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Harnessing Biotechnology for Life Sciences Research: Innovations in Genetic Engineering, Bioinformatics, and Environmental Biotechnology

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Annotation: The revolution in Life Sciences research (LSR) has been made possible by the availability of state-of-the-art, high-throughput and high-resolution biochemical, biophysical, structural and sequencing techniques. The LSR community requires a new generation of scientific instrumentation that can meet this demand. Such equipment requires specialized skills, fine-tuning and constant repairs, thus demanding an enormous burden from LSR laboratories. The LSR community needs to be freed from these non-scientific tasks so that scientists can concentrate on the science. Unfortunately, in many cases such high-end equipment is not readily available to life scientists, for example in mid-tier LSR laboratories of developing countries. Countries such as Brazil or Russia are trying to ameliorate this situation by investing billions into cutting-edge LSR techniques in mega-facilities such as synchrotrons or free electron lasers. In this case access is very limited; not to mention travel expenses for

researchers from many countries having no free access to Brazilian or Russian mega-facilities.

Modern research broadly depends on state-of-the-art high-end equipment. In LSR these are MRIs, X-ray diffractometers, electron or atomic-force microscopes, mass-spectrometers, sequencing machines, etc., which give rise to enormous amounts of data requiring specialized analysis and interpretation. These techniques are not just machines and methodologies, they are scientific instrumentation, which demands specialized skills to be operated and maintained. As a rule, such high-end equipment is expensive, energy-consuming, in need of constant maintaining and tuning, which place a huge burden on laboratories. Biophysics, structural biology, and broadly biochemistry are disciplines needing such advanced instrumentation to provide the necessary information about structure and dynamics of biological objects involved in life processes, e.g. proteins. Some groups are trying to meet this demand by developing scientific instrumentation in home laboratories instead of commercially immobilized devices.

1. Introduction to Biotechnology

Advances in science can be optimally utilized by converting laboratory research into implications. Biotechnology is one such umbrella term that covers a vast area of research employing significant digitization. From explant generation to the design of respective gene constructs, validation of constructs by molecular biology techniques, VIGS, and CRISPR development as well as its transformation, everything is simply a click away. Application of in silico design to laboratory execution in performing biotechnology-based transfer is highlighted here [1].

Biotechnology is the technology of hope. It refers to the working with living systems or their derivatives to make or modify products or processes for specific use. It is multi-disciplinary with interaction between fields like microbiology, molecular biology, biochemistry, chemical engineering, information technology, phyto-biotechnology, marine biology, environmental

biotechnology, etc. in which major impact on all aspects of life exists [2]. In recent years, biotechnology has made rapid strides in healthcare, agriculture, research and development, environment and energy. The technology is continually developing and constantly impacting humans and the world around us in 5 ways. From diagnostics and therapeutics in health, safety from man-made or natural calamities in marine, waste treatment in environment, safer food in agriculture, and awareness and innovative approaches to sustainable energy in energy are discussed here.

2. Genetic Engineering: Principles and Techniques

Molecular biology refers to two complementary areas of the biological world—the study of biological macromolecules and cellular processes at the molecular level, and the principles and processes of transfer, maintenance, and expression of genetic information in organisms. It is more narrow and precise than cell biology or biochemistry, yet more expansive than microbiology or genetics. This difficult definition reflects the masking of molecular biology as a discipline by its own success. As key molecular biology principles and techniques have become common and popular, and as they have been applied outside of traditional life sciences disciplines, the perception that molecular biology is simple, or even trivial, has been fostered. However, to the biologist, the advent of the molecular biology age has necessarily created paradigmatic shifts, conceptual revolutions, and distinct life sciences disciplines, only vaguely paralleled in fields such as quantum physics or mathematics. As the molecular revolution expands, it will impact additional areas, and continue to provide powerful tools for understanding and manipulating human and animal biology, health, vigor, and beauty [3]. Essentially genetic engineering, for the purpose of this review refers to the transfer of DNA between cells, especially between cells of different species. In the past it was necessary for such a transfer to occur naturally, but with the advent of molecular biology, techniques have been developed that enable the manipulation of DNA in vitro and the generation of recombinant DNA molecules that do not occur in nature. The process by which such molecules can be delivered to sensitive cells in non-viral vectors and taken up and integrated into the host genomes will be described. The use of viruses as vectors will be briefly mentioned, although this area has developed a large literature of its own. The field is so vast that only certain selected techniques will be described, but nowhere outside specialized journals can one find the wide-ranging, intelligible, and informative overview of genetic engineering techniques comparable to the book that has been produced by [4].

2.1. CRISPR-Cas9 Technology

In recent years, CRISPR-Cas9 technology has emerged as a powerful genomic editing tool, rapidly transforming life sciences research and biotechnology production. Initially discovered in Escherichia coli, CRISPR systems, together with accompanying Cas proteins, form an adaptive immune system that can specifically and accurately target foreign nucleic acids. A type II CRISPR system containing a single protein and a crRNA-tracrRNA complex were shown to be sufficient to mediate the interference of foreign nucleic acids in bacteria. This simplicity has led to the development and widespread use of CRISPR-Cas9 technology as a versatile and powerful analytic tool to manipulate or engineer the genomes of living organisms.

Mechanistically, a double-stranded DNA break introduced by Cas9 is predominantly repaired by error-prone non-homologous end joining with an associated reliance on cellular repair mechanisms, introducing indel mutations that can result in targeted gene knockouts. In addition, insertion of a donor DNA can be coupled with the Cas9-mediated DSB to model disease mutations, create fluorescent protein fusions, or engineer the use of efficient and precise homologous recombination repair. Used in combination with co-injections of Cas9-gRNA RNP or plasmids expressing Cas9 or gRNA, CRISPR-Cas9 technology has been successfully employed to create knockout and knockin animal models. Widely published protocols for the utilization of CRISPR-Cas9 in various cell types and organismal models have led to an explosion of published reports taking advantage of this technology.

Recent studies have uncovered an extensive diversity of non-canonical CRISPR-Cas9 systems lacking the essential signature genes of type II CRISPR-Cas9 systems. These discoveries have reminded researchers of an increasing need for new and robust alternative CRISPR technology to expand the toolkit available for genomic manipulation in diverse organisms and cell types. Such new technologies are required to be simple to adopt, versatile in their applications, robust, highly effective in a variety of systems, and affordable. Expanding on lessons learned from discovery of the first and most widely-used CRISPR-Cas9 technology, recent studies have identified new CRISPR systems that overcome many of the limitations of existing systems, expanding the robust nucleic acid editing toolkit available to cell and molecular biologists. [5][6][7]

2.2. Gene Cloning Methods

The type of gene cloning or amplification chosen mainly is determined by the type of product desired and the starting material. The major techniques are: its introduction into a suitable vector and either: Resynthesis; In silico degenerate oligonucleotide amplification; Genomic library screening; cDNA library screening; PCR amplification; Low-frequency mRNA screening; Genomic restriction fragment screening; Amplification by PCR, semicon; Reverse transcriptase-PCR. All but the first three routes work with DNA, RNA or cDNA. The first, resynthesis, requires the sought sequence to be known; and library screening works only with large gene fragments in the case of those cloned into bacteriophage and in the case of yeast artificial chromosomes of cosmute vectors.

Cloning vectors contain prokaryotic origin of replication; an antibiotic resistance gene to allow selection of the transformed bacteria and a unique restriction site. Depending on the type of the vector, 1-10 or more kb of DNA can be inserted into it. Vector systems include plasmids, bacteriophages, cosmids and yeast artificial chromosomes. The introduction of the fragment into the vector first necessitates re cleavage at the chosen restriction site, followed by ligation to covalently join the two pieces of DNA. The introduction of the vector into the phage grows clones; these form plaques which can be harvested and isolated. Digestion again with the original restriction enzyme to regenerate compatible sticky ends allows the vector to be re-cleaved and losasmid, cosmid and phage clones isolated. Selection is possible using their origin of replication and antibiotic resistance. A suitable control is to transform with the vector alone to check for containment. Various sizes of fragment can be analysed by agarose gel electrophoresis and any non-matching bands characterised. Hybridization screening is by far the most versatile and sensitive method and involves labelling the known probe by incorporation of radioactive or other tags. The filter charged with bacteria is then treated to allow the probe to hybridise.

A second piece of DNA (the probe) with a high and known degree of sequence similarity on average to the target gene is needed. Primers of usually one or two hundred bases that bracket the region of interest on the known sequence can be designed for the amplification of that region from cDNA, genomic or other sources by polymerase chain reaction. By using engineered bases and synthetic oligonucleotides, construct-in binding sites for new restriction enzymes, a second initiation site for T7 polymerase for the generation the second strand and (or) tails with certain affinities for other binding sites are possible. The plasmid or other system containing the nucleic acid to be cloned is cleaved with the chosen enzymes and after phenol-chloroform extraction, either ligated. Vector systems include the bioassay-competent, infectious plasmid clones, and packaging vectors from blade plasmids for bacteriophage vectors, cosmids and BACs for much larger inserts. Various vectors are independently transformed into the bacterium which later mated and co lysogenic carriers are screened in the first instance for loss of part of the probe after growing in a selective broth. [8][9]

2.3. Transgenic Organisms

Biotechnology techniques have revolutionized the Life Sciences. Fundamental discoveries made by Scientists in the field of molecular genetics have provided a toolbox of approaches. These tools can probe, alter and expand the genetic loci of organisms of fundamental interest. Modified

organisms, referred to as the transgenic organisms or genetically modified organisms (GMOs) can be utilized for research as well as applications with the manufacture of pharmaceuticals, analysis of biological processes, and genetic engineering of crops. However, successful transfer of these powerful techniques to new systems requires extensive consideration of key issues.

Transgenic organisms provide an effective and powerful methodology for functionally analyzing genes and gene products. When co-expressed with the desired regulatory and effector constructs, Transgenic organisms can provide a cost effective and high throughput methodology for screening the activity of novel regulatory sequences in a native context.

Transgenic organisms complemented with genetically-encoded or exogenously added fluorescent tags provide powerful biological tools for investigating proteins. These altered organisms can be used to follow protein localization, degradation, and abundance as well as protein interactions nor modifications. Transgenic animals have been used to engineer organisms that can express fluorescence proteins in specific tissues providing a dynamic platform to track gene expression throughout embryogenesis or following cellular injury [10]. In the same manner, transgenic plants have been used to supplement fluorescent peptides to determine the trafficking of proteins throughout the endomembrane network.

Transgenic organisms can also be modified to express secreted targets or express proteins within organelles that retain translational products within membranes. Once purified, proteins expressed from organisms engineered in this manner can be adapted for use in fluorescence resonance energy transfer (FRET), dual-labelling microscopy, and resonance energy transfer luminescence microscopy [11]. All of these transgenic organisms have been successfully used to rigorously analyze the biogenesis or processing pathways of proteins in a dynamic manner.

3. Bioinformatics in Life Sciences

Modern biology is experiencing a deep transformation. A rapid expansion of molecular-level measurements using omics technologies has taken place in biology and recently also in medicine. Thus, many complementary approaches have become available to build a detailed picture of the inner structure and functioning of organisms. The burgeoning discipline of bioinformatics has emerged from this experimental wealth aimed at handling and reconciling the new data. It has permeated much of biological and biomedical research, and it is now emerging as a key a priori interdisciplinary area that is gaining critical mass in countries around the world. With tens of thousands of biologists-researchers at the interface with advanced math, stats, IT, and algorithms, it addresses a wide array of problems: from central questions in systems biology to more applied issues such as biometric marketing or drug discovery [12]. The strong tradition of open access for large volumes of raw data and high-quality algorithm implementations makes bioinformatics a unique case of open science. Data in bioinformatics is characterized by an ongoing exponential growth in both space and speed, vastly outnumbering algorithms to annotate the respective.

Evidently, tremendous progress has been made towards formalizing computation in the life sciences. Biology is now a bona fide computational science, with estimates of 107 CPU hours per year spent on bioinformatics in Europe alone and similar orders of magnitude elsewhere. The integration of large-scale measurements of multiple omes has improved largely the understanding and modeling of biological systems and of their perturbations, resulting in significant contributions in health and environmental applications [13]. This experience often referred to as the ‘golden age’ of bioinformatics is both a success story and a cause of concern. There is no guarantee that the large and rapidly growing bioinformatical culture built in the last two decades will scale up with data. Most, if not all, estimate of bioinformatics crash at some point. Reproducibility problems arise at every level, with downstream implications on quality and accuracy of annotations. Rather than dismissing poor quality results as untrustworthy, a more stringent internal control might be investigated. However, while the availability of cheaper and better instruments and components leads to improvement, it might not suffice to address all major issues.

3.1. Data Analysis Techniques

Biological Interaction Networks encompass a wide variety of networks each presenting a unique perspective of the underlying biology if appropriately annotated and integrated. Recent inventions of high-throughput platforms provide novel means to obtain large amounts of transcriptome data for every known organism. There is little work dealt with the integration of gene profiles with large biological interaction networks for pattern discovery. A pattern discovery framework was implemented which allows mining of highly significant patterns. The framework is evaluated based on the Arabidopsis GeneNet. A variety of evaluations are performed on the mined patterns; these evaluations capture the biological significance of the mined patterns in genome, transcriptome and phenotype levels. The framework is designed in a general way, can be extended to include other biological networks or plant species. Network analysis is very essential in biology. The classical biological networks captured on board are usually compact and small, whereas in the post-genomics age quite large biological objects are available. These objects are biological interaction networks encapsulated a wide variety of interactions. For each molecular type, biosystems experience biological interactions on different time scales. The occurrences of these interactions can further be explored based on different ways. Interesting patterns signify some insights of the targeted biological interaction networks. However, such a task is very challenging due to the bulk and large scale of modern biological networks. Pattern discovery is a crucial and challenging issue in analyzing biological interaction networks. To capture significantly enriched patterns, the nature of the biological interactions contained in the large networks need to be inspected and modeled. Biological interaction networks encompass a wide variety of networks each presenting a unique perspective of the underlying biology if appropriately annotated and integrated. Specifically these networks can be classified into four main types. Experimental observations of interactions provide a blueprint of biology. Mining positive interaction data generates significant implications on the biological interactions. Contrarily each regulatory interaction also has some contraries. With multiple types of biological interaction networks on board designed for plant biologists, gene profiles can provide insights on novel metabolic events at which the biological interaction networks would reset. [14][15][16]

3.2. Genomic Databases

Genome Databases

Genomic databases are the locations for storing, sharing, retrieving, and comparing information related to the genomes of various individuals and organisms, all in a standardized manner. Initially, these databases were shared on CD-ROMs and small tapes. But, rapid development of technology and high-speed internet has resulted in the development of specific databases for almost all model organisms and a group of organisms with common specificity. Some of the databases related to the genomes of viruses, archaea, bacteria, invertebrates, vertebrates, plants, and humans are given below.

Virus genomes are the simplest among all living organisms. They are acellular organisms. However, sequences of viral genomes and proteins and their functional information are very much needed to compare the tentatively related viruses and to apply toward the related viral outbreaks. Virology databases contain sequence data and biological data related to viruses. Moreover, some of these databases have software tools for bioinformatics analysis. Virus-Host DB contains data of lytic and lysogenic bacteria-bacteriophage interaction, which can help researchers study novel interactions. VCDB hosts a collection of viral circular DNA genomes and software tools for circular virus genome analysis. The IPTG site provides a resource of researchers who have significant experimental experience on viral genome and protein manipulation and virus isolation studies, and researchers can submit their contact information on it. The ViralZone integrates widely used information on virus classification, structure, genome, life cycle, and virology databases and bioinformatics tools related to virus sequences and structures in a user-friendly sequence. Details of the databases can be found in [17].

A database related to archaea should possess an archaeal genome annotation system. There are several publicly available archaea genomic databases: the online databases and the downloadable databases. There are only three online databases; those are: the Genomic data for archaeal phylogenetic analysis, Archaea genome and amino acid sequence search, and a database for archaeal genome annotation.

3.3. Computational Modeling

Growing awareness of the role of bioprocesses and biosystems in biotechnology and biomedicine has increased the demand for in silico modeling in the biopharmaceutical industry and academic/industrial partnerships to advance in silico modeling in downstream processing and cell-based assays. Cell culture can be broadly separated into upstream bioprocesses (cell line generation, media development, and bioreactor operation) and downstream bioprocesses (harvesting and purification). Predicting a biological output given a bioprocess input has served some critical use cases in therapeutic development at drug, target, and candidate selection. The biopharmaceutical industry considers in silico models to be an established research and development tool [18]. Machine learning tools have been deployed extensively to relate preclinical input data from high-throughput experimental screening to whole-animal pharmacokinetic modeling and clinical outcomes and guide drug dosage and administration regimens. However, life sciences in general and the biopharmaceutical industry in particular may be dominated by hoping for the best rather than along the lines of reductions in dimensionality and innovations that allow complex systems to be appropriately modeled, queried, and searched. There is no avalanche of in silico models relevant to the biological, biopharmaceutical, and bioindustry sectors.

Despite success stories globally, there are still challenges of understanding and conversion of breadth and depth of biological knowledge, large uncertainties in input-output responses of biological systems, and the absence of standardized nomenclature across domains in biology that hampered in silico modeling. The scientific computing community has advanced strongly in this regard and has amassed a wealth of process systems knowledge, algorithms, and tools on modeling and simulation. The low awareness level of process systems modeling tools often keeps life sciences researchers still stuck in their respective fields. The establishment of a governance model and the design of translational case studies are two major analytical undertakings thought to accelerate the development and adoption of in silico models in the pharmaceutical industry. Due to investments in process systems, the pharmaceutical industry is immediately positioned to provide a suite of solutions to the issues faced by the biopharmaceutical industry. [19][20]

4. Environmental Biotechnology Applications

Environmental biotechnology deals with maintenance of a pollution-free environment, waste treatment, monitoring of environmental changes, and pollution prevention. It consists of a series of approaches utilizing direct or indirect biological processes in waste treatment, pollution prevention, and monitoring of environmental changes. Environmental biotechnology deals with problems related to environmental pollutants such as heavy metals, petroleum carbons, plastics, pesticides, etc. Scientists have developed various biotechnological procedures for the elimination of these pollutants. The development of biotechnology has provided advantages in designing new biological processes of waste treatment. Microbial bioremediation utilizes higher living organisms or certain microbial species for decontamination. All living organisms possess the inherent potentiality to degrade various pollutants.

Biodegradation of industrial wastes can be achieved by providing the suitable growth conditions required for the development of natural organisms associated with the process. Mainly, bioremediation is achieved by using indigenous microbes, which are subjected to various treks under natural and laboratory conditions. Also, the genetic properties of the microbes involved in bioremediation are evaluated, which lead to their possible cloning in suitable genetic systems. The explosive cost of conventional processes catalyzed the pursuit of a more cost-effective form of

treatment based on biological processes derived from nature. A wide field of application has arisen using microorganisms, and a variety of bioprocesses are now employed to treat waste. Knowledge of environmental microbiology in conjunction with genetic engineering approaches has given rise to a range of developments.

Enzyme bioreactors are being developed to pretreat industrial and food waste components for removal through sewage systems. Various enzymes are being obtained from commercial sources. A number of simple bioreactors along with consortium of microorganisms are being evaluated in laboratories and pilot plant studies. Since enzymes are specific to substrate(s), better results are being obtained. The production of biofuel from waste can solve the fuel crisis. It can also reduce the problems of pollution. Anaerobic fermentation of waste produces biogas. Enzymes are produced from microbes that can degrade waste products containing starch, cellulose, and lignocellulose. These industrial wastes can be converted into sugars, which are subsequently fermented to produce ethanol. Ethanol can be used to replace petrol and dodecanol can be used to replace diesel. Microbes may be engineered to produce enzymes required for conversion of plant materials into biodegradable plastics.

Methane can be derived from bacteria that degrade waste products. Methane can be used as fuel or in industrial processes to derive other products. Insect- and pest-resistant crops have been developed which have reduced the use and environmental load of insecticides. Bioengineering of plants with the Bt toxin gene and their subsequent release in the environment has helped to solve the problems of cotton pests to a large extent with negligible side effects on the environment. Modern biotechnology-based waste treatment is being adopted since a decade, and a number of biotechnological industries are in operation in various countries. Biotechnological processes may create opportunities in new areas for waste treatment for various types of wastes. These need to be identified and addressed. [21][22]

4.1. Bioremediation Techniques

Bioremediation techniques are increasingly important for the rapid detection and remediation of environmental contaminants. These processes are environmentally friendly and safe and their unique biocatalytic capacitates allow the removal of a wide range of contaminants from various environmental matrices. Pollution caused by heavy metals and organic compounds is considered one of the most serious global environmental issues, since they can accumulate in food chains and threaten both ecosystems and human health. For example, innumerable cases of water source pollution have occurred due to continuous disposal of heavy metals into rivers. Recently, intensive industrial activity has aggravated contamination by organic compounds. Therefore, environmental remediation is of paramount importance and bio-remediation technology is one of the most promising strategies.

Bioremediation is the use of biological organisms to destroy or reduce hazardous wastes on a contaminated site. The biological remediation techniques include land farming or ex-situ bioremediation, bio-cells, bio-piles, composting, bioreactors, phytoremediation, microbial flora and sludge, and seaweeds. Some biological agents of bioremediation are microbes, enzymes, and plants. A few examples are bacillus sp., pseudomonas sp., azotobacter, aspergillus niger, Ganoderma, Penicillium, and ionophore antibiotics. Bioremediation is a potent management tool to control environmental pollution and to recover contaminated soil. Advanced knowledge on the biochemistry and genetics of hydrocarbon degrading bacteria and mycoremediation would aid in developing microbial consortia and fungal cultures that can be used in bioremediation research and technology [23].

Bioremediation can be defined as “the biobased removal of contaminants from a site.” Various biological materials are used to obtain advanced processes, some created or selected by researchers, and others probably improved in situ. The technology comprises both expensive and inexpensive methods. The expensive approach is the total excavation and treatment of contaminated materials in industrial plants. The inexpensive region comprises those biobased

methods that select native microorganisms able to degrade compounds of anthropogenic origin and/or those that foster bioprocesses at in situ conditions.

4.2. Waste Management Solutions

Waste management solutions revolve around adopting a comprehensive approach that incorporates technological innovation, raises consumer awareness and corporate social responsibility, promotes consumer behavior change and gives more value to surplus food. The Food Recovery Hierarchy outlines actions which organizations, individuals and families can take to prevent and manage wasted food. We have aimed to showcase modern techniques that enable us to turn organic by-products or waste into valuable materials and energy. Valorization of biological waste materials appears as one of the most promising avenues to limit waste and avoid depletion of natural resources. The waste into value concept promises carbon neutrality and local employment. Strategies of bio-valorization are often based on traditional methods and techniques. Microbiology, together with molecular biology, is likely to improve the fermentation processes in the fields of biofuels and biogas. More selective collection and processing methods are likely to increase the yields and value of bio-derived products, such as green urea and phosphate from human and animal excrements. New innovations in the field of household waste may provide fascinating opportunities [24].

4.3. Sustainable Agriculture Practices

Limited food resources significantly harm human health and development, primarily in low-and middle-income countries (LMICs) where crop production is largely limited by heat, drought, and flooding [25]. Agriculture also contributes heavily to climate change via greenhouse gas emissions from livestock production, fertilizer application, land use change, biomass burning, and deforestation. Some climate change impacts, including more extreme weather, temperature, and precipitation, are expected to worsen, worsening food security and threatening sustainability. Climate extrinsic factors such as rising levels and concentration of fertilizer application and rising prices of essential yields and inputs threaten to overwhelm mitigation progress made by some farmers and governments. The realities of climate change are predicted to make it increasingly difficult for farmers to achieve their desired productivity and yields. It is increasingly necessary to build adaptation into crop breeding and biotechnology tools to help farmers manage climate change.

Predicted climate change impacts on human health, agriculture, and economic growth and productivity suggest a significant threat to sustainable development, especially in LMICs. Sustainable development is theoretical, precluding a clear set of measurables but can be understood with varying degrees of success. Predictably, food systems will need to be transformed by modifying the biochemistry, physiology, and enzymology of organisms to support sustainability goals. Investment across human, social, physical, natural, and economic assets is critical to moving toward sustainability. Better understanding, valuation, and incorporation of externalities are needed to achieve sustainable development. Open access data on food systems challenges and barriers to development is crucial for improving global understanding of the nature and scale of the problem. A full accounting framework for food systems is also necessary to more accurately assess their contribution to national sustainability priorities.

5. Innovations in Synthetic Biology

Synthetic biological circuits can serve as powerful tools to explore the principles that govern biological systems, advance the understanding of human biology, and exploit such knowledge to help improve the understanding and treatment of diseases. Therapeutics targeted to the molecular mechanisms of human diseases hold great promise for both efficacy and reduced side effects. In this regard, many different types of disease-targeted therapeutic agents are being developed, from small molecules, peptides, and proteins to nucleic acids. However, a current limitation of available therapeutic modalities is that they exclusively rely on passive target recognition, which relies on

complimentary inter-molecular interactions between the agent and target(s) and lacks precision control over specificity and timing of actions. Such limitations can be overcome by utilizing the principles of synthetic biology to construct “targetable” dynamics circuits in human cells that combine both receptor/circuit interaction and target/circuit interaction to elicit a therapeutic output at the target(s) [26] and [27]. In addition to minimizing damage to by-stander normal cells/tissues, such circuitry can also potentially reduce the probability of drug resistance evolution by manipulating the dynamics of drug action to activate drug/action close to the timing and location of its targets. To demonstrate the feasibility of multi-targeted, RNA-regulated circuits, a simple, two-substrate AND gate circuit framework that can produce a therapeutic output of widely used herpes simplex virus thymidine kinase pro-drug activated drug was previously constructed. Such a circuit was constrained with an RNA aptamer for the selection of activator at the target that inhibits parallel circuit of drug on-off in non-target cells. Its effective inhibitory action was characterized in transient transfection experiments in cell lines and in xenograph models.

5.1. Metabolic Engineering

The term metabolic engineering, first coined to designate twelve different methodologies to study cellular metabolic processes, was later adopted to also cover the subject area that seeks to improve cellular behavior by modifying metabolic engineering pathways and was defined as the optimization of an already existing natural cellular process to produce it up to a maximal yield and productivity. Metabolic engineering tries to apply information toward the optimization of the biological synthesis trajectory of a desired compound. In recent years, the homogeneity of these two subject areas has become blurred, putting forth the need to distinctively categorize both of them. The constraints and needs imposed by the classical synthetic biology methodologies on metabolic engineering techniques and methods for the modeling of mathematical optimization problems to optimize the behavior of engineered systems make of paramount importance the clear distinction of both subject areas. A deeper understanding in this respect would allow researchers from these different communities to proactively familiarize and benefit from the complementary methodologies offered by both domains.

In post-genomic times, the combination of high-throughput measurement of cellular components together with high-throughput characterization and perturbation techniques offer an unprecedented view of cellular behavior. The generation of complementary new techniques and methods, most of them described as “-omics”, has been vital in the development of both areas. Some of these technologies can be applied to insert genes of partial or complete metabolic pathways for the synthesis of a specific compound. They can also be used to eliminate genes from the organism that interfere with the synthesis of the compound of interest. For that purpose, diverse gene knockout technologies, such as classical insertional mutagenesis, transposons or tailor nucleases, can be employed. Additionally, these methodologies allow carrying out point mutations that reduce the activity or expression of native proteins to modify the metabolic flux. Targets for this type of intervention are either the genes coding for the enzymes that are apparatus of anabolic blocks or fast growing that are behind catabolism involved in the generation of metabolic intermediates that waste carbon or energy as in the case of polyhydroxybutyric acid production. The techniques and methods currently exist are not only not effective but also depend on the organism on which they are being applied. Although state-of-the-art transformation systems are available for a handful of organisms, in many others, such methodologies must be developed from zero. Therefore, high efforts and investments should be made in this regard to successfully advance in metabolic pathway engineering in a high-throughput mode ([28]).

5.2. Biological Circuit Design

The design of biological circuits is perhaps the most exciting and advanced most area of biotechnology. Biological logic circuits designed using synthetic biology toolkit can alter the properties of living matter to sense their environment and respond by modification of their genetic programs and metabolism. These circuits are comprised of one or more biomolecular devices such

as DNA, RNA and protein. A combination of devices can be wired to simulate the desired logic operation. An important goal of biotechnology is to design and deploy advanced logic circuits programmed to simulate complex multilayer logic functions capable of thinking, reasoning and imitating human-like behavior. Moreover, the same logic circuits would also be needed to design adaptive circuits capable of evolution for acquisition and improvement of complex functions in a random environment [29].

A biological circuit represents information as a chemical concentration and as a biological circuit changes, this information is transmitted from molecule to another at different time scales. Biological circuits are perhaps the most exciting and advanced most. A close cousin to electronic circuits is indeed biological circuits. Biological circuits are devices that compute or process information (or energy) in chemical form; they exist in the heart of every cell and many diseases arise from dysfunction [30].

6. Ethical Considerations in Biotechnology

The developments in biotechnology raise some ethical considerations. Ethical questions with respect to biotechnology can vary depending on the applications or the perspective on which they are posed. In the life sciences research and pharmaceutical developments, issues of freedom of research can arise. At the policy level, ethical (and social) aspects of biotechnology can also concern issues of responsible use of technologies in various areas of application.

This paper will concentrate on ethical questions addressed to biotechnologies themselves, i.e., issues that concern the technologies independently of how they are used, in a similar manner as questions on the ethics of nuclear technologies can be asked apart from the applications [31]. This is a challenging topic for two main reasons.

The ethical discussion about the biotechnology as a whole has at the moment much more questions than answers, and it may seem overly ambitious to try to give an overview of what issues might need ethical examination. However, there have been a number of studies in recent years on specific issues that can be considered suitable starting points for framing the ethical discussion. Besides, the “transparency” claim implies a proactive approach regarding ethical consideration.

Nevertheless, biotechnology encompasses a wide variety of technologies. The ethical discussion concerning biotechnology is generally organization specific, depending on the specific nature of management and on the context in which the organization operates. In this paper, biotechnology as genetically modified organisms (GMOs) will be confined to a set of issues that can be considered widespread and relevant for future discussions. It has been used in a wide variety of commercial and experimental applications in the life sciences and agricultural sector and procedures for public policy development concerning GMOs have already been elaborated on in some countries. Hence, the GMOs form a relevant and interesting case for examining a number of general issues on ethics in relation to biotechnology, and for considering follow-up steps.

On the other hand, the biosafety issue is just one of the many ethical questions that might be relevant for the biotechnology as a whole, even if arguably appropriate starting points. Environmental pollution, safety of products for man and animal, and the rapid decrease of genetic biodiversity are some of the ethical questions that can only be approached with regards to the specific techniques or applications of biotechnology.

6.1. Bioethics Frameworks

Although ethical challenges in biotechnology are multiple and ongoing, including those tied to development of technologies, additional challenges arise when/if they are adopted on a grander scale in local public health research, as in public education and promotion scenarios. A framework for public deliberation that can account for these challenges would incorporate roles for adherents of the aforementioned frameworks and would also include those who seek to understand and

assess the plans of the research enterprise under consideration. The latter comprise a multi-disciplinary group that includes scientists, public health researchers, practitioners, risk assessors, media and communications researchers/practitioners, legal scholars, and specialists in civil society/building deliberative processes. Synergy between these groups would be driven by the belief that serious missteps in applied bioethics by the public health research enterprise could invite Hobson's choice challenges from civil society. Such challenges in turn could catalyze immediate calls for costly policy action by governmental oversight bodies and/or dismissal of the research avenues proscribed by the plans.

Even nuanced and self-confident groundwork about the prion and microb-Ean cases will not facilitate any instrumental deliberation about their analogue plans if they lose credibility. In situations where a bioethics framework could inappropriate, the consequences could be severe: biological defense research archives could be destroyed and immediate cessation of work could ensue. Non-scientists would best decide if the reference frame of the Danger of God is appropriate to a biotechnology application/or bioweapon case; scientists and/or those who would be responsible for starting the debate need to consider this course of action before proceeding. The Danger of God reference frame stands to exclude bioethics from the discussion altogether [32].

If adopting and framing such a daunting a standpoint is indeed desired, civil society would use all of its power, including mobilizing third party experts, to impact public perceptions of biotechnology and its practices. This could incur consequences of cathedral grandeur; public money could be sought to stage any such deliberated process and investigative committees involving eminent scholars would be called together. For the actual immediate work of bioethics, however, the Danger of God would impose a challenge that no subframe could easily mediate (with the important caveat that the future unknowns around persistent emergent properties could still offer alternative unapproachable categories). [33][34][35]

6.2. Public Perception and Policy

Social acceptance of biotechnology is slow in developing countries like India, where it is being studied as a necessary component of life sciences research, teaching, or commercial applications. There are allegations against GM crops for their supposed environmental impacts and hazards to general public health [36]. In developing countries, issues with biotech agriculture cover mainly GM crops and foods, while concern with human applications is less, except with stem cell therapy in a few urban pockets. Biotech research is conducted primarily in the commercial/academic sector, while policymakers, politicians, and risk assessors are new and trust deficient. The initial trust building, awareness, and participation of various stakeholders are key in policy formulation and decision making. Although biotechnology has impacted life sciences research and there are concerns with its use, attempts were made to study the using channel and their effectiveness in reaching out to the life sciences research community in India.

For the present study, the life sciences research community and their perception and knowledge level towards the rapid advancements in biotechnology were examined. The survey was conducted in March–July 2017 using an online questionnaire as a survey tool. Questions concerned the impact of biotechnology on life sciences research, laboratory safety, intellectual property rights, capacity building, bioethics, and public acceptance. There was a wide geographical distribution with respect to termination and representation of various sectors (academia, industry, and government). Majority strongly endorsed that biotechnology will have a positive impact on life sciences research. The vast majority agreed that such impacts will depend on the level of awareness and understanding of these advancements. Majority agreed that they are aware about issues of laboratory safety, IPR, and biosecurity associated with biotechnology. Majority were positive on biotechnological advancements improving public acceptance of science.

7. Regulatory Landscape for Biotechnology

The biotechnology regulatory landscape stems from the need for assurance that biotechnology

products meet state safety and efficacy standards and for an open forum in which to consider the science underlying biotechnological advances and the dangers they present. In the beginning, the oversight process was vested in the federal sector, leading to dramatic rifts based on the intrusion of the regulatory process into realms beyond the purview of the law. This legal analysis examines developments in state biotechnology regulatory policy based on analysis of current Maine law with a focus upon biotechnology product labeling practices. Imperative for forwarding the development of biotechnology regulation are recognition that current legal avenues are inadequate and entry to the legislative process by "insider" advocates – those possessing exploitable knowledge of the biotechnology industry and the accessibility of the legislative process – acting in the public interest to find resolution.

Biotechnology includes a wide variety of applications. Though biotechnology is touted as the "next industrial revolution," proponents claim, there are other views regarding this development. Indeed, many scientists, among them Nobel laureates, suggest that genetic research is the most frightening endeavor ever to be gripped by novelty. Such diversity of opinions raises the matter of oversight and regulation of biotechnology activities. Knowledge and both understanding and the ignorance of the science itself, opportunities and threats to the possibilities of the new biotechnology systems abound. Yet, because of projections of both great rewards and possibly catastrophic holocaust, knowledge and understanding of these forces must advance ahead of both the research and the technology itself, else they risk being lost, neglected, or ignored [37]. Projections regarding what biotechnologies portend for the future range from natural restraints built into the pro-cum-hist genes of microbes to thoughts on end-of-the-race biogenetics and the fate of the human race. Meanwhile, biotechnological developments forge ahead. The age of biotechnology is indeed upon us [38].

7.1. Global Regulatory Bodies

With the advent of novel biotechnologies such as CRISPR and gene therapy systems, biotechnology holds great promise for research and therapeutic use in the life sciences. Because of the wide range of uses of biotechnological products, these technologies and the relevant products are increasingly scrutinized by regulatory agencies globally. The regulatory policy constantly evolves in accordance with technological advancements in biotechnology while attempts are made to ensure the safety and efficacy of widely used products. In 2016, when a CRISPR/Cas9 gene-editing system was used in the first clinical trial to cure transthyretin-mediation amyloidosis (ATTR) in patients in Texas, local concerns were raised if the tests were approved for safety and efficacy [37]. After the clinical trial, the United States Food and Drug Administration (FDA) announced newly established guidelines for review of editing techniques of such viruses. In 2021, a female patient died of severe adverse reactions and multiple organ failure from her CRISPR gene-editing therapy, with a subsequent crash of its company stock, and a denial of the trial's renewal application was reported to the FDA. In 2022, it became public that a patient treated by the same company had received a unapproved concurrent mRNA FDA vaccine after the coding viral sequence was delivered into the patient's cells. In 2023, the company FDA passed as regulatory tidbits appeared in news coverage again after unregulated adoptive transfer of the CAR T cell product.

The life sciences are experiencing an explosive advance with the introduction of novel experimental capabilities in multiple innovative platforms, with external factors creating significant tensions between the need for this biotechnological innovation and responsibility to minimize the risks posed. The pace of progress and resultant steps taken by researchers up to the line create opportunities for major scientific discoveries with transformative health benefits worldwide. Front-running countries and regions in life science research aim to establish initiates to promote scientific growth and high-tech investments. However, the newly established and existing regulations do not apply to the newest biotechnologies, exacerbating the risk of eventual regulatory gaps in the race for compliant research. Concerns include the dual-use potential of biotechnological knowledge and the impact of illicit and unregulated studies to potentially create

catastrophic threats to humanity. With the involvement of notable scientists and founders, another potential danger arises that researchers are able to conduct studies abroad without oversight or regulation on unwanted biotechnologies that are banned at home. [39][40][41][42]

7.2. Compliance and Safety Standards

Important aspects of Bio-Recycling considered in the context of an effective laboratory biosafety and good laboratory practices are summarized below:

1. Compliance and Safety Standards HSE explains the differences between biosafety and biosecurity. As per the HSE guidelines, a term "Biological Safety" refers to Practices, Containment, Safeguards and Isolation designed to prevent Release or Escape of Bio-hazards Bio-CSi for Bio-Risk Mitigation after observing Bio-Safety Containment Levels i.e. BSL1-4. Bio-Risk Mitigation helps Lab-work continuity. Aspects of Bio-CSi are aimed to prevent unintentional release of pathogens/living modified organisms. Under the "Biological Security", it is to safeguard Dangerous Pathogens (or GMOs). Bio-SSi safeguards hold clandestine production or usage of bio-agents. Thus, Bio-Si incorporates aspects from "Bio-SM" aspects which prevent calculated/scientific misuse of biologics either by individuals/ethnic groups/countries [43]. Bio-SM is a broader than biological security which aims to prevent misuse of Biotechnology and bio-group [44]. Thus a "Bio-Harm" occurs when biological Technologies or Agents or Knowledge cause "negative effects" e.g Causing Natural Disasters by Chemical/Bio-Weapons or causing Malaria as Bioweapon by infecting guided mosquitoes or Terrorist Dissemination of infected food, etc.

2. Minimum Best Laboratory Practices Laboratories with bio-agents having Hazard Group Classification of 1, 2 & 3 on occasional basis should ensure proper practices for the safety of laboratory personnel and the environment. This describes minimum acceptable best laboratory practices from the containment and exposure point of view that should be practiced in any BSL-2 Containment Laboratory. These include restrictions on access and storage of bio-chemicals; pre-use procedures for equipment, glasswares and disposables; procedures during the experiments; and post-experiment procedures. When possible, all manipulation on culturing bio-agents should be done inside a BSC with a HEPA filter safety cabinet preferably under a Main Service Unit. Basics of arranging benches and placing of equipment inside a BSC in such a way that air flows in a downward direction and practically no turbulence zone is created are discussed. The cycle of air movement within in a BSC and its effectiveness in protecting the personnel and preventing contaminations are explained. Finally the proficient use of equipment and supplies and office general precautions regarding consumables, waste disposal and personnel hygiene are emphasized.

8. Future Directions in Biotechnology

The past 20 years have witnessed remarkable advances in the area of biotechnology, with many new tools, techniques, and instruments developed and commercialized for use by the pharmaceutical industry. At the same time, omics and related technologies have rapidly matured and are now routinely used in laboratories conducting drug research. The impact that these advancements have had in terms of both new opportunities and improved productivity will be discussed in this article [45]. Selected future trends that are likely to have a significant impact on drug research over the next decade will also be discussed.

New biological knowledge has been acquired thanks primarily to advances in genomic technologies. Next-generation genome sequencing, automation, and high-throughput analysis have dramatically reduced the cost of sequencing a base pair of DNA. There is speculation that it will be cheaper to sequence an individual's entire genome than to purchase a cup of coffee. The rapid accumulation of publicly available genomic sequence information has provided researchers with a genetic database that is now being mined at an unprecedented pace. Much of the new information that has been acquired has already been incorporated into dialogue databases. Proteomic technologies have improved dramatically, with a multitude of new techniques developed for

protein separation and identification, along with advanced high-resolution mass spectrometry. Additional new technologies have provided a better analytical toolkit for drug-target identification, validation, and selection. These include the introduction of new chemical probes for specifically studying pharmacologically important classes of proteins, such as kinases, lipid kinases, G-protein-coupled receptors, and other receptors that are key targets for new drug development.

In summary, pharmaceutical scientists have taken advantage of every opportunity or technique available to aid in the long, costly, and unpredictable drug discovery process. The techniques described herein have changed the way drug research is conducted, refining the process that optimizes the useful pharmacological properties of an identified novel chemical lead and minimizing the unwanted properties. The promise of genomics, proteomics, metabolomics, pharmacogenomics, epigenomics, toxicogenomics, systems biology, and bioinformatics to radically change the drug discovery paradigm is eagerly anticipated.

8.1. Emerging Technologies

Technological innovations have always been a cornerstone of scientific advancement. Perhaps exemplified most vividly in the physical sciences by the rise of the telescope and microscope, the development of scientific techniques has equally, if differently, changed the face of life sciences research. There too, innovations in technology have changed the scope and approach of scientific work at all levels from the biochemist to the biologist [45]. Correlatively, availability of inexpensive kits to genotype or sequence biological samples brought these techniques to a large number of life sciences laboratories such that they transformed the scope and day-to-day practice of science. These technological developments brought with them a wave of ethical concern over the methods by which this information is gathered, the interpretation of the vast amounts of DNA sequences and correlatively, what happens to the information once it is obtained. Yet even though biotechnology has developed swiftly and scientific usage of biotechnology has greatly increased, awareness and understanding of just what biotechnology is and how it can be (mis)used for research, industry, or social control remains low.

The promise of biotechnology is wondrous, varied, and vast. Simply put, biotechnology refers to techniques that make chemicals, molecules, or organisms designed or customized by the manipulation of biology, cells, or biomolecules more widely though not uniquely defined to also include ‘substantially improved’ natural products. Biotechnology offers dramatic and very appealing innovations. At the level of fermentation, biotechnological adaptation of an organism to produce a chemical of interest could make it into a factory producing a highly complex pharmaceutical, natural product, or chemical that is much less complex. At the genetic level and in vitro, biotechnological approaches to gene assembly, and polymerization using DNA polymerases of nucleic acid substrates could also provide the means to just such products. Such biotechnological methods must draw on sophisticated molecular biology techniques, extensive knowledge of the organism or the process, and perhaps the experience of chemical synthesis, extensive data on chemical production or knowledge of drug design and manufacture to even begin to test their feasibility.

8.2. Interdisciplinary Collaborations

Building and maintaining effective collaborations across disciplines can be challenging, given the differences in goals, methods, key concepts, and training. Some of these differences are explicit and tangible, making them visible and easy to address. Others are much more subtle and intangible, such as key concepts that arise from the distinct paradigms of the various disciplines and their basic assumptions. In establishing collaborations, it is critical for the biologist to understand these differences and their consequences in order to communicate and operate effectively with collaborators. However, its subtleties and complexities mean that discipline-bridging knowledge might not always be accessible from textbooks or other academic sources and is often learned from experience with success or failure. This talk will focus on what the biologist

needs to know to establish effective collaborations for experimental and computational work on complex biosystems. It will emphasize some fundamental concepts of modeling and computation that biologists will encounter when collaborating with theoreticians and informaticians [46].

This biotechnology educational module stems from one of the workshop discussions held at the Machine Learning Methods for Complex Biosystems workshop. This workshop brought together academic researchers from computer science, statistics, physics, and biology industries, and students seeking postdoctoral positions or jobs in industry. The discussions highlighted key differences and similarities in the goals, methods, and training of theorists/informaticians and experimentalists, and emphasized the implications of these differences for effective collaboration. It was discussed that the differences between these disciplines are visible and tangible in terms of training [47]. Recent developments in machine learning methods provide unprecedented opportunities for analyzing data for high-throughput screens and domain-wide studies, for organizing and integrating data available across separate repositories and studies, and for extracting key parameters and principles governing complex biosystems from sparse data. On the other hand, inquiries into the motivations, future directions for the field, and any regulatory or ethical concerns and implications did not get the same level of discussion.

9. Case Studies in Biotechnology Research

The majority of life-sciences research is conducted by biotechnology professionals working in small to medium enterprises. The biotechnology sector is expected to harvest the benefits of these advances, invaluable in designing new constructs, pathways, or production platforms. Understanding biotechnology through case studies not only provides insights into research design but also helps future biotechnology professionals navigate potential pitfalls, take bold steps, and prepare for the unforeseen challenges and surprises likely to arise during research. Before diving into research designs, it is important to know what can be achieved with all the tools, metabolism sources, reagents, and knowledge obtained recently. For biological research, observing nature and the laws that govern it is the preferred approach. It may take many years of gathering knowledge, but understanding the system comes from direct observation of its natural workings. It is this knowledge that eventually generates hypotheses that can be tested in a controlled manner, be it with a bioreactor, a 96-well plate, or any other device that allows sampling and perturbation. As knowledge grows, intricate systems often get too complex to be studied straightforwardly. This generates another type of research with the sweet promise of unveiling new phenomena through well-designed experimental changes. Computer simulations are often helpful in this regard. Again, being aware of the limitations of the models and faithfully describing the relevant biology is critical for success. However, many systems remain too complex, dynamic, or intricate to dissect, hypothesize, or simulate. For these situations, experimentation becomes a proverbial shot in the dark. Despite years spent in research, being trained in programming computer simulations to model the system better, or digging into the nuts and bolts of each metabolite or protein involved, it would not be easy to solve the problem at hand.

The following case studies will illustrate how these research-learning cycles played out, from the early years of investigating the groESL chaperonin system of Schizosaccharomyces pombe, attempts to understand how S. pombe leaderless mRNAs are translated, and the risk of modernizing these luciferase-based constructed closet systems to the more common Escherichia coli 5'-UTR systems as a mean to generate tighter sensor systems. The elongation factor EF-Tu and the leaderless translation of an E. coli mRNA captured this enthusiasm and naivety of novice biotechnologists, the astonishing complexity of this bacterium only decades into the research career, and the importance of combating nanopore sequencing revenue losses from investing in educational and research purposes. Attempting to construct more versatile glycerol 3-phosphate dehydrogenase-based fluorescence assays and luciferase- or fluorescent protein-based sensors while exploring a novel cloning-to-sequencing pipeline that seduced a desperate and naive novice into a year of hell will illustrate the complexities involved in bridging unlikely partners such as Pseudomonas fluorescens-an almost promiscuous source of novel strategies to combat materially

ubiquitous organic pollutants-and Saccharomyces cerevisiae-a habitual workhorse of synthetic biology. Lastly, the bioinformatics perspective will be considered. Failure to confront the immense potential of accessible, affordable, fast, and reliable bioinformatics platforms and databases may hinder the competitiveness of biotechnology.

9.1. Successful Biotech Startups

Biotech startups are sparse. Multibillion-dollar companies such as Illumina and Regeneron have not spun off pure biotech startups in a decade [48]. Here we provide the most visible biotech opportunities that have emerged from the current wider economic turmoil: immuno-oncology, RNA-based therapeutics, cell-therapy platforms, and next-generation sequencing and gene editing tools. The biotech landscape is rapidly changing. This analysis can be used by biopharma companies to identify where to prioritize partnerships, by VCs to assess the profitability of technological bets, and by biotechs to evaluate competitors. Creating and optimizing nucleotide analogs bolstered by high-throughput screening could accelerate the development of proprietary anti-cancer mRNA vaccines and other RNA-based therapeutic modalities. Exploring epitranscriptomics could expose weaknesses in RNA-based therapeutic platforms and help craft best-in-class RTPs. The establishment of humanized and tumor-antigen-edited mouse models could open up a new platform for developing immune-oncology monoclonal antibodies, especially those targeting specific post-translationally-modified epitopes [49].

The recent pandemic-induced investment boom had created a desire and capacity for new biotech startups in all three local communities. However, in retrospect, that push created an overcrowding effect in the industry, exacerbating the drought in seed funding that was starting to surface by mid-2021, despite still being a period of disproportionally high fund-raising activity. Questions have been raised in investment circles as to whether small private biotech companies had become too numerous, too similar, and too early-stage to collectively organize an attractive entry/exit strategy versus pursuing public funding—or simply whether the pipeline had overly congested. The rapid initial public offering of the first half of 2021 had all but dissipated, leaving behind a wasteland of devalued private biotechs and disappointed investors, a far cry from the promise of reaping a stock market windfall from an ongoing wave of much-ballyhooed SPAC biotech IPOs that were running out of diligence valuation time.

9.2. Innovative Research Projects

Several innovative research projects have been initiated that challenge and, where appropriate, expand established methodologies. These enhancements include more sustainable approaches or new analytical techniques, providing opportunities for both working within and challenging the discipline of life sciences research.

The legacy of radioactive waste disposal at the Dounreay Nuclear Power Development Establishment has resulted in environmental ‘hot spots’ arising from the legacy of waste disposal practices [50]. Research undertaken as part of the biobank initiative focuses on establishing if biotechnological approaches could be adopted for sustainable bioremediation of these contained hot spots.

The dispersal of a fine-grained, moderately radioactive, backfill matrix and resulting radioactive particle fallout along the disused Dounreay to Vitrified Nuclear Waste Transport pipeline and its associated off-site environments presented a hazard to the surrounding ecosystem and human health. The applicability of piezoelectric dnazymes in environmental monitoring and biosensing technologies was examined, focusing on the evolution of nucleic acid biosensors to detect the nano-scale particles which had entered the environment via the pipeline. This led to the initial examination of ‘probes’ containing chemically modified bases, which had been designed to hybridize selectively with the target DNA from a small sub-set of the particulate trail. An improvement in the selectivity of target detection was noted using those modified probes and work will continue with additional chemically modified probes.

Enzyme-substrates are often critical probes exposing new interactions. A biocidal protein modelling strategy was used to design methyltransferase-split luciferase biosensors for bioassay development and increasing understanding of biocide-lipid interactions. The biobanking strategy provides high-throughput screening of microbial samples for ‘scale-up’ biosensors from micro- to mini-well.

10. Conclusion

Biotechnology is the application of science and technology to create products, process and to improve upon existing products and process for human welfare by manipulating living organisms or their components. It is an interdisciplinary science, which covers many different branches of life science and engineering including microbiology, genetic engineering, molecular biology, biochemistry, bioinformatics, tissue culture, bioprocess engineering, and industrial biotechnology. Advances in recombinant DNA led to the development of new tools for core biotechnology. The results have opened the door for new life sciences approach based upon genomics, proteomics and metabolomics. The rapid pace of advances in genomics and bioinformatics is revolutionizing life sciences research. Methods for single cell analysis are on the verge of providing new fundamental knowledge and new tools for drug discovery and development, diagnostic and therapeutic medicine, toxicology, and food safety. Automated data analysis tools are expected to generate unprecedented understanding of the functional codes of cells, biochemical networks, and their links to health and disease.

Biotechnology is emerging as a booming industry in India and also contributing a lot to the growth of Indian economy. Human resource development has been regarded as a pre-requisite for the success of any industry. Therefore both, the government and industry have given a lot of thrust on creating necessary skilled human resources at different levels, from diplomas engineers to PhD scientists across the country. Growth of biotechnology industry has been attributed to phenomenal growth of R&D and capability building in biotechnology at the Institute level within short span of time. Quality research in biotechnology, front ranking patenting as a result of R&D, has fetched good commercial opportunities in therapeutics, diagnostics and agricultural biotechnological products.

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