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Frontiers in Advanced Biotechnology: Integrating Ai, Nanomedicine, and Genetic Engineering

Alia Jaber Khayoun Zabala
University of Anbar College of Science Department of Biotechnology

Nour Khalid Mohammed Atiyah
University of Babylon College of Sciences Department of Microbiology

Zainab Zahir Naji Hamid, Iman Ibrahim Abdul Hassan
University of Diyala, College of Science Department of Life Sciences

Mohammed Hamoud Nayef Mukhlef
University: University of Fallujah College of Applied Sciences, Department of Biotechnology

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Annotation: The advancing cell visualization and recording techniques are enabling new opportunities to study the relationship between cell types and the emergent dynamics of mesoscale cellular organization. While we are at the beginning of cellular imaging, the advent of new technologies raises the hopeful prospect of long-term and large-scale visualization of cellular activity in this new regime of activity. This talk will introduce how deep learning methods can analyze cellular morphometry to predict cellular dynamics in terms of intracellular calcium rhythms, extend this work to spatiotemporal dynamics of gene expression, and also summarize future directions to unite conventional summary statistics with deep learning and applied learning methods with physics-based modeling to fully translate emerging imaging techniques into understanding of cellular self-organization

and dynamics.

Engineering approaches to modify or control gene expression in mammalian cells are hot topics in synthetic biology. An important sub-topic is to design and implement artificial transcription factors in order to achieve intentionally programmed control on gene activity. Computer-aided design methods allow for a wider range of artificial transcription factor effects than before, including tunable activity, user-defined expression profiles, or complex operation. Next-generation artificial transcription factors with native binding domains or cell-permeable designs have advanced the applicability of artificial transcription factors beyond transient life. Next-generation orthogonal delivery modules including RNA, DNA, and protein carriers have advanced collaboratively on both the engineering aspect and research feasibility. Synthetic gene circuits designed as layered networks can achieve complicated dynamic activities that are consistent with theoretical expectations and thus provide a calibrated platform for testing synthetic biology modules. Integration of genetic and biochemical circuits under the same framework allows for deeper processing of intracellular signals when purely genetic circuits are insufficient. In the meantime, synthesis of mass spectrometry-compatible proteomics circuits, inner-cell-surface-detectable glycoengineering circuits, and output-sensing circuits points to a promising future of synthetic biology with lived design-intent understanding of production by-products.

1. Introduction to Advanced Biotechnology

Rapid developments in advanced biotechnology and its multiple applications have redefined the future of medicine, agriculture, food production, and bio-energy. Advanced biotechnology integrates biomaterials, genetic engineering, tissue engineering, molecular imaging, and nanotechnology for the development of novel healthcare systems for the prevention, diagnosis, and treatment of acute chronic diseases. Similarly, novel bio-informatics tools, sensors, and systems for plant molecular biology, breeding, and bio-fuel generation generate an enormous amount of biotechnological data that need to be addressed and correlated for further investigation and applications for next-generation plant systems. These state-of-the-art facilities allow the exploration of microbes, plants, and animals at multiple levels of biological organization to produce Low-Calorie sweeteners, surfactants, antibiotics, and other drugs, bio-fertilizers, bio-pesticides, herbicides, bio-fuel, animal health feed, and bio-energy which are non-toxic, biodegradable, cost-effective, and eco-friendly. All researchers from around the globe at different stages of their careers are encouraged to submit original, research articles, review articles, and short communications addressing various aspects of biotechnology within these broad frontiers. Genomic, proteomic, metabolic, and biochemical analysis of various biological systems to explore the organisms of interest. Microbial diversity for useful enzymes, metabolites, toxins, and surfactants; Plant diversity for useful genes, mRNAs, miRNAs, natural products, and metabolites; Mammalian diversity for useful genes, proteins, and metabolites; Agri-biotech including bio-fertilizer, bio-pesticide, bio-energy-generating microbes, engineered seeds, and bio-sensors. Nanotechnology, nanobiotechnology, biosensors, nanobiosensors, and other bio-nanotechnological applications. Bioinformatics tools for biotechnology applications and analysis. Synthetic biology applied to engineering biological systems for biotechnology applications. Bio-simulation and high-throughput automation technologies of interest to biotechnologists. Novel cloned genes, receptors, and potential drug molecules of interest to biotechnologists. Biotechnological applications of cellular and genetic therapies. Bioprospecting, diversity, biogeography, and discovery of previously undescribed hosts of interest to bioprospectors. [1][2][3]

2. The Role of Artificial Intelligence in Biotechnology

Artificial Intelligence (AI) is continuously evolving and expanding from the domains of technology and engineering into many fields, including biotechnology. AI is defined as the capability of a system to imitate intelligent human behavior. In recent years, advancements in machine learning have fueled many technological breakthroughs, including everyday devices such as smart speakers and voice recognition software. AI is intended to enable machines to perform tasks that require human-like attributes such as reasoning and problem-solving [4]. This transformation has directly affected applications in biotechnology and medicine, powering personalized health care, regenerative medicine, metric-based diagnostics, and biomedical engineering. The initiation of AI in the health care ecosystem has been on predictions for prognosis, informed and automated diagnoses, and recommendation services for health professionals.

In discovery, development, and deployment, drugs and vaccines have traditionally been selected based on in vitro studies using high throughput functional screening and assay platforms. In vitro and in vivo proof-of-concept studies are crucial early steps in basic research to develop a screening platform for candidate drug molecules, antibody or vaccine candidates, or gene or vector constructs to prevent/control a disease. Integration of these platforms with micro/nanotechnology enabled high throughput analysis of drug/drug candidates in micro or nanoscaled individual rather than macroscale batch analysis. However, the most high throughput screening platforms are of in vitro studies only. For high throughput drug discovery and clinical trials, continuous improvement and optimization tools from machine learning and AI have been

applied to preclinical and clinical to mitigate multiple sabotage mechanisms [5]. The AI-powered continuous optimization platform enables proactive real time integration of adjusted path and project plans into the ongoing process of drug discovery and clinical. This tool empowers scientists and clinicians with a proactive strategy to explore the challenge of models per chips, chips retrieval, drugs storage, sample freeze-thaw and tracking to project priorities, candidate toxicity, genotoxicity and dilemma.

AI dramatically reshapes high throughput screening and analysis of drug molecules, as well as vaccine or antibody candidates. It minimizes efforts and resources in identifying candidate therapeutic agents, greatly speeding up drug discovery. It has applications in pharma screening data from huge libraries with millions of compounds. With a population of big data, AI can also assist existing drugs in drug repurposing and repositioning by maximizing the use of high throughput screening libraries and miniaturized tests in identifying existing small molecules of safety profiles with new undiscovered pharmacological actions aimed at new targets of action. First, AI can be employed to cluster chemical compounds of high similarity to the previously identified drugs to test their effects based on target similarity.

2.1. AI Algorithms in Drug Discovery

Despite the great advancements in AI, ML, and DL, the academic community claims that their application to drug discovery is still in an early stage [5]. There is no doubt that to improve drug efficacy, it is imperative to re-examine existing compounds in new drug targets and new drug combinations. Using AI and ML algorithms in drug discovery reveals the hidden interactions of compound combinations and enables the discovery of potential synergistic drug combinations. Drug combinations can provide better treatment than single drug administration by enhancing the therapeutic effect and reducing the adverse effects. Drug discovery based ML methods can predict drug combinations and complex biological networks. Existing methods can be categorized into three types based on drug data, drug combination data, and drug target data.

With the rapid advancement of deep learning methods, fully integrated models have received increasing attention due to the rapid growth of various drug-related genomic, transcriptomic, and proteomic data on the publicly available databases [6]. A two-step population-level framework that learns drug-gene interaction features is proposed. The drug-gene interactions are represented based on both drug and gene similarity networks instead of using one-hot encoding. A graph neural network model is then designed to recover the drug-drug interaction network and to predict the drug combination. A multi-graph neural network (GNN) model for drug combination synergy prediction based on the multi-source drug and protein networks is developed. A method using continuous representations of compounds to systematically assess drug interaction predictions and combine hits from several proprietary predictions is proposed. One major concern with the AI model prediction for the drug discovery process is the risk of generating a false positive or false negative prediction. Therefore, how to decisively validate AI-drug prediction designed for high-throughput experiment construction for unconventional candidate compounds output selection remains a great challenge in the field. Furthermore, with increased attention and supports from governing and funding agencies, the drug discovery application based on AI can be expected to flourish rapidly.

2.2. Machine Learning for Genomic Analysis

An increasing number of proliferation events in human history, including various forms of biological knowledge, biomolecular resources, and computational infrastructures to support advanced biotechnological research, led to today’s new wave of biotechnology, Advanced Biotechnology. Frontier efforts in this context are described under the new research area of Advanced Biotechnology. Their distinctness is underscored via a brief exposition of essential technology and human factors. Connecting these developments and challenges is an unprecedented potential of an accelerating pace of views to assemble the intricacy of biology into broadly adoptable and broadly accessible quantitative models, computable by existing computers

and interpretable by those trained in other fields. All these developments lead to today's greatest hope of biotechnology, actively contributing to biological research and use in new-life-form bioengineering. The knowledge-intensive and automated approaches, though not peer-reviewed yet, are promising alternatives to many previously painstaking human efforts in biology, such as the 15-year effort of the Human Genome Project.

The data-intensive fields of genomics and machine learning are in an early stage of convergence. Genomics researchers increasingly seek to harness the power of machine learning methods to extract knowledge from their data; conversely, machine learning scientists recognize that genomics offers a wealth of large, complex, and well-annotated datasets for developing biologically relevant algorithms. Researchers inquired to identify common challenges and receive recommendations to better support genomic research efforts using machine learning approaches, including reducing biases in training datasets, prioritizing transparency and interpretability of machine learning methods, and developing privacy-preserving technologies. Genomics and machine learning have a shared history dating back nearly a quarter century, with the first applications of machine learning methods on DNA sequence data reported soon after the Human Genome Project. Since the advent of next-generation DNA-sequencing methods, massive volumes of exome, genome, and transcriptome sequencing data have been generated, often with rich and complex metadata annotations. This rich data landscape provides a natural resource for using machine learning to derive biologically and clinically meaningful insights. Machine learning has consistently been a versatile tool for annotating genomes and extracting knowledge from raw DNA sequence data. Diverse applications of machine learning in genomics include genome sequence assembly, gene identification, annotation of gene function, genomic variant calling, modeling of sequence evolution, and genotype-phenotype predictions. [7][8][9]

2.3. AI-Driven Personalized Medicine

Recent developments in precision oncology are making the personalisation of ATMPs feasible. A critical issue is the readiness of the regulatory approaches to keep up with these developments. Firstly, the class of ATMPs and the need for direct patient-specific evidence are discussed, motivating the need for a shift in regulatory thinking. Secondly, the AI-enabled innovations that are bringing the personalisation of therapy planning and of ATMP design to the patient's bedside are presented. Finally, the bottlenecks in current regulatory processes for these emerging technologies are described along with solutions that could optimise safe approval pathways. The scientific feasibility of patient-specific ATMPs at the convergence of mRNA technology, genetic engineering, 3D bioprinting, and personalised medicine is being extensively explored. There is also increasing recognition that patient-specific integration of rich molecular and clinical data from clinical metabolites, imaging, genomics, transcriptomics, machine learning, and medical literature is critical to the successful development, screening, and application of precision medicines [10].

AI approaches are rapidly evolving into mature systems with the potential to impact many aspects of medicine. The enormous potential of generative models even more so for patient-specific gene-therapy-and-immunotherapy-drug development, as well as for synthesis programming. Furthermore, there is now the potential for development through complementary advancements of multi-modal AI models which integrate multiple data modalities. Generalist medical intelligence has been proposed which, once sufficiently advanced and fed, could flexibly interpret combinations of medical data of any type and nature, including those from electronic health records, imaging, laboratory results, genomics, and medical literature.

3. Nanomedicine: Revolutionizing Treatment Approaches

Nanomedicine, as a topic of research, application, and treatment for diseases, is described as an emerging branch of biotechnology, hence the aim of this article. Nanotechnology opens a vast field of research and application. It can be mainly divided into three segments. The first is pharmaceutical nanotechnology, which will have applications in biological fields including the

pharmaceutical and biomedical fields. Pharmaceutical nanotechnology will include study of bio-molecules and their interactions impacted by nanoscale (sub 100nm) modification, along with drug delivery systems like liposomes, immunoliposomes, nanoparticles, nanoemulsions, self-emulsifying systems, etc. The nanomedicine will be capable to detect lethal diseases, like cancer in very early stages. There will be a possibility to treat genetic diseases by targeting or repairing specific genes, tissue, and cells. Existing treatments like chemotherapy and radiotherapy will be made more specific and efficient so that specific 'bad' cells can be treated or destroyed, sparing the healthy ones. In future, nanomedicine will have both capabilities of detection and treatment [11].

Next, surgical nanotechnology involves using engineered nano-scaled tools, machines, and instruments to perform surgeries with minimal incision and maximum precision. The concept of future surgeons involves robots performing surgeries inside patients with unmatched precision. Collagen targeted-tissue engineering scaffolds will be developed for coronary artery repair. Nanobots will be able to fix mutations in DNA, repair broken neurons, remove blood clots, and address diseases at the cellular or molecular levels. The health status of individuals will be continuously monitored through nano-scaled biosensors implanted in the body. Over the last couple of years, the impact of non-invasive imaging on assessing and improving the potential of nanomedicine has greatly expanded. Some nanomedicine formulations have been designed for diagnostic purposes. Improved fluorescent markers for diagnostic and screening purpose have been one of the first applications of nanomedicine [12].

Nanomedicine radically changes cancer therapy by increasing the number of highly effective therapeutic agents, which is a highly desirable option in the treatment of incurable diseases. It increases the safety window of these agents by increasing their biological half-life and reducing systemic side effect. The positive impact of nanomedicines on the quality of life in life-threatening diseases like cancer is evident in clinical trials. With clinical implications never before anticipated, these technologies provide more efficacious and safe medicines. They can also cause unwanted human toxicity, liberate undesired drug, or provide the need of advanced formulation technologies for stability among other ASTM concerns. Eventually, as nanomedicine is a new area of pharmaceutical study and application, there is very little data concerning possible risks and safety.

3.1. Nanoparticles in Drug Delivery

A promising field in biotechnology and nanomedicine is the use of nanoparticles, as well as nanomaterials in general, for drug delivery. This is a very active field of research that has seen major breakthroughs in recent years, as nanotechnology has matured and become widely adopted by the pharmaceutical industry. Nanoparticles are typically between 1 and 100 nm in size and ensure precise release of drugs in the right locations by passing cellular membranes via endocytosis. There are many elaborate and intelligent ways to "pack" drugs into nanoparticles for transport, including liposomes, dendrimers, polymers, and many others. It is crucial for the nanoparticles to be biocompatible, as they will come into direct contact with tissues and cells. It is also important to consider the size and charge of the nanoparticles, as these will affect their biochemical properties, administration routes, tissue targeting, and excretion routes. Despite the immense potential of nanoparticle drug delivery, there are still several major biological barriers that need to be addressed, and stringent testing of any nanoparticles for safety and toxicity will need to be performed. Overall, nanoparticle delivery of drugs is a major field of research in biotechnology and medicine that has seen rapid progress and offers very promising solutions to current medical issues, although there are still many challenges that need to be addressed.

3.2. Nanotechnology for Cancer Therapy

Nanomedicine is the application of nanotechnology to achieve advances in health care at the molecular level [13]. It defines a new approach, the "nanobot", as a computerized device in the 102-104 nm range, that would be implanted in the body to detect and destroy cancer cells on an individual basis or as prophylactic measures. Nanotechnology is applied in medicine as

"diagnostics" and "therapeutics" [14], that is, as a novel tool that would significantly improve upon existing approaches for early detection, diagnosis, treatment, and imaging of disease, and "nanosurgery", that is, as a nanocomputed needle and robotic-based device that would perform surgery at the nanoscale. Recombinant DNA technology, monoclonal antibody technology, and soft lithography have opened up the biological world on the nanometer scale.

Nanotechnology is used in chemotherapeutic agents that could overcome existing limitations. Nanoparticles coated with organic molecules increase solubility and drug bioavailability. Protein- and polysaccharide-coated silica-coated liposome can target drug delivery to specific organs. Magnetic nanoparticles that concentrate on tumor sites enhance drug delivery efficiency. Liposome-peptide aptamer conjugates target drug delivery with high specificity. Nanocrystal technology to improve radiotherapy by increased LENTERA delivery and decreased normal tissue-associated toxicity is a shape-dependent, metalspecific, and controlled release radiosensitization concept. Interdigitated microscale electrodes are used with gold nanoparticle-coated liposome to achieve true release of the encapsulated agent in a local region of the tissue.

Recent studies show potential avenues where nanotechnology can bring substantial improvements to medical diagnostics and intervention and where need exists for development. The challenge is to rapidly turn this potential into affordable reality. Nanotechnology has the unique potential to bridge biology and medicine at new scales and levels of organization, and thereby to put biology in precisely controlled environments and to observe and influence molecular interaction. In addition, with nanotechnology it could bring a new sensing modality to medical diagnosis. On the other hand, the controlled manipulation of nanosystems is not a small step from current technology. Further research is needed in all areas of characterization, assembly, stability, and interaction at the nanoscale before nanotechnology can reach medicine. [15][16][17]

3.3. Diagnostics Using Nanoscale Devices

Nanobiosensors are analytical devices consisting of biorecognizers and transducers, allowing measurement of analytes. In particular, DNA-based nanosensors, which constitute a class of nanobiosensors based on nucleic acids made of several molecular components, can be used for detection of nucleic acids, proteins, and a variety of biologically-relevant species. They involve various types of configurations, working mechanisms, and materials to enhance analytical performance and for facile use and practical applications. During the last 40 years, new principles, methods and materials have continuously emerged, forming an exciting landscape of DNA nanobiosensing technologies, bringing various applications in the detection and recognition of pathogens, disease biomarkers and drugs from different sample matrices such as blood, sputum, and wastewater [18]. The successful evolution of DNA nanobiosensors is encountered with challenges, which need to be overcome for the next level of evolution. As a highly important type of DNA-based nanobiosensors, nanoGOLD-based labelfree electrochemical detection of miRNAs was realized by employing a g-graphene-based biosensing strategy and a co-NH2 acrylic acid polymer-dispersed gold nanoparticles composite for signal amplification, providing a detection limit of 1 aM. Nevertheless, the development of such platforms is hindered sometimes by the lack of detailed knowledge about specific biochemical interactions, appropriate amplification methods and adequate affinity agents and validated markers. Therefore, stimulator separated electrochemistry-induced fluorescence resonance energy transfer-based bioassay platforms have been successfully proposed, achieving much lower concentration detection limit as low as femto-Mole level. However, to achieve high sensitivity, efficiency and multiplexity for the biomarker identification of a wide variety of diseases, it is necessary to develop novel platform DNA nanobiosensors [19].

4. Genetic Engineering Techniques

Genetic engineering, the manipulation of a genome’s DNA by technologies from molecular biology, is at the frontier of basic and applied science, with unprecedented interest across most areas of biology and biotechnology, and is coming to be regarded as the most important area of

biology in the twenty-first century [20]. A genome's DNA can be modified, usually by either insertion or deletion of specific sequences. This is referred to as targeted modification. Alternatively, longer sequences can be added, acting as extrachromosomal elements and not taking part in the normal genomic functions. By convention, such inserts are referred to as transgenes, and the basic methods for producing transgenic organisms, cells, or tissues are summarized. Microinjection of DNA into a one-cell fertilized egg has been traditionally the first and most direct method for producing transgenic animals, using plasmids or bacterial artificial chromosomes, serrated from DNA obtained from the nuclear or germline genome.

By contrast, homologous recombination has been exploited to add DNA or other modifications, usually larger, to it or to delete it selectively from a normal genome [21]. These methods could take advantage of cell culture techniques to obtain efficient transduction, despite producing a few transgenic individuals. Depending on the vector and the method used to deliver it, either single or double-stranded DNA, or either linear or circular forms, could be tested for efficacy. Genomic integration of random transgenes is problematic, due to their random insertion location, affecting their expression as a consequence of insertion into transcription units or regulatory sequences, and producing aberrant and potentially detrimental transcripts. Hereditary diseases or malformations are routinely modelled in mice by random integration of mutated genes. Any target in any genome can be modified now using a combination of two RNA molecules, one with complementary sequence to the previously known DNA target, the other encoding for a genetically engineered nuclease capable of fixing the break that the first will induce.

4.1. CRISPR-Cas9: A Game Changer

The profoundly significant CRISPR-Cas9 technology has arisen well ahead of the pack, often cited in all types of review and research articles. This technology enables genome editing in a simple and efficient way, allowing scientists to precisely delete or insert nucleotides in a DNA sequence. CRISPR-Cas is a bacterial immune system that can acquire, express, and utilize specific RNA sequences to recognize and degrade foreign nucleic acids. CRISPR-Cas9 is capable of introducing site-directed double-strand breaks in DNA sequences, which are then repaired via either non-homologous end joining or homology-directed repair. This technology raises many ethical issues, like the risks taken by generating enhanced animals or plants or the risk of generating a worldwide ecological impact. Since it is society as a whole who should decide how to use this technology it is up to scientists to educate the people so they can make an informed decision. Scientists have a responsibility to involve the public in their work, because transparency is key to trust. This responsibility is similar to that held by politicians regarding decisions that may impact future generations [22].

The CRISPR-Cas technology has become the most precise genome editing technology. Studies using CRISPR-Cas technology have increased in recent years, revealing its potential in modern medicine. After a brief overview of CRISPR-Cas systems, this technology focuses on the CRISPR-Cas9 system, detailing its components, mechanisms, and applications in genome editing. It is estimated that over 800 publications mentioning CRISPR-Cas technology were published in 2012. In October 2015, this technology was at the core of one of the most popular discussions among scientists and ethicists about a study in which this technique was used in human embryos. The CRISPR-Cas9 technology is the second most cited publication in 2014, 2015, and 2016 and the first for 2017, the present. After the first enzyme directed to be used to create DNA double stranded breaks, other CRISPR-Cas systems have been used, such as the CRISPR-Cas12a and Cas13 systems. It is believed that the future development of this technology can lead to a method for multiplex non-coding RNA delivery. In clinical uses of other genome editing technologies, like ZNF, Talen, or homology recombination have failed, probably due to off-target effects, difficulty in delivery, or the need for donor DNA templates. In contrast, there are many studies showing that engineered Cas9s with a mutation that destroys the endonuclease function retain the ability to bind target DNAs and repress transcription. Many clinical trials are in progress to use ex vivo and in vivo somatic cell editing in patients. It is expected that in the near future editing the

human genome with CRISPR-Cas9 will aid in the treatment of genetic and infectious diseases, as well as cancer. Advances in CRISPR/Cas9 technology and delivery modalities for gene therapy are overcoming barriers to clinical translation. Many studies have shown promising results, but validating the safety of CRISPR-Cas9 for clinical application must address several elements, including ethical implications [23].

Although some challenges remain, CRISPR-Cas technology will become a safe and applicable method used in a variety of therapeutic approaches. The BRCA1 study demonstrates the simplicity and potential of this technology, enabling a fast and cheap procedure to modify a single nucleotide, eliminating hereditary breast and ovarian cancer from patients' cells. Such a safe treatment would help not only the patient but also prevent cancer development in future generations. This study is an example of how this technology could be used in eggs or zygotes to eliminate genetic diseases from gametes or embryos. In this regard, many studies have been performed in several model organisms like zebrafish or monkeys giving rise to viable embryos carrying and transmitting the desired mutation. The uses of CRISPR-Cas system go beyond medical applications. CRISPR-Cas systems are being used to advance modern agriculture and biotechnology, contributing to the development of drought-resistant crops, which would be especially important for regions vulnerable to climate change. For now, the technology is being using to create precise deletions or insert the genes of interest into the genome of many organisms. However, there is still much work to be done for fully functional systems in many organisms. CRISPR-Cas9 allows the targeted delivery of transcribing arrays of long non-coding RNA to orthogonal genomic loci, where they form upregulated nuclear foci. CRISPR-Cas9 provides endless possibilities to improve the world.

4.2. Gene Therapy Approaches

A broad variety of diseases known as genetic disorders are brought on by mutated genes that can either cause loss-of-function phenotypes due to deletions or point mutations or gain-of-function anomalies brought on by molecular hyperactivation such as aberrant expression of pathological gene variants. These diseases afflict about 1 in 200 people worldwide. Among them, over one thousand are dominant neurodegenerative disorders, including Alzheimer’s disease, where the development of intracellular Aβ plaques and tau tangles occurs due to the hyperactivation of genes such as APP, PSEN1, and MAPT. Despite their high prevalence, ailments brought on by undruggable targets have eluded safe treatments so far. It is wonderful that a variety of platforms for CRISPR/Cas9-based genetic therapies have emerged in the lab as gene editing technologies have matured extensively.

Scientists believed that these observations would inspire novel gene therapy approaches with high therapeutic hopes to treat genetic diseases and hence initiated numerous preclinical studies, translations and efficacy tests. However, despite quickly completing numerous preclinical studies in the late 2010s, the development of CRISPR/Cas9 EDG therapies was slowed down due to severe translation challenges to ameliorate all of the aforementioned safety concerns. At the same time, the promising development of AAV vectors in gene therapy with the delivery of traditional transgenes was also hindered due to the emergence of neutralizing anti-AAV antibodies in patients. Of a great concern, a huge immune, oncogenic and manufacturing safety hurdle for virus and virus-like nanoparticle-based human therapies is hard to tackle, while a small but predictable immune side-effect would be a general issue. Though extensively investigated since 1990s, one-crash-treat-once gTOx therapies as ephemeral interventions with a high dose could not overcome severe manufacturing and safety hurdles due to the unanticipated recombinants and off-target gene edits by either viral or non-viral nanoparticles. Therefore, not only new vectors and encoding remedies, but also new delivery and formulations are highly expected to improve the current safety and efficacy profiles.

Gene therapies as ephemeral interventions are able to ameliorate human diseases caused by the monogenic birth of defective genes. Compared with durable genome editing therapies, they suffer

unpredictably and uncontrollably. Gene replacement with a working copy of the deficient transgene is expected, as the mutations of 50% of genes in the human genome are recessive loss-of-function mutations. An ideal way to treat recessive disorders via gDNA replacement is to deliver an intact transgene with its promoter in a copy of 1–5000 that cannot be transformed irreversibly by random insertion into the genome. There is palpably an ideal huge target tissue size to achieve sufficient protein expression to restore the normal physiological level of transgene, however, no immune hurdle for the massive foreign transgenes. Meanwhile, the delivery and transduction of both gDNA and RNA are highly cautioned due to the huge size considerations over packaging capacity. [24][25][26]

4.3. Synthetic Biology Applications

Synthetic biology is an overarching engineering discipline that integrates biology with mathematics, engineering, computer science, and other interdisciplinary sciences to research, develop, and design biological systems for applications in synthetic medicine, biomanufacturing, and bioremediation. Recent rapid developments of high-throughput DNA synthesis and sequencing technologies combined with advances in bioinformatics and modeling are transforming the engineering biological systems from a test of life. To integrate information of biomolecular assembly processes, synthetic biology is acquiring a major focus on constructing genetic toolboxes for functional exploration, assembly rules for genomic design, and advanced modeling for in silico design synthetics.

A rapidly developing field of modern biotechnology is biosynthetic technology, which aims to design a novel biological system to create or optimize valuable biomolecules not created naturally or not produced by a certain strain. To build a new biosynthetic pathway and engineer a producing strain or a host, the most fundamental requirement is to have a genetic toolbox. With the increased development in research, innovation, and policy interest in recent years, biosynthetic technology has developed rapidly, combining engineering, electronics, computer science, and mathematics based on classical genetic engineering and metabolic engineering. Recently, synthetic biology has made essential breakthroughs in the energy, chemical industry, and medicine industry, particularly in programmable genetic control at multiple levels of regulation. Synthetic biology has provided new opportunities for biotechnology as well as challenges [27] [28].

5. Ethical Considerations in Biotechnology

The rapid advancement of biotechnology presents new ethical challenges that have never occurred before. Genetic methods in biotechnology, such as gene editing, reverse transcription, and expression of antigens by transgenic microbes, plants and animals, will have significant and profound consequences on the environment, agriculture, animal husbandry, food, medicine, health, law, society and even other fields. Though a lot of benefits are anticipated like eliminating human genetic disease, curing oncology and infectious diseases, it is unknown how many problems to human beings will arise. As similar issues raised by physical and chemical biotechnology also exist in biological biotechnology, such as enviro-biotechnology and materials based on biomacromolecule, new ethical issues also await to be explored and researched patiently [29]. Research ethics have never received so much attention as in the past few years. As China’s science and technology have achieved important progress, there are also significant ethical challenges in genome editing and artificial intelligence. AI is pervasive in use, from algorithms in an app of mobile phones to big data analysis in top-level decision making by governments of countries. AI also plays a more important role, and could be a powerful tool for positive and beneficial changes [30]. The introduction of disruptive technologies such as AI has multidimensional impacts on an individual and society. However, it is unclear whether AI can develop beneficially with social culture and social governance. It is time to focus on AI safety issues now. Moral and ethical questions arise in the process of development and application of AI; these questions also bring high risks and may bring very unpredictable problems into the community. What are the ethical issues in AI? What are measures to improve the ethics of AI? It

is known that which AI has big data, fast speed, complicated algorithms or great unknown consequences will also have ethical issues. Some ethical issues are macroscopic, medium-sized and microscopic. The unexpected behavior of everything is also a kind of ethics. Many ethical issues in AI are miscellaneous. Therefore, it is necessary to develop reasonable ethical regulations for each emerging technology. It is claimed that the development speed of science and technology (S&T) may be much higher than that of ethics, which may cause many problems.

5.1. Bioethics in Genetic Engineering

Since the discovery of the DNA structure described by Watson and Crick in 1953, the generation of knowledge about the molecular genetic bases began [31]. It was determined that the double helix contained all the genetic information of individuals made up of the four bases, adenine, thymine, guanine, and cytosine. After this event, the human genome was sequenced, discovering that it is made up of 3 billion base pairs, overseeing the production of millions of different proteins. These advances have allowed the development of gene therapy, through which it is sought to interfere in gene expression through corrective manipulation based on sequence cutting and pasting techniques. Advances in genetic engineering have allowed the study and understanding of the complex genomic system of expression. The use of these techniques involves diverse and complex techniques in vivo and in vitro, mainly based on the use of vectors that seek to introduce a specific or modified gene.

Three principles of bioethics were proposed in the Belmont report in 1978: beneficence, autonomy of patients, and justice. Later, Beauchamp and Childres added a fourth one: non-maleficence. These principles constituted the study of ethical issues related to biomedical research. In this concept, non-maleficence highlights the premise of Primum non nocere, translated as “first, do no harm”. The use of a gene scouting procedure for a certain biotechnology process is a very sensitive issue and has turned the spotlight of debate on gene patenting terms. The consequences that may arise from its improper use generate the greatest number of questions and fears. Avoiding the improper use of sequences processed in the following decryption is critical. Effective systems of nucleic acid biosecurity have been defined to counter and restrict these avoidable manipulations. The gene editing technique based on CRISPR Cas and its various uses and applications are described in detail.

The prokaryotic CRISPR-Cas immune system is currently in the sights of biotechnologists for genetic modification applications. The combination of this immunity with the enzymes Cas9 and Cpf1 with a RNA guide complementary to a predetermined sequence generates tremendous interest in the scientific community. This technology allows the execution of a repair to insert, delete, or mutate specific bases on genomic targets, guiding an RNA sequence synthesized through complementary base pairing and capable of forming hairpin structures.

5.2. Regulatory Frameworks for AI in Medicine

The contribution of AI to medicine is unquestionable; however, the industry needs to come to grips with AI technologies’ actual use cases before stakeholders create necessary and effective safeguards. The healthcare and wellness industry strives to reap the benefits of AI, but the AI itself questions gained benefits, as does the healthcare industry in regard to trust. Transparency, accountability, equity, and sustainability must be incorporated across the life cycle of AI/ML-enabled health technologies, from disparate data sources to the amalgamation of datasets into models and the model outputs [32]. These issues of interest set the stage for a broadly-defined regulatory framework. In recent years, multiple healthcare system stakeholders have come together to elevate concerns about the safe and effective use of AI in healthcare settings, all while promoting the uptake of AI as a technology [10]. Several key stakeholders/organizations can be found within this regulatory and governance landscape. These groups, which include industry trade associations, global regulatory authorities, medical associations (including healthcare professional associations), and a patient-centered group, were formed to promote the introduction and development of regulations that would balance the anticipated AI medical device benefits

with stakeholder safety.

Governance issues in healthcare AI technology comprise many of the same issues as in traditional MedTech and software and IT industries, where gregarious thought leadership is widespread and actively pursued. AI concerns are already being entrenched into rapid development Data Governance Acts and Laws, Audit Frameworks, EU AI Acts, the US AI Bill of Rights, Right to be forgotten, and similar AI transparency and accountability laws across the globe. Nevertheless, AI offers unique complexities and has the potential to add new dimensions to MedTech regulation strategies. Again, there is much groundwork in thought leadership that needs to be adopted and reworked for the medical technology industry in combination with exploration of new thinking.

5.3. Public Perception of Nanomedicine

Nanomedicine, a promising branch of nanotechnology, raises public perception issues similar to those in other nanotechnology fields [33]. In the relatively unregulated field of nanotechnology, a gap exists between corporate research funding and multifaceted investigation of implications. The lack of strong regulations and safety assessments promotes rapid technological progress globally but necessitates transparency in ethical implications, human rights, and health concerns. A conference addressed long-term public health and safety implications in nanotechnology research and settings, emphasizing multidisciplinary inquiry to understand sociotechnical dynamics. Despite therapeutic promise, unanswered health and ecological safety concerns hinder human use of nanomedicine. To disseminate nanomedical education, awareness programs incorporating ethical implications and participatory engagement tools are needed. Pre-service healthcare professionals deserve inclusion in development.

Perceptions of nanosciences and nanomedicine among graduate students, physician faculty, and non-physician healthcare professionals in academic health centers revealed low awareness levels. Age, respondent type, science, and clinical experience markedly impacted perceptions of nanomedicine as inherently harmful or beneficial. Importance rating scores were high for nanomedicine anxiety, confidence in nanomedicine, deliberative concerns, harmful use awareness, and overall positive perception, while distrust, price concerns, susceptibility, and harmful health behaviors received lower scores. Education and experience intent ratings indicate a need for targeted statements and outreach efforts on incorporation into practice or daily living. Overall positive sentiment toward nanomedicine technologies exists, balancing confidence and hesitation, and lowering harmful use awareness through engagement directly with vulnerable populations.

6. Integrative Approaches in Biotechnology

In the last few decades, dramatic advances have been made in the understanding of biology at the molecular level and in the manipulation or fabrication of things far smaller than can be seen in an optical microscope. Biotechnology may be defined as the application of Biology to create new products or processes. The great advances that have been made in proteomics, genomics, some aspects of metagenomics and microbiology may all be considered areas of Biotechnology. Nanotechnology, on the other hand, focuses on making things smaller than a micron (the visible limit of an optical microscope). This may include manipulation or fabrication of nanomaterials as well as the applications of these materials to a variety of fields (especially medicine) or using them to probe living systems [34]. It is now possible to carry out on in vivo fluorescent (or bioluminescent) imaging of a zebrafish embryo by dressing it with nanocrystals for hours on end, a feat unthinkable until very recently. Nanotechnology—based generally on new materials or in some cases instruments—enables access to previously unprobed spatial and temporal domains of biological systems. Fundamentally, biology operates on the nanoscale. Biology (or more precisely molecular biology) is the science principally concerned with understanding the function of life (including moisture control, self-repair, pattern formation etc.) based on a microscopic structure (molecules). Molecules—made of atoms (determined by Chemistry)—are the things whose collective action takes life forward. The understanding of protein folding or membrane rearrangement is principally concerned with the chemistry of these biological structures. The mills

of life (e.g. ribosome, proteasome, chaperonin) operate on the nanoscale, as do the discrete unit trusts of biology (plasmid, genes). Yet how biology transmits its functional effects on the nanoscale is apparently disregarded by nanotechnology. To a certain extent this may be forgivable given the modest progress made in interrogating biology at the nanoscale. Following the seminal structural reveal of photosystems in 1980s, the field of structural biology with its emphasis on resolution milestones has sexily unfolded the structures of many biomacromolecules at exquisitely high atomistic detail. There is now a chance to switch the focus to function. This is beginning to be met with technologies, based on nanomaterials in particular, that exploit the physical principles at the nanometer scale and can either probe or intervene to elucidate the chemistry of biology. It is expected new effects will arise from the interplay of nanotechnology with biology. Nanotechnology could be a size-matched tool to interrogate the chemistry of biology; this was hitherto in essence a crucial grand challenge that needed tackling at the molecular or even atomic level. [35][17][36]

6.1. Combining AI and Nanotechnology

The development of autonomous swarm intelligence in nanotechnology cancer drug delivery systems is becoming attracting more attention. The detection and treatment of malignant tumors using smart technologies in a time-efficient and targeted manner have gained importance due to the failure of traditional technologies based on chemical therapy approaches in treating some cancer types. Swarm-intelligent mobile robotic micromachines have been proposed as smart and novel alternatives. In contrast to other approaches, this strategy does not require the addition of foreign materials, and medical nanobots can be created by modifying traditional nanoparticles. Advances in micromotors, nanorobots, and hybrid nanovectors have narrowed the gap between theory and reality in nanomedicine. Nano-micromotor systems driven by electricity, light, and magnetism have been produced to analyze their environmental and electrical properties for monitoring applications at the nanoscale, providing real-time feedback, and discovering targets. In addition, recent developments in soft devices for target monitoring are highlighted to understand the networks behind cancer invasion and metastasis better. In this review, the challenges posed by autonomous swarm intelligence of intelligent cancer nanobots are systematically discussed, and a complete framework is proposed, which includes the minimal swarm intelligence needed regarding environmental adaptation, control architecture design taking advantage of bioinspiration, integrated active and passive utilizing distributed sensing and actuation, and control implementation in a laboratory setting. Additionally, future perspectives integrating AI are depicted, which could lead to breakthroughs in nanotechnology for biomedical applications.

Nanomedicine is an emerging field in healthcare that investigates biological interactions of nano-sized agents designed to diagnose and treat diseases. The global market of nanomedicine was estimated at USD 178 billion in 2018 and is expected to reach USD 353 billion by 20256. In 2017, scientific publications about nanomedicine peaked at 8,153, and the overall annual publication rate for nanomedicine literature showed a consistent upward trend over the past 2 decades. Nanomedicine aims to improve the pharmacodynamics and pharmacokinetics of therapeutic agents in vivo and is expected to impact both therapeutic and diagnostic fields. Nanomedicine outperforms conventional medicine and has potential medical applications. Nanomedicine engineering is, however, extremely challenging owing to various safety and therapeutic challenges.

6.2. Genetic Engineering and Nanomedicine Synergies

There have been tremendous advances in the development of drug delivery systems or carriers, both at the experimental level and the application level, driven by new materials, synthesis methods, characterization tools, animal models, and logistical biosafety studies. The advances have coupled with increasing understanding of biology, biocompatibility, pharmacology, and disease pathology. So far, almost all potential carriers that can be imagined have been synthesized, and many have been tested in therapeutic applications. The burgeoning related fields, such as

synthetic biology and genetic modification, offer infinite possibilities on the creation and reprogramming of biological systems for drug development and delivery. Alternative physical stimuli-based approaches, such as photothermal and sonodynamic therapy-based modalities, can convert any nanomaterial into theranostic nanomedicine. Furthermore, by modifying established scaffold molecules or existing drugs, a range of theranostic molecular drugs with fully distinct modes of action can be generated. Together with the elucidation of basic cellular signaling and redox systems, true tumor microenvironment-mimicking nanomedicines that can capitalize on the inherent pro-survival nature of cancer cells and perturb critical redox balance to trigger an irreversible "overdosing" mode of action will pave the way toward considering nanomedicine for routine use in cancer treatment. Many existing advanced drug carriers are bioinspired and made from biological molecules. With an ever-accelerating development of synthetic biology and genetic engineering, there will be tremendous opportunities to design and generate entirely tailor-made synthetic cellular systems from bacteria to viruses which should be well-controlled on all levels of biosafety, biodegradability, and biodistribution. A complementary synergy-by-design strategy combining both nanotechnology and genetic engineering will harvest the best of these two worlds and could open the ballgame of the next paradigm shift in drug delivery. The next breakthroughs hinge on the interdisciplinary efforts of material chemists, molecular biologists, systems biologists, virologists, pharmacologists, and clinicians focusing on delivering drugs in smart ways with multiscale and synergistic mechanisms. Considerable existing knowledge in synthetic biology, genetic engineering, virology, tumor biochemistry and pathology, can be rationally mined to engineer nanomedicine/cellular devices adaptable to an arbitrary drug type. Cross-validation and collaborative efforts are required to build systems biocompatible and small animal models immune from biases correlated with species evolution trajectory and tumor pathology. Upon successful deployment of the first generation of theranostics, widespread engineering of imaging agents for biomedicine would trigger the biomedical industry revolution. [37][38][39]

6.3. Case Studies of Integrated Solutions

Recent advances in artificial intelligence (AI) and nanomedicine are revolutionizing the way medicine is administered to patients, moving from conventional approaches to individualized treatments. AI offers advanced capabilities for handling vast data while nanomedicine provides powerful tools for delivering individualized treatment regimens. An integrated AI and nanomedicine platform can alleviate the challenges of administering individualized medicine [40]. New ways of treating diseases are required due to the failure of many conventional approaches. From drug discovery to prescriptive treatment regimens, a holistic paradigm shift from treating groups of individuals to treating individuals is needed to maximize treatment efficacy while minimizing side effects. This transformation requires a thorough understanding of disease development and delivery methods tailored to patient needs. With current advancements in AI and nanomedicine, real-time assessment of diseases and intricate personalized treatment design with sophisticated delivery nanovectors could summon a new era of medicine. This section aims to provide three case studies of integrated AI and nanomedicine platforms for novel personalized treatments of three common disorders; hypertension, allergies, and migraine. Essential knowledge of the three diseases that lead to complex treatment paths will be summarized. A comprehensive fibroblast growth factor 23 (FGF23) screening-based integrated AI and smart pharmacokinetics-nanomedicine steering platform for individualized biotherapies will be demonstrated. In addition, a comprehensive pharmacogenomics screening-based integrated AI and hepatic disease-specific organoid-on-chip platform for nanomedicine-prompted tailoring regimens will be unveiled. Finally, a comprehensive omics screening-based AI-driven personalization of dietary intake and nanoparticle-enabled meal protocols for food allergies will be shown. These case studies demonstrate how treating complex diseases necessitates AI's highly efficient exploration of vast data coupled with nanomedicine's secure, precise, and efficient drug delivery and release. As a new discipline, the convergence between nanotechnology and AI holds great promise for future

advancements in healthcare.

7. Future Trends in Advanced Biotechnology

Advances are expected in the following subfields and issues of advanced biotechnology in the near future: Genetic Engineering, Nanomedicine, and Artificial Intelligence (AI). Also, safety and ethical considerations are expected in those fields [41].

7.1 Genetic Engineering

Recent advances in biological engineering have challenged established paradigms in multiple fields. Metabolomics and human microbiome studies have generated a wealth of data; novel tools for in-situ imaging of biomolecules have emerged, and artificial intelligence approaches and big data analytics have begun transforming how biologists think about modelling and simulation. This rapid pace of change raises questions of what is currently unknown, how future developments might unfold and how responsible research and innovation can be brought into play.

The issue is the need for a set of transatlantic concerns, challenges and possible pitfalls arising from recent advances in systems biology and its applications in synthetic biology and bioengineering, as imaging and modelling across spatial and temporal scales are pushing at the boundaries of current computational paradigms.

7.2 Nanomedicine

Nanotechnology is a field that deals with materials at the atomic, molecular, or macromolecular scale (typically, smaller than 100 nm). Nanotechnology in medicine is the utilization of nanoparticles for diagnosis, monitoring, drug delivery, and other methods to treat disease. Nanomedicine is likely to have the highest growth and greatest market potential of the five areas listed here; its expected growth is on the order of 20% per year, for a total market capitalization of $300 billion by 2020. Nanomedicine has the greatest number of potential applications, spanning drug delivery, diagnostics, imaging, monitoring, biomaterials, and implants.

Nanotechnology, in general, is liable to face a number of public acceptance and risk management hurdles in the future. Strong opposition to genetically modified organisms (GMOs) has spread from Europe across the Atlantic, and luminaries in the fields of synthetic biology, nanotechnology, and artificial intelligence—among others—view bio-competition with the same lens one would view an arms race.

7.1. Emerging Technologies and Innovations

Over a century ago, novel ideas regarding the treatment of ailments emerged. Contemporary medicine was taught in quaint lecture halls with anatomy and physiology carved by hands in plaster casts. Soon thereafter, the concept of germ theory became accepted, leading to a greater understanding of why diseases developed. Following this, greater mechanistic elucidation of diseases emerged while treatments were refined, particularly with the renaissance of surgery and antibiotics [40]. These scientific discoveries were revelatory, ground-breaking, and landmark; however, treatments were still limited to the elucidation, explanation, and refinement of a handful of concepts. As science advanced, this mechanistic basis would enable modern medicinal practices that radically altered the lives of patients. Now, some discoveries can be considered revolutionary due to the understanding of the human body as an operating system with components that can be digitized, transformed, and engineered. However, with this transformation, the difference in complexity and reflexivity compared to diseases/objective confounds treatment deployment.

For centuries, conventional medicine was governed by physician expertise, patient trust, and prevailing standards of care; nonetheless, asymmetry in information hampered reasoning surrounding treatment and outcome harmonization. Current medical practices generally focus on treating symptoms and ailments for large groups of people. Unfortunately, following these clinical practice guidelines can elicit differences in treatment response, therapeutic effect, and adverse reaction based on genetic variations within various populations. Moreover, most clinical practice

guidelines are series oriented towards a single condition. However, patients often exhibit multimorbidities. This discrepancy in treatment application can lead to the incentive of developing new consolidated clinical practice guidelines that account for more than a single disease matrix. Recent studies have shown that the synchronous application of independent clinical practices to manage multimorbidities is associated with adverse drug-drug or drug-disease responses, fail to elicit robust and resistant pathways of health, and can magnify symptoms due to overstimulation. Hence, this discrepancy in treatment application may further drive a need to improve conventional practices.

7.2. Predictive Analytics in Biotechnology

Innovative study of genetic variations for diagnosis is better and permitted by the integration of newly accessible technologies. These newly advanced technologies are regularly adopted in concert with deep learning approaches to formulate a unified and systematic integrated targeting mechanism. Here the scope of utilizing advanced AI and ML algorithms, deep neural networks (DNN)-based methods, for both supervised and unsupervised tasks, is dissected. Newly developed metabolomics technologies generate a distinctive metabolic profile or fingerprint for variable times and metabolomics data at different levels. Multi-omics data can assist documenting causality mechanisms ranging from root causes of aberrations at DNA, RNA, and protein down to therapeutically actionable co-modulation of cellular phenotypes, tissues, and organs. By volume, biotechnological perturbations are notorious for compound heterogeneity and divergence that magnify difficulties in identification, selection, and signalize multi-omics detection [42].

The big data streams of translational medicine, especially multi-layered -omics data, are on the rise. However, most biomedical data are heterogeneous, high dimensional, and under-sampled. Meanwhile, sense-level answering to a biomedical why question is a challenge in bridging the modalities of human language and biological data. Target information descriptor passage retrieval from biomedical literature and multi-omics biomolecular data is a key necessity for addressing the challenge. Automatic retrieval of well-grounded target descriptor passages from text is enabled by novel neural architecture called pre-trained transformer (PT). Beyond text, PTs can be leveraged to further advance representation learning modules for specifying target descriptor biomolecular evidence from multi-omics data. Boundless public biobank repositories with well-curated subject input make the BM potential and large-scale. Accurate and automated mechanism-learning methodologies address many demanding issues in understanding causal-chemical mechanisms. This will speed up biomolecular response or feedback mechanism targeting and detection.

7.3. The Role of Big Data in Biotech

In this era of “big data,” unprecedented amounts of multi-omic data from multiple disease domains are generated at an astonishing speed. For a long time, biobanks have been recognized as vital resources for underlying biological factors associated with human health and disease, and this need is anticipated to grow further exponentially. Thus, more so than before, biobanks face hurdles regarding storage, management, quality assurance, accessibility, and reuse of samples and relevant data. These challenges are further intensified due to the complex ethical and privacy implications of data sharing despite this urgency. Most biobanks have been operating in silos and haven’t been connected to date, leading to wasted samples and limited opportunities to answer novel research questions on an unprecedented scale. Multiple international initiatives have been launched to uncover the potential of population biobanks at the local and international levels [43]. Currently, large amounts of clinical data are produced in healthcare, contributing to high demand for advanced analytical solutions. Additionally, driven by new technologies, developments such as wearables and multi-omic tests are gaining ground, leading to innovative approaches in health monitoring, data analysis, and preventive measures. Such data sources require innovative solutions to integrate all data types into a cohesive whole. At the same time, leveraging these data sources requires societal trust in safeguarding sensitive individuals’ data, which can be achieved by improving the process of data utilization.

Ripe for revolution, health data research can benefit from rapid developments in the AI field, as transferability and fairness of AI-powered algorithms require work [44]. Biobanks, with their extensive sample and data collections, provide an ideal setting to advance the capabilities of AI methodologies. However, in order to understand how health data can be effectively leveraged in the current AI development schemes, biobanks also need to keep pace with the technological world, affecting tech adoption, demand forecasts, and service orchestration within the biobank. Moreover, widely publicized data breaches undermine individual and societal confidence in solutions based on extended data use, which needs to be actively counteracted through focused design choices in enacting acquisitions and no-take-back incentives. In this regard, this article discusses up-and-coming storage options for biobanks, elucidating four data management processes for tech adoption, relating them to biobanks and specifying open questions for future research. [45][46]

8. Conclusion

This Special Issue explored how emerging technologies, highlighting AI, genetic engineering, and nanomedicine, individually and in conjunction, impact drug delivery and biomanufacturing. Various topics related to the main theme were presented and discussed: (1) AI-enabled approaches, e.g., in regulatory frameworks for synthetic biology; (2) Soft materials for drug delivery, e.g., engineered bacteria or virus-like nanoparticles in drug delivery deployed in bioimaging and diagnostic techniques; (3) Synthetic biology allows gene editing in pest control, i.e., integrating xeno-nucleotide platforms to enable regulated fate control for gene drives and CRISPR systems. Exploring synergies between research fields, especially in addressing limitations, challenges, and safety, is an integral part of this very new field of biotechnology.

Emerging fields of research and applications, and industries are, by definition, difficult to govern fully. As noted in several contributions to this Special Issue, the intersection between AI and biotechnology creates a lively and shifting governance challenge. The attempts to govern ostensibly well-defined application domains, such as biomanufacturing, explored in this Special Issue run the dual risk of being either insufficient, short-lived, cherry-picking or becoming too universal, restrictive, or rigid .

The intricacies of concurrent and mutually influencing cycles of innovation and governance should be front and center in future research. Here, specific attention to the governance challenge for this intersectional area is in order on method and data. Research on the alignment between academia, government funding, and their favored languages and methods, also referred to as “governance by knowledge regime,” is urgent; similarly, research on oversight by algorithmic academia in funding decisions should be encouraged.

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