investment allocations; a new BIO 2030 document seems to be under preparation.

Australia

Australia[58] has a population of 25.89 million (2021 Census) with a GDP of $1.708 trillion (nominal; 2023) and $1.718 trillion (PPP; 2023). It ranks 13th on GDP (nominal 2023) and 19th (PPP GDP 2023). Agriculture constituted 2.8 per cent (2017) of GDP, while the dominant sectors were Services: 62.7 per cent; Construction: 7.4 per cent; Mining: 5.8 per cent and Manufacturing: 5.8 per cent. Australia is a highly developed country and its economy is mixed.

Presently in Australia, there is no official national bioeconomy strategy. The government is however interested to develop it's agricultural, forest and marine resources, using sophisticated modern technologies and therefore has provided political guidance and support,[59] identifying priority areas in several thematic areas of the bioeconomy in these sectors. Australia has defined plans and strategies for generating bioenergy. Their Bioenergy Roadmap.[60] is anticipated to contribute to around $10 billion in extra GDP per annum.

Australia has a strong emphasis on developing products and services using techniques of synthetic biology. They have defined synthetic biology as 'the rational design and construction of nucleic acid sequences or proteins and novel combinations thereof, using standardized genetic parts'. Australia is moving into synthetic biology application domains[61] by developing appropriate expertise systematically through (a) Foundation

Technologies, (b) Environment and Bio control projects, (c) Industrial Biotechnology projects, (d) projects in Health and Medicine, and (e) programmes in Agriculture and Food. They are also working on rationalising and maximizing the impact of each project on their economy. The domain of application of Foundation Technologies includes an advanced robotic high-throughput DNA componentry assembly, cell line engineering, and analysis facility, which they have termed as Bio Foundry; development of synthetic biology parts and tools((termed as bio bricks) that can be applied to a wide range of application areas for exploiting their biological and genetic heritage; and developing organelle control devices which would serve as engineering tools targeting mitochondria and chloroplasts. The aim of projects in Environment and Biocontrol is to contribute to a world class capability in delivering solutions based on synthetic biology. Industrial Biotechnology projects would be towards producing fibers and chemicals. Projects in Health and Medicine would aim to design new synthetic biology tools and platforms that would improve health and further global health research. The novel design of next generation yeast and crop production platforms is aimed at, in Agriculture and Food areas. Efforts would concurrently be made to enable the public to understand the benefits of the developments. The necessary social, ethical and legal frameworks required to deliver safe and efficacious solutions by using synthetic biology techniques and technologies would also be prepared.

Thus far Australia has invested at least Australian dollars (A$) 80 million in developing research capabilities in synthetic biology. It is anticipated that by 2040, synthetic biology may turn out up to A$ 27 billion in revenue annually and would create 44,000 new jobs for the country.62 The contributions from synthetic biology are thus thought to be quite significant. The techniques and technologies used in synthetic biology are almost the same that are used in uplifting bioeconomy in other developed countries. Although Australia does not officially have bioeconomy programmes, they are focused on developing technologies that are most relevant to promoting bio economies elsewhere, and therefore the efforts of the country were included in the paper.

Impact of Bioeconomy towards Global GDP

The present GDP of the world[63] was estimated at US$101.56 trillion in 2022(International Monetary Fund); US$96.51 trillion in 2021(World Bank); and US$85.33 trillion in 2020(United Nations). Estimate made by different agencies vary. For example, the 2022 World GDP was reported[64] at US$95 trillion as of 2022. The figures provide a broad flavour about the world economy. The global biotechnology market[65] was estimated at

US$1224.31 billion in 2022. The present contributions of bioeconomy to the world GDP are therefore assessed to be about 1.2 per cent to1.3 per cent. The contributions shall substantially rise in future as cutting-edge novel biotechnologies are invented during future years.

Discussion and Concluding Remarks

The worldwide bioeconomy is centered on fostering economic prosperity by harnessing biological resources, including plants, animals, microorganisms, derived biomass, and organic waste. Through advanced technological applications, it facilitates the production of diverse goods, ranging from food, animal feed, pharmaceuticals, bio-based polymers, plastics, chemicals, and value-added products to biofuels and energy. The overarching objective is to achieve these outcomes while concurrently reducing greenhouse gas emissions. Harnessing bioeconomy is anticipated to enable recycling of wastes and more promotion of environmental sustainability. Bioeconomy is a social necessity to address major human needs such as food, medicines, safe drinking water, healthy dwelling places with science-based washrooms and bathrooms. Advancement of bioeconomy in counties is anticipated to elevate the health, longevity and living standards of people besides societal reforming to promote equal opportunities for skill development.

The demand for certain inputs for people for improving the living standards promotes competition between and among certain crucial needs such as food, feed, fuel, pharmaceuticals and healthcare infrastructure. Countries and societies would resort to trade-offs strategy, depending on their priorities, and one universal solution would not emerge. Therefore different kinds of innovations shall be promoted in different countries. However, safe and nutritious foods grown through various innovative technologies, using different life forms other than plants, shall be a major priority all over to produce protein-rich biomass in closed systems, thereby minimizing the use of land. Adverse impacts emanating from packaged foods dispensed in plastics-based containers would draw more attention, and innovations in bioplastics are anticipated to be a major direction in novel technology development. In order to reduce respiratory illness while preparing foods using solid fuels (plant biomass and animal dung based), more use of liquefied as well as biogas is foreseen. Advent in the generation of more efficacious new medicines and increased production of patent expired effective biomedicines (produced by r DNA technology and other connected and linked technological advancements) for increasing longevity and maintaining better health are other areas of innovation are bound to intensify.

Economic advancement causes generation of more wealth. Bio economic advancement causing creation of more wealth needs to be rationally distributed so that there is more equity among people in the possession of wealth. As a social objective, bioeconomy needs to address the inequality dynamics among people, and come up with policies to minimise and rationalise severe existing inequality. Growing inequality among people in different countries is a great global concern. The world needs more talented people to contribute to new inventions in science and technologies. The world cannot progress without major new inventions. Inventions emanate from people. There is increasing evidence that innovative people are born in every community. But to nurture talents, there is a need to enable people to have access to good health, high-quality education and to ensure safety. Access to these services by all would reduce inequality, and more talented people would develop from both sexes. Talented young people would not reach their full potential if they are inhibited by social circumstances. In bioeconomy objectives, while creating new job opportunities is flagged, there is a need to take action to reduce inequalities, especially in developing and poor countries, at least in maintaining good health, access to high-quality education and ensuring safety at all ages.

In countries practicing globalisation, competition and open market economy, while countries have been able to increase their wealth phenomenally, the income inequality has also grown along with increased lack of opportunities for poor individuals, resulting in diminished access to basic needs such as nutritious food, pure drinking water, sound health, adequate education for skill development, access to cheaper energy sources, and many others. Therefore, unless governments have simultaneously taken up programmes to mitigate such needs rationally, the gap is seen to swell. Multiple components emanating from practicing bioeconomy and improving the efficiency across productive factors can assist in bridging the gap between 'haves and have-nots', especially in access to food, good health and renewable energy in a sustainable manner. The technological developments in relevant areas should, therefore, be identified for each country by the governments, and appropriate programmes and action plans need to be pursued. There is no better alternative to acquiring own skills and developmental initiatives.

Acceptance of biobased products and technologies involving manipulation of genes, cell lines, and natural life forms applied to benefit various relevant sectors such as food, feed and fodder; health of people, industry and improvement of polluted environment has strong societal acceptance issues. Safety and efficacy are the two main points on which societal acceptance or rejection depends. To develop a strictly science-based society is almost impossible. The element of ethics, social acceptance issues, including rights to choose and legal provisions, are anticipated to flare up. Countries would have to resolve multiple issues and, therefore, there is a need to spend time on such issues through united global forums on a precautionary principle concurrently, as global advancements in bioeconomy take place.

Advancement in wealth creation by developing products involving the manipulation of genes, cell lines, and natural life forms has strong societal acceptance issues. The element of ethics, social acceptance issues, including rights to choose and legal provisions need to be worked upon through united global forums on a precautionary principle for bringing out undisputed resolution.

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Utility of Bioenzymes for Sustainable Food Systems: A Narrative Review

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Abstract: Due to its numerous benefits to sustainability, product quality, and consumer health, the use of bio-enzymes in food systems has grown in significance. The importance of these enzymes in the creation of sustainable food is highlighted in this abstract. By increasing the bioavailability of vital nutrients and lowering the amount of anti-nutrients, bio-enzymes serve a critical role in boosting the nutritional value of food. By displacing artificial additives and preservatives, they also assist in the production of products with cleaner labels. Reduced food waste, increased shelf life, and consistency and flavour of food items are all made possible by bio-enzymes. Additionally, their eco-friendly sourcing and sustainable production methods meet the rising demand for food production that is environmentally conscious. The significance of bio-enzymes is growing in an era of increased sustainability goals, consumer awareness and environmental implications. The review presents studies on the utility of bio enzymes in food production and processing and in improving food quality, nutritional value, and safety and its role in the environmental impact and exploration of the latest technological developments and innovations in the food industry along with the identification of literature gaps and areas where research is scarce.
Keywords: Bio enzymes, Bio catalysis, Ecofriendly food production, Food processing, Enzymes in food, Sustainable food systems.

Introduction

In recent years, there has been growing recognition of the need for sustainable food systems that can meet the nutritional needs of a growing global population while minimising negative environmental impacts. Traditional agricultural and food production practices often rely on non-renewable resources, contribute to greenhouse gas emissions, and generate waste. As a result, there is a growing interest in utilising bio-enzymes and biofuels to promote sustainability in food systems. Achieving sustainable food systems now appears to be possible with the help of biofuels and bio-enzymes (Herrero *et al*., 2020).

In living organisms, bio-enzymes serve as catalysts to speed up chemical reactions. They are naturally occurring proteins. They have a wide range of uses in numerous industries, including the food business. Biofuels, on the

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other hand, are renewable fuels that can replace fossil fuels since they are made from organic matter, such as plant biomass or animal waste (Ayub *et al*., 2023).

A solution named as "Garbage Enzyme" was developed in 2006 by Thai researcher Dr. Rosukon Poompanvong, utilising organic solid waste (Novianti & Muliarta, 2021). The simple fermentation of organic waste materials, such as fruit and vegetable peels, flowers, or leaves, mixed with molasses and water, is employed to produce bio enzymes. The concoction is made up of three parts organic waste, one part molasses, and ten parts water, or 3:1:10 ratio. In addition, the mixture's primary ingredients include hormones, amino acids, alcohol, acetic acid, vitamins, minerals, salts, and enzymes (such as lipase, amylase, protease, and cellulase). This mixture is fermented for three months to provide a dark brown liquid known as garbage enzyme or eco enzyme, which has an odour similar to vinegar (Samriti, 2019).

Biotechnology utilises bio-enzymes in bioprocessing, where biological systems are employed to produce valuable products using genetic engineering and fermentation. This includes the use of enzymes in the production of bio-based materials, biofuels, and other bio-derived products. Various industries such as detergents, textiles, pharmaceuticals and food and beverages are using the bio-enzymes to obtain a sustainable cost-effective and environment-friendly products. Enzymes have been found to be useful in bioremediation processes to degrade pollutants, and they play a role in wastewater treatment and soil improvement. By naturally fertilising the land with enzyme residue, tainted water is purified and more leaching is prevented (Keus, 2015).

By using such Eco-enzymes, wastewater sludge can be used as a potential organic fertilizer and disinfectant, an antibiotic agent for endodontic treatments, and also as a hand sanitiser. Its versatile properties include its ability to act as a disinfectant, biofertiliser, and cleaner for wastewater, all while lowering the need for landfills that generate methane emissions, a major contributor to global warming (Barman *et al*., 2022). Thus, the bio-enzymes are useful instruments in the wider discipline of biotechnology because of their versatility; they have an impact on many industries and help develop novel and sustainable solutions. The value of bio enzymes and biofuels comes from their capacity to address a number of significant sustainability issues in food systems. They provide chances to increase resource efficiency, lower greenhouse gas emissions, encourage waste reduction, and aid in the growth of circular economy practices. Sustainable food systems can be developed, assuring food security, minimising negative environmental effects, and promoting economic growth (Esfandabadi, 2022).

In the food sector, sustainability is essential to protect the environment, save resources, maintain food security, promote public health, complete social obligations, satisfy customer needs, and manage risks. A more resilient, egalitarian, and sustainable food system that benefits people, the environment, and future generations can be achieved through adopting sustainability approaches by the industry. The usefulness and advantages of bio enzymes in sustainable food systems is crucial in this regard. This review examines the potential of bio enzymes in enhancing the processing efficiency, and waste management by converting the biowaste to value added products, improving the shelf life and the quality attributes of the product, and improving the specific functional properties of the food product while highlighting the beneficial contributions to the development of a more resilient and sustainable food system. Hence, the present review focusses on assessing the available literature to develop a comprehensive understanding of the potential, challenges, and opportunities and guide future efforts towards a more sustainable and efficient food production and processing.

Rationale for the narrative review:

The usage of bio enzymes for giving a thorough overview of the state of research and commercial practices has grown significantly as people's awareness of the need for sustainable food systems has increased. The review highlights the role of these eco enzymes in enhancing the bioeconomy. Researchers, legislators, business people, and the general public would all benefit from the review's information on the function of bio enzymes in advancing sustainable food production, processing, and waste management. The evaluation can shed light on potential new developments and future approaches for the use of bio-enzymes in food systems. Researchers, industry participants, and policymakers may work together more to discover fresh uses, get around obstacles, and boost the adoption and use of these technologies. The review can identify literature gaps and areas where research is limited or scarce.

Objectives of the Review:

1) Analyse the utility of bio enzymes in food production and processing and in improving food quality, nutritional value, and safety.
2) Investigate the environmental impact of bio enzymes in the context of sustainable food systems.
3) Explore the latest technological developments and innovations related to bio enzymes in the food industry.

Methodology: Different databases such as Scopus, Web of Science, PubMed and Google Scholar were searched by utilising the Boolean operators "OR" and "AND" to find the relevant articles. MeSH subheadings and appropriate keywords were employed, such as Bio enzymes, Food production, food processing, Enzymes in food, Sustainable food systems, Enzymes in food and or Food industry, Food processing, Garbage-enzymes, Eco-enzymes for the identification of the pertinent studies. Fifty-four full research papers in English language, published between 2003-2023 were included in the review and studies with only abstracts published and research articles found in non-English language were excluded.

Overview of Bio-Enzymes and their Utility in Sustainable Food Systems

Currently, the global food system is accountable for over 30 per cent of greenhouse gas emissions, with food loss and waste alone responsible for 8–10 per cent. The need for animal-based protein will rise as a result of rising earnings, urbanisation, and the projected increase in world population to approximately 10 billion by 2050 (Fiora, 2019). This calls for a revolution in food manufacturing, consumption, and production processes worldwide during the next three decades. In order to feed an additional two billion people while also combating climate change, we now have a striking opportunity and responsibility to build a more equitable, resilient, and sustainable food system. A developing strategy to replace chemical agents in numerous industrial domains is the use of bio enzymes. Bio enzymes, also referred to as biological catalysts are proteins which assist and quicken chemical processes in living things. Microorganisms generate bio enzymes that convert natural resources, such as food and agricultural waste, into soluble nutrients, enhancing the bioavailability of such elements. Bio enzymes have received a lot of interest recently due to their use in sustainable food systems. They have many advantages, such as better product quality, reduced waste, higher resource efficiency, and reduced environmental impact (Kee *et al*., 2023). Although the use of bio enzymes is not a different idea, its potential in the current chemical-dominated global market has been grossly underestimated. These biological catalysts can contribute to a sustainable food and drink industry.

Characteristics of Bio-enzymes

The crucial traits of bio enzymes include the unique composition and three-dimensional structure of amino acids specialized in catalytic activity. The substrate is recognised and bound by the enzyme, which then catalyses the desired chemical reaction. This is made possible by the precise arrangement of amino acids in the active site and other sections of the enzyme. The structure of an enzyme can be altered or changed, which can result in altered catalytic activity or function loss (Lakra *et al*., 2022). Proteases have a distinct protein structure that enables them to target and cleave particular peptide bonds in proteins, leading to protein hydrolysis. For example, proteases are essential for the development of flavour and texture in the making of cheese. Peptides and amino acids are produced as a result of the proteases' action on the casein proteins found in milk. These breakdown byproducts help give many types of cheese their distinctive flavour and scent (Gurumallesh *et al*., 2019). Additionally, every bio enzyme exhibits selective catalysis. By being specific, bio enzymes guarantee that they carry out certain tasks inside biological systems. Different mechanisms, such as post-translational modifications, feedback inhibition, and allosteric regulation, can be used to regulate an organism. This enables precise control over cellular functions and metabolic pathways. Extreme pH or temperature conditions can be tolerated by certain bio enzymes. Bio-enzymes are generally reusable catalysts. They are not consumed or permanently altered during the catalytic reaction and can participate in multiple reaction cycles. This reusability contributes to the cost-effectiveness and efficiency of bio enzymes in various industrial processes, such as during the brewing process, bio enzymes are used to break down proteins and starches, respectively, such as amylases and proteases. These enzymes aid in breaking down proteins to increase flavour and stability and turn starches into fermentable sugars. The leftover grains or biomass from brewing can be used as animal feed or anaerobically digested to produce biogas or during the baking, enzymes such as amylases, xylanases, and lipases are used to increase volume, improve texture, and prolong the shelf life of baked goods and any waste or unfinished goods can be recycled or used again after baking, for example, by composting them or using them to make animal feed (Handique *et al*., 2023).

Utility of Bio-Enzymes in the Food Production and Food Processing Industry

It has been shown that bio enzymes can be used in a variety of settings, including agriculture and food industry and community settings, to utilise food waste. Likewise, the Bio enzyme use is extensive since it is entirely natural and aids in waste lessening. As we are accentuating on sustainable food production, the bio enzymes which accelerate food production and ease food processing are particularly useful.

Proteoses

Proteoses are particularly important in cheese-making processes to impart and develop the texture, flavour, and aroma of different types of cheese. They are added during the coagulation stage to break down milk proteins, primarily casein, into smaller peptides and amino acids. This enzymatic action helps develop specific proteases, such as chymosin (rennet), to coagulate milk proteins and form curds in cheese production. Advances in enzyme engineering techniques have allowed for the development of more efficient and specific proteases for cheese production (Sharma *et al*., 2020). Researchers are exploring genetic modifications and protein engineering to enhance the performance of proteases, resulting in improved coagulation properties, cheese texture, and flavour development. By optimising fermentation conditions, pH levels, temperature, and incubation times, they aim to maximize the proteolytic activity of enzymes, leading to better cheese quality and yield (Sharma *et al*., 2016). The use of microbial proteases derived from genetically modified microorganisms or newly discovered strains has gained attention. When dairy, fruit, vegetable, legume, fish, and meat products are fermented, bioactive peptides are released. In addition to their capacity to produce bioactive peptides, lactic acid bacteria, Bacillus spp., yeasts, and mould have a proteolytic specificity that contributes significantly to the production of particular bioactive peptides in traditional fermented foods (Chaurasia *et al*., 2023). Protease supplies from new and different sources are being investigated for meat fermentation. This entails looking into proteases produced from plants, microorganisms, or recombinant enzymes.

Finding proteases with particular functions and traits that can improve fermentation and aid in the production of distinctive meat products is being researched (Parlindungan et al., 2023). According to reports, soy-based fermented foods (SFF) are highly effective at preventing thrombus, which is one of the major risk factors for cardiovascular disease. This is largely because these foods contain bioactive compounds, particularly fibrinolytic enzymes (FE) produced by microorganisms during the fermentation process. The microbial fibrinolytic enzymes (MFE) from SFF were consequently been the main focus (Yao et al., 2021). Some plant proteases are used to coagulate milk proteins and aid in the production of cheese curds, such as those found in figs (ficin) and pineapples (bromelain) (Patel et al., 2013). They provide an alternative to proteases originating from animals, such as rennet. Plant proteases have a function in the brewing and beverage industries, particularly in the manufacturing of beer. They are employed to break down malted grain proteins, enhancing wort filtration and beer clarity. Additionally, proteases are utilised to alter the functional characteristics of food proteins, such as coagulation and emulsification, as well as their flavour, nutritional value, solubility, and digestibility (Graca et al., 2023). In the baking industry, proteases are frequently employed to make bread, baked goods, crackers, and waffles. These enzymes are employed to speed up the mixing process, lessen dough consistency and uniform (Aruna et al., 2014).

Amylase

The field of amylase applications in food production is continuously evolving, with ongoing research and development. Amylase is a common ingredient in baking products and is used to enhance the texture, handling characteristics, and overall quality of baked foods. It aids in the breakdown of flour's intricate starch molecules into simpler sugars that yeast can ferment and release carbon dioxide from. This gas generation helps dough leaven and gives bread, pastries and other baked goods their light and fluffy texture. Immobilisation techniques have advanced the use of amylase in food production. Immobilised enzymes have increased stability, reusability, and ease of separation from the finished product, among other advantages (Bashir *et al.*,2020). In order to increase the performance and cost-effectiveness of amylase applications, many immobilisation techniques have been investigated, including encapsulation, covalent binding, and adsorption onto solid substrates. Amylases with improved characteristics have been created using genetic engineering techniques for use in particular food applications. Researchers have altered amylases to enhance their substrate specificity, thermal stability, pH tolerance, or resistance to inhibitors through protein engineering and directed evolution. These developments allow for the creation of customised amylases with enhanced functionality for various food processing requirements (Jujjavarapu, 2019). Likewise, new methods for process optimisation have increased the efficiency with which amylase is used in food production (Far *et al.*, 2020).

Lipases

Animals, plants, and microorganisms all manufacture lipases, which are widely distributed enzymes The adoption of recombinant manufacturing technology is essential due to the rising economic interest in these proteins in the food and nutraceutical industries. Utilising cell factories for the heterologous manufacture of lipases has increased the productivity of lipase production bioprocesses while decreasing the cost of enzymes. One of the most frequently employed cell factories among them is Komogataella phaffi (P. pastoris) (Vellero *et al.*, 2012). To safeguard lipases throughout processing, improve their stability, and regulate their activity in certain food matrices, microencapsulation, and delivery systems based on nanotechnology protein engineering, bioinformatics design, directed evolution, saturation mutagenesis, site-directed mutagenesis, and DNA shuffling have all been used to improve lipases activity (Reyesal *et al.*, 2022). These developments make it possible for lipases to be released in a targeted and regulated manner, improving their performance in food-related applications (Hamdan *et al.*, 2021). However, the natural form is frequently chosen in the food business as a valuable bio enzyme in food production, offering opportunities to enhance flavours, improve texture, and modify fat content in various food products such as flavour enhancers in a variety of cheeses such as blue cheese, parmesan. Lipases can be used to modify oils and fats to lower their amount of harmful trans fats. Additionally, they can be utilised to create structured lipids that have particular health advantages, including a lower calorie count or an enhanced fatty acid profile. The creation of food products with better functionalities and nutritional profiles is made possible by lipases (Teng *et al*., 2021). Lipase is widely used in cheese production to enhance flavour and aroma. Certain types of cheese, such as blue cheese and Parmesan, require the addition of lipase to develop their characteristic flavours. Lipase acts on the milk fat, releasing free fatty acids that contribute to the unique taste and aroma of these cheeses and also helps in the modification of fats and oils, leading to improved emulsification, aeration, and stability of dough and batters. Lipase can also enhance the textural attributes of baked goods, such as the softness of bread and the creaminess of fillings, using certain lipase-mediated reactions such as catalysis of triglycerides into free fatty acids, resulting in fat modification or reduction, which may have implications for product formulation and nutritional considerations.

Cellulases

The typical sources of cellulase are microorganisms like bacteria and fungus. These enzymes are highly substrate-specific and efficient at dissolving cellulose into less complex sugars, making them useful tools in a variety of industries. Particularly diverse uses for cellulase can be found in the food business, food service, food supply, and food preservation. Cellulases can, in fact, improve the flavour and aroma of food products, extract the essential oil from olives and the polyphenols found in tea, hydrolyse roasted coffee, lessen the roughness of dough, clarify fruit juices, and tenderise fruit. However, they have mostly been ignored in the food industries. Future possibilities, scientific and technological advancements, and the use of cellulases in the food sector are all projected to increase their potential. Potential applications for cellulase in the food sector include bacteria (Paenibacillus and Bacillus) and fungus (Trichoderma and Aspergillus) (Ejaz *et al*.,2021). In the juice industry, cellulases are applied in combination with other macerating enzymes for increasing process performance and yield, improving the extraction methods, clarification and stabilisation of juices (D'souza *et al*., 2021). They can also reduce the viscosity of nectar and puree from fruits such as apricot, mango, plum, papaya, pear and peach, and are used for the extraction of flavonoids from flowers and seeds. The preference for cellulase-mediated extraction over conventional methods is due to higher yield, less heat damage and short processing time. Cellulases are utilized for the extraction of phenolic compounds from grape pomace (Toy *et al*., 2022). B-Glucosidases in combination with, pectinase alter the structure, flavour and aroma of fruits and vegetables along with reducing the bitterness of citrus fruits and improve the aroma and flavours of wines Cellulases are used with other enzymes for efficient olive oil extraction ((Uzner *et al*., 2021).

Pectinase

Pectinesterase, which converts the polymer of pectin into monomers through the reactionary process of trans-elimination, and Polygalacturonase, which breaks down pectin into smaller fragments through the process of hydrolysis, are two different types of pectinases depending on how they react with their substrate. Pectin is broken down by the enzyme pectin lyase through the reactionary de-esterification process. Two enzymes that work on the glycosidic bonds of polygalacturonic acid and hydrolytic cleavage, respectively, are polygalacturonase (PG) and polymethyl galacturonase (PMG) (Samanta, 2019). Furthermore, fruits are a great source of pectinase. It plays a part in fruit ripening and functions as a natural accelerator. Microorganisms also contain pectinase, which is employed extensively in industry.

Nowadays, enterprises use microorganisms to generate pectinase in a controlled manner because they have a propensity to multiply themselves. Pectinase is made by a variety of yeast, bacterium, and fungus strains. Plants produce pectinase that is more active and so more resistant to alkali, acid, and high temperatures. Pectinase generated by bacteria, on the other hand, exhibits poor activity and is less resistant to high temperatures, acid, and alkali (Hernández-Beltrán *et al*., 2020).   This is the reason why industries prefer to recombine several microbes to produce pectinase with higher activity. Pectinases break down pectin, a complex carbohydrate found in fruits and vegetables. They are used in fruit juice extraction, wine clarification, and to enhance the texture and clarity of fruit products. Pectinase increases the effectiveness of several food processing procedures like clarifying, filtration, and extraction by breaking down pectin. Food processing becomes more sustainable as a result of the decreased need for surplus water, energy, and other resources. The clarity, stability, and sensory qualities of food and beverage items are improved by pectinase enzymes. Pectinase treatment improves juice clarity and decreases haze in the fruit juice business, creating visually appealing products (John *et al*, 2020). This enhances the items' general quality and marketability, lowering the risk of food waste and helping to create a sustainable food system. Hence, Pectinase effectively extracts juice from fruits, minimising waste and maximising fruit consumption while promoting a more sustainable use of agricultural resources.

Other enzymes:

Likewise, Catalases break down hydrogen peroxide into water and oxygen. They are used in the food industry to prevent oxidative damage and maintain food quality, such as in the processing of fruits, vegetables, and dairy products. Phytases break down phytic acid, a form of phosphorus found in grains and oilseeds. They are used in animal feed and food processing to improve nutrient availability and reduce environmental phosphorus pollution. Invertases convert sucrose into glucose and fructose. They are used in the production of inverted sugar syrups, candies, and sweeteners. Lactases break down lactose, the sugar found in milk, into glucose and galactose. They are used in dairy processing to produce lactose-free or reduced-lactose dairy products. Invertase allows for the production of fruit-based sweeteners using a more sustainable approach. It facilitates the hydrolysis of sucrose, a naturally occurring sugar present in fruits, into glucose and fructose, the primary sugars in fruit-based sweeteners. Fruit juices or fruit purees can be used as substrates for this enzymatic conversion process.

This encourages a more diverse and sustainable agricultural system and lessens reliance on large-scale sugar monocultures. In general, growing fruits uses less water than conventional sugar crops (Tan et al., 2023). Water resources can be preserved by employing fruits as a source of sweets, resulting in more sustainable water management techniques. Glucose oxidases convert glucose into gluconic acid and hydrogen peroxide. They are used in food preservation, as they can inhibit microbial growth and extend the shelf life of food products. The requirement for artificial preservatives or chemical additives can be decreased by using glucose oxidase as a preservative, encouraging a more environmentally friendly method of food preservation. Glucose oxidase can also be employed to enhance the texture and calibre of bread goods. Glucose oxidase aids in converting extra glucose in the dough into gluconic acid and hydrogen peroxide. The pH is lowered by the gluconic acid, which improves bread volume and dough formation, and reduces the use of chemical additions, like dough conditioners or oxidising agents, in the making of bread, lessening the impact these compounds have on the environment (Chen et al., 2020).

Environmental Impact of Bio Enzymes for Sustainable Food Systems

In the context of sustainable food systems, instead of using conventional chemical processes for manufacturing food, bio enzymes offer an alternative that may have advantages for sustainable agriculture, reduced chemical use, energy efficiency, waste reduction, biodegradability, and water conservation.

The environmental implications of bio enzymes in sustainable food systems are examined through the available recent evidences.

Reduction of Chemical Additives

Various studies have demonstrated that bio enzymes, such as proteases and amylases, effectively replaced chemical additives like emulsifiers and stabilizers in bakery and dairy products. Animal rennet has been replaced by microbial proteases from Mucor or Endothia parasitica. However, it has been discovered that pure chymosin is more specific than microbiological rennin. It has been demonstrated that pepsin and chymosin-like enzymes from harp seal and fish species that can withstand freesing temperatures can curdle milk, although they are similarly less specific than microbial enzymes. The most important upcoming development in the manufacturing of microbial rennet is the introduction of microbial chymosin made by a genetically modified organism (Ravindran *et al*.,2018).

Study by Sambaraju *et al*. (2023), explored anaerobic fermentation of jaggery, plant waste (generally speaking, fruit, vegetable, flower, or plant waste), water, and microorganisms in a plastic container. Six distinct samples were taken from various fruit and vegetable peels to test their effectiveness and suitability in various industries. After filtering, the liquid portion was utilised to characterise bio-enzymes, while the solid Eco-enzyme is a sort of naturally occurring substance that is typically extracted from citrus fruit peels, trash, and other sources. It is a smart solution made from the fermentation of fresh kitchen trash, such as fruit and vegetable peels. It is a kind of vinegar produced by converting food waste and sugar into alcohol through fermentation. Eco enzyme is a fermented liquid created mostly from sugar, fruit peels, and water in a 1:3:10 ratio (Benny *et al*., 2023). Citrus Eco-enzyme, citrus fruit extracts and citrus flavonoids, due to their phenolic composition and antioxidant activities, have the potential to have favourable biological traits.

Miguel *et al*., 2013 asserted that asparaginase has a high potential for decreasing the synthesis of acrylamide during baking. Asparaginase (L-asparagineamidohydrolases, EC 3.5.1.1) catalyses the hydrolysis of asparagine to aspartic acid and ammonium, hence eliminating the precursor to the synthesis of acrylamide. Asparagine and a carbonyl source undergo the Maillard reaction, which results in the formation of acrylamide, which is categorised as a potential human carcinogen Although asparaginase is present in all living things, including animals, plants, and microbes, filamentous fungus like Aspergillus oryzae and A. niger have been investigated for the purpose of producing enzymes for use in industry (FAO, 2007)

Potential Use in Sanitation and Hygiene in Food Industries

Toxic chemical compounds are largely affecting the worldwide food sector due to anthropogenic and natural sources. As a result of chemical contamination at various phases of food processing, food safety is at risk. Pesticides and other chemicals, such as Polychlorinated Biphenyls (PCBs), are examples of persistent organic pollutants (POPs), which have a long-lasting harmful impact on the environment. As heavy metals, antibiotics, and POP contamination can have a negative impact on human health, they must be regulated by effective legislative actions and appropriate monitoring criteria that are based on reliable scientific evidence. The bioremediation of contaminants is one of the already in place solutions that work well. The sustainability and economic impact of these technologies as a control technique in the food sector, however, require further study. These garbage enzymes or bio enzymes work as enzymatic cleaning agent for food industries as an eco-friendly alternative to chemical cleaning agents in the food industry. The application of GE (garbage enzymes) to treat leachate from metropolitan municipal landfills and domestic wastewater showed a reduction of approximately 55-74 per cent. The concentrations were significantly lowered, but they still didn't match the disposal guidelines however (Rani *et al*., 2020).

Energy saving using Bio- Enzymes

Sustainable processing is now of greater significance than ever because of the urgent need to meet the ambitious net zero targets to reduce carbon emissions and the effects of climate change. The use of inexpensive, renewable materials, nature-inspired, highly selective biocatalysts operating optimally under mild circumstances, and decreased energy consumption/ carbon footprint are all desired characteristics of bioprocessing that can help it meet the challenge of sustainable processing. There has been a lot of interest recently in developing intensified bioprocesses because bioprocessing productivity is far from ideal for meeting the large-scale demand for food, drugs, biofuels, and bio-based chemicals (Bodhoo *et al*., 2020). Significant progress has been made in tailoring and utilising the technologies in the toolbox traditionally applied in chemical process intensification. Enzymes have the potential to provide a low-energy method of recycling some of the textiles and single-use plastics that cause the most pollution, but the cost of this technology will largely determine its global adoption. Researchers have recently demonstrated that one common plastic manufactured by enzyme-based recycling can be economically competitive with conventional PET derived from fossil fuels, consume up to 80 per cent less energy, and emit up to 40 per cent fewer greenhouse gases than virgin manufacturing (Zhu *et al*., 2022).

Energy Efficiency and Environmental Advantages Compared to Conventional Methods

Compared to conventional approaches, bio enzymes are extremely effective catalysts that enable chemical reactions to occur at lower temperatures and softer conditions. In a variety of industrial operations, including food processing, textile manufacture, and biofuel generation, this can result in significant energy savings. Utilising bio enzymes can lessen the demand for high-temperature processing, hence reducing energy needs and related expenses. Perhaps the easiest way to describe the immense catalytic activity of enzymes is to use the constant kcat, also known as the turnover rate, turnover frequency, or turnover number. The number of substrate molecules that can be transformed into products by a single enzyme molecule per unit of time (often per minute or per second) is represented by this constant. For instance, a single carbonic anhydrase molecule may catalyse the conversion of nearly 500,000 molecules of its substrates, water (H2O) and carbon dioxide (CO2), into the product, bicarbonate (HCO3), every second. This is an incredibly impressive feat. The turnover rate (mole product s−1 mole enzyme−1) of certain enzymes such as Carbonic anhydrase is 600,000, catalase is 93,000, β–galactosidase is 200, Chymotrypsin is 100 and tyrosinase is 1 (Robinson, 2015).

Latest Technological Developments and Innovations Related to Bio Enzymes in the Food Industry

In recent years, there have been a number of technological advancements and advances in the field of bio-enzymes in the food sector. In order to increase the stability and reusability of bio enzymes in food processing, immobilization techniques have been developed. In order to facilitate easy separation and reuse, immobilization entails attaching the enzyme to a support substance, such as nanoparticles, polymers, or matrices. With the help of this technology, enzyme use in many food processes is now more efficient and affordable (Brandy & Jordan , 2009). Bio enzymes can now be modified and optimized for use in certain food-related applications because of advancements in enzyme engineering techniques, including protein engineering and directed evolution. Enzymes can be modified to have better activity, stability, substrate specificity, and tolerance to difficult processing conditions using genetic engineering and mutagenesis (Pang *et al*., 2021). The combination of bio-enzymes and nanotechnology has created new opportunities for food processing. In food systems, nano-scale carriers like nanoparticles and nanofibers can shield enzymes, improve their stability, and deliver regulated release. Potential uses for nanobiotechnology include nutrient delivery, flavour enhancement, and food preservation. Over the past forty years, advances in water purification techniques have been made, with the utilization of nanomaterials and nanomembranes being the most significant. TiO2, ZnO, CuO, Ag, CNTs, and mixed oxide nanoparticles, for example, are modern examples of manufactured materials that employ nanoparticles and nanomembranes (polymeric membranes) (Manikandan *et al*., 2022). Bio enzymes and membrane technologies offer creative approaches to food preparation. Enzymatic membrane reactors can be made by immobilising enzymes on or inside of membranes. In processes including juice clarifying, wine production, and milk fractionation, these systems offer benefits like improved reaction speeds, higher-quality products, and less energy and water use (De *et al*., 2022). Multiple enzymes act sequentially in enzyme cascade reactions to create desirable food components or flavours. Recent developments in enzyme cascade systems have made it possible to synthesize complex molecules more effectively and sustainably, including flavour compounds, natural sweeteners, and functional food components (Niu *et al*., 2022).

Biosensors for evaluating the safety and quality of food have been developed using enzymes. Biosensors can quickly and on-site analyse food samples by identifying specific chemicals or pollutants. High sensitivity, specificity, and cost-effectiveness are just a few benefits that enzyme-based biosensors provide, making them useful instruments for applications in the food sector (Rotario et al., 2016). Recent technical and scientific studies based on optical sensing approaches, such as fluorescence sensors, target-responsive hydrogels, chemiluminescence assay, tube enzyme-linked immunosorbent assay, enzymatic fiber-optic biosensor, phosphorescence, lateral flow immunoassay, double-signal fluorescence strategy, wearable glove-based sensors, and paper-based sensors, have made novel advancements and stipulated scientific insight for the on-site detection of pesticide residue (Umapathi et al., 2022). To comprehend the interactions between enzymes and their substrates and to forecast enzyme behavior, computational techniques such as molecular modelling and simulations have been used. These methods support the creation and improvement of bio enzymes for better catalytic stability, specificity, and efficiency (Bahaman et al., 2020). Continued research and application of these advancements will further enhance the role of bio enzymes in achieving a more sustainable and technologically advanced food industry. The Table 1 below summarises the various applications of bio enzymes for maintaining a sustainable food system.

Table 1 "Sustainable Food Solutions: Harnessing the Power of Bio-enzymes"

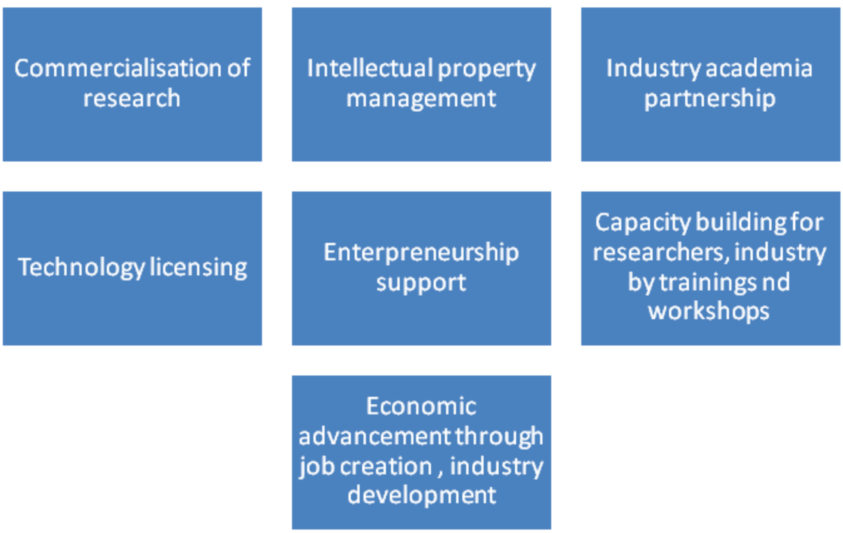
Source: Author's own compilation.

Role of Technology Transfer Offices in India's Biotechnology Sector

As one of the top hubs for bio innovation and biomanufacturing today, India has been identified as an emerging sector and an essential element of the nation's effort to become a $5 trillion economy by 2024 through the rising biotechnology market in India. As per the Invest India reports, 51 Biotech-KISAN (Biotech Krishi Innovation Science Application Network) hubs have been financed by the Department of Biotechnology. These hubs connect Indian farmers with the top scientists and institutions, enabling them to access knowledge on soil health, irrigation, and innovative Agri technologies. This is enabled by the Technology transfer, and knowledge transfer from academic and research organisations to the commercial sector is greatly aided by the work of Technology Transfer Offices (TTOs). TTOs have grown to be crucial intermediaries in India's biotechnology industry, bridging the disparity between research and commercialisation (Markan & Verma, 2019). TTOs are involved with negotiating licencing deals and submitting patent applications arising from biotech research and inventions, TTOs progress the conversion of research discoveries into applications that are advantageous to both industry and academia by fostering collaboration (Debackere, 2018). Asia and Pacific Centre for Transfer of Technology (APCTT), National Research Development Corporation (NRDC), Technology Information Forecasting and Assessment

Council (TIFAC), Biotech Consortium India Limited, Technology Bureau of Small Enterprises (TBSE) are some of the examples of TOTs functioning in India involved in various initiatives, including promoting industry-academia collaborations, technology transfer, and the development of biotechnology parks and incubators through consultancy for investment opportunities, regulatory requirements, setting up incubators, preparation of biosafety dossiers, investment plans, identification of industry partners for technology commercialisation and trainings and sector- specific workshops. The Figure 1 summarises the applications of TOTs in the biotechnology sector.

Figure 1: Contribution of TOTs towards sustainable biotechnology ecosystem



Source: Author's own compilation.

Gaps Identified through the Literature Review

Sustainability Studies on Bio-Enzymes and The Life Cycle *Assessment Studies*

The overall environmental impact of employing bio-enzymes in food production by measuring the net sustainability benefits, such as decreased water and energy use, greenhouse gas emissions, and waste generation, needs to be evaluated through research. There are limited studies on the life cycle assessment of the bio enzymes.

Resource efficiency studies

There haven't been many studies that quantify the increases in resource efficiency that come from using enzymes. choosing enzymes that consume less energy and waste.

Need for a Regulatory Framework

The legal framework governing the use of enzymes in food production is still developing. To comprehend the complexity and guarantee adherence to the changing laws governing food safety and labelling, research is required.

Limited Data on Long-Term Health Implications

There is a scarcity of research available on the long-term health effects of eating food products that have been treated with bio enzymes. To fully comprehend the potential health impacts and security issues connected with their intake, more research is needed. It is crucial to comprehend how bio enzymes interact with other components in complicated food matrices. Clarification of the impact of various meal compositions on enzyme activity and efficacy requires more study.

Synergy of Enzyme Combinations

There are few studies examining the synergistic impact of mixing several enzymes in food systems. An important field of research on how enzyme combinations can improve the sustainability and efficiency of certain processes is still developing.

Conclusion

Bio-enzymes have the potential to make a major contribution in defining the future of our food, rendering it healthier, and more environmentally friendly, and adding value to waste streams. For the production of food ingredients to be healthier and more sustainable in the future, enzyme research and development is progressing, considering its benefits as a renewable resource. Due to advancements in bio-enzyme engineering, businesses are now transitioning to a circular economy, where resources are used, and waste is recycled, from a linear economy, where resources are used but waste is ignored. The natural biocatalysts are now being used as tools to valorise agri-food and by-product waste, recover key nutrients, and turn some by-products into revenue returns. It is evident that the advancement and future of bio-enzymes is a significant contributing aspect to making this happen if the food industry wants to become sustainable, accessible, and move towards becoming carbon neutral.

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Sustainable biofuels and carbon footprints

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Abstract: Due to the sharp rise in world population, it is predicted that in the next 20 years, the world's energy demand would increase by 48 per cent. Currently, fossil fuels provide 80 per cent of the world's energy needs. However, the increasingly diminishing supply of fossil fuels combined with their damaging effects on the environment has generated a lot of interest in sustainable biofuels. This will facilitate the shift to a bioeconomy that must be carbon neutral. Biofuels are obtained from biomass like wood and straw, released by direct combustion of dry matter and converted into a gaseous and liquid fuel. In the ensuing decades, biofuels are anticipated to play a significant role in the transition to green energy and sustainable development. Due to their contribution to energy independence, urban and rural development, improvement of the ecological footprint, and decrease in carbon emissions, biofuels offer many appealing qualities. Despite technological advancements, the sustainability aspects of biofuel production methods are of inherent importance. In this review, we have discussed the significance of biofuel, the energy demand and supply statistics and how biofuels are the upcoming fuels playing a very important role in uplifting the global bioeconomy. but on the other aspect, it has been observed through various reports that the Carbon footprint of biofuel is also going to be a severe challenge in the coming days. Thus, before framing the policy on biofuel, it is necessary to look after all possible alternates to reduce the carbon footprint because unless the carbon emission remains the same issue, then the use of biofuel for global change may effect the bioeconomy with negative implications.
Keywords: Biofuels, Biomass, Carbon footprint, Bioeconomy, Sustainable development.

Introduction

Environmental Sustainability of Biofuels and its Contribution in Sustainable Economy

In certain cases, the term "conventional biofuels" is used to describe the first types of biofuels since they were initially developed using standard methods and equipment. Some common examples are fermentation, distillation, and transesterification. When compared to their first-generation counterparts, biofuels from the second generation are made from other than food feedstocks like agricultural byproducts, residues of forests, and waste

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materials (including urban solid waste), as opposed to specific energy crops like Miscanthus and other lingo-cellulosic plants. Biodiesel made from microalgae using traditional transesterification or hydrotreatment of algal oil is a third-generation biofuel. Since studies on methods for producing second and third-generation biofuels are still in its infancy, these fuels are sometimes referred to as "advanced biofuels" (Thangavel and Sridevi, 2015); (Khan *et al*., 2021); (Gheewala, 2023).

Table 1: Estimation of Global Biofuel Demand from 2010 to 2050 (International Energy Agency, 2011)

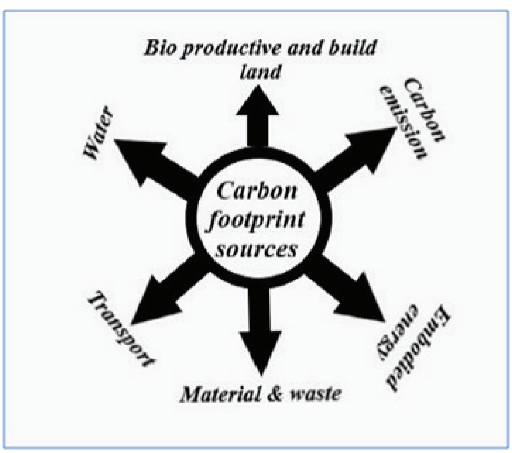
Year	Biofuel Demand (Exajoules)	Conventional Bioethanol (Exajoules)	Cane based Bioethanol (Exajoules)	Crop Residue based Bioethanol (Exajoules)	Biomethane (Exajoules)	Conventional biodiesel (Exajoules)	Advanced biodiesel (Exajoules)	Total (in Exajoules)
2010	1.29	0.44	0.00	0.53	0.00	0.00	0.00	2.26
2015	1.35	0.90	0.15	0.68	0.15	0.08	0.00	3.31
2020	1.50	1.44	0.45	0.90	0.38	0.15	0.23	5.05
2025	1.20	1.88	1.05	0.98	1.13	0.83	0.38	7.45
2030	0.98	2.11	1.88	0.90	1.96	1.35	0.98	10.16
2035	0.45	2.48	2.56	0.60	3.61	2.41	1.28	13.39
2040	0.15	2.63	3.46	0.23	5.34	3.16	1.66	16.63
2045	0.08	2.86	4.14	0.08	7.98	5.04	3.76	23.94
2050	0.00	3.24	5.04	0.00	10.91	6.70	5.87	31.76

Source: Author's own compilation.

To encourage sustainable expansion, regulatory legislation like the RED (Renewable Energy Directive) and RFS (Renewable Fuel criteria) provide a wide range of sustainability criteria for biofuels, one of the most crucial of which is their life cycle greenhouse gas emissions. The Renewable Fuel Standard (RFS) mandates a minimum 50 per cent diminution of emissions of greenhouse gases from advanced biofuels and a minimum 20 per cent decrease from conventional biofuels (National Service Center for Environmental Publications (NSCEP) n.d.). This report gives the details of the competition between traditional and cutting-edge biofuels in terms of their prospective impact on bioenergy use, and a typographical representation is shown in Fig.1. Because advanced biofuels are not yet cost competitive, they are often more costly to produce than existing biofuels. What is often neglected in discussions about biofuel is the industry's contribution to global animal feed supply and land utilisation for feedstock production.

The transport sector is responsible for about 20 per cent of the world total energy use. Despite the fact that they only account for around 3 per cent-4 per cent of global road transport fuel and just 5 per cent of overall bioenergy consumption at now, transport biofuels are the fastest booming bioenergy industry. Most capacity expansion and financing need is expected for next generation biofuels in the longer term, and strong competition from other renewable energy projects with lower risks (wind and solar) can be experienced. Although only a small portion of the world's biomass has recently been used for biofuels production, there is a lot of buzz around liquid biofuels for transportation. (Popp *et al*., 2014); (Calvin *et al*., 2021).

Figure 1: Various carbon footprint sources



Source: Author's own compilation.

Projected world primary energy demand by 2050 is expected to be in the range of 600 to 1000 EJ/year compared to about 500 Exajoules (EJ) in 2008. The expert assessment suggests potential deployment levels of bioenergy by 2050 in the range of 100–300 EJ/year. However, there are large uncertainties in this potential, such as market and policy conditions, and there is a strong dependence on the rate of improvements in the agricultural sector for food, fodder and fiber production and forest products. The entire current global biomass harvest would be required to achieve a 200 EJ/year deployment level of bioenergy by 2050. Scenarios looking at the penetration of different low carbon energy sources indicate that future demand for bioenergy could be up to 250 EJ/year (Haberl *et al*., 2007); (Roux *et al*., 2021).

It is reasonable to assume that biomass could sustainably contribute between a quarter and a third of the future global energy mix. The total annual above ground net primary production (the net amount of carbon assimilated in a time period by vegetation) on the Earth's terrestrial surface is estimated to be about 35 Gt carbon, or 1260 EJ/year, assuming an average carbon content of 50 per cent and 18 GJ/t average heating value (Pospíšilová 2003), which can be compared to the current world primary energy supply of about 500 EJ/year.

Greater yield potential, decreased losses and wastes throughout the food chain, and reduced inputs will influence the amount of land available for non-food crops. However, these volumes will remain limited relative to total energy and transport sector fuel demand. Limited biomass resources will be allocated to the sector (materials, chemicals, energy) that is most able to afford them. The cost of biomass conversion into alternative final fuels including bio-derived power, ethanol blends, biodiesel, and bio-derived jet fuel, will have to be weighed against the price of currently available fossil fuel-based products. Alternative fuel and energy source prices, government actions (such as excise rates), and the emission intensity of different industries will all have a role. No additional farmland is needed for bioenergy production, and there are few to no environmental dangers associated with using waste and residue as a fuel source. Several factors may discourage the use of these "lower-risk" resources. Using residues and surplus forest growth, and establishing energy crop plantations on currently unused land, may prove more expensive than creating large-scale energy plantations on plowable land. In the case of residues, opportunity costs can occur, and the scattered distribution of residues may render it difficult in some places to recover them (IEA 2020). Future policy structures, such as greenhouse gas emission reduction objectives, will determine the extent to which these potentials may be realised. Cost, logistics, and resource and environmental concerns all play a role in determining whether or not biomass is used (The Intergovernmental Panel on Climate Change (IPCC) 2011).

The risk-adjusted net present value (r-NPV) method, which recently emerged in the biotech industry, uses the development attrition rate as a discount factor to reflect risk during each development phase. Notably, there is limited research on the attrition rate and development period of new substance drugs and the research results are not consistently presented (Woo *et al*., 2019). Enzymatic biofuel cell (EBC) attracts much attention recently in the fuel cell community because of its unique feature to enable the enzyme as a catalyst, rather than a precious metal, to oxidise the fuel. The embedment of carbon nanotubes, commonly used in the anodic electrode of EBC to electrically wire the enzyme, suffers from their complicated synthetic procedure and fragile assembly. In this regard (Duong *et al*., 2019) demonstrate a facile and low-cost route to achieve the desired immobilisation of the glucose oxidase on a robust, flexible conducive carbon cloth. (Sakamoto *et al*., 2019) prepared a CNT-enzyme complex with highly oriented immobilisation of enzyme onto the CNT surface.

The complex showed excellent electrical characteristics and could be used to develop biodevices that enable efficient electron transfer. The growing power demands of wearable electronic devices have stimulated the development of on-body energy-harvesting strategies. Jeerapan *et al*. (2019) review the recent progress on rapidly emerging wearable biofuel cells (BFCs), along with related challenges and prospects. The brown midrib mutants (bm) of maize, with reduced lignin content, can be exploited for the development of cultivars with better digestibility. Choudhary *et al*. (2019) study enabling technologies for utilisation of maize as a bioenergy feedstock. The improvement of maize as a feedstock and biological conversion strategies of lignocellulosic biomass are assessed. Kumar et. al. (2020) aim to present an insight into currently available pre-treatment technologies for the deconstruction and fractionation of lignocellulosic biomass for the development of lignocellulosic feedstock based biorefinery. Kumar, et. al., (2020) will enable a better understanding of already available processes and help overcome the limitations and develop an improvised technology to ease the pretreatment process to make the concept of biorefinery a reality. Ott *et al*. (2020) present the ecological effects of energy development and production on grassland systems.

During energy production operations, noise and road traffic reduction plans and atmospheric monitoring will enable more informed mitigation measures. Khan *et al*. (2021) investigate the benefits, limitations, and trends in different generations of biofuels through a review of the literature. (Khan *et al*., 2021) also addresses the newer generation of biofuels, highlighting the social, economic, and environmental aspects, providing the reader with information on long-term sustainability. The development of highly active and stable noble metal-free ORR electrocatalysts remains as one of the major challenges. (Feng *et al*., 2021) report cobalt/nitrogen co-doped porous carbon materials (Co-N-C) originated from well-designed bimetal-organic frameworks (Zn100-xCox-ZIF) as efficient ORR electrocatalysts in both pH-neutral and alkaline solutions.

Biofuels and progress in Biotech and Synthetic Biology: Prospect

The biotech industry's use of the risk-adjusted net present value (r-NPV) approach has introduced a more sophisticated method for evaluating projects. This method incorporates the development attrition rate as a discount factor (Montagna *et al*. 2020). However, there is a lack of research on the attrition rate and development period of new substance drugs, highlighting the need for a more comprehensive understanding. Recent research in enzymatic biofuel cells (EBC) has focused on the use of enzymes as catalysts to reduce reliance on precious metals (Mukherjee *et al*., 2022). Duong *et al*. 2019 presented a cost-effective method for immobilizing glucose oxidase on a flexible, conducive carbon cloth, addressing the challenges associated with the complicated synthesis of carbon nanotubes. Meanwhile, (Sakamoto *et al*. 2020) showcased a CNT-enzyme complex with highly oriented immobilisation, exhibiting superior electrical characteristics for the development of efficient biodevices. All this research focuses on and addresses the progress, challenges, and prospects of wearable biofuel cells (BFCs) in response to the surging demand for wearable electronic devices. Choudhary *et al*. 2020 explored the potential of brown midrib mutants (bm) in maise for the development of cultivars with enhanced digestibility, contributing to advancements in bioenergy feedstock. Kumar *et al*., (2020) provided insights into pre-treatment technologies for lignocellulosic biomass, aiming to facilitate the development of lignocellulosic feedstock-based biorefineries. The ecological impacts of energy development and proposed mitigation measures during production operations (Ott *et al*., 2021). Lastly, the challenge of developing noble metal-free ORR electrocatalysts and introduced cobalt/nitrogen co-doped porous carbon materials as efficient solutions in diverse pH environments (Qin *et al*., 2021).

Recent advancements in synthetic biology and metabolic engineering have significantly improved the efficiency of advanced biofuels. Shanmugam *et al*., 2020) discuss the use of CRISPR-Cas-based techniques for genetic manipulation, emphasising the importance of reducing off-target effects for safer and more successful implementation. These strategies instill confidence in the use of these methodologies for enhanced biofuel production. The integration of biotechnological advancements into modern city development and their seamless integration within the Internet of Things (IoT) framework. The transformative impact of these developments on urban landscapes paves the way for innovative and sustainable urban solutions. These advancements have the potential to and revolutionise the way cities are built and operated, creating a more sustainable future for urban dwellers (Gotovtsev 2020).

India's Biofuels Alliance in the G20 Summit: A Step Towards Sustainability

On September 9, 2023, the G20 New Delhi summit announced the formation of the Global Biofuel Alliance (GBA) to encourage the development and acceptance of sustainable biofuels and to establish applicable standards and certification. The GBA is made up of 19 countries and 12 international entities. Argentina, Brazil, Canada, India, Italy, South Africa, and the United States are among the G20 members who support the alliance. Bangladesh, Singapore, Mauritius, and the UAE were the four G20 Invitee countries that endorse GBA. Iceland, Kenya, Guyana, Paraguay, Seychelles, Sri Lanka, Uganda, and Finland are the eight non-G20 countries. The World Bank, Asian Development Bank, World Economic Forum, World LPG Organisation, International Energy Agency, International Energy Forum, International Renewable Energy Agency, and World Biogas Association are among the international organisations (Kala, 2023).

It aims to provide an overview of the Biofuels Alliance launched by India at the G20 Summit. The alliance signifies a strategic move towards sustainable energy solutions, fostering international cooperation in the development and promotion of biofuels. India has been actively pursuing green energy initiatives to address environmental concerns and reduce dependence on fossil fuels. The G20 Summit provided a platform for India to introduce a Biofuels Alliance, emphasising the importance of biofuels in achieving global sustainability goals. Promotion of Sustainable Energy: The alliance focuses on promoting biofuels as an environmentally friendly alternative to conventional fossil fuels. Biofuels are derived from organic materials and contribute significantly to reducing carbon emissions.

Research and Development: Collaborative efforts in research and development will be a key aspect of the alliance. Member countries will share knowledge and expertise to enhance the efficiency and viability of biofuel production.

Policy Harmonisation: The Biofuels Alliance aims to create a framework for harmonising policies related to biofuel production, distribution, and consumption. This will facilitate smoother international trade and encourage investment in the biofuel sector.

Capacity Building: The alliance will prioritise capacity building initiatives to support member countries adopting and implementing biofuel technologies. This includes training programs, technology transfer, and sharing best practices.

Alliance Structure: The Biofuels Alliance will be structured with a Secretariat responsible for coordinating activities, sharing information, and organising collaborative projects. Regular meetings and conferences will provide a platform for member countries to discuss progress and address challenges. The consequences of India's Biofuels Alliance in the G20 Summit were:

Economic Growth: The alliance anticipates significant economic growth through the development of a robust biofuel industry. This includes job creation, investment opportunities, and the establishment of a sustainable energy sector.

Environmental Impact: By promoting the use of biofuels, the alliance aims to reduce greenhouse gas emissions, mitigate climate change, and contribute to global efforts in achieving a carbon-neutral future.

Global Energy Security: Diversifying energy sources through biofuels enhances global energy security by reducing reliance on finite fossil fuel resources and minimising geopolitical risks associated with traditional energy supplies.

The launch of the Biofuels Alliance by India at the G20 Summit represents a commendable step towards a sustainable and greener future. This initiative underscores the importance of international collaboration in addressing shared challenges related to energy security and environmental sustainability. As the alliance progresses, it is expected to make significant contributions to the global transition towards a more sustainable energy landscape.

According to a study released by the Ministry of Petroleum and Natural Gas, Government of India, India has made great strides in the development of biofuels through initiatives like the National Biodiesel Mission and the Ethanol Blended Petrol Program. Several interventions by the Indian government have facilitated an increase in average ethanol blending from 1.53 per cent in 2013-14 to 10.02 per cent in 2021-22, the introduction of E20 fuels, commissioning of Asia's first 2G Ethanol bio-refinery in Panipat, Haryana. The commissioning of 40 compressed bio-gas plants with a total capacity of 225 tons per day and, the introduction of M15 (petrol blended with 15 per cent Methanol) and the research and testing of 15 per cent

Methanol in Diesel, and so on. As a result, the 10 per cent blending target was met months ahead of schedule, and the 20 per cent blending target was moved up from 2030 to 2025. Additionally, 130 specific ethanol plants in deficit states have signed long-term offtake agreements, guaranteeing an annual volume of 4.3 billion litres of ethanol for offtake. By 2025, a 20 per cent ethanol blend will save foreign exchange of more than 6.6 billion US dollars annually, reduce greenhouse gas emissions by 21.6 million MT annually, boost farmers' cumulative income by more than 5.1 billion US dollars annually, and generate thousands of new job opportunities (Biofuels Study Report, 2023).

Competition between Conventional and Advanced Biofuels

Long-term diversification and decarbonisation of transportation need substantial development of advanced biofuels. Despite several claims and the completion of several studies on second-generation bioethanol, none of these facilities are yet producing bioethanol on an industrial scale. In order to come up with a product that can compete with first-generation bioethanol, processing costs will need to be reduced further. The pre-treatment process yields a number of useful byproducts, including lignin, which can be burned to power the ethanol plant's operations, used as a dispersant and binding agent in concrete admixtures, substituted for phenolic and epoxy resins, or used as the primary component in thermoplastic material blends, polyurethane foams, or surfactants. By using both first- and second-generation feedstocks, bottlenecks may be avoided and product competitiveness increased(Paulova *et al*., 2013).

Many nations already generate conventional biofuels using standard methods and feedstock. Large-scale extraction of traditional biofuels, other than sugarcane ethanol, is unlikely to be sustainable in the future since it would divert feedstock and land from food cultivation and forestry. In addition, they are somewhat costly and provide marginally lower GHG emissions than fossil fuels (Kumar, Tirkey, and Shukla, 2021).

Advanced biofuels promise to be more sustainable, with higher carbon emissions reductions. They are based on biomass resources and land not used for other primary needs, such as food production and farming. Agriculture and forestry lignocellulosic wastes, fast-rotation crop residues (perhaps produced on small, non-arable land), the organic part of municipal garbage, and micro-algae all qualify as feedstock. The conversion of these resources into biofuels requires processes that are currently under commercial demonstration or under development, with small plants in operation and large plants under construction or planned all over the world (Yana et al., 2022).

Algae Based Advanced Biofuel: A Domain of Bioeconomy

Algae represent another potential feed-stock that is suddenly attracting attention and venture capital to dozens of startups. Chevron is working with NREL to produce transportation fuel from algae. The high-risk, high-reward Defense Advanced Research Projects Agency has a project to use it to make jet fuel.

Algae have many potential advantages from the point of view of carbon impact. It doesn't compete with food crops for land or even necessarily fresh water, since many species can grow in brackish or briny water. It reproduces in hours, which means it is potentially far more productive than terrestrial plants. Algae naturally produce oils that have a roughly 50 per cent higher energy content than ethanol and can fit more easily into the current fuel infrastructure. A major part of algae's productivity potential stems from the fact that a critical limiting factor in plant growth the very low concentration of CO2 can easily be mitigated in water, merely by bubbling in a highly concentrated source, such as the exhaust emissions from a fossil fuel fired power plant. However, the need for such a carbon source places some limits on locations (Yaashikaa, Devi, and Kumar, 2022).

Does Biofuel reduce the Carbon footprint!

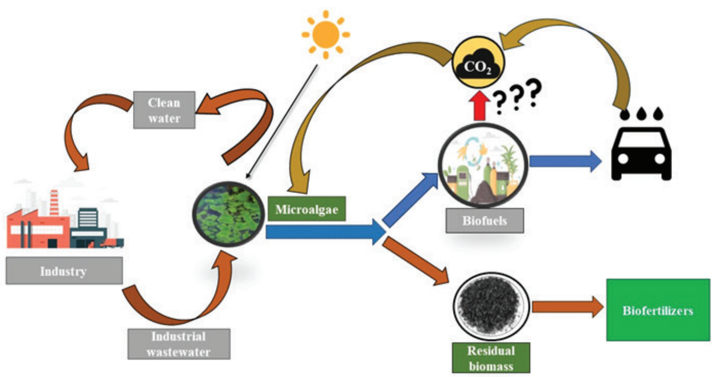
The entire quantity of greenhouse gases created by a product or service from the moment it is thought of as a product or service all the way through the time it is used is referred to as the carbon footprint. There are a variety of approaches, both analog and digital, that may be used to calculate a precise carbon footprint. In the definition of the carbon footprint, scope-3 emissions are automatically included. Third phase biofuel emissions are those that occur farther upstream in the supply chain. In the real world, businesses may utilise the carbon footprint of a product either as a selling point or as a purchasing guide in order to attract customers. In the context of the fight against climate change, the concept of the "carbon footprint" may be used to differentiate between "high" and "low" categories of economic activity (Brankatschk and Finkbeiner 2017); (Brandão, Heijungs, and Cowie 2022).

Carbon footprint of Biofuels

The amount of carbon that is included in each kind of biofuel was calculated using the information that was presented in (Defra 2013), specifically for bioethanol, biodiesel, and biomethane, in that order. This information was then used to calculate the carbon footprint of one liter of biofuel (Defra 2013). The total carbon footprint was obtained from the concatenated results for the individual footprints per litre of bioethanol, biodiesel and biomethane multiplied by the annual IEA biofuel projections out to 2050 (IEA 2020). In 2010, it was estimated at 0.085 billion worldwide hectares, and it is projected to increase to 0.64 billion hectares by 2050. Sugarcane bioethanol and high-tech biodiesel production are mostly to blame for this expansion. Sugarcane bioethanol produced 0.80 kg CO2 per litre of biofuels, whereas advanced biofuels were found to produce 1.22 kg CO2 per liter of biofuels. Consequently, sugarcane contributed 18 per cent of the total carbon footprint in 2010 and is expected to exhibit a similar proportion by 2050.

Carbon footprint is one of the significant factors that been calculated to understand how basic substrates, medium and sources of biofuel generate an amount of carbon footprint and how it is affecting the biofuel driven economy (Jeswani, Chilvers, and Azapagic, 2020). The major question arises here that the biofuel which is going to be the futuristic fuel and globally governments are making a policy for these alternate fuels, but at some extent hike in carbon footprint has been measured in some microalgae-based biofuels. Recent studies reveal that microalgae-based biodiesel may produce and burn more carbon than its petroleum-based counterpart(Khan *et al*. 2021). The biofuel's poor performance is due to its manufacturing process, which requires more energy than the final product can produce as shown in Fig. 2.

Figure 2: Schematic representation of Bioeconomy and Carbon emission



Source: Author's own compilation.

As a group, biofuels, fuels made from renewable natural resources, such as plants, coffee grounds, and vegetable oils emit less carbon dioxide into the environment than fossil fuels. And microalgae, phytoplankton that grow in fresh and salt water, have qualities that made them particularly hopeful candidates. Because it contains a significant amount of lipids that may be turned into fuel, some types of phytoplankton are capable of producing up to 30 times the amount of energy that is produced by other types of biofuels. And phytoplankton develop quickly, thriving in a broad range of temperatures and ecosystems, even on wastewater land, and do not need the diversion of food towards fuel production, in contrast to maize, soybeans, and other biofuel crops. Yet these advantages alone don't translate to energy efficiency. As per the report published in International Journal of Life Cycle Assessment in April 2023, a recent study provides a significant data on the increased emission in Carbon footprint by algal biofuels (Bradley *et al*., 2023).

Conclusion

Biofuels are considered carbon neutral because the carbon dioxide emitted when they are burned is offset by the carbon dioxide that was absorbed by the plants during photosynthesis. But, the modern research is contradictory resulting in higher emission of carbon footprint and that led the global civilisation to rethink before framing the policies. The organic material that makes biofuels is made of carbon dioxide absorbed by plants from the atmosphere as they grew. When the plant biomass is burned, it releases this absorbed carbon dioxide back into the atmosphere which might increase the pollution of CO2 in the atmosphere which clearly do not fulfill the futuristic objectives of Biofuels. The use of biofuels can help to reduce our reliance on fossil fuels and contribute to a more sustainable energy system. However, it is important to carefully evaluate the environmental impacts of biofuels in order to ensure that they are being used in the most sustainable and responsible way possible. By using biofuels as an alternative energy source, we can reduce our reliance on fossil fuels, which can help to reduce our impact on the environment and contribute to a more sustainable energy system that is more locally based. The transition to biofuels will affect the economic sectors of agriculture, manufacture, reprocessing, recycling, and transportation. By opening up new markets for crops and other agricultural goods, the establishment of a biofuels sector has the potential to play a significant role in the promotion of economic expansion in rural areas that have fewer opportunities for employment. Except providing new livelihood opportunities for local families, they could also represent a sustainable and innovative option that will contribute to rural development. But certain negative implication can possibly withdraw these alternate sources from potential replacement candidate against fossil fuel.

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Role of Industry 4.0 in Biotechnology to Produce Environmentally Sustainable Biotechnology Products

Punit Kumar* and Archana**

Abstract: Due to the rise of global population, pollution, and the limitation of natural resources, sustainability is now becoming a fundamental requirement of industries. Sustainable processes support all the dimensions of ecological, social, and economic parameters. Industry 4.0 concept originated from the German industry, and the main aspect is the use of advanced technology for efficient production. Industry 4.0 comprises technologies such as digital technology, machine learning, robotics, Internet of Things, and cyber-physical systems etc. Industry 4.0 is capable to transform the traditional manufacturing units into smart factories. The biotechnology industry uses the principles of molecular biology, genetic engineering, and fermentation technology etc to produce a variety of products. Similar to the industrial revolution, the biotechnology industry also underwent a similar revolution. Biotechnology industry uses technologies like recombinant DNA technologies, metabolic engineering, and fermentation technologies. Biotechnological processes have certain limitations, like instability of biological catalysts, complex biological systems, and difficulties in upstream and downstream processes. Biotechnological processes are environment friendly and are considered, creating less harm to nature as compared to chemical industrial processes. In this article authors have discussed the role of Industry 4.0 technologies in the production of environmentally sustainable biotechnology products.
Keywords: Industry 4.0, biotechnology, smart factories, sustainability, digital technology, Internet of Things, automation

Introduction

Since the inception of human civilization, there has been continuous development in science and technology. These developments have revolutionised all sectors including, research, space, medical, and industries. Throughout history, industrial revolutions changed the processes and tools that were used to make products and created an impact on more than one type of industry. Initially, things and products were produced for domestic utilisation, later on, development, demands and markets led to the distribution of products outside the localised boundaries. These trades increased the profits. Simultaneously, new markets and new demands were identified that created the requirements for more production. More profits

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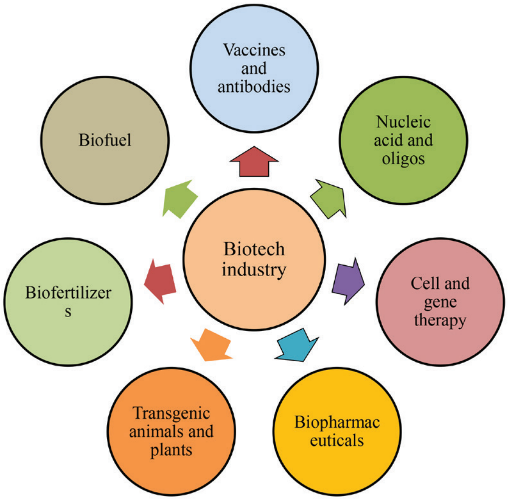
attracted the investment to establish more production units that were further transformed into industries. The initial production activities were performed using simple tools and equipments in small warehouses that were further transformed into manufacturing facilities using new technologies. Thus, the industrial revolution led to the transformation of handicraft economy into machine industry (Simon, 2023). Now, we can clearly analyse how advanced technologies and production tools substituted less sophisticated tools. Nowadays, industries are using more intelligent tools. These advancements have allowed us to make goods in big quantities and for profit. Industrial revolutions significantly transformed the social and economic structures of countries. These are associated with economic development, increase in productivity, and advanced welfare in the countries, including high-quality goods and services.

Though, the Industrial Revolutions made economic developments but industrial activities are also associated with critical environmental concerns, such as; pollution, emission of greenhouse gases, deforestation, loss of biodiversity, climate change and unsustainable developments. Out of these, the rapid depletion of Earth's resources and unsustainability became some of the important global challenges that should be considered during technological development. Moreover, The United Nations' global initiative towards sustainable development goals (SDGs) strongly supports inclusive social and economic development (Morrar et al., 2017; United Nations Sustainable Development Goals, 2015; United Nations, 2023).

The Fourth Industrial Revolution (Industrie 4.0 in German) was started in Germany in 2011 as an initiative of the German government (Vogel-Heuser & Hess 2016). The idea was formulated at the Hannover Fair in 2011, and it was officially announced 2013 by the German government as an initiative to transform the manufacturing sector. It transformed the Cyber Physical Systems concept into Cyber Physical Production Systems. This project was a high-tech strategy for automation and digitization of the manufacturing industry (Daudt & Willcox, 2018).

Biotechnology has contributed to improve the healthcare, environment agriculture, and industry etc. (Figure 1).

Figure 1: Some important products of biotechnology based industries



Source: Author's own compilation.

Biotechnology is making significant contributing towards energy supply (biogas, biofuels, bioethanol, and microbial fuel cells etc), health protection (antibiotics, enzymes, vaccines, cell and gene therapy, diagnostics, and nanotechnology etc), food supply (biofertilizers, high yielding varieties, hybrids, genetically modified crops, and tissue culture etc), biomolecules (fermentation, genetic engineering, and metabolic engineering etc), and environment protection (biodegradation, bioremediation, manipulations of biogeochemical cycles, waste management, biomonitoring), and finding of new biotherapeutics etc (Awais *et al*., 2010; Gavrilescu & Chisti, 2005; Martin *et al*., 2021; Rabaey & Verstraete, 2005; Singh, 2017; Verma *et al*., 2011). Biotechnology is also showing advancements in synthetic biology, which is offering alternatives to fossil-derived materials (Matthews *et al*., 2019). Moreover, biotechnology is also playing a key role in achieving the Goal 2, Goal 3, and Goal 9 of sustainable development goals. Biotechnology also has the ability to transform life and generate new products and services (UNESCO, 2023). Furthermore, biotechnology is providing its importance in technology that can significantly contribute for the sustainable development (Primer, 2001). Moreover, the involvement of industry 4.0 approaches is playing important roles in biotechnology.

In this paper, authors have discussed the background and history of Industry revolutions, development of biotechnology, and the role of industry

4.0 in the biotechnology sector. Including this, the role of industry 4.0 is also discussed to produce environmentally sustainable biotechnology products.

Development of Biotechnology

The biotechnology term was first used in 1919 by Karl Erkey (Verma *et al*., 2011). It involves the utilisation of techniques to manipulate living organisms or their components to generate useful services and products. Thus, techniques used in biotechnology use the information obtained by modern discoveries in different fields, including biochemistry, molecular biology, cell biology, microbiology, bioinformatics, genetic engineering, and industrial microbiology (Bhatia 2018). Moreover, it would be good to say that biotechnology is the integration of different principles of biological science and engineering to utilize living organisms (microorganisms, plants, and animals) in industry, research and technology for verity of applications. At present, principles of biotechnology are being utilised in medical, agricultural, pharmaceutical, and industrial sectors with the ultimate goal to benefit humanity.

The development of biotechnology has been categorized into three main stages, such as Ancient Biotechnology, Classical Biotechnology, and Modern Biotechnology. The ancient biotechnology (Pre, 1800) is associated with early uses of biotechnology for humans, such as the production of curd, cheese, vinegar, bread and liquor. Moreover, some other applications of ancient biotechnology were food preservation, improvement in crop and animal varieties by cross-breeding. Classical biotechnology existed from 1800 to middle of 20th century. This phase is associated with the starting of the scientific development of biotechnology. In this phase, remarkable developments were performed, such as laws of inheritance, the structure of chromosome, initiation of vaccination, the theory of genes, and the discovery of antibiotics, etc. The modern biotechnology phase comprises major scientific discoveries, such as the double helix model of DNA, synthesis of DNA, genetic engineering, gene cloning, DNA fingerprinting, gene sequencing, artificial gene synthesis, protein synthesis, genomics, proteomics, hybridoma technology, recombinant DNA technology, gene editing, cell and gene therapy etc (Verma *et al*., 2011).

At present, biotechnology is making a significant contribution as an industry in energy production, healthcare, food and beverage, diagnostics, and environment protection, etc. All these factors are driving bioeconomy forward.

Sustainable Production of Biotechnology Products

Sustainable industry is assumed to be economically viable, environmentally compatible, and socially responsible. Thus, sustainable production of products comprises all the processes associated with production that are ecofriendly (or cause minimum harm to the environment), reduced use of resources, and economically viable.

An Increase in population and industrialisation is causing global environmental issues such as waste generation, depletion of natural resources, generation of greenhouse gases, pollution, and loss of biodiversity etc. The unsustainable manufacturing processes are one of the main factors that are suggested to cause pollution, intensive use of energy and raw materials, and poor discharge of waste (Olah *et al*., 2020). Thus, it becomes important to use resources in an optimised way, reduce the effects of waste, and waste management. Biotechnology industry harnesses living organisms or their products and processes to produce the products and services for humans (Gavrilescu & Chisti, 2005). In association with sustainable development, Biotechnology has the capacity to alleviate real-world environmental problems such as waste, pollutants (micropollutants also), non-degradable materials (chemicals, and plastics etc), and lignocellulosic biomass through microorganisms and biocatalysts.

The sustainable production of biotechnology products is based on technological innovation. It is found that for a given level of production, biotechnology reduces the cost and environmental footprint as compared to chemical processes. Biotechnology was found to reduce the capital and operating cost by 10-50 per cent. Including this, it was also observed that biotechnology can develop new products with unique properties, cost and environmental performances that are difficult to be obtained byproducts produced by conventional chemical synthesis methods (Primer, 2001).

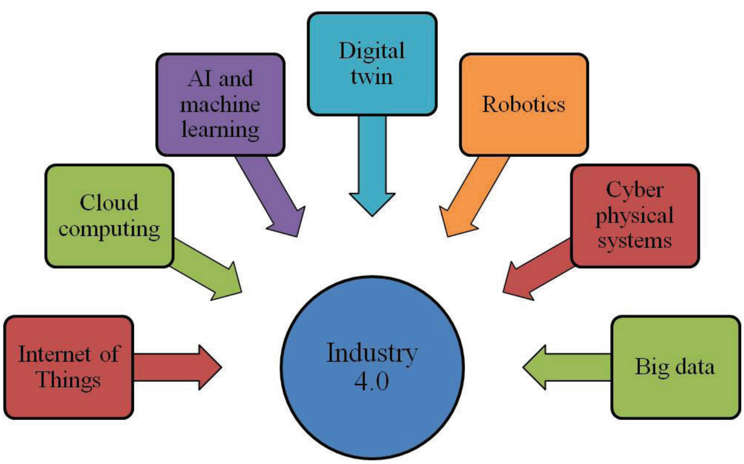
Biotechnology processes are considered sustainable as all bio-organic chemicals, products are biodegradable and renewable. Moreover, byproducts of one biochemical reaction are substrates for another biochemical reaction; thus, technically, biotechnological processes do not generate any waste. Biotechnology processes have the potential to transform waste into renewable energy. For example, lignocellulosic waste may be used in the production of biogas (Wei, 2016). Biotechnology is actively contributing to biofuel production, ethanol production, biodiesel production, bio-methane production, and biogas production (Kilbane, 2016). In this way biotechnology is contributing to sustainable development by reducing the consumption of fossil fuels.

History of Industry Revolutions and Industry 4.0

Every industrial revolution is associated with benefits and challenges to the social and economic status of the country where such revolutions are taking place (Morrar *et al*., 2017). The duration of industrial development has been divided into different stages. Industrial Revolution 1.0 was started in the 18th century and covered the duration of about 1760-1840. This industrial revolution witnessed the transformation of hand-based production into machine based manufacturing. The Industrial revolution 2.0 led to the development of telecommunication technologies, technologically improved machines, and establishment of the assembly lines in the industries etc. This phase also marked an improvement in industry culture (Morrar *et al*., 2017; Simon, 2023). Industry 3.0 was led by the invention of the internet, transistors, and Integrated Circuits. This phase witnessed the involvement of electronics and digital technology for manufacturing (Pereira & Romero, 2017; Simon, 2023). This phase is also referred to as the digital revolution and computer era (Simon, 2023). More important, internet was considered a public infrastructure technology (Carr, 2003). The Industrial 3.0 revolution started partial automation in manufacturing.

The present stage is categorised as industry 4.0. It is a collective term for technologies comprising digital technologies, and automation in industrial manufacturing processes. This revolution is also associated with the development of Smart Factory (Dutton, 2014). The important key elements of industry 4.0 are fully automated data acquisition, evaluation and quantification, and analysis (Figure 2).

Figure 2: Technologies that are driving Industry 4.0



Source: Author's own compilation.

Including this, there is a requirement for a digital data acquisition approach (Uhlemann *et al*., 2017). In industry revolution 4.0, Cyber physical systems (CPS) are playing an important role (Wu *et al*., 2020). The Industry 4.0 technologies offer a large number of objectives, such as; IT-enabled manufacturing of goods, facilitating communication between parts, implementing human-machine interaction (HMI) paradigms, automation, and predictive control. The organisations have incorporated key digital technologies for Industry 4.0, such as; artificial intelligence (AI), big data, Machine Learning (ML), cloud computing, digital twin, Internet of Things (IoT), robotics, remote sensing, and CPS (Ahsan & Siddique, 2021; Chen *et al*., 2017; Gupta & Jauhar, 2023; Javaid *et al*., 2022; Rifkin, 2014).

The industry 4.0 led the way for social and technological transformation. Industrial 4.0 is enabling digital transformation into smart machines that collect data and analyse this data by AI. IoT devices connect machines, and exchange the information without human intervention to provide real time information about manufacturing facilities.

Industry 4.0 and Environmental Sustainability

It is found that industrial production processes are associated with air pollution, poor waste discharge, and the intensive use of energy, raw materials, and information. The traditional industrial production processes exhibit a negative impact on environmental sustainability as the production process takes place in a weak sustainability model. Thus manufacturers are constantly trying to identify the methods to decrease the operating cost associated with production processes.

Sustainability is associated with optimized utilisation of resources during the entire production cycle. Sustainable manufacturing produces products using economically viable procedures with decreased negative environmental impact while preserving the natural resources and energy. Innovative technologies play a critical role in managing the production of manufacturing units and their environmental impacts. Therefore, the adoption of new technologies has the capability to provide solutions to the existing environmental challenges. The industry 4.0 technologies have unlocked the doors for industrial development by improving the efficiency and production in modern industrial units (Ali *et al*., 2022).

Industry 4.0 demonstrates the interrelationship between different aspects of industrial manufacturing through advanced information and communication systems. It enables the transformation of traditional manufacturing units into smart factories. Industry 4.0 technologies have the potential to integrate manufacturing lines, teams, business processes, regardless of international boundaries and other aspects. These technologies provide more knowledge about the production environment of industry, supply and delivery chains, and the market. These technologies monitor production processes, and enable the operators to collect big data and analyze to recognise the crucial areas of production. The study of de Soto *et al*. (2018) demonstrated that the involvement of robotics in the production has improved the productivity and higher production with reduced cost. The adoption of Industry 4.0 would lead to reduced negative impacts on the environment with respect to the use of energy, raw materials, information, and production of high-quality products (Bai *et al*., 2020; Olah *et al*., 2020; Javaid *et al*., 2022). Thus, the huge economic and sustainability potential of Industry 4.0 is leading manufacturers to optimise their value chain's production and its associated processes. It is reported that Industry 4.0 technologies create an innovative ecosystem that allows integration of resources. These technologies enabled firms to transform production system, decision-making, and operations (Benitez *et al*., 2020).

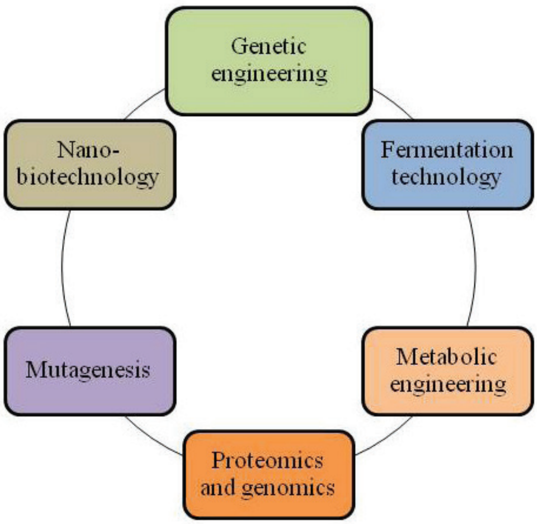
It is also observed that sustainable organisations should support triple bottom lines (economic, environmental and social) of sustainability. The case study conducted by Braccini *et al*. (2019) demonstrated that the adoption of Industry 4.0 technologies supported the economic, environmental, and social dimensions of sustainability.

Utilisation of industry 4.0 approaches (such as digital technology, artificial intelligence, and machine learning, etc.,) may play an important role in the sustainable production of biotechnology products. The combination of different technologies is the core value of Industry 4.0. Though, the examination of each technology separately is crucial for determining the right combination of technologies for each specific case (El Merroun *et al*., 2022). Real time monitoring and predictive control using AI could improve the robustness of the processes, minimise waste generation, maintain the quality of products, and also improve cycle times. Here, we discuss two approaches by which Industry 4.0 technologies may provide sustainable production of biotechnology products while managing global environmental problems. Biotechnology industry is research driven sector hence, one approach focuses on the involvement of Industry 4.0 technologies in research and development, where these technologies could contribute to improve the catalytic properties of enzymes, identification of new enzymes, structure determination, genetic engineering, metabolic engineering and fermentation process optimisation etc. Second approach focuses on the involvement of Industry 4.0 technologies in the establishment of smart factories.

State of Biotechnology Industry at Global Level

The development of biotechnology led to the development of industrial activities involved in the production of antibiotics, production of vaccines, production of enzymes, production of recombinant proteins, production of biomolecules, and production of personalised therapies (Figure 3).

Figure 3: Some important technologies used in biotechnology based industries.



Source: Author's own compilation.

Besides this, the demand for biobased materials is constantly increasing from the consumers and industry (Danielson *et al*., 2020). All these factors are driving bioeconomy forward. It is assumed that in the last three decades about 260 novel biotechnology products have been approved. The research and development in biotechnology started in 1980s. In 1973, scientists genetically engineered E. coli bacteria with foreign genes via the process of recombination. In 1977, a biotechnology company (Genentech) produced somatostatin by recombinant E. coli. Following this, the company also produced human hormone Insulin. Since the initial advancements in biotechnology from 1973, nowadays the biotechnology industry is focusing on gene therapy, nanobiotechnology, human microbiome, immunotherapy, CRISPR-Cas9 gene editing, CAR-T cell therapy, and many more fields (Smith, 2022).

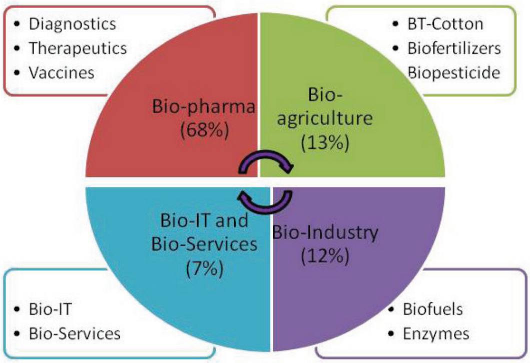
At present, there are more than 10000 biotechnology industries across the world. These industries have been established in almost all the countries across the world and major biotechnology activities are focused in North America, Europe, and Asia Pacific. Some of the major companies performing biotechnology-based businesses are Abbott, Amgen, Bayer, Biogen, Genentech, Johnson and Johnson, Merck, Novartis, Pfizer, Roche, Sanofi, and Samsung Biologics, etc. Although biotechnology-based industries are established around the world, but maximum share of biotech industries is occupied by the North America. The countries which have a high number of biotechnology industries are Australia, Canada, China, France, Germany, India, Japan, Singapore, South Korea, UK, and the USA. The biotechnological sector is continuously developing worldwide. The main factors behind the growth are initiatives taken by governments, favourable regulations, collaborations and investment.

As per the IBISWorld report, there are 11076 global biotechnology businesses in 2023, and the global biotechnology business growth rate in 2023 was 4.8 per cent. Moreover, in the last five years (20018-2023) biotechnology sector has shown the growth rate of 5.9 per cent per year (Industry statistics, 2023). Another report published in 2022 (BioSpace, 2022) suggested that biotech industry is expected to grow at the CAGR of 17.83 per cent during the 2021-2030. This report also suggested that in 2020 biotech industry was valued about USD 852.88 billion, and it is expected to be worth USD 3.44 trillion by 2030. In the biotech sector, the healthcare sector (biopharmaceuticals) occupies the highest share of 48.7 per cent. Including this, other sectors like fermentation, bio-services, agri-biotech, bio-services are also contributing to the growth of the biotech sector. Moreover, due to advancements in the informatics tools, bioinformatics sector is expected to grow at CAGR of 21.5 per cent from 2020-2030 (BioSpace, 2022).

State of Indian Biotechnology Industry

The biotechnology industry in India mainly comprises Bio-agriculture, Bio-Industrials, Biopharmaceuticals, Bio-IT, and Bio-services etc (Figure 4).

Figure 4: Sector wise share of Indian biotechnology sectors in 2022



Source: Invest India (2023)..

As per the government report (Biotechnology, Make in India 2023), there were more than 2500 biotech companies in India in 2022. Some examples of major companies with biotech related business in India are Aurobindo Pharma, Alembic, Biocon, Bharat Serum and Vaccine, Panacea Biotech, and Serum Institute of India etc. India's biotechnology industry has grown to USD 80 billion in 2022, and further, it is expected to be worth about USD 300 billion by 2030. The expected CAGR during 2022-2025 is expected about 17 per cent. India is a major biotechnology hub across the globe. Including this, India is among the top 12 biotechnology destinations across the world, top 3 in South Asia and also contributes about 3 per cent share in biotechnology industry at global level. Moreover, India has the2nd largest number of USFDA approved manufacturing facilities outside the USA. The number of Indian start-ups has also increased about 100 fold during 20014-2022, and their number has increased by more than 5300. Furthermore, the Government of India aims to increase the number of biotech start-ups to more than 10000 by 2025 (Biotechnology, Make in India 2023; Invest India, 2023).

India's biotechnology sector is expanding continuously. For its further growth, the department of Biotechnology (DBT) is entering into different collaborations with leading global organisations. Moreover, Government of India has taken many initiatives such as establishment of Biotechnology Parks/Incubators, development of bioclusters, Make in India Facilitation Cell (Biotechnology), National Portal for Biotech researchers and Start-Ups (BioRRAP), and foreign direct investment policy etc. (Biotechnology, Make in India, 2023). Biotech Consortium India Limited (BCIL) is also playing a key role in technology transfer. BCIL has experience of more than 3 decades in the transfer of technologies to industries from research institutes and universities. Technology Transfer Office has been setup at BCIL with the support of Department of Biotechnology - Biotechnology Industry Research Assistance Council - National Biopharma Mission (DBT-BIRAC-NBM). Till date, BCIL has transferred about 60 technologies (like biofertilizers, biomedical devices, biopesticides, diagnostics, and vaccines etc.,) which are developed in India to many industries in India and abroad. Including this, Technology Transfer Office also invites innovators and technology developers across the world to explore the technology transfer prospects and intellectual property management. Moreover, BCIL is also providing services in setting and operationalisation of biotech parks/incubators (Biotech Consortium India Limited, 2023).

Application of Industry 4.0 in Biotechnology

The biotechnology processes comprise the biomolecules and organisms. Microorganisms produce a variety of biomolecules via fermentation processes. Microorganisms are genetically engineered, and fermentation conditions are optimised to enhance t productivity. Microorganisms may produce a variety of organic chemicals for industrial applications such as adipic acid, succinic acid, diols, diamines and many other synthetic polymers (Lorenzo, 2018). In the recent time, the biotechnology is also being used as synthetic biology (SynBio) to produce products that are produced by chemical and manufacturing industries (Hanson & Lorenzo, 2023). Moreover, biological systems are also producing the products that would be costly to produce by traditional manufacturing methods. Still, chemical and manufacturing industries are reluctant to adopt bio-based processes due to the difficulty of transforming of laboratory scale bioprocesses into economically viable industrial processes (Lorenzo, 2018). Including this, the instability of biological catalysts, difficulties in downstream processing, and complexity of biological systems also pose difficulties for new engineering technologies in biotechnology industry (Zamacona, 2021). Thus, for the adoption of new technologies in biotechnology based industries, various issues on the biological and industrial sides need to be addressed.

Like the industrial revolution, biotechnology also undergone technological revolutions. The Industry 4.0 technologies, such as digitalisation, robotics, automation, and machine learning etc., are enabling biotechnologists to perform research, development, and creating favourable production conditions. These technologies look promising in the development and advancement of biotechnology (Massabni & da Silva, 2019). Big data and AI are becoming key factor in biotechnology to provide competitive and sustainable advantage. Big data analysis and machine learning are assumed to be helpful in synthetic biology. Automation, additive manufacturing, and simulations are considered helpful in providing optimised production conditions (Zamacona, 2021). The biotechnological developments are increasingly dependent on the use of big data that is produced by high-throughput methods and is stored in databases (Oliveira, 2019). It is found that machine learning, and artificial intelligence etc., are becoming helpful in data analysis, data integration, and process optimisation. Including this, it is also expected that big data analysis will be a key factor in experiment design, drug discovery, genomics, pharmacogenetics, pharmacogenomics, and proteomics etc. (Oliveira, 2019).

The digitalisation and automation are providing smart manufacturing solutions that are governed by Industry 4.0. To enhance the efficacy of the production, there is an increased need of modelling tools such as machine learning, including multivariate data analysis. The Data Integrity (DI) in biopharmaceutical industries is also a key factor for product quality. Smart manufacturing solutions like cloud platforms are considered to play an important role in maintaining the DI throughout the processing (Alosert *et al.*, 2022). Thus, Industry 4.0 technologies are paving the way for automated laboratories, automated manufacturing platforms, and the integration of production units into large manufacturing facilities.

Transformation of Biotechnology into New Age Global Industry

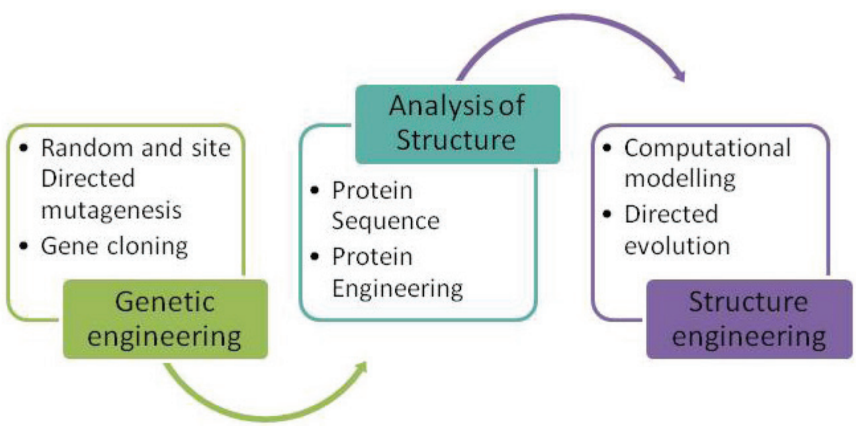
Industry 4.0 technologies such as Internet of Things (IoT), artificial intelligence, machine learning, robotics, big data analytics, and automation etc., have capabilities to transform biotechnology in a new age global industry where advanced technologies are involved in research and development and manufacturing. These technologies could be helpful in establishing a collaborative network between different research laboratories, different pharmaceutical and biotechnology manufacturing facilities across the world to maintain the productivity, competitiveness and supply cycle.

The Internet of things technologies are assisting researchers in minimising the manual handling of specimens, better control over environmental factors, and effective data management using the sensors (Kamal, 2022). Artificial intelligence is widely used in drug discovery (David *et al.*, 2020), drug safety (Diaw *et al.*, 2022), genomics (Lin & Ngiam, 2023), proteomics, cancer biomarker discovery (Xiao *et al.*, 2021), and metabolomics (Barberis *et al.*, 2022) etc. Machine learning is helpful in the analysis of complex metabolomic data, disease modelling and diagnosis (Galal *et al.*, 2022). Robotics and automation are playing key role in biotechnology research and development facilities and manufacturing facilities. Automation is improving reproducibility, research efficiency, enhanced production, and safety (Holland & Davies, 2020). Many companies are utilising robotic and automation platforms in the production, synthesis of DNA, and production of new microbial strains. Various examples demonstrate that biotechnology companies are using robotics technology to enhance efficiency, such as Amyris producing new bacterial strains, Ginkgo Bioworks working on robot-assisted strain design technology, Zymergen and Counsyl are generating biological data using automated robots and isolating the strains and proteins through deep learning, and Transcriptic and Riffyn are working to develop a platform technology for fast production and analysis of large amount of complex biological data through cloud-based synthetic biology software (Kim, 2019). Recently the world has seen the potential of digital technology and computational approaches to develop vaccines for COVID-19 in a short span. The rapid development of effective vaccines against this virus offered long-term control.

Industry 4.0 Technologies in Research and Development in Biotechnology

Biomanufacturing processes comprise biocatalysts, microorganisms, animal cells and plant cells. At the cellular level, biochemical processes are performed by enzymes (biocatalysts), and thus, enzymes are used in industrial applications for bioprocess, production, and improving the quality of products. For sustainable production of biotechnology products, and to manage the environmental issues (like resource depletion, and waste generation), the catalytic properties of existing enzymes should be increased or new enzymes with higher catalytic properties may be isolated or synthesised (Figure 5).

Figure 5: Some important approaches for redesigning the biocatalyst for improved biocatalysis



Source: Author's own compilation.

In this direction, various approaches such as; site directed mutagenesis (Yang *et al*., 2019), genetic engineering, metabolic engineering (Nevoigt, 2008), directed evolution (Kumar & Singh, 2013), and high throughput screening etc., are playing a key role (Sharma *et al*., 2019). Many of scientific reports are available that demonstrate role of these approaches to increase the biocatalytic potential of industrially important enzymes.

Site-directed mutation has been used to improve the enzymatic activity of an industrially important enzyme (5-carboxy-2-pentenoyl-CoA reductase) for increased biosynthesis of Adipate. Adipate is used as raw material to produce lubricants, nylon-6,6, pesticides, polyurethane foam, and synthetic rubber (Yang *et al*., 2019). While routine chemical methods producing these items are found to generate greenhouse gas, toxic chemicals and pollutants.

α-amylases are used biocatalysts in baking industries, starch saccharification, and textile desizing. Due to the acidic nature of starch, the acidic amylases are demanded from industry. However, acid stable, Ca++ independent, and thermo stable α-amylases are commercially not available. Biotechnological approaches are playing key role to produce α-amylases such as; α-amylases gene cloning and expression, structural conformational studies, protein engineering of α-amylases, directed evolution, study of molecular dynamics and computational modelling (Sharma & Satyanarayana, 2013).

Saccharomyces cerevisiae has a long history of application to produce alcohol and Baker's yeast. It is widely used in the food and beverage industries. Activity of S. cerevisiae could be increased by metabolic engineering approaches (Lian *et al*., 2018; Nevoigt, 2008; Ostergaard *et al*., 2000). Including this, genetic engineering approaches (random mutagenesis, site directed mutagenesis, and recombinant DNA technology, etc.) are also being explored to improve the activity of S. cerevisiae.

The potential of biocatalysis has been observed in the synthesis of COVID-19 drug, where engineered Ribosyl-1-Kinase was used to synthesise Molnupiravir in a short and sustainable process. The engineered enzyme shortened the synthetic pathway by 70 per cent and about 7-fold more yield (McIntosh *et al*., 2021). Similarly, engineered Cytidine Deaminase has been reported to produce N-hydroxy-cytidine which is a key intermediate for the synthesis of Molnupiravir (Burke *et al*., 2022). Including this, a large-scale manufacturing process for Molnupiravir has been developed. This process is demonstrated 1.6 fold improvement in yield (Fier *et al*., 2021). Recently, scientists have used smart library design and machine learning approaches to engineer the iron/α-ketoglutarate dependent halogenase WelO5 (Büchler *et al*., 2022).

These examples reflect that enzyme engineering is a promising approach for the sustainable production of biotechnology products because a lesser amount of raw materials will be used for the generation of the same or more amount of products. Thus, resources will be less used and less amount of waste would be generated while productivity will be increased. However, the approaches like directed evolution, protein engineering, structure prediction (using X-Ray crystallography, NMR) are time-consuming.

Industry 4.0 technologies could be explored in research and development. Artificial intelligence and digital tools may be used for the analysis of genomic and proteomic data, enzyme active site determination, protein design, reverse genetics and artificial synthesis of novel enzymes possessing high bio-catalytic activity. Metagenomic screening is emerging as a novel tool to identify enzymes with high metabolic activity. Industry 4.0 technologies may integrate the research output of different research groups, analysis of available DNA and protein databases, in silico screening, enhance the pace of biocatalyst identification, optimisation and improve the biocatalytic properties (active site modification, substrate tolerance, pH tolerance, temperature tolerance, control of feedback inhibition), cofactor recycling, structure-guided engineering, computational modelling. Out of these, may processes may be automated. It is expected that computational tools will lead the revolution in enzyme engineering (Büchler *et al*., 2022).

Machine Learning (ML) methods have been used in bioprocess development, strain selection, strain improvement, and bioprocess optimisation etc (Helleckes *et al*., 2023). ML approaches are also used in protein engineering via directed evolution (Yang *et al*., 2019). AI technology could be used in protein engineering, and pathway design to construct microbial cell factories. AI technology is being used for metabolic engineering to increase biological production via protein engineering and pathway design. Including this, AI technology is also explored in directed evolution (Jang *et al*., 2022). AI with Microfluidic technologies may be used in biotechnology research, prognostics, diagnostics, the development of personalised medicines, and the development of regenerative medicine (Zare Harofte *et al*., 2022). Digital Twin technology is virtually representation of complex bioprocesses. Bioprocess Digital Twin platforms of cell cultures may developed to regulate the manufacturing environment of mammalian cells (for example CHO cells) and bioreactors (Park *et al*., 2021).

Industry 4.0 Technologies in Smart Manufacturing in Biotechnology

Industry 4.0 technologies have immense potential for the sustainable production of biotechnology products. In biopharma, automated platforms will improve the productivity, competitiveness, modernise manufacturing and environmental sustainability (Silva *et al.*, 2020). It is expected that the adoption of 4.0 technologies in biotechnology will take biomanufacturing to new heights.

Industry 4.0 technologies allow communication between machine and people in regulated environment equipped with self adapting capabilities (Artico *et al.*, 2022). Integration of technologies like AI, machine learning, Internet of Things (IoT), and cloud computing etc., are transforming production facilities into smart factories. These smart factories are equipped with embedded software, advanced sensors, and robotics that monitor and optimise the production processes (Soori *et al.*, 2023). These technologies increased automation, predictive control, self optimisation of processes, optimised usage of resources that improve the productivity and environmental sustainability.

Smart manufacturing led by Industry 4.0 technologies offers benefits in manufacturing, monitoring the production processes, and waste management. The technologies like Artificial Intelligence (AI), robotics, and Machine Learning will lead to the establishment of smart manufacturing units that will increase the productivity and reduce waste generation. These approaches are capable to improve the economics of production through sustainable production of existing and novel products. AI approaches are capable to improve the design and processing engineering strategies in bioprocessing (Yang *et al.*, 2023). Big data and Artificial Intelligence are playing key roles in smart ecosystem design. Big Data and AI are fundamentally generating competitive and sustainable advantage (Artico *et al.*, 2022). Machine learning approaches are useful in monitoring, scale-up and control of bioprocesses (Helleckes *et al.*, 2023). An automated and high-throughput platform has been developed with the help of ML for de novo synthesis of artificial enzymes (Wu *et al.*, 2023).

Future Prospects

The future of biomanufacturing seems to be very promising as the demand for biotechnology based products, medicines, and therapeutic proteins is increasing. The aim of biomanufacturing is to provide high quality products at affordable cost. However, the process for manufacturing of biotherapeutic molecules is complex, costly and associated with high failure rate. It also contains regulatory challenges. Industry 4.0 technologies guided manufacturing is expected to replace traditional biomanufacturing production model. These technologies have the capacity to increase the productivity, efficiency, and sustainable production of biotechnology products while managing global environmental issues. Moreover, the adoption of such technologies will create jobs for trained and skilled manpower.

Although industry 4.0 technologies seem to be very promising in bioprocessing and biotechnology but there are certain challenges to adoption of industry 4.0 technologies that need to be addressed. Some of them are; the complexity of biological systems to be automated, regulatory requirements, lack of qualified professionals, lack of availability of funds, and lack of organisational strategies for implementation etc. Some other challenges are market uncertainty of the firm's business, competition, financial and knowledge constraints.

Many companies have established advanced facilities that use principles of Industry 4.0 and biotechnology. For example, Gingko Bioworks perform bioengineering using a platform based on automation, data analysis and software development. Strateos offers cloud based biological research and testing services (Zamacona, 2021). Merck & Co., pilot plant facility at West Point, PA (USA), is performing bioprocess research and development activities using analytics platforms that leverage cloud-based software. Merck Sharp & Dohme established the Werthenstein BioPharma facility (Switzerland) that is involved in the development and analysis of new large molecule drugs using automated analysis technology. Human vaccine research facility of GlaxoSmithKline Biologicals is exploring the artificial intelligence–based predictive controllers to improve the robustness of manufacturing processes, improving quality of products, and reducing waste (Macdonald, 2020). Amgen's Singapore manufacturing facility has implemented a platform to perform centralised monitoring of processes across the entire manufacturing network (Innovate, 2021).

Conclusion

Industry 4.0 technologies have immense potential in the biotechnology sector for sustainable production of products, as these technologies could improve the performance and productivity. However, biological systems and processes seem to be complex for modelling and automation. Though the involvement of industry 4.0 technologies like automation, AI based production and robotics could improve the production efficiency, waste minimisation, and forecasting of demands etc. The technologies like automation, digitalisation may contribute in research and development in biotechnology by contributing the analysis of protein structure, gene sequences and play an important role in genetic engineering, protein engineering and fermentation technology etc. It is also assumed that the adoption of these technologies will also increase the employment opportunities of skilled manpower in industries. However, digital transformation of biomanufacturing facilities exhibits some obstacles, but it could offer long term advantages in bioprocessing utilising process control real time monitoring.

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RIS
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Technology Transfer Offices and Life Sciences Based Innovations : An Indian Perspective

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Abstract: Transfer of technology (ToT) developed in research institutes to industry has been one of the most discussed areas in the recent past. ToT helps in accelerated commercialisation for rapid industrial growth and generates revenue for the institutes by monetising research outcomes. The role of TTOs in the process of developing, protecting intellectual property and disseminating technologies through licensing to spinouts or established companies has generated special interest. TTOs are academic or commercial entities that facilitate the management of intellectual property rights and ToT by bridging the gap between research and industrial needs. They provide support for collaboration and mediate relationships between different innovation stakeholders, namely academia and industry. The present article highlights the role and importance of TTOs in the Indian context with a backdrop of the ecosystem of developed countries. It also suggests the need for having TTO at individual research organisation for better outreach and academia-industry connects. The study suggests a need for having a larger network of professional TTOs, harmonised policy for managing IP and technology and a robust tech-transfer system which will help all the stakeholders leading to creation of a large number of start-ups, job-creations and, overall, in building the robust innovation and tech-transfer ecosystem for industrial growth
Keywords: Intellectual Property, Technology transfer, TTO, Licensing, Commercialisation, Spinout

Introduction

Concerted and multi-stakeholders' efforts, which facilitate the transition of scientific outcomes, knowledge and intellectual property from its creators, mainly universities and research institutions, to the uses of public and private sectors, is called technology transfer (TT). It transforms inventions and scientific outcomes into new products and services for the benefit of society. Association of University Technology Managers, popularly known as AUTM, defines it as, "the process of transferring scientific findings (such as inventions) from one entity to another (i.e., industry) for further scaling up, validation, refinement and commercialization" (McDevitt *et al*, 2014).

Key drivers for industrial growth include a strong base of innovation research in universities and research institutions. In the present time, the priority of institutions has changed towards research and technology

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development, including IP creation and its commercialisation. India, which is a fast-developing country, the creation of IP and its commercialisation are of the matter of high priority for rapid industrial growth. The Innovation Index of India, published in 2021, mentioned that the overall spending on R&D has been comparatively at a lower side. The overall share of gross expenditure on R&D (GERD), as a percentage of GDP, was about 0.7 per cent. in which the private sector contributes just 0.1 per cent. Developed countries like Denmark, the United States, Sweden, and Switzerland spend about 3.0 per cent, 2.9 per cent, 3.2 per cent and 3.4 per cent, respectively. In the case of Israel, expenditure on R&D is 4.5 per cent of its GDP, which is the highest in the world.

As per the views expressed in the Economic Times (2022) quoting the report of NITI Aayog, it has been emphasized that if India has to achieve its goal of a $5 trillion economy, countries' GERD needs significant improvement and needs to touch at least 2 per cent. India ranked 40 in the Global Innovation Index in the year 2022 as compared to 48 in 2020 as per the report of WIPO published in 2020 (WIPO, 2020). This situation can be improved significantly through a robust technology transfer system by facilitating the creation of a large number of spinouts and licensing of promising technologies to existing companies. Industry should be motivated to invest in acquiring research findings and technology development.

Life science industry, specifically biotechnology, has been identified as the sunrise sector by the Indian government. One of the driving technologies of the future is biotechnology. Professionals working in this area need to orient themselves towards rapid changing technologies. The power of digitalization has enabled biotechnology towards the development of new products and processes from the speedy understanding of genetic information of cells/microorganisms. Integration of technologies with robotics, 3D printing, and artificial intelligence are technologies that will impact biotechnology on a large scale.

In 2022, the Indian Bio-Economy grew from USD 70.2 billion to USD 80.12 billion in 2021 in spite of the pandemic period. The nation has set an ambitious target for the BioEconomy to touch the $150 billion threshold by 2025. It has the potential to reach $270-300 Billion by the year 2030 (India Bio-economy Report, 2022). The above ambitious target would be achieved through supporting start-up innovation ecosystem, IP-driven research, technology development and commercialization. The robust technology transfer system is the key to rapid growth in which TTO has to play a very important role.

TTO and its Role Specially in Industry 4.0

As per the legal status, TTOs can be either an academic institute embedded entity or independent commercial organizations which facilitate IPR management and technology transfer by bridging the gap between research and industry. TTOs provide assistance in making collaboration and facilitate stronger relationships between different innovation stakeholders namely academia and industry. The broad objectives of a TTO include – generating affiliations with enhanced collaborations with industry, commercialising research outcomes for public benefits, rewarding the inventors and assisting them in planning applied research with commercial potential and monetize the research towards generating additional resources for institutes which can be utilised for further research (Tornatzky, 2000).

In India, the ratio of TTOs for alarge number of institutions is significantly less as compared to other countries having a knowledge-based economy. According to the Department of Science and Technology, a total of 216 institutions are operational in different subject areas. UGC website provides updates that 1074 universities, including 430 private universities are operational in India. Considering this large number of institutional and university base, there is a need to have a widespread network of TTOs across the country to meet the demand of building the innovation and technology transfer ecosystem.

With the presence of a large number of institutions, diverse geography and socio-economic status of India, an ecosystem is relatively different from any small European country. However, this base provides a clear indication of the need for focused research through industry participation, research leading to technology development and emphasis on monetising the IP Assets in India. TTOs are crucial for building a culture of innovation and technology management.

Society and government will be greatly benefitted if research outcome is converted into products, leading to revenue generation for the institute as well as the government. In India, shifting of gear is required from publishing to patenting and, moreover, patenting with technology focus. Further emphasis is required for monetising promising research outcomes towards capitalising technological advancement.

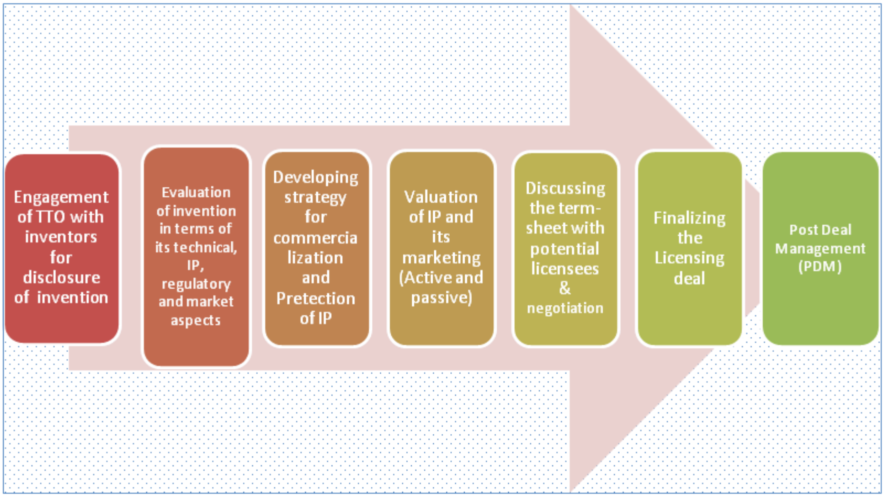
In general, Industry 4.0 relies on transforming the industrial manufacturing process by digitalising and adopting new technologies. The expected market share of Industry 4.0 is projected to be more than 71.7 billion US $ and it is expected that it will exceed 150 billion US $

soon (Ammar *et al*., 2021). It is relevant to mention here that the Impact of industry 4.0 technologies i.e. artificial intelligence, mechanization, use of robotics/drones, 3D printing, on the Biotechnology sector is quite evident. In biotech research and industry, new sensors, equipment with better efficiency and artificial intelligence are being applied along with automation, big data, advanced process analysis and the internet of things (IoT), which has greatly impacted the speed and outcome of the work (Sezer *et al*., 2018). TTO has to play an important role in the speedy transfer of such technologies and knowledge from the developer/inventors to the user towards contributing in rapid industrial growth. Razan *et al*. (2022) highlighted that technology transfer plays a key role in the commercialization of new technology and skill development for students and scientists. It creates a conducive climate for university-industry collaborations, including industry 4.0 technologies. A license agreement could be the most preferred method for technology transfer as it allows the university to retain the IP rights, and at the same time, it gives the industrial partner the right to develop and use the technologies under stipulated conditions.

Process of Technology Transfer for Successful Commercialisation

To initiate the process, TTO engages with the researchers, scientists or inventors in order to understand the invention in an organised and systematic manner. Once disclosure is received by TTO, it is evaluated mainly in terms of its IP strength and market potential. The evaluation also includes technical and regulatory aspects in order to have a complete SWOT analysis. Based on the assessment, IP protection and licensing-strategy are finalised. In the process, IP is valuated based on various approaches, namely cost-based, market-based and income-based approaches or in a combination of these. IP or technology is marketed among the potential licensees by TTO. Term-sheet is discussed with the interested potential licensee. Once the deal is finalized or the term sheet is approved by the licensor and licensee, the licensing agreement is executed. After licensing, TTO monitors the progress of technology commercialization in terms of attaining the milestones, which is also called post-deal management (PDM. PDM is one of the very important processes of technology licensing or commercialization. This process is outlined in Figure 1

Figure 1: Generalized process of technology-transfer



Source: Author's own compilation.

Various Models of Technology-Transfer

There are various models of transferring the technologies. Some of the very prevalent modals of technology transfer and its commercialization are listed below:

- **Licensing:** This is an industry preferred method to grant legal rights to a licensee to use IP for manufacturing products and services. The consideration is provided for its exclusivity or non-exclusivity. In addition to this, the field of use and territory are other important parameters in the licensing agreement.
- **Spinouts:** It is the way of licensing startups affiliated with inventors in the capacity as agreed by host institutions: Sometimes, spinouts is an ideal means to increase the TRL or perfect the technology. In the evolving entrepreneurial ecosystem for life sciences ventures in India, it is very important that the startup has the involvement of experienced entrepreneur as co-founder. Defined institutional policies should be in place in order to provide supportive environment to spinout.
- **Co-development:** Sometimes, research results need further validation or development is needed to match with requirement of the industry. Option of co-development can be explored. Co- ownership can be discussed and negotiated considering the contributions of parties in background IP and foreground IP generation.

- **Assignment:** Assignment of IP is the transfer of ownership to the second party. It is also called the sale of IP rights. In the case of start-ups, sometimes it becomes crucial to transfer to IP rights enabling them to raise funds. In case of a large portfolio, sometimes TTO prefers to assign the IP in place of licensing in order to minimise the cases of PDM. However, in case of assignment, due caution is required in deciding the terms or value of IP.

Global and National Scenario: A brief Overview

In many countries, ToT is governed by an Act enforced by the respective governments. For instance, Denmark has an Act on Inventions at Public Research Institutions, which is effective from June 1, 1999. This act defines that for any inventions originating through public funding, the University as an employer has the right to acquire all rights to that which the employee has invented in relation to his/her work. In other words, earlier, there was Professor Privilege in Denmark, which later flipped into University-owned IP after this Act (Baldini, 2006). Quite before the above, the USA has mandated technology ownership by public research institutions and technology licensing under the Bayh-Dole Act of 1980. One of the objectives of this Act was to encourage investment from the private sector in federally funded research for societal benefits (Markel *et al*., 2013). South Africa has also a similar provision under the Intellectual Property Rights from Publicly Financed Research and Development Act, Act 51 of 2008(IPR-PFRDAct) (Uctu & Essop (2022). IPR-PFRD Act clearly specifies that designated institutions should establish a TTO. The IPR-PFRD Act emphasised faster rate of transfer of technologies developed in universities or public research organisations to industry, which can result into accelerated technological innovation.

Similarly, the Japanese version of Bayh Dole Act, which was implemented in 1999, revolutionised university research commercialisation in Japan by increasing the number of applications of filing patents by universities and enhancing the process of ToT to Japanese industries (Takenaka, 2005). It is noteworthy to mention here another innovation-driven country in Asia i.e Israel. ToT is one of the main reasons for the economic growth of Israel where universities are called Economic Engines". Israeli universities can own a for-profit company called Technology Transfer Company (TTC). TTCs handle the IP of universities and are responsible for the research commercialization policy of the university. Government and private sector both invest heavily in start-ups (Messer-Yaron, 2014).

In India, the situation is different from the above countries, there are many regulations governing technology transfer, including Indian Contract Act, 1972, Competition Act, 2002, Copyright Act, 1957, Trademark Act, 1999, Patent Act, 1970 etc, make it comparatively complex process.

Institutions under the ambit of CSIR or ICMR or ICAR or DBT have defined policies on IP protection and broad guidelines for technology management and commercialisation. Among Universities in India, the policy is quite variables, many of them have not published/documented their policy framework, whereas some of them having a broad guideline on IP management and up to some extent, on technology licensing. It is felt that a harmonised policy in the country, including the University system, will pave the way for effective IP management and its speedy commercialization.

National innovation system (NIS) and level of University Industry linkages (UILs) are different in countries. Based on the requirements of country, innovation policy should be devised.. NIS of any country revolves around many factors, such as (i) performing R&D, (2) financing R&D, (3) human resource development, (4) diffusing technology, (5) promoting entrepreneurship, and (6) formulating technology and innovation policy.

In Indian academics, focus on the commercialisation of research outcomes is evolving. Still, academicians emphasize on publishing research papers rather than aiming at technology development and commercialization. The study conducted by Ravi & Janodia, in 2021 suggested that (i) Indian universities must leverage expertise commercialisation of research findings, (ii) more focus should be given to the commercial viability of research, and (iii) devise mechanisms to collaborate with industrial partners.

Many Indian universities have either established IP and technology transfer cell or TTO in view of the UGC guidelines to assess the outcome of teaching facilities in which score is allotted for of patents and its commercialisation (The Gazette of India, Authority, 2018). Govt of India launched “Make in India” in 2014 towards facilitating inventions, Intellectual Property protection, and build the best manufacturing infrastructure in the country. Later, a national IPR policy was published and the government prioritized to bring the administration of IP laws under the Department of Industrial Promotion and Policy (DIPP) (Joseph and Abrol, 2016). These are all different efforts made at various levels to shift the gear towards technology or product-based research.

Guidelines governing ToT in Biotechnology and Healthcare Sector in India *(System laid down by DBT and ICMR)*:

In India, the Department of Biotechnology is steering the research and technology development in agriculture, healthcare, environment, energy and other allied areas in life-science. Biotech-based technologies have various limitations in terms of ToT, which include low market readiness, requirements for further development and investments to commercialise research leads, a limited number of biotech companies and long gestation period of biotech products from promising research leads to commercialisation. In addition to this, start-up companies (which are growing significantly in the recent past) are not willing to license technologies which are in general available on non-exclusive basis.

It is noteworthy to mention that DBT earlier adopted only non-exclusive licensing provisions in order to promote market competitiveness and increase affordability. Major policy shift happened in July 2023 when DBT approved "Intellectual Property Guidelines", which seems to be highly significant for accelerating technology transfer and commercialization. This change has been summarized in Table:1

Table 1: Comparative status of changes in modalities post implementation of DBT- Intellectual Property Guidelines 2023

Before July 2023	After July 2023
Agreement executed between DBT and the fund recipient specifies that any IP that emerged through the support of DBT has to be transferred to the industry ***only on a non-exclusive basis***	It was decided to revise the grant agreement in order to provide options for ***all forms of licensing***. Technology having low TRL (Upto 5) can be licensed out on an exclusive basis, whereas technology with TRL 6 and more can be transferred on non-exclusive basis. Exclusivity in ToT is expected to attract good companies
Name of DBT was to be included as Co-applicant in application for IP arising out of funding	This procedural requirement is removed now. IP is to be filed in the name of the host institution only.

Source: Author's own compilation.

The above guidelines of DBT provided further clarity on the following aspects:

- **Decision making:** Institutional Committee of DBT Autonomous Institution has been empowered to make decisions.
- **Commercialisation focus:** Piling up IP for long periods without transfer or licensing has been discouraged.
- **Mechanism of licensing:** It will be decided on a **case-to-case** basis by the inventor and the host institute through the institutional IP committees and informed to the Government.
- **Exclusive licensing**, for products/technologies that are intended for large-scale public deployment, agreements should include a clause of **affordability** in Indian.
- **IP Assignment requests:** The same would be dealt with case to case basis under approval of competent authority with approval of competent authority for encouraging spin-outs.

For healthcare technologies of public research institutions mainly developed through funding of the Indian Council of Medical Research (ICMR), limitations for ToT remain the same, similar to the as mentioned for biotechnologies in the previous section. ToT of these technologies are governed by ICMR Guidelines for Technology Transfer and Revenue Sharing – 2021. In this case, non-exclusive licensing is the preferred mode for increasing competition and maximizing public access. However, licensing on an exclusive basis is also considered by the competent authority of ICMR as a special case, particularly licensing to start-up companies created with the support of ICMR.

Royalty model of ICMR on net Sales is well defined based on TRL (reproduced below at Table 2), which is in addition to upfront or milestone payment as per valuation of particular technology:

Table 2: Royalty model of ICMR

TRL	Royalty per cent on net sale
1 -3	1-2 per cent
4-6	3-5 per cent
7 and above	5 per cent and above (On approval of competent authority

Source: Author's own compilation.

Various Operational Technology Transfer Offices or Organizations (TTOs) in India

There are many TTOs operational in India with the mandate of technology transfer/ commercialisation and allied activities for supporting the innovation ecosystem. Some of the leading TTOs are being discussed here. NRDC and AgIn are example of specialised TTOs set up by the Government of India under respective ministries for extending the technology transfer services to various institutions functional in their domain.

National Research Development Corporation (NRDC): Govt of India set-up NRDC in the year 1953. NRDC functions under the Department of Scientific and Industrial Research, Ministry of Science & Technology. NRDC has the mandate of developing, promoting and transferring technologies coming from various national R&D institutions. NRDC has been operational over the past seven decades and forged strong links with various R & D organisations nationally and internationally. NRDC is known for its large repository of the wide range of technologies spread over almost all areas of industries. NRDC has been exporting promising and proven technologies to industries both in developed as well as developing countries (https://dsir.gov.in/national-research-development-corporation)

Agrinnovate India Ltd. (AgIn): Department of Agricultural Research & Education (DARE), Ministry of Agriculture, Government of India created AgIn in the year 2011. It acts as a focal point between the Indian Council of Agricultural Research (ICAR- an autonomous organisation under DARE) and the Stakeholders for the purpose of technology transfer and commercialisation. AgIn facilitates the production, marketing and popularisation of ICAR's products, processes and technologies in agriculture and allied sectors, such as seed, planting material, vaccines, diagnostics, bio-technological products as a specialised agency in the agriculture domain. (http://agrinnovateindia.co.in/index.html)

Biotech Consortium India Limited (BCIL) was set up in 1990 by the All India Financial Institutions with shareholding of IDBI bank and other corporate for facilitating technology commercialization in the area of Biotechnology. It is also engaged in project management and consultancy assignments in the area of biotechnology.

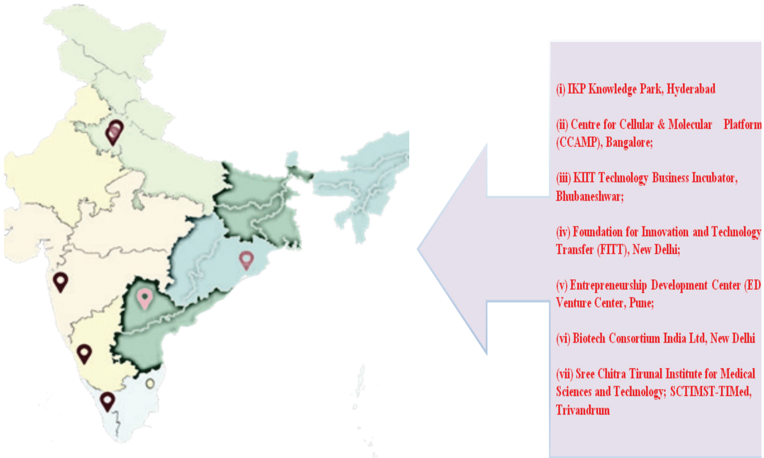
New Space India Limited (NSIL) Government of India incorporated NSIL in 2019 as a Public Sector Undertaking under the Department of Space (although it's not for life science, but its establishment shows the strong commitment of the government to technology transfer) towards helping companies in scaling up for space related programme by ToT mechanisms and addressing the need of upcoming global commercial satellite market.

The above developments indicate that there is a good platform for the technology transfer ecosystem in India. Considering the large country with a significant number of institutions, universities and a pool of researchers, there is a need for having a network of TTOs in the country for propelling towards enhanced technology transfer and commercialisation. Setting up of Regional Level TTOs (RTTOs) is an important step in this direction. RTTOs are briefly discussed in the following section.

RTTOs under NBM of DBT-BIRAC

The National Biopharma Mission (NBM) is an Industry-Academia collaborative Mission, for accelerating early development of biopharmaceuticals, titled "Innovate in India" (i3) under the umbrella of DBT-BIRAC. The NBM has taken the initiative to strengthen the technology transfer ecosystem with the support of the World Bank. In this direction, NBM established seven Regional Technology Transfer Organizations (RTTOs) to foster technology transfer by bringing under their fold nationwide public research organizations. These 7 RTTOs are housed in host organizations namely (i) IKP Knowledge Park, Hyderabad; (ii) Centre for Cellular & Molecular Platforms (CCAMP), Bangalore; (iii) KIIT Technology Business Incubator, Bhubaneshwar; (iv) Foundation for Innovation and Technology Transfer (FITT), New Delhi; (v) Entrepreneurship Development Center (EDC), Venture Center, Pune; (vi) Biotech Consortium India Ltd, New Delhi and (vii) Sree Chitra Tirunal Institute for Medical Sciences and Technology; SCTIMST-TIMed, Trivandrum. These RTTOs have been assigned to different territories for engaging themselves them different institutions towards supporting them in innovation management and technology transfer (BIRAC: Technology Transfer Offices, 2012). Locations of these 7 RTTOs is depicted at Map (Figure 2)

Figure 2: Map depicting the location of Regional Technology Transfer Offices supported by DBT-NBM-BIRAC



Source: Author's own compilation.

There are models of embedded or in-house or dedicated TTO for Institutes or universities as well as standalone TTO working with various institutions. Basic process of technology transfer remains similar in both types of TTO. In-house TTO being an integral part of Institute, the flow of invention is smooth, whereas stand-alone TTO is required to establish formal linkage with the institution. Standalone TTO gets IP at various stages of prosecutions, while in-house TTO gets the invention details at an early stage, which is beneficial for early transaction. At the same time, managing conflicts becomes easy for standalone TTO being the external agency.

TTO as an Effective Platform for Robust Innovation Management and Technology Transfer System: The role of TTO is highly important in the journey of technology commercialisation right from identifying the invention or receiving the disclosure of the invention from the inventor and taking it to the transfer to the suitable entity through licensing out or facilitating in creating spinout. It helps in making a strategy for the protection of IP in which close coordination between TTO and the inventor is crucial. In certain cases, the inventor is also advised to generate additional data or information in order to form robust patent claims, which may attract industry for in-licensing.

TTO has good connectivity with inventors on one hand and active engagement with industry partners on the other hand towards identifying the technological problems; they are strategically suited for bridging the technological gap and finding new opportunities. This helps in establishing connection even at an early stage, i.e innovation disclosures being received at the TTO and having a potential licensee or industry partner for negotiation at a very early stage to take the technology forward. Before proceeding with IP protection, evaluation and marketing of invention; clarity on inventorship is also important. Inter-institutional agreement becomes important for joint inventorship and the same has to be thoroughly assessed to understand rights and revenue sharing by the parties. Another important aspect is that TTO helps institutes or universities to build patent portfolios having good commercial potential in order to incentivise and monetize the research programme. It is well established fact that the professional TTO helps in the technical evaluation of invention, the right valuation (neither undervalued nor overvalued) and identifying the right commercialisation strategy (spinout or licensing to an established company).

To conclude, TTO has proved as an effective platform for institutes/ universities for managing the innovation and technology. In the presence of effective TTO, inventors can focus on their core research activities without worrying or engaging them in procedural aspects of IP and technology transfer related activities.

Few Case Studies Highlighting Contribution of TTOs in Technology Commercialisation

- **Long Legacy of Technology Transfer and Commercialisation by NRDC:**

  With the establishment of NRDC as a Not for Profit company, there was a beginning of an organised Tech Transfer System in India almost 7 decades before. NRDC was the brainchild of Sir Shanti Swarup Bhatnagar, known as the "Father of Indian Research Laboratories". It has signed more than 5000 license agreements and contributed significantly to India's ambition of building a science- and technology-driven economy (http://www.nrdcindia.com/.).

  Many important technologies were transferred, and their commercialisation was facilitated by NRDC for the last many decades. One of many success stories is the production technology of infant food from buffalo milk. This technology was developed by CSIR-

Central Food Technological Research Institute, which was transferred to Gujarat Cooperative Milk Marketing Federation Limited, known as Amul in 1960. India witnessed the importance of technology development by research institutions and commercialisation by industry partners with the involvement of technology transfer organisation like NRDC in its initial years post independence period. This development greatly contributed to the availability of indigenous products, which were earlier being imported from other developed countries like New Zealand and Switzerland, resulting in saving foreign currency, providing economic options to consumers and uplifting the economy of farmers/ milk producers (Shashidhara LS, 2017). Since then, many impactful technologies were expeditiously transferred by NRDC and also facilitated handholding to licensees.

- **Transfer of technology developed through funding of DBT – BIRAC**

  Several promising technologies were developed through funding from the Department of Biotechnology (DBT), Government of India. Technologies are developed at autonomous institutions under DBT as well as other institutions under the extramural grant in aid support by DBT. ToT of White Rust Resistant (WRR) Mustard varieties is a suitable example of the impact of TTO for the speedy transfer of technology to several companies on a non-exclusive basis for larger benefits of the farming community. This technology-transfer was facilitated by BCIL as authorised by the Biotech Industry R&D Assistance Council (BIRAC). BCIL has 70 technologies of various domains, including agri-biotech, medical biotech, medical devices, etc including the above technology. This technology was developed by Delhi University South Campus and there was a need to utilize the benefits of this research to the public. There was huge scope to integrate the value of the commercialised lines/varieties by multiple players of the seed business. It is noteworthy that Indian mustard (Brassica juncea) is the most important and major edible oil seed crop. White rust (Albugo candida) is the most prevalent disease which causes major yield losses in Indian Mustard (Lakra *et al*, 1989). In a short span of time, this technology was transferred to 8 prominent Indian Seed companies, namely M/s Ajeet Seeds Pvt. Limited, Aurangabad; M/s Bioseed Pvt. Ltd, Hyderabad; M/s Ganga Kaveri Seeds Pvt. Ltd., Delhi; M/s Kalash Seeds Pvt Ltd, Jalna; M/s Rallis India (Metahelix Life Sciences Limited) Bangalore;

M/s Rasi Seeds Pvt. Ltd., Tamil Nadu; M/s Tierra Agrotech Pvt. Ltd., Hyderabad and M/s Pioneer HI - Bred Private Limited, Hyderabad (www.biotech.co.in). Licensee companies incorporated this gene/trait in already commercialized varieties for better impact and crop yield.

- **ICAR –Agrinnovate Infusing Technologies with Agriculture for Sustainable Future**

  ICAR- Central Institute for Subtropical Horticulture (CISH) developed technology called "ICAR-FUSICONT" to control Panama Wilt disease caused by Fusarium species affecting banana, specially G-9 variety. This technology is highly significant as Indian tissue culture companies (more than 70 per cent) undertake mass multiplication and production of this species due to high market demand. Approximately 350 million plantlets were produced every year for plantation by farmers on thousands of hectares of land, significantly contributing to the economy.

  The above technology is a bio-formulation based on the antagonistic fungal of Trichoderma reesei and bacteria Lysnibacillus fusiforms grown in specific media/ substrate. This technology is also useful for vegetables (tomato, potato, capsicum, chillies) and spice (cumin and fenugreek) crops other than bananas. Agrinnovate India Ltd, as TTO of ICAR, facilitated successful validation and transferred to Ms Innoterra India on a non-exclusive basis (ICAR , 2022). This signifies the role of TTO in the speedy translation and scaling up of technology by taking the promising research outcome to a suitable industry partner for the benefit of the public.

Spinouts as an Effective Tool for Tech Commercialisation through TTO

Spinouts, in general, is an entity to which the technology from a university or research institution is licensed out in which the university or research institution has taken equity ownership in the licensee. It could be easy to license an IP or technology to a well-established and financially sound company. However, in case, technology needs more maturation through further research, it is equally important to have a company around the technology through the support of institutions. The process ensures that the Institute does not leave its ownership of the technology before adequate compensation. Having equity is part of that compensation. In Denmark, it was seen that approximately 50 per cent of the technologies are being transferred to spinout companies and the same is considered as an effective way of job and wealth creation. In the case of spinout, it is critical to attract investor(s). TTO plays a very important role not only in the creation of spinouts but also in raising funds subsequently. Inventor of the technology can be affiliated with Spinout Company as a non-executive director. Extent of involvement of the inventor in spinouts should be approved by the Director/Head of the Institute. As the TTO, it is critical to decide the way forward towards identifying the path to market with the best way for the success of technology for the benefit of the public at large. Department of Biotechnology (DBT), Govt of India has also come up with guidelines vide No. office order - BT/NBDB/13/01/2018 towards "Encouraging Development and Commercialization of Inventions and Innovations" towards allowing innovators to have an equity stake in techno enterprises / spinoffs while in professional employment with their research academic (Compendium of Instructions Issued for Departmental Officials, 2021)

Availability of seed funds and access to the biotech incubator /park or central equipment facility of the institute by the spinout plays an important role in the onward journey of commercialisation. Location of such a platform is critical. Proximity of a leading research institute/university for biotech park/incubator provides an ideal ecosystem through frequent interaction with professors/mentors and other resources required for the success of spinout. This also facilitates speedy technology transfer from research group to spinout or start-up. Globally, the ecosystem developed by Stanford University in California through Stanford Industrial Park is a great example of academia and industry collaboration through speedy technology transfer, paving the way for the development of Silicon Valley (Gromov, 2013). In India, biotech clusters like Genome Valley in Hyderabad and incubators housed within leading institutes like IITs have made significant progress in technology development and commercialization. However, it needs momentum through strengthening the technology transfer ecosystem in order to realise its full potential.

Conclusion

- Technology transfer systems evolved in the US and Europe during the 1980s and 1990s with the enactment Act on Innovation and tech-transfer. The Indian ecosystem of technology transfer, especially in life science, is in the process of evolving with the presence of specialized TTO. Although there is a significant presence of TTOs with success stories of technology transfer in the biotech/life science sector, there is a need for a larger network of professional TTOs considering the number of universities/institutions in the country. It would be good to have TTOs in the individual research organization connecting to the state-level lead TTO (hub and spoke model) for greater outreach and stronger academia-industry connect.

- There is a need to implement harmonised guidelines/policies on managing IP and technology across the country in order to rule out confusion among stakeholders. Such guidelines should focus on increasing industry-academia collaboration and enhancing the share of industry funding for research.
- In life-science/biotechnology, where most of the technologies developed at the Institutional level have a low technology readiness level (TRL), emphasis on creating spinouts should be given over licensing to existing established companies. These spinouts will be an effective model for the maturation of technology, attracting better revenue for the institute and also facilitating in generating a large number of start-ups, leading to job creation.
- The concept of applied or product-centric research and technology development in academic institutions has started getting new impetus through the implementation of the National Education Policy 2020 by the Government of India. Recent move on cabinet approval of setting up the National Research Foundation (NRF) will provide it a further boost. Merging of autonomous institutions of the Department of Biotechnology as a single society in the form of the Biotech Research and Innovation Council (BRIC) will avoid potential overlap, leading to focused research towards generating IPs/ technologies through government funding.
- Various funding schemes of Government of India through Indian Council of Medical Research (ICMR), Indian Council of Agricultural Research (ICAR), Council of Scientific and Industrial Research (CSIR), DBT-Biotechnology Industry R&D Assistance Council (BIRAC), Department of Science and Technology (DST), Technology Development Board (TDB) etc with network of large number of bio-incubators and parks are catalyzing creation of technology-based bio-entrepreneurs towards making India Self-reliant and global hub of production of biotech products and services. Robust technology transfer system through TTOs would definitely play a very important role in building and operationalization of the entire ecosystem.

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