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Research Article

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Exploring Biomedical Engineering (BME): Advances within Accelerated Computing and Regenerative Medicine for a Computational and Medical Science Perspective Exploration Analysis

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Abstract

The field of molecular engineering in medicine has made significant strides in recent years, transforming healthcare, diagnostics, and therapy development. However, the COVID-19 pandemic highlighted the ongoing need for further innovative progress and detailed investigation. This research delves into the interdisciplinary domain of biomedical engineering with molecular engineering, examining its impact on the domains of regenerative medicine, biomaterials, tissue engineering, and the acceleration of health science through advanced biotechnologies. The primary objective of this research is to conduct an in-depth exploration of biomaterial applications and their roles in regenerative medicine, along with advancements in tissue engineering, organ-on-a-chip device mechanics, and the transformative potential of bioprinting in creating functional tissues and organs. This research also includes a case study analysis of drug discovery, immune engineering, precision medicine, and gene editing, with insights into the processing, design, and screening pipelines for biologics, as well as the future role of therapeutics and drugs in healthcare. Throughout this exploration, meaningful discussions with conclusions are drawn regarding the advanced technologies investigated, employing systematic technical computing methods at each step of the research process. The rapid advancements in terms of technological computing have brought about significant growth and transformation in various types of domains of biomedical engineering, particularly in the field of medical science and human health. With the progress in artificial intelligence (AI), computer vision, deep learning, image processing, machine learning there has been a revolutionary change in healthcare, addressing a wide range of medical conditions and human anatomy perspectives. The integration of these immersive technologies has not only improved in the realm of medication and disease control but has also provided solutions for complex tasks and issues related to human anatomy threats within the health sector. This research also focuses on the impact of accelerated computing in biomedical engineering, providing insights into the modern utility of toolsets in Bioinformatics and mechanics with artificial intelligence within medical science and also diving into understanding the human anatomy. Additionally, it explores the concept of functional genomics and its potential to provide insights into future disease and health issues, paving the way for advancements in healthcare for the foreseeable future and beyond.

Keywords: Artificial Intelligence (AI), Biomedical Engineering (BME), Bioinformatics, Biomaterials, Biomedical Image Processing, Biomedical Computing Applications and Devices, Biomedical Health Devices, Biomedical Health Informatics, Biomedical Instrumentations Measurement and Applications, Deep Learning, Functional Genomics, Machine Learning, Medical Data Informatics, Medical Science, Molecular Engineering, Regenerative Medicine

1. Introduction

Recent years have witnessed remarkable transformations in medical science, ushering in groundbreaking discoveries that have revolutionized healthcare across various domains. These advancements have not only enhanced disease diagnosis and treatment but have also significantly elevated patient care standards, instilling newfound hope and fostering improved quality of life [1-3]. Among the most promising areas of innovation lies regenerative medicine, a field dedicated to restoring, replacing, or regenerating damaged tissues and organs through cutting-edge approaches such as cell therapy, tissue engineering, and gene therapy. Stem cell therapy, tissue engineering, and gene therapy offer unprecedented potential to revolutionize the treatment landscape for previously incurable conditions. The development of implantable artificial organs represents a monumental stride in medical science, with researchers successfully fabricating artificial organs like hearts, kidneys, and skin grafts using a blend of polymers and biological tissues. These advancements hold immense promise in extending and enhancing the lives of patients awaiting organ transplants. Nanotechnology stands as a pivotal player in medicine, facilitating targeted drug delivery, mitigating side effects, and potentially offering remedies for previously untreatable diseases. Recent breakthroughs include leveraging nanoparticles for more efficacious and less detrimental cancer therapies and devising imaging agents capable of selectively targeting and visualizing diseased cells. The advent of gene editing technologies, notably CRISPR-Cas9, stands poised to revolutionize medicine by enabling precise genetic modifications with implications for curing genetic disorders and combating diseases like Alzheimer's, HIV, and cancer.

However, ethical considerations and safety concerns must be diligently addressed [4]. Artificial intelligence (AI) and machine learning are reshaping healthcare by analyzing vast troves of medical data to enhance diagnosis accuracy, tailor personalized treatments, and monitor patient health [5-7]. Noteworthy applications encompass AI systems adept at diagnosing skin cancer, predicting patient mortality, and identifying early signs of psychosis. CAR T-cell therapy emerges as a groundbreaking innovation in cancer treatment, harnessing genetically modified T cells to target and eradicate cancer cells, showing promising efficacy in treating various lymphoma types and holding potential for broader cancer therapeutics. The advent of mRNA vaccines, exemplified by the transformative COVID-19 vaccines, marks a paradigm shift in vaccine technology, offering rapid development, cost efficiency, and adaptability to emerging viral variants, with far-reaching implications for disease prevention and treatment [7].

Advancements in 3D printing have facilitated the creation of bespoke implants, anatomical models, and prostheses, reducing the necessity for invasive surgeries and elevating patient care standards. Telemedicine has emerged as a prominent force, particularly amid the COVID-19 pandemic, facilitating remote access to medical services, enhancing healthcare accessibility, and potentially curbing costs. Virtual reality (VR) is revolutionizing medical education by providing students with immersive, simulated environments to practice medical procedures, thereby enhancing skills and patient safety. Wearable health monitoring devices like fitness trackers and smartwatches have transformed personal health management, furnishing real-time data on physical activity, heart rate, sleep patterns, and more, empowering individuals to proactively manage their health and enabling healthcare professionals to remotely monitor patients for early disease detection and prevention. These recent strides in medical science hold the promise to reshape healthcare delivery, enhance patient outcomes, and pave the way for novel treatment and prevention modalities [1,3,8].

The context of this research revolves around all the various domains associated within the realm of biomedical engineering. Biomedical engineering, also known as medical engineering, combines principles of engineering and design with medicine and biology to address healthcare challenges. It encompasses a wide range of applications, including diagnostics, therapy, and the management of medical equipment in hospitals. As a relatively new field, biomedical engineering has evolved from an interdisciplinary specialization to become a distinct discipline. Much of the work in this field involves research and development in various subfields. Biomedical engineers contribute to advancements such as biocompatible prostheses, medical devices for diagnosis and treatment, imaging technologies like MRIs and EKG/ECG/EEGs, regenerative tissue growth, and the development of pharmaceutical drugs and therapeutic biologicals [9]. The field of biomedical engineering plays a crucial role in advancing healthcare and improving patient outcomes. Biological engineering, also known as bioengineering, applies the principles of biology and engineering to develop practical and economically viable products [10,11].

This field draws knowledge and expertise from various scientific disciplines, including mass and heat transfer, kinetics, biocatalysts, biomechanics, bioinformatics, and more. It encompasses the design of medical devices, diagnostic equipment, biocompatible materials, renewable energy systems, ecological engineering solutions, agricultural engineering advancements, and catalysis processes. Bioengineering research includes the development of engineered bacteria for chemical production, innovative medical imaging technologies, portable disease diagnostic devices, prosthetics, biopharmaceuticals, and tissue-engineered organs. Bioengineering intersects with biotechnology and biomedical sciences, similar to how other engineering fields relate to various scientific domains. Bioengineers also collaborate with doctors, clinicians, and researchers to mimic or modify biological systems, applying engineering principles to replace, enhance, sustain, or predict chemical and mechanical processes within the biological realm. Biomedical engineering has emerged as a distinct and specialized field within engineering. It has transitioned from being an interdisciplinary specialization to being considered a field in itself. The majority of work in biomedical engineering revolves around research and development across various engineering subfields. Prominent applications of biomedical engineering include all the development of biocompatible prostheses, diagnostic and therapeutic medical devices, imaging technologies like MRI and ECG, regenerative tissue growth, and pharmaceutical drugs and therapeutic biologicals to a certain degree.

Biomedical engineering involves collaboration among technologists, biologists, and medical professionals. Its primary goal is to acquire fundamental knowledge about the physical characteristics and functioning of biological materials. This knowledge is then applied to create devices, perform surgeries, and develop new techniques that enhance people's health and overall quality of life. Notable achievements within the biomedical engineering resulting from this collaboration include dialysis machines for kidney replacement, hip and knee prostheses, materials and technologies for heart and blood vessel surgeries, and artificial hearts. These advancements have significantly contributed to improving healthcare outcomes and have positively impacted the lives of individuals around the world.

2. Methods and Experimental Analysis

For the conduction of this research various methods were applied to formulate the optimum perspective results and data analytics with visual representations which is included regarding the context of this research. The methodology and methods were processed within a step-by-step systematic iterative approach towards the investigation that revolves around the impact of Artificial Intelligence (AI), Accelerated Computing, Biomedical Peripherals, Molecular Engineering and Regenerative Medicine for technical computing functionality within Biomedical Application systems within the landscape of Biomedical Engineering. To start, a very detailed and comprehensive background available knowledge research was conducted towards the gathering of the existing knowledge and along with that, available potential context which are identifiable in terms of research gaps. Next, the required data information and its processable collection were mapped inside the KNIME data analytics platform which was convoluted in terms of data mining, performed using different methods with a wide range of functionality tools, and all the sampled data also underwent preprocessing with post processing to ensure that, the quality remained with optimum relevance associated with the perspective domains. Afterwards, all the performance analytics with visualization representations for those functionality techniques were programmed into design illustration prototyping which were evaluated using suitable metrics and then compared with a variety of traditional and existing technical computing approaches. After that, all the produced results were analyzed, interpreted in the context of the research objectives, with a discussion towards the implications for Biomedical Engineering Applications in line with AI, BME, Medical Data Informatics, Regenerative Medicine which resulted in many future speculations. Finally, all the findings were summarized and all limitations were acknowledged with suggestions for any type of future research prospect in the respective domain were also mentioned. This methodology actually enabled a comprehensive exploration of how the designed prototyping toolsets investigation and computing peripheral features can enhance the Biomedical Engineering perspective and how Regenerative Medicine in terms of Molecular Engineering falls within the digital world, paving the way for a better and improved terminologies with promising outcomes and advancements in the field.

2.1 Background Research and Iterative Exploration of Investigations for Available Knowledge

The field of regenerative medicine holds immense promise within biomedical engineering, focusing on enhancing cell activity to promote tissue regeneration. Often, damaged or injured tissues exhibit limited natural healing potential, impeding crucial processes like cell migration, proliferation, and differentiation. Scientific advancements have been made to augment these natural healing abilities, potentially leading to patient-friendly tissue regeneration methods [12-16]. However, conventional cell culture conditions, primarily reliant on polystyrene dishes, fail to replicate the complex cellular interactions found in native tissues. This discrepancy in cell conditions results in diminished cell activity in vitro compared to in vivo settings, impacting essential functions such as differentiation, proliferation, metabolism, and cytokine secretion. Consequently, discrepancies arise between in vitro drug screening outcomes and preclinical or clinical studies due to variations in cell condition and activity [17-19].

To advance regenerative medicine, it is imperative to enhance cell function and activity both in vitro and in vivo. Biomaterials play a pivotal role in augmenting cell activity for regenerative medicine, facilitating advancements in tissue regeneration potential. Collagen, a natural biomaterial abundantly present in the body and a crucial component of the extracellular matrix (ECM), has been extensively utilized to promote cell activity in various tissues, including bone, cartilage, muscle, and cancer. For instance, collagen scaffolds, coupled with controlled drug release systems, have facilitated bone regeneration, while collagen-fibrin hydrogels have supported osteogenic differentiation of cells. Moreover, anisotropic collagen scaffolds have stimulated muscle bundle assembly and invasive cancer cell migration, showcasing collagen's versatility in tissue engineering and drug research. Gelatin, derived from collagen, presents another valuable biomaterial. Gelatin-based hydrogels offer high biocompatibility and support cell sheet viability, growth, and function. These hydrogels can release growth factors like basic fibroblast growth factor (bFGF), which enhance cardiac contractile function and promote the expression of specific proteins like β-casein in epithelial cells. Gelatin sheets, when combined with ovarian tissues and bFGF, significantly enhance stromal and endothelial cell proliferation. In wound healing applications, gelatin sheets impregnated with platelet-rich plasma accelerate capillary and tissue formation. Furthermore, gelatin-based hydrogel systems with drug release capabilities are employed to mimic cancer cell invasion, enabling the evaluation of cancer cell behavior in response to various stimuli like transforming growth factor-β1. Alginate, a natural polysaccharide derived from seaweed, finds widespread use in cell encapsulation systems for tissue engineering and drug research [20-32]. Alginate-based hydrogels support embryonic stem cell differentiation into primordial germ cells and promote osteogenesis and mineralization when encapsulating mesenchymal stem cells. Injectable alginate-based hydrogels have been developed for cell delivery to damaged tissues, offering advantages such as oxygen permeability and biocompatibility [33,34].

These injectable gels eventually disappear after transplantation, avoiding long-term interference with tissue regeneration. Moreover, alginate-based hydrogels have been utilized to create cancer tissue models that mimic cancer invasion and metastasis, facilitating anti-cancer drug screening. Chitosan, a biopolymer derived from chitin, is renowned for its biocompatibility and versatility, finding applications in various regenerative medicine approaches such as blood vessel regeneration, cartilage formation, bone regeneration, intervertebral disc therapy, and skin tissue engineering [35,36]. Chitosan-based scaffolds and membranes mimic native tissue properties, promoting cell adhesion, proliferation, and expression of tissue-specific markers. Chitosan nanohybrids and composites exhibit enhanced bioactivity and osteoconductivity for bone regeneration. Additionally, chitosan hydrogels support nerve regeneration and serve as drug delivery systems, fostering stem cell and neuron culture and migration. Silk fibroin, derived from silkworms, boasts unique properties for tissue engineering applications. Silk fibroin scaffolds support bone and cartilage regeneration, creating a microenvironment conducive to osteogenic and chondrogenic differentiation. These scaffolds can be optimized by incorporating other materials like gelatin to enhance cell growth and tissue-specific gene expression. Additionally, silk fibroin membranes have been investigated for their effects on acoustic energy transfer and tensile strength in cartilage and tympanic membrane regeneration. Agarose stands as a widely utilized biomaterial in regenerative medicine due to its distinctive properties. Composed of D-galactose and 3.6-anhydro-L-galactopyranose units, agarose can absorb water and facilitate the permeation of oxygen and nutrients to encapsulated living cells. It forms gels through hydrogen bonding and electronic interactions, eliminating the need for harmful crosslinking agents. Importantly, agarose exhibits low immunogenicity [37-39]. Researchers leverage its tunable properties to create gels of varying stiffness for tissue engineering applications.

Combining agarose with polydopamine enhances water content, cell adhesion, collagen deposition, and angiogenesis, making it a valuable tool for regenerative medicine, including nerve and cornea regeneration. Matrigel, derived from a complex protein mixture found in mouse Engel berth-Holm-Swarm tumor, serves as an alternative basement membrane for cell culture when replicating human basement membrane integrity is challenging. Matrigel is particularly valuable in cancer research, aiding in invasion assays, morphology evaluation, and gene expression studies [40,41]. When combined with other biomaterials like alginate, Matrigel maintains high malignancy, spreading, migration, and invasion activities of cancer cells, crucial for studying cancer cell behavior in a biomimetic matrix. Matrigel-assisted tissue engineering holds promise in cancer tissue engineering and anti-cancer drug validation, enhancing the accuracy of in vitro experiments. Poly (lactic acid) (PLA) and poly (lactic-co-glycolic acid) (PLGA) stand out as biomaterials with significant applications in regenerative medicine. PLA, boasting an elastic modulus similar to bone, finds suitability in bone tissue engineering, especially when combined with hydroxyapatite (HA), crucial for ECM remodeling and homeostasis. Porous PLA-HA scaffolds support efficient culture of osteoblast cells, with HA distribution enhancing cell adhesion and wettability. PLGA, known for its biodegradability and biocompatibility, supports nerve cell culture, promoting axonal growth and nerve regeneration, with PLGA conduits showing promise in peripheral nerve regeneration when combined with substances like salidroside [42,43].

Biomaterials play a vital role in various aspects of regenerative medicine, from supporting cell culture to aiding tissue engineering and drug delivery. Natural biomaterials like collagen, gelatin, alginate, chitosan, and silk fibroin offer diverse advantages, including biocompatibility, controlled drug release, and support for tissue-specific differentiation. These biomaterials have been instrumental in advancing regenerative medicine's potential for tissue regeneration and disease treatment, contributing to the development of in vitro models to study disease mechanisms and drug responses accurately. Bioengineering is an interdisciplinary field that applies engineering principles to solve problems in the life sciences. Throughout history, the design and production of medical devices, including prosthetic devices, have been prevalent. Examples of ancient prosthetics, such as wooden digits found in Egyptian tombs, highlight early attempts to replace missing body parts. In the late 1700s, Luigi Galvani's experiments explored the relationship between electricity and animal physiology. This paved the way for using electrical impulses within the body for diagnostic purposes, as seen in the field of electro cardiology. Galvani's student, Alessandro Volta, later invented the first battery in the early 18th century, leading to the application of electricity for therapeutic uses. Additionally, Wilhelm Roentgen's discovery of X-rays in the 19th century revolutionized diagnostic procedures by utilizing electromagnetic radiation. In the 20th century, the world witnessed remarkable discoveries and breakthroughs in bioengineering. Mechanical, electrical, and chemical engineering principles converged to create complex medical systems. These advancements included the development of dialysis, pacemakers, artificial hearts, responsive prosthetic devices, and DNA testing that underlies within various genetic technologies [1,4,8,10,11,44-54,].

As we enter the 21st century, bioengineering remains a dynamic field for technological breakthroughs and exciting new developments that hold the potential to significantly enhance the quality of life. Biological engineering is a discipline rooted in the biological sciences, similar to how other engineering fields are based on specific scientific principles. The term "bioengineering" was coined in 1954 by scientist Heinz Wolff, marking the recognition of this field as a distinct branch of engineering. Initially, bioengineering focused on electrical engineering due to its application in medical devices and machinery. As engineers and life scientists collaborated, they realized the need for a deeper understanding of biology in engineering work. This led engineers interested in biological engineering to devote more time to studying biology, psychology, and medicine to enhance their knowledge in these areas. In recent years, the term biological engineering has also been applied to environmental modifications aimed at soil protection, slope stabilization, watercourse management, and ecological enhancement [2,3,55-63]. Agricultural engineering has also been encompassed within biological engineering due to their shared focus on living organisms. The first biological engineering program in the United States was established at the University of California, San Diego in 1966, followed by similar programs at MIT and Utah State University. Many agricultural engineering departments worldwide have also rebranded themselves as agricultural and biological engineering or agricultural and biosystems engineering. Biological engineering spans a wide range of scales and complexities, applying engineering principles to systems ranging from the molecular level (such as molecular biology and biochemistry) to cellular and tissue-based systems (including devices and sensors) to whole organisms and even entire ecosystems [64].

It encompasses various fields, including microbiology, pharmacology, immunology, neurobiology, and neuroscience, and offers a broad base of knowledge to address diverse biological challenges. Bioinformatics is an interdisciplinary field that focuses on developing methods and software tools to analyze and interpret biological data. It combines computer science, statistics, mathematics, and engineering to unravel the complexities of biological information [65-67]. As an umbrella term, bioinformatics encompasses a broad range of biological studies that utilize computer programming as a crucial part of their methodology. It also refers to specific analysis "pipelines" that are commonly used, particularly in the field of genomics. Bioinformatics plays a vital role in identifying candidate genes and nucleotides, such as single nucleotide polymorphisms (SNPs) [68-70]. The identification of these genetic variations helps in understanding the genetic basis of diseases, unique adaptations, desirable traits in agricultural species, and differences between populations. Beyond its practical applications, bioinformatics also seeks to uncover the underlying organizational principles within nucleic acid and protein sequences [5,6,71-75]. By studying the patterns and structures of these biological molecules, researchers aim to gain insights into their functions and evolutionary relationships. In other words, bioinformatics serves as a powerful tool in biological research, enabling scientists to analyze large-scale biological datasets, identify genetic variations, and explore the organization and function of biological molecules. It contributes to advancing our understanding of various biological phenomena and has significant implications in fields such as medicine, agriculture, and evolutionary biology [76-80].

Biomedical engineering encompasses various subfields that contribute to advancing healthcare and improving human well-being. Biomechanics focuses on studying the mechanical aspects of biological systems at different levels, from whole organisms to cell organelles, using principles of mechanics. Biomaterial's science explores the interaction of materials with living systems and has applications in medicine, biology, tissue engineering, and materials science [81]. Biomedical optics combines physics, engineering, and biology to study the interaction of biological tissue and light for sensing, imaging, and treatment purposes. Tissue engineering aims to create artificial organs and tissues for transplantation, utilizing biological materials and engineering techniques [7,82,83]. Genetic engineering involves the direct manipulation of an organism's genes, finding applications in various fields such as crop improvement and the production of pharmaceuticals. Neural engineering focuses on understanding, repairing, replacing, or enhancing neural systems using engineering approaches [7,83]. Pharmaceutical engineering is an interdisciplinary science that combines drug engineering, drug delivery systems, pharmaceutical technology, chemical engineering operations, and pharmaceutical analysis to improve medicinal treatment. Each of these subfields contributes to the advancement of biomedical engineering and has the potential to significantly impact healthcare and quality of life.

Functional genomics is a field within molecular biology that aims to understand the functions and interactions of genes and proteins. It utilizes the vast amount of data generated by genomic and transcriptomic projects, focusing on dynamic aspects such as gene transcription, translation, regulation of gene expression, and protein-protein interactions. Unlike the static aspects of genomic information, such as DNA sequence, functional genomics takes a genome-wide approach to study these questions using high-throughput methods [5,6,66-70]. The definition of function in functional genomics is often based on the "causal role" of a gene or protein, referring to its sufficiency and necessity for a particular function. The goal of functional genomics is to comprehensively understand the functions of genes and proteins, aiming to eventually encompass all components of a genome. This includes studying the biochemical, cellular, physiological properties, and natural genetic variations of genes and proteins. Functional genomics encompasses various techniques and applications. It involves studying aspects of the genome itself, such as mutations and polymorphisms, as well as measuring molecular activities using techniques like transcriptomics, proteomics, and metabolomics. Multiplex techniques are commonly used to measure the abundance of gene products or analyze the effects of gene variants and mutants. By integrating these measurements, functional genomics seeks to provide a more comprehensive understanding of how the genome specifies function and contributes to systems biology approaches. Functional genomics plays a crucial role in unraveling the complex functions and interactions of genes and proteins, providing insights into biological processes and improving our understanding of various diseases and biological systems.

2.2 Biomedical Applications on Health Informatics and Regenerative Medicine

The field of biomedical engineering has made significant advancements in recent years, leveraging technology, medicine, and resources to address a wide range of health issues. This has fostered an environment that inspires creativity and innovation, enabling biomedical engineers to create solutions that have never been possible before, ultimately improving the lives of billions of people worldwide. One area where biomedical engineering has made tremendous progress is within the development of the healthcare inventions. Biomedical engineers have designed groundbreaking technologies such as prosthetic limbs, artificial hearts, bionic contact lenses, and even the camera pill, which can capture internal processes using a built-in camera, battery, light, and transmitter. These inventions have revolutionized the way we approach healthcare and provide individuals with previously unimaginable solutions to their specific healthcare needs. The impact of biomedical engineering is not limited to inventions alone. Through their research into bodily functions, biomedical engineers contribute to the development of new medicines and drugs to treat diseases, including cancer. They have also played a key role in advancing medical procedures such as laser surgery, offering long-term solutions to health problems that were once considered challenging to address. To give an idea concerning the matter figure 1 provides a visualization of physical and cyber healthcare systems with overview of the healthcare data spectrum.

Collaboration between biomedical engineers and other healthcare professionals, such as doctors, nurses, surgeons, and technicians, has resulted in the creation of essential tools and devices. This includes MRI machines, dialysis machines, diagnostic equipment, and ultrasound devices. These advancements have significantly enhanced the diagnosis, treatment, and monitoring of various medical conditions, improving patient outcomes and overall healthcare delivery. Biomedical engineers also study the intricate biological processes within the human body, aiming to understand why it functions the way it does and how different biological systems operate. This knowledge has led to the development of innovative technologies such as wearable sensors and pacemakers. These devices offer patients comfort while allowing remote and real-time monitoring of their health conditions. By leveraging biological insights, biomedical engineers have made significant strides in providing personalized and efficient healthcare solutions.

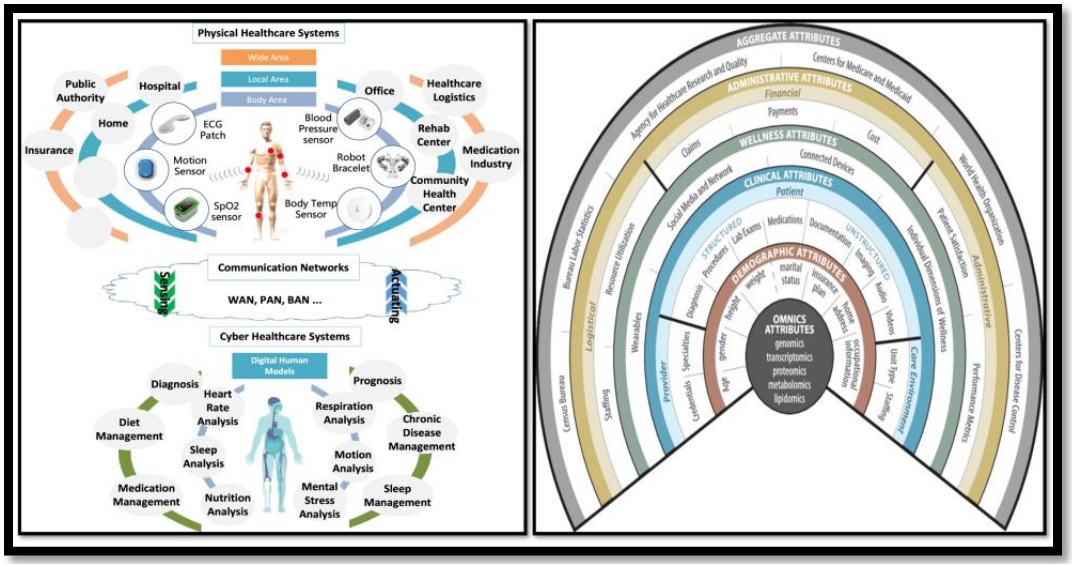

Figure 1: An Overview Visualization of Healthcare Systems and the Healthcare Data Spectrum

Biomedical engineering has transformed and enhanced healthcare services in numerous ways. The field's innovations, ranging from groundbreaking inventions to new medicines, vital tools and devices, and technologies that monitor and support biological processes, have revolutionized the healthcare landscape [9,84,85]. By combining engineering principles with medical knowledge, biomedical engineers have unlocked the potential to improve health outcomes, enhance patient experiences, and ultimately make a positive impact on society as a whole.

The role of biomaterials in regenerative medicine and biomedical applications is paramount, holding the potential to replace damaged tissues and organs and treat chronic diseases. Recent advances in biochemistry, molecular biology, engineering, and material sciences have expanded opportunities for their clinical use. These biomaterials act as scaffolds, resembling the extracellular matrix (ECM), which naturally supports tissues and organs, providing structural support, mimicking the physiological microenvironment, and contributing to various molecular and signaling events that maintain cell morphology and function. The ability of biomaterials to mimic the native ECM is crucial for effectively regenerating damaged tissues. Natural hydrogels, such as chitosan, collagen, and decellularized tissues, offer inherent biodegradability and biocompatibility, making them suitable for tissue engineering. Synthetic hydrogels like polyethylene glycol (PEG) provide advantages such as large-scale production and tunable properties, enhancing their utility in 3D cell culturing and tissue engineering. Tuning hydrogel properties facilitates a better understanding of cell-substrate interactions and the creation of tissue models, ultimately improving tissue regeneration efficiency. However, challenges persist in translating these biomaterials into practical applications. Many synthetic hydrogels are synthesized under harsh chemical conditions, requiring careful removal of unreacted reagents to prevent cross-contamination. Achieving the dynamic and heterogeneous nature of the native cellular microenvironment remains a challenge. Manufacturing and processing techniques are being adapted to synthesize biomaterials with desirable features safely. Photochemical reactions offer spatiotemporal control over hydrogel properties, enabling precise three-dimensional adjustments.

Understanding the molecular pathways between cells and biomaterials is crucial for developing biomaterials that elicit specific cellular responses, enhancing tissue regeneration control. The structural, mechanical, and biochemical properties of synthetic scaffolds still fall short of replicating complex human tissues, and achieving precise regulation of physiological processes within biomaterials remains challenging. Integrating key biomolecules and signals for bioactivation is essential. Monitoring cellular behavior in synthetic microenvironments and tracking introduced signals are integral to developing effective and cost-efficient biomaterials for clinical use. Microfabrication technologies provide a diverse range of sizes, shapes, and architectures to create complex functional engineered tissues and organs. Bridging the gap between scientific knowledge and biomaterial development, along with a deep understanding of their role in tissue regeneration, is crucial. Advances in synthetic technology are paving the way for new generations of multifunctional biomaterials, holding promise for the rapidly growing field of regenerative medicine. Biomaterials stand at the forefront of regenerative medicine, serving as a bridge between scientific innovation and practical clinical applications. Their ability to mimic the native cellular microenvironment and support tissue regeneration is driving advancements that have the potential to transform healthcare and improve patient outcomes.

In the realm of organ and tissue products, numerous companies have made significant advancements with promising outcomes for healthcare medication. Ongoing research and development continue to drive progress in this area, with Table 1 providing an illustration to better understand the matter.

Product	**Tissues/ Organs**	**Description**	**Company**
AlloDerm®	Skin	Acellular dermal matrix for soft-tissue augmentation and replacement	Life Cell Corp.
Apligraf®	Skin	Allogeneic fibroblasts on a bovine collagen I matrix with upper keratinocyte cell layer	Organogenesis
Dermagraf®	Skin	Allogeneic fibroblasts on a vicryl mesh scaffold	Shire Regenerative Medicine, Inc
GraftJacket®	Skin	Acellular dermal matrix for soft-tissue augmentation and chronic wound treatment	Wright Medical Technology Inc.
TransCyte®	Skin	Allogeneic fibroblasts on a nylon mesh with upper silicone layer	Shire Regenerative Medicine, Inc
Oasis® Wound Matrix	Skin	Decellularized porcine small intestinal submucosa	Cook Biotech
Integra® Bilayer Wound Matrix	Skin	Type I bovine collagen with chondroitin-6-sulfate and silicone	Integra Life Sciences
Epicel®	Skin	Autologous keratinocyte cell sheets	Genzyme
Carticel®	Cartilage	Autologous chondrocytes	Genzyme
NeoCart®	Cartilage	Autologous chondrocytes on type I bovine collagen	Histogenics
VeriCart™	Cartilage	Type I bovine collagen	Histogenics
AlloMatrix®	Bone	Demineralized bone matrix combined with calcium sulfate	Weight Medical Technology Inc.
Osteocel® Plus	Bone	Allogeneic bone with mesenchymal stem cells	NuVasive
Pura-Matrix™	Bone	Hydrogel composed of a self-assembling peptide	3DMatrix
Osteoscaf™	Bone	Poly(lactic-co-glycolic acid) and calcium phosphate scaffold	Tissue Regeneration Therapeutics
INFUSE® bone graft	Bone	Recombinant human bone morphogenetic proteins-2 in combination with bovine type I collagen	Medtronics
Lifeline™	Blood vessels	Autologous fibroblast tubular cell sheet integrated with endothelial cells	Cytograft Tissue Engineering
Omniflow®	Blood vessels	Polyester mesh with cross-linked ovine collagen	Binova
Anginera™	Heart	Allogeneic fibroblasts on vicryl mesh	Theregen
CardioValve® SynerGraft Pulmonary Heart Valve	Heart	Decellularized allogeneic pulmonary valve	Cryolife

Table 1: Selection of the Commercially Available Biomaterials for Regenerative Medicine

3. Advancements within the Medical Science and Regenerative Medicine Domains

The field of biomedical engineering is at the forefront of transformative medical technology advancements that have the potential to revolutionize healthcare. With a focus on incorporating innovative tools and techniques, biomedical engineers are driving significant changes in how we receive treatment and improving the overall quality of patient care. One of the most exciting developments in biomedical engineering is the rise of robotics in surgery. Surgical robots offer various advantages, such as increased precision, reduced natural shakes, and the ability to perform minimally invasive procedures. These advancements lead to smaller incisions, faster recovery times, and a lower risk of infection. Biomedical engineers are also exploring the possibility of telesurgeries, where surgeons can control robots remotely to perform surgeries, enabling expert medical care in remote areas. Tissue engineering is another area where biomedical engineering is making remarkable strides. The advent of 3D printing has opened doors for creating functional organs and tissues that can potentially be transplanted into patients. Biomedical engineers are also utilizing 3D printing to develop tissue models for studying diseases, treatment responses, and the physiological impacts of various factors. For example, researchers have successfully printed 3D models of blood vessels, allowed in-depth analysis of healthy and diseased tissues and enhanced our understanding of the cardiovascular system. The integration of artificial intelligence (AI) and virtual reality (VR) into biomedical engineering has paved the way for groundbreaking applications in medicine. AI algorithms can assist in the identification and analysis of medical images, aiding in the diagnosis and treatment of diseases. VR technology is being utilized to create realistic simulations of patient anatomy, enabling doctors to practice complex procedures before performing them on real patients.

Additionally, VR is being used as a training tool for medical professionals, providing immersive experiences and enhancing their skills in communication, empathy, and patient care. The Big Data types are illustrated in figure 2 providing the visualization of data science in terms of medical data. These advances in biomedical engineering are not limited to research labs or academic settings. Many of these technologies are already finding their way into medical facilities, benefiting patients directly. From improved X-ray technology to robotic-assisted surgeries and the training of medical professionals using VR, biomedical engineering is reshaping healthcare and paving the way for longer, healthier lives. Biomedical engineering is driving transformative advancements in medical technology. The incorporation of robotics, tissue engineering, AI, and VR is revolutionizing the way we approach diagnosis, treatment, and training in healthcare. With the potential for minimally invasive procedures, enhanced imaging capabilities, and improved patient outcomes, the impact of biomedical engineering is set to positively impact the lives of individuals across the globe.

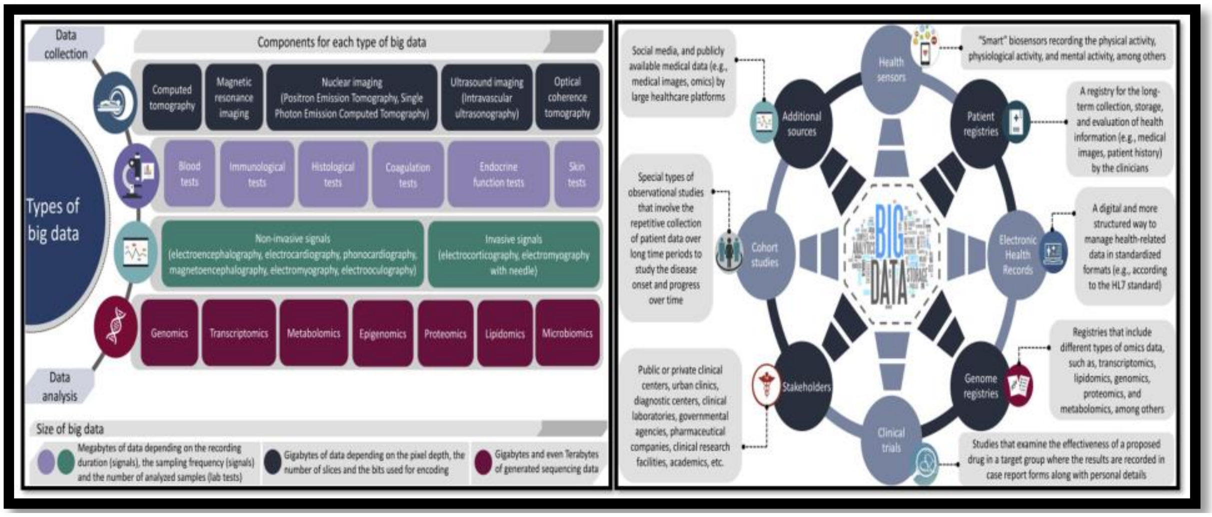

Figure 2: Data Science types in Terms of Medical Data

Regenerative medicine stands as a dynamic field dedicated to repairing and rejuvenating damaged or diseased cells, tissues, and organs, with the overarching goal of restoring proper function to these biological components, often disrupted by injury, illness, or natural aging processes. It encompasses various strategies, including tissue engineering, therapeutic stem cell utilization, and the production of artificial organs. Traditionally emphasizing biomaterials, stem cells, and growth factors, recent developments have expanded the scope to include an immune-centric approach, making it a thriving area of exploration. Traditional regenerative methods, such as autografting, where a patient's own tissues are employed to facilitate healing, have been common but are not without complications, particularly graft rejection. To address these challenges, there's growing interest in harnessing the power of the immune system. Active control of immune responses presents a promising avenue for regenerative therapies. A deeper understanding of the immune mechanisms involved in tissue regeneration could shed light on graft and biomaterial acceptance, offering alternative solutions to traditional autografting. The immune system's response to tissue damage plays a pivotal role in assessing the integrity of the healing process, involving both innate and adaptive immunity. Key players include macrophages, neutrophils, and various molecules triggering inflammatory responses, clearing cellular debris, remodeling the extracellular matrix, and synthesizing cytokines.

Recent research developments reveal significant overlap between innate and adaptive immunity, with danger signals like damage-associated molecular patterns (DAMPs), neutrophils, and macrophages modulating tissue healing. In the realm of immunomodulation in regenerative medicine, two prominent strategies have emerged: biomaterials and scaffolds. Biomaterials, including metals, ceramics, polymers, and composites, carry the risk of rejection due to being foreign to the human body. However, an innovative approach involves delivering biomaterials through immune components acting as immunomodulators, potentially triggering pro- or anti-inflammatory responses. Success depends on the biomaterial's physicochemical properties, including form, crosslinking level, hydrophobicity, and nature. Another promising avenue is using decellularized extracellular matrix (ECM) as a scaffold. This technique involves removing cells from excised tissues, leaving behind a scaffold structure influencing cellular processes and fostering pro-regenerative conditions. Researchers have explored this approach in bioengineering livers using decellularized scaffolds, enhancing therapeutic potential through structural modifications like crosslinking with Nano-graphene oxide, showing promise in improving liver function and offering an alternative to traditional organ transplantation. These advancements in immunomodulation, biomaterials, and scaffolds underscore the exciting potential of regenerative medicine to transform healthcare, offering new solutions for healing and tissue restoration.

3.1 Recent Innovations: BME and Tissue Engineering

Recent trends in biomedical engineering are revolutionizing healthcare and paving the way for advancements in prosthetics, surgical devices, diagnostics, imaging methods, and more. The field is rapidly growing, incorporating innovative technologies and interdisciplinary approaches to improve medical outcomes and enhance patient care. One significant trend is the proliferation of wearable devices and implantable technologies. Wearable health devices and implantable, such as fitness trackers and cardiac monitors, provide real-time data that enable early detection of symptoms, personalized treatment, and remote monitoring. These technologies have the potential to improve diagnosis, reduce healthcare costs, and optimize patient care.

Nanorobotics is another emerging trend in biomedical engineering. By manipulating biological matter at the molecular level, nanorobots hold promise in fighting diseases. These microscopic robots can be programmed to perform functions like searching for pathogens or monitoring vital signs. Recent breakthroughs in nanotechnology have shown potential in shrinking tumors and offering less harmful alternatives to treatments like chemotherapy. Brain-computer interfaces (BCIs) are devices that allow signals from the brain to direct external activity, offering hope to individuals with motor disabilities. BCIs measure brain electrical activity and enable users to control external devices like prosthetic limbs. While ethical questions surrounding BCIs exist, ongoing research is improving accuracy and expanding their applications. BCIs have the potential to augment human cognition and perception, blurring the line between humans and technology. 3D bioprinting is an emerging technology that combines cells, growth factors, and biomaterials to create tissue-like structures. Scientists have already achieved significant milestones, such as 3D-printing a human-sized heart using human cells. The potential of 3D bioprinting extends to printing artificial skin cells for burn victims and eventually creating replacement organs. This technology has the potential to revolutionize organ transplantation and improve treatment options for various medical conditions. Biomedical engineering is at the forefront of healthcare advancements, integrating technology, biology, and engineering to improve medical outcomes and enhance patient well-being. Wearable devices, nanorobotics, brain-computer interfaces, and 3D bioprinting represent some of the exciting recent trends that are transforming the medical landscape and offering new possibilities for the future of healthcare.

Tissue engineering and regenerative medicine represent cutting-edge fields in medical research, focused on overcoming the challenges associated with repairing or replacing damaged or diseased tissues and organs. Tissue engineering, an evolution of biomaterials development, intricately combines scaffolds, cells, and biologically active molecules to create functional tissues with the goal of restoring, maintaining, or enhancing compromised tissues or entire organs. Noteworthy examples include FDA-approved engineered tissues like artificial skin and cartilage, though their widespread clinical use is currently limited. Regenerative medicine extends beyond tissue engineering, encompassing research on self-healing processes, where the body leverages its mechanisms, often with the assistance of foreign biological materials, to regenerate cells and reconstruct tissues and organs. The terminology of "tissue engineering" and "regenerative medicine" is increasingly interchangeable, reflecting the field's aspiration to move from treating complex diseases to curing them. These fields find applications not only in medical therapeutics but also in non-therapeutic areas, such as biosensors for detecting biological or chemical threats and tissue chips for assessing experimental drug toxicity. The central concept revolves around manipulating cell behavior, their interactions with the environment, and their ability to form tissues and organs. The tissue engineering process typically begins with the creation of scaffolds from various materials, serving as the foundation for tissue development and facilitating the exchange of signaling molecules.

Cells, sometimes guided by growth factors, are introduced into this environment, leading to tissue formation. Advanced approaches involve the simultaneous mixing of cells, scaffolds, and growth factors, allowing tissues to self-assemble. Utilizing pre-existing scaffolds derived from donor organs, with cells removed, serves as another method, providing a template for growing new tissue. For instance, bioengineered liver tissue grown on decellularized scaffolds shows promise in drug testing, offering an alternative to animal models. Despite progress, tissue engineering and regenerative medicine still play a relatively minor role in clinical practice. While procedures like supplemental bladder implantation, skin grafts, and cartilage replacements have been performed, fully reproducible transplantation of more complex organs, such as the heart, lung, and liver, remains a challenge. However, these engineered tissues serve as crucial research tools, especially in drug development, accelerating the screening of potential medications and advancing personalized medicine while reducing costs and animal testing.

Ongoing research, fueled by organizations like the National Institute of Biomedical Imaging and Bioengineering (NIBIB), is driving innovation in tissue engineering and regenerative medicine. Breakthroughs include engineering mature bone stem cells for successful transplantation and creating lattices to help engineered tissues develop essential vascular networks. Novel solutions, like a biological gel and adhesive combination, show promise in regenerating cartilage tissue, offering hope for joint-related issues. Efforts in kidney regeneration from a patient's own cells represent promising steps toward addressing kidney disease and donor organ shortages. These advancements reflect a commitment to pushing the boundaries in tissue engineering and regenerative medicine. In various medical disciplines like orthopedics, cardiology, neurology, and dermatology, tissue engineering has offered solutions for repairing bone defects, addressing non-healing fractures, and potentially restoring function in spinal cord injuries and peripheral nerve damage. Breakthroughs in vascularized constructs have the potential to revolutionize patient care across specialties.

A critical frontier lies in organ transplantation, with tissue-engineered organs emerging as potential solutions to the persistent shortage of donor organs. While challenges like achieving full functionality and long-term viability persist, progress in bioengineered organs envisions a future where organ transplantation is not constrained by donor availability. However, tissue engineering faces challenges, such as creating adequate vascularization within large tissue constructs and addressing immunological responses for effective host integration. Ongoing research explores strategies, including angiogenic factors, advanced bioprinting, and immunomodulatory biomaterials, to enhance tissue engineering's potential. Tissue engineering holds immense promise and ongoing research endeavors offer a promising avenue for addressing critical medical challenges, enhancing patient outcomes, and revolutionizing healthcare across various disciplines.

3.2 Emerging Advances in BME and Organs-On-A-Chip

Biomedical engineering has led to numerous inventions and innovations that have significantly impacted the field of healthcare. Prosthetics, including artificial limbs and dentures, have greatly improved the quality of life for individuals with missing or impaired body parts. Bionic contact lenses have enabled enhanced vision capabilities, while bionic exoskeletons have provided mobility assistance for individuals with disabilities. Robotic and laser instruments have revolutionized surgical procedures, making them more precise and less invasive. Implantable medical and drug delivery devices have facilitated targeted treatments and improved patient outcomes. Medical imaging technologies like X-ray and MRI machines have allowed for accurate diagnoses and monitoring of conditions. Radiation therapy has become a powerful tool in cancer treatment, while transcutaneous electrical nerve stimulation (TENS) devices have provided pain relief for various conditions. Nanomaterials have opened up new possibilities in drug delivery and tissue engineering, and bioprinting has allowed for the creation of functional human tissue and organs. The advent of genome editing technologies has paved the way for precise modifications in genetic material, enabling potential treatments for genetic diseases. In addition to these specific inventions, there are several trends in biomedical engineering that are shaping the future of healthcare. Tissue engineering and bioprinting offer the potential for creating artificial tissues and organs, at the same time revolutionizing transplantation procedures. Organs-on-chips, microbubbles, and transdermal patches are emerging technologies that show promise in diagnostics and drug delivery. Wearable medical devices, such as fitness trackers and health monitors, provide real-time data for better disease management and preventive care. Surgical robotics and nanorobots are advancing surgical precision and capabilities. Medical virtual reality is being used for training, therapy, and surgical planning. Artificial intelligence is being integrated into medical imaging to improve diagnostic accuracy. Personalized medicine, which mainly tailor's treatments to an individual's genetic profile and lifestyle, is becoming more feasible with advancements in biomedical engineering.

The Internet of Medical Things (IoMT) is playing an increasingly important role in biomedical engineering. It encompasses the interconnectedness of medical devices and applications, allowing for real-time monitoring, diagnostics, and data analysis. IoMT enables personalized and remote healthcare delivery, enhancing patient outcomes and convenience. From wearable devices to imaging machines and smart beds, IoMT is transforming the healthcare landscape and improving the overall patient experience. Not only that, biomedical engineering has also led to a wide range of inventions and innovations that have transformed healthcare. From prosthetics to imaging technologies, these advancements have improved patient care, enabled new treatment modalities, and enhanced quality of life. Emerging trends such as tissue engineering, bioprinting, wearable devices, surgical robotics, and IoMT are driving further advancements in the field, promising a future of personalized and technologically advanced healthcare.

Organ-on-a-chip (OOC) technology is a pioneering approach in biomedical engineering, particularly within the realm of bio-MEMS (Micro-Electro-Mechanical Systems). These innovative devices are multi-channel 3-D microfluidic cell cultures integrated into a single chip, meticulously designed to emulate the activities, mechanics, and physiological responses of entire organs or organ systems. OOCs have emerged as potent tools bridging the gap between traditional cell culture and in vivo studies, offering a more sophisticated in vitro approximation of complex tissues. This advancement holds significant promise for drug development and toxin testing, potentially reducing reliance on animal models.

While numerous publications report successful replication of organ functions on OOCs, it's crucial to recognize that this technology is still in its infancy. Researchers employ various designs and approaches to simulate organs ranging from the brain and lung to the heart, kidney, liver, and more. However, early OOCs may oversimplify the intricate network of physiological processes within the human body, potentially overlooking significant biological phenomena.

To address these limitations, ongoing efforts in microphysiometry aim to accurately model more sophisticated physiological responses through microfabrication, microelectronics, microfluidics. One significant achievement facilitated by organ chips is the study of the intricate pathophysiology of human viral infections. For instance, liver chips have enabled groundbreaking research into viral hepatitis, allowing researchers to delve into the effects of viruses on specific organs in a controlled and accurate manner. In parallel, lab-on-a-chip (LOC) devices have also made substantial progress in the last decade. These devices integrate various laboratory functions onto a single chip, primarily focusing on the handling of particles within the microfluidic channels. This miniaturization of laboratory functions offers several advantages, including reduced reagent consumption, increased portability, better process control, and lower fabrication costs. The laminar flow properties of microfluidics have been harnessed for various cellular biology applications, such as studying cell motility, stem cell differentiation, biochemical signaling, and embryonic development. Transitioning from traditional 2D cell cultures to OOCs has been a significant step forward in cellular biology. While 3D cell culture models already improve cell differentiation and tissue organization compared to 2D cultures, they still fall short in mimicking many aspects of an organ's cellular properties. OOCs address these limitations by efficiently transporting nutrients and other soluble cues throughout 3D tissue constructs, replicating tissue-to-tissue interfaces, spatiotemporal gradients of chemicals, and notably the mechanically active microenvironments. In essence, organs-on-chips represent the next wave of 3D cell culture models, offering a more accurate portrayal of the biological activities, dynamic mechanical properties, and biochemical functionalities of living organs. This breakthrough technology holds immense potential for advancing our understanding of human physiology and disease, drug development, and toxicity testing. Organ-on-a-chip (OOC) technology is revolutionizing our approach to studying various organs and their functions, offering a sophisticated bridge between traditional cell culture and in vivo research.

Noteworthy developments include brain-on-a-chip, gut-on-a-chip, lung-on-a-chip, heart-on-a-chip, kidney-on-a-chip, liver-on-a-chip, prostate-on-a-chip, blood vessel-on-a-chip, skin-on-a-chip, and endometrium-on-a-chip platforms, each providing unique insights into organ physiology, disease modeling, and drug testing. Human-on-a-chip technology is a remarkable advancement in biomedical research, aiming to replicate the complexity of multiple organs working together in a controlled, in vitro environment. These microfluidic platforms offer a more accurate representation of human physiology compared to traditional laboratory techniques, holding immense potential for improving drug development, toxicology studies, and disease modeling while reducing reliance on animal testing.

3.3 AI, Deep Learning, Machine Learning Advancements within BME and Bioprinting

Machine learning has become an essential tool in biomedical research due to its ability to address complex datasets and provide valuable insights. One common use of machine learning is for making predictions based on measurable data [84]. For example, in psychiatric medicine, machine learning has been used to predict mood based on smartphone recordings of everyday behaviors [85]. In neuroscience, machine learning techniques have been employed to decode neural activity and infer intentions from brain measurements, enabling advancements in prosthetics and interactive devices [9]. Machine learning also serves as a benchmark for evaluating human-generated models, helping to identify missing principles or misguided approaches. Additionally, machine learning aids in understanding complex systems by determining nonlinear relationships between variables and identifying shared information between components of a system. As datasets in biomedical research continue to grow in complexity, machine learning becomes indispensable. Humans are limited in their ability to comprehend and model complex datasets, often missing important patterns and structures. Machine learning techniques excel in capturing complex relationships and can handle large, multifaceted datasets. Moreover, machine learning addresses challenges posed by nonlinearity and recurrence, which are prevalent in biological systems. By embracing the complexity inherent in biomedical data, machine learning provides better fits and more accurate predictions compared to simpler models. Machine learning also supports the collection of a large number of variables, as it can improve predictions even when the contributions of individual variables are unclear.

The application of machine learning in neuroscience serves as a compelling example of its capabilities. In neural decoding, machine learning techniques have outperformed traditional linear approaches in predicting intentions based on brain activity. Neural network-based methods, along with ensemble methods that combine multiple techniques, have achieved remarkable results. Machine learning also challenges the common practice of using simple models in neural encoding, where signals from neurons are analyzed in relation to external variables. Machine learning algorithms, such as neural networks and extreme gradient-boosted trees, have surpassed generalized linear models in capturing the complex relationships between neural activity and external variables. By setting benchmarks and providing more accurate descriptions of neural computations, machine learning enhances our understanding of the human brain. While machine learning techniques may seem complex, their implementation has become increasingly accessible. With the availability of user-friendly software packages and automated machine learning tools, biomedical scientists can easily apply machine learning to their research without extensive knowledge of specific algorithms. This empowers researchers to focus on formulating scientific questions and interpreting the results generated by machine learning models.

Machine learning has become a necessity in biomedical research due to its ability to address complex datasets, make accurate predictions, benchmark human-generated models, and enhance understanding. From predicting mood based on smartphone data to decoding neural activity and modeling complex biological systems, machine learning offers valuable insights and advancements in various biomedical disciplines. As datasets continue to grow, machine learning's capacity to handle complexity and capture nonlinear relationships will be crucial in furthering our understanding of biological processes and improving healthcare outcomes. The field of 3D printing, also known as additive manufacturing, has become increasingly prominent across various industries, with healthcare being a notable area of growth. Within healthcare, 3D bioprinting, which incorporates living cells into the printing process, is emerging as a significant advancement. Projections indicate that the global 3D bioprinting market will exceed $4.7 billion by 2025. One of the primary goals of 3D bioprinting is to address the shortage of organs by enabling the fabrication of complex tissues and organs. While fully functional human organs are still in experimental stages, simpler tissues like skin and cardiac patches have already been successfully bio-printed. These bio-printed tissues find applications in drug testing, toxicity assessment, tissue engineering, and more. The advantages of 3D bioprinting include the creation of anatomically accurate structures, porous designs, incorporation of multiple cell types, and precise delivery of growth factors and genes. However, a significant challenge remains in achieving vascularization within bio printed tissues, which is essential for larger, complex organs' survival. In the realm of bioprinting ink, Boston-based company Cell ink has taken a unique approach by developing standardized bioinks composed of various materials infused with human cells.

These bioinks, compatible with most 3D bioprinters, are designed for specific tissue types and hold potential for future applications in human tissue replacement. Notably, laser direct-write (LDW) printing has shown promise for achieving single-cell spatial resolution, with researchers at Tulane University pioneering this technology to deposit various cell types with exceptional precision. LDW printing has been utilized to create complex tissues like collagen fibers, muscle fibers, and neural circuits, offering opportunities to investigate disease mechanisms, tissue functionality, and cancer cell behavior. Moreover, 3D bioprinting extends beyond tissue creation to designing cost-effective lab tools. Researchers at the University of Southern California utilize 3D bioprinting to build modular microfluidic systems, simplifying fluid mixing for diagnostic tests and microbioreactor processes. These systems facilitate precise fluid mixing and can generate uniform microdroplets for various applications, incorporating off-the-shelf components to drive down costs and enhance device functionality. Looking ahead, the field of 3D bioprinting is expanding into 4D, where printed structures can dynamically respond to their environment. Companies like GE Healthcare are interested in technologies that improve and streamline the bioprinting process, utilizing high-power microscopes and digital modeling tools to control printing more effectively.

Noteworthy applications include Organovo's use of 3D bioprinting to create therapeutic liver tissues, termed Novo Tissues, for treating rare liver diseases. Despite challenges, the potential for bio-printed tissues to address unmet medical needs is evident. In terms of materials, a recent study introduced a novel additive manufacturing system combining 3D printing with plasma treatment. This system enables the creation of complex scaffolds with varying properties, offering greater control over scaffold characteristics for tissue engineering applications. Bioprinting is revolutionizing healthcare by pushing the boundaries of tissue engineering, drug testing, and medical device fabrication. As research continues, the potential to create functional human organs and personalized medical treatments using 3D bioprinting becomes increasingly feasible, promising a brighter future for healthcare innovation and patient care.

3.4 Functional Genomics, Drug Delivery Systems and Immune Engineering: Case Studies Analysis

Machine learning has revolutionized the field of biology and bioinformatics, enabling researchers to analyze complex biological data, make predictions, and gain deeper insights into various biological processes. In genomics, machine learning techniques have been applied to regulatory genomics, structural genomics, and functional genomics. They have helped predict gene expression, classify protein structures, and identify gene functions and interactions. Machine learning methods combined with natural language processing have also facilitated the analysis of large genomics-related datasets, aiding in relation extraction and named entity recognition. One of the significant applications of machine learning in genomics is genome sequencing. Next-generation sequencing techniques, empowered by machine learning algorithms, have drastically reduced the time and cost required to sequence genomes.

Machine learning has also played a crucial role in gene editing processes, such as CRISPR, by assisting in the selection of the correct DNA sequence for editing. In proteomics, machine learning has contributed to the analysis of protein components, their interactions, and their roles within organisms. Mass spectrometry-enabled proteomics has been enhanced by machine learning algorithms, which help identify proteins from mass spectral peaks and improve the accuracy of protein recognition. These advancements have facilitated the diagnosis of diseases and expanded our understanding of protein patterns. Microarrays, used to detect gene expressions, have benefited from machine learning techniques, particularly in gene classification and clustering. Machine learning has made it easier to identify significant interactions in complex experiments and analyze large-scale microarray datasets. It has also enabled the prediction of future gene stages and the discovery of relationships between genes and diseases. Text mining, powered by machine learning and natural language processing, has been valuable in extracting and analyzing information from biological publications. This technology enables researchers to process and analyze large volumes of documents, aiding in large-scale protein and molecule interaction analysis, translation of content into different languages, searching for drug targets, and automatic annotation of gene and protein functions. In systems biology, machine learning has become instrumental in modeling complex biological interactions and behaviors. It helps capture the interactions between biological components and simulate the behavior of biological systems. Machine learning techniques, such as probabilistic graphical models and genetic algorithms, have been used to model genetic networks and regulatory structures. They have also facilitated the identification of relationships between phenotypes and genotypes, shedding light on the critical genetic composition of organisms. Machine learning has transformed the field of biology and bioinformatics by providing powerful tools to analyze and interpret complex biological data, make accurate predictions, and enhance our understanding of biological processes. It has accelerated research in genomics, proteomics, microarrays, text mining, and systems biology, opening up a whole new avenue for discoveries and advancements in the field of biology.

The case study analysis delves into the complexities and opportunities surrounding the oral delivery of immunotherapeutic, focusing on the pivotal role of biomaterials and drug delivery systems (DDS). While oral administration offers convenience and non-invasiveness, it encounters hurdles like enzymatic degradation, pH fluctuations in the gastrointestinal tract, and mucosal barriers, particularly daunting when handling delicate immunotherapeutic agents like antibodies, mRNA, and DNA. The human intestine, rich in immune cells, emerges as a promising site for immune modulation via oral delivery. Notably, oral administration can induce tolerance to intravenously delivered therapeutics, mitigating the production of antidrug antibodies and preserving efficacy. Immunotherapeutic agents like interleukins, growth factors, and small molecules, such as rapamycin, hold significant potential for oral delivery, facilitated by DDS tailored to target specific gut sites for immune modulation.

Despite DDS promise, overcoming natural GI barriers is imperative for successful oral immune engineering. Biomaterials, especially those with mucoadhesive properties, prove instrumental in enhancing drug residence time within the gastrointestinal tract. Mucoadhesion involves forming chemical bonds, like hydrogen or ionic bonds, with mucosa. Thiolated polymers, for instance, bolster mucoadhesion through strong covalent disulfide bonds with the mucosal layer, facilitating local delivery for diseases necessitating precise immune modulation, like ulcerative colitis and inflammatory bowel diseases. Nanoparticle systems armed with specialized mucolytic agents offer promise by breaking down mucus substructures, enabling drug carriers to penetrate the mucosal layer. Combining targeting mechanisms, such as self-nanoemulsifying drug delivery systems (SNEDDS) with mucoadhesives, enhances drug solubility and adhesion, bolstering bioavailability for delivering anti-inflammatory cytokines, growth factors, and other immunotherapeutic to specific gut sites for targeted immune modulation.

Overcoming the epithelial barrier requires leveraging mechanisms like passive diffusion, carrier-mediated diffusion, active transport, or transcytosis to access systemic circulation. Strategies include employing transient permeabilizing agents, prodrugs, and cell-penetrating peptides (CPPs) to enhance drug transport. Active transport systems, such as molecular motors, facilitate uniform vaccine distribution in the gut, augmenting immune responses against mucosa-related infections.

Current strategies for oral-to-systemic immunotherapeutic delivery spotlight biomaterial developments to heighten drug bioavailability. Both natural and synthetic biomaterials, like chitosan-based nanoparticles and innovative devices like the MucoJet, aim to enhance immunotherapeutic absorption through the gastrointestinal tract, marking significant strides in making oral drug delivery a viable option for immunotherapeutics. Nonetheless, challenges pertaining to safety, cost, and clinical translation persist, underscoring the pivotal role of biomaterials and drug delivery systems in revolutionizing immune-related disease treatment through targeted and efficient drug administration.

3.5 Functional Genomics and the Advances for Precision Medicine with Gene Editing

Machine learning and artificial intelligence (AI) have made significant contributions to the healthcare industry, enhancing patient care and improving quality of life. These technologies are being used in various applications to transform healthcare delivery. One important area is drug discovery and manufacturing, where machine learning is used in the early stages to assist in finding alternative options for multifactorial disease therapy. Precision medicine and next-generation sequencing techniques have proven valuable in this process. Medical imaging and diagnosis have also benefited greatly from machine learning and AI. Computer vision technologies, powered by deep learning and machine learning algorithms, enable advanced analysis of medical images. This technology is used in applications such as tumor detection, radiology interpretation, and quantitative analysis of 3D medical images. Projects like Microsoft's Inner Eye are utilizing machine learning to improve medical image analysis and diagnosis. Personalized medicine is another promising application of machine learning in healthcare. By leveraging predictive analytics on patient data, machine learning algorithms can assist in generating personalized treatment options. This approach goes beyond traditional diagnostic methods and takes into account individual patient characteristics, health history, and genetic information. Machine learning algorithms can analyze large datasets and identify patterns that can guide personalized treatment decisions. Machine learning is also being used in stroke diagnosis and treatment. Pattern recognition algorithms help in diagnosing, treating, and predicting complications in neurological diseases, including stroke.

Algorithms such as Support Vector Machines (SVM) and 3D Conventional Neural Network (CNN) are used to predict motor deficits in stroke patients, aiding in personalized rehabilitation planning. In the field of biology and bioinformatics, machine learning tools have revolutionized data analysis and modeling. Deep Variant is a deep-learning tool used for genome data mining. It accurately predicts common genetic variations and provides scalable, cloud-based solutions for complex genomics datasets. Atom wise algorithms enable the study of the 3D structure of proteins and other molecules with atomic precision, facilitating drug discovery. Cell Profiler, a software powered by machine learning methods, allows for the quantitative measurement of individual cell features from microscopy images, enabling a very high-throughput analysis of biological samples. Machine learning, particularly through deep learning algorithms, extracts meaningful information from large datasets such as genomes or images, and builds models based on the extracted features. These models can then be used for analysis and prediction on other biological datasets. The application of machine learning in biology and bioinformatics has accelerated research, enabling the discovery of new patterns and relationships in complex biological systems. Machine learning is transforming healthcare and biology by enabling more accurate diagnosis, personalized treatment, and advanced data analysis. These technologies have the potential to revolutionize the field, leading to better patient outcomes and advancements in biological research.

Precision medicine is rapidly advancing, promising personalized treatments for patients, but several challenges hinder its widespread adoption. This investigation offers insights into solutions to these challenges and the diverse methods and technologies needed to realize precision medicine's potential. One groundbreaking aspect is the use of advanced therapies like genome editing, such as CRISPR-Cas9, enabling tailored modifications to correct genetic mutations and treat previously untreatable diseases. However, there's a need for alternative benefit-risk assessment calculations due to small sample sizes in treatment development.

New statistical methods, like pairwise comparison of patient outcomes, are crucial for accurate assessment. Population-scale genomics can identify disease risks and medicine suitability before disease onset, shifting care from reactive to proactive. Initiatives like Estonia's 100,000 Genomes Project highlight the potential of genomic data collection for personalized care. Despite advancements, challenges remain, including data privacy, regional regulatory differences, and ethical concerns. Collaboration between industry, regulators, and public trust is vital. The recent Diamond session on "Precision Medicine, Gene Editing, and Gene Therapy" emphasized the field's progress, challenges, and opportunities. Gene therapy and editing are making strides, driven by increased research, growing market, and societal acceptance. Affordability, safety, and regulatory balance remain concerns. Access to precision medicine, particularly for rare diseases, must improve, and regulatory oversight must address ethical concerns. Managing genomic data storage, analysis, privacy, and sharing poses challenges. Addressing off-target effects in gene editing is crucial. Opportunities exist in data accessibility, patient engagement, and education to accelerate research and improve public understanding. Looking ahead, precision medicine can shift toward preventive care, benefiting population health and reducing healthcare costs. Stakeholders must collaborate internationally to address ethical concerns and align regulatory requirements. Patient safety must remain paramount as precision medicine progresses.

4. AI Perspectives within Healthcare Informatics: Drug Design, Discovery, Screening

Artificial intelligence (AI) has revolutionized the healthcare industry by improving patient care and outcomes. AI in healthcare has the potential to transform the way we diagnose diseases, develop treatments, and prevent illnesses. The use of AI technology, such as machine learning and natural language processing, has enabled medical professionals to make more accurate diagnoses, personalize treatments, and streamline clinical processes. Machine learning, one of the most common AI techniques in healthcare, has facilitated medical diagnosis and treatment by processing large amounts of clinical data, identifying patterns, and making predictions with higher accuracy. It has been used for precision medicine, predicting treatment success based on individual patient characteristics, and detecting correlations and changes in health data that may indicate health risks. Deep learning, a subset of machine learning, has also been applied to tasks such as speech recognition and natural language processing, aiding in medical record analysis and clinical decision-making. To better understand AI enabled mechanics in terms of healthcare figure 3 gives a visual representation of the matter.

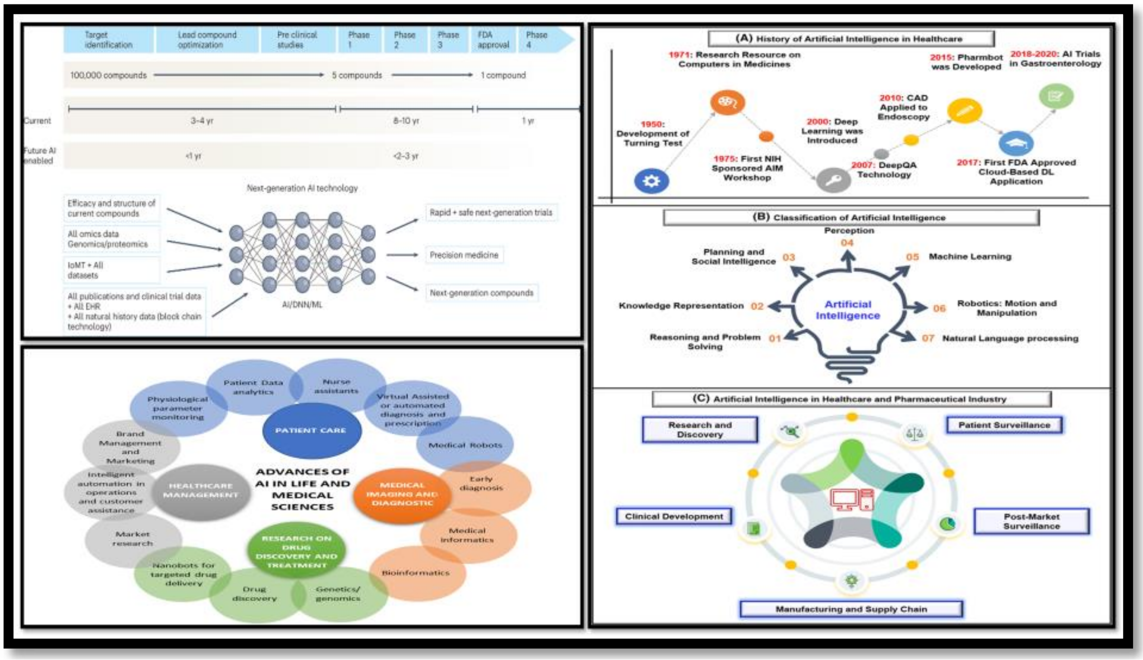

Figure 3: AI Enable Healthcare Visualization

Natural language processing (NLP) is another AI technology transforming healthcare. NLP enables computers to interpret and use human language, allowing for improved diagnosis and accuracy, personalized treatment recommendations, and streamlined clinical processes. By extracting valuable information from medical records and health data, NLP helps healthcare professionals make informed decisions and manage complex data more efficiently. Rule-based expert systems, although less prevalent today, have played a role in clinical decision support by providing sets of rules for specific knowledge areas. However, machine learning approaches are gradually replacing rule-based systems, offering more flexibility and accuracy in healthcare analytics and decision-making. AI within healthcare has diverse applications, including diagnosis and treatment, administrative tasks, and data analysis. By automating administrative processes, AI reduces human error, saves time, and allows medical professionals to focus on patient care. Challenges associated with AI adoption in healthcare include data privacy and security, patient safety and accuracy, integration with existing IT systems, physician acceptance and trust, and compliance with regulations. Addressing these challenges is crucial to ensure ethical and responsible use of AI in healthcare. Looking forward, AI in healthcare holds tremendous potential for further innovation and advancement. The use of AI-powered tools and algorithms can enable faster disease detection, personalized treatments, and automation of processes such as drug discovery and diagnostics. The future of AI in healthcare promises improved patient outcomes, increased safety, and reduced costs.

However, the successful adoption of AI in healthcare relies on overcoming challenges and ensuring collaboration between AI technologies and medical professionals. Moreover, AI has transformed healthcare by enhancing diagnosis accuracy, personalizing treatments, streamlining processes, and improving patient care. As AI continues to advance, its impact on healthcare is expected to grow, leading to further advancements, better health outcomes, and improved patient experiences. Artificial intelligence (AI) is making significant strides in various clinical applications, revolutionizing healthcare practices. In the field of cardiovascular medicine, AI algorithms are being developed to aid in diagnosing and risk stratifying patients with conditions such as coronary artery disease. Wearable devices and internet-based technologies are also being used to monitor cardiac data, enabling early detection of cardiac events outside of the hospital. AI has shown promise in dermatology for diagnosing skin cancer and classifying various skin diseases. It has achieved high accuracy levels in skin cancer detection, surpassing human dermatologists in some cases. Gastroenterology is another area where AI can enhance endoscopic procedures, allowing for faster disease identification and visualization of blind spots. Infectious diseases are being tackled with the help of AI, with applications ranging from predicting treatment outcomes and identifying antimicrobial resistance to diagnosing diseases such as malaria, meningitis, and tuberculosis. Musculoskeletal applications of AI include identifying causes of knee pain, particularly in underserved populations, to improve diagnosis and management. Oncology has seen significant progress in using AI for cancer diagnosis, risk stratification, molecular characterization of tumors, and drug discovery.

AI algorithms have shown promise in detecting breast cancer and prostate cancer with high accuracy rates. Ophthalmology benefits from AI applications for screening eye diseases, with FDA approval granted for the use of AI algorithms in diagnosing diabetic retinopathy. AI can assist pathologists in analyzing digital pathology images, aiding in the diagnosis of diseases such as breast cancer, gastric cancer, and colorectal cancer. Primary care is also utilizing AI for decision support, predictive modeling, and business analytics to improve patient care and treatment outcomes. In psychiatry, AI is being explored for predictive modeling of diagnoses and treatment outcomes, as well as the development of chat-bot therapy for conditions like anxiety and depression. Radiology is an area where AI is making significant strides, particularly in interpreting medical imaging scans. Deep learning models have demonstrated accuracy comparable to that of human experts in identifying diseases through CT and MR imaging. AI also offers non-interpretive benefits to radiologists, such as reducing noise in images, enhancing image quality, and automatically assessing image quality. Disease diagnosis and classification benefit from AI techniques, including artificial neural networks and Bayesian networks. AI-assisted diagnosis based on electronic health records (EHRs) is helping physicians make more accurate diagnoses and treatment decisions by leveraging mass data and identifying similar cases. Telemedicine is another area where AI is gaining traction, enabling remote patient monitoring and providing real-time alerts to physicians based on sensor data. EHRs are being analyzed and interpreted using natural language processing, making reports more concise and standardized.

AI algorithms are also used to predict disease risk based on patient records and family history. Drug interactions pose a threat to patients taking multiple medications, and AI is being utilized to identify potential drug-drug interactions by analyzing medical literature and user-generated content such as adverse event reports. While AI holds great potential in these clinical applications, challenges remain. Validation of AI models against human performance is essential, as is addressing issues of bias, interpretability, and privacy. Further research and clinical trials are needed to assess the true clinical utility of AI in various healthcare settings. Overall, AI has the potential to revolutionize clinical practices, improve patient outcomes, and enhance the efficiency and accuracy of healthcare delivery. The healthcare industry is witnessing the implementation of artificial intelligence (AI) through the collaboration and mergers of large health companies, allowing for greater accessibility to health data. These partnerships provide a foundation for the development and integration of AI algorithms. Many companies are exploring the incorporation of big data in healthcare, focusing on data assessment, storage, management, and analysis technologies. Several prominent companies have contributed to the advancement of AI algorithms in healthcare. IBM's Watson Oncology is being developed in partnership with leading cancer centers to assist in personalized cancer treatment.

Microsoft's Hanover project analyzes medical research to predict highly effective cancer drug treatments. Google's DeepMind platform is being used by the UK National Health Service for risk detection and cancer tissue analysis. Tencent is working on various medical systems and services, including AI-powered diagnostic imaging and intelligent healthcare through their WeChat platform. Intel has invested in startups like Lumiata, which uses AI to identify at-risk patients and develop care options. Neural ink, founded by Elon Musk, has developed a next-generation neuroprosthetic that interfaces with neural pathways in the human brain. AI is also transforming healthcare delivery in developing nations by improving access to diagnosis and treatment. With the increasing capabilities of AI over the internet, machine learning algorithms can accurately diagnose life-threatening diseases in areas where healthcare resources are limited. AI enables a level of personalized care that is often lacking in developing countries. The regulatory landscape for AI in healthcare is evolving. Regulations such as the Health Insurance Portability and Accountability Act (HIPAA) and the European General Data Protection Regulation (GDPR) protect patient data and privacy. The U.S. FDA has published an Action Plan for the regulation of medical devices incorporating AI. The U.S. Department of Health and Human Services has issued guidance on the ethical use of AI, emphasizing principles such as respect for autonomy, beneficence, non-maleficence, and justice. Similar regulations and guidelines exist in other countries, such as Denmark and the European Union, to ensure responsible data use and protect individual rights.

AI is revolutionizing the healthcare industry by improving clinical decision support systems, expanding access to care, and enhancing patient outcomes. Large companies are investing in AI research and development, and regulations are being developed to address ethical concerns and protect patient data. The implementation of AI in healthcare holds great promise for improving healthcare delivery, particularly in underserved areas and developing nations to a great extent. Drug discovery, the process of identifying new therapeutic compounds, remains challenging despite advancements in biotechnology and computational tools. Drug design is crucial, involving the creation of molecules that interact effectively with specific biological targets. Computational modeling and bioinformatics play key roles, especially in the era of big data. Therapeutic antibodies and biopharmaceuticals are gaining prominence, requiring advanced computational techniques to enhance their properties. The drug development journey includes preclinical research, clinical trials, and regulatory approval, focusing on optimizing drug properties like affinity, selectivity, efficacy, stability, and bioavailability. The Special Issue published on IEEE "Drug Design and Discovery: Principles and Applications" features research articles and communication pieces contributed by experts worldwide. One notable article discusses the use of the computational platform CANDO for repurposing existing drugs to combat Ebola virus outbreaks. This platform integrates computational predictions and in vitro screening results to identify potential treatments efficiently, reducing time, cost, and resources. Another study explores the synthesis of novel compounds with potential antitumor properties by combining nitric oxide (NO) release with diterpenoids. This innovative approach showcases hybrid compounds as a strategy for discovering new anticancer agents. Understanding protein-protein interactions is crucial in unraveling cellular networks. A recent study introduces a machine learning method called iPPBS-Opt, which uses pseudo amino acid composition and stationary wavelet transform to predict protein-protein binding sites.

This method simplifies the prediction process and aids in drug discovery and biomedical research. In terms of drug safety, an investigation into the nephrotoxicity of the widely used antibiotic vancomycin sheds light on its molecular targets in human kidney cells. This knowledge can lead to improved therapeutic strategies and reduced side effects in clinical applications. Additionally, the Special Issue covers research on antimalarial agents, antiviral compounds, antimicrobial agents, antiepileptic drugs, and anti-inflammatory agents. These studies explore novel compounds, their synthesis, and their biological activities, contributing to efforts to discover effective treatments for various diseases. The articles collectively highlight the importance of computational methods, innovative compound design, and comprehensive pharmacological evaluations in drug discovery and development. These multidisciplinary approaches aim to accelerate the identification of promising drug candidates with enhanced safety and efficacy profiles, benefiting patients worldwide.

5. Biologics the New Future

According to a recent report by Global Data titled 'Future of Pharma—Looking Ahead to 2022,' the pharmaceutical industry is witnessing a steady rise in biologics, which are expected to surpass small molecules in terms of sales revenue. The report predicts a significant increase in biologics sales over the next five years, with a projected $120 billion more in sales by 2027 compared to innovative small molecules. Quentin Horgan, Managing Analyst for the Drugs Database at Global Data, describes biologics as "primary engines of value creation" and expects this trend to continue. Biologics are anticipated to dominate sales for both large-cap and mega-cap bio/pharma companies, reflecting the industry's shift towards these drugs not only in terms of approvals but also in manufacturing processes. Global Data forecasts that nearly all subtypes of biologics will experience substantial growth in sales revenue, collectively accounting for 55% of all innovative drug sales by 2027. Monoclonal antibodies, such as OPDIVO (Ono Pharmaceuticals), Dupixent (Regeneron Pharmaceuticals), and Keytruda (Merck), are currently driving biologics sales and are expected to contribute to 46% of biologics sales in 2027. Keytruda, primarily used for oncology indications, is projected to make up 4% of all biologics sales in 2027. While monoclonal antibodies will continue to dominate, the report highlights that gene therapies and gene-modified cell therapies will experience the most substantial growth.

Between 2022 and 2027, both molecule types are forecasted to witness a remarkable increase of over 1,000 percent in sales. Notably, gene therapy sales are expected to be driven by pipeline therapies, such as RPA-501 by Rocket Pharmaceuticals, which is currently in Phase I of clinical trials. This underscores the evolving landscape of the pharmaceutical industry towards biologics and the potential for groundbreaking advancements in treatment modalities. An opinion article explores whether small molecules or biologics will shape the future of pharmaceuticals, drawing parallels with technological advancements. Small-molecule drugs, characterized by low molecular weight, have been foundational in traditional medicine and are known for their predictable pharmacokinetics, simpler dosing, and cost-effectiveness. However, their simplicity exposes them to fierce generic competition post-patent expiration. In contrast, the industry is shifting towards biologics, which include complex drugs like monoclonal antibodies, gene-based therapies, and cellular products. These drugs play a vital role in fields like oncology but face challenges such as high cost, complexity in manufacturing, fragility, and patient immune responses. Despite these challenges, analytics predict that biologics will dominate the pharmaceutical landscape due to their efficacy in addressing complex diseases. As technology advances and production costs decrease, biologics are expected to become more accessible, potentially reshaping the future of medicine.

6. Results and Findings

The future of AI in healthcare holds tremendous potential to transform the industry in various ways. One significant advantage of AI is its ability to analyze large volumes of data quickly and accurately. By leveraging machine learning algorithms, AI can identify patterns and predict outcomes based on extensive datasets, leading to improved diagnoses and treatment plans. Medical imaging is another area where AI can make a significant impact. AI algorithms can be trained to detect abnormalities in images such as X-rays, CT scans, and MRIs, accelerating diagnoses and reducing the risk of human error. Personalized medicine is another area where AI can excel. By analyzing a patient's medical history, genetic information, and lifestyle factors, AI can provide tailored treatment recommendations that meet each patient's unique needs. Remote patient monitoring is also a promising application of AI in healthcare. By continuously monitoring patients and detecting early warning signs of complications, AI can enable healthcare professionals to intervene before conditions worsen, resulting in better patient outcomes and reduced hospital readmissions. A summary of the research exploration results and findings are illustrated within figure 4 and 5 providing an experimental visualization design for future healthcare.

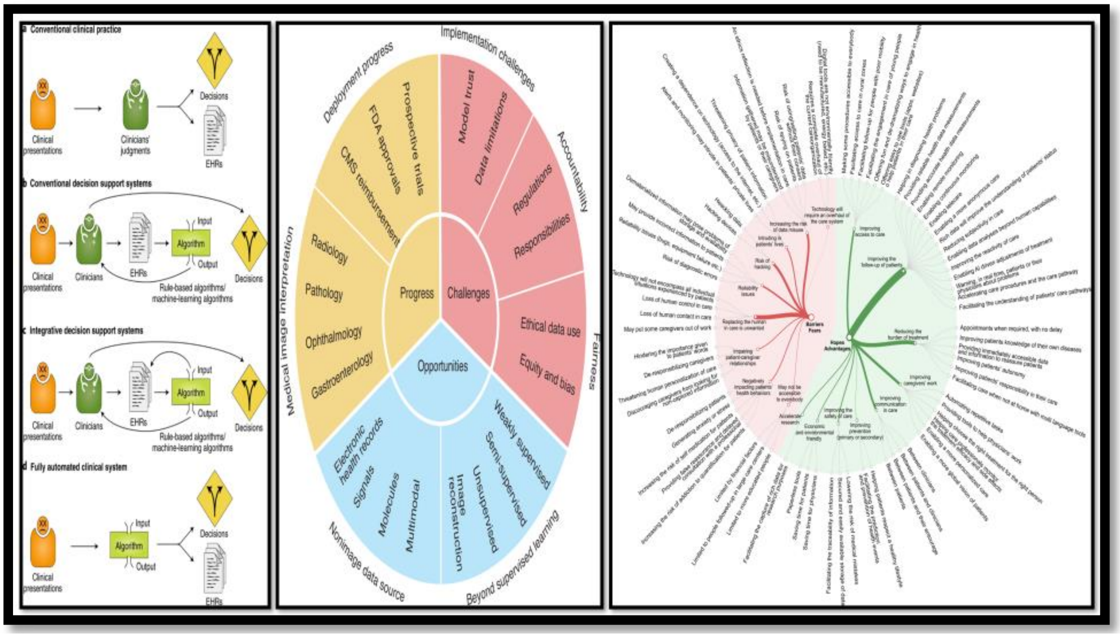

Figure 4: A Visual Representation of the Findings from the Research Results

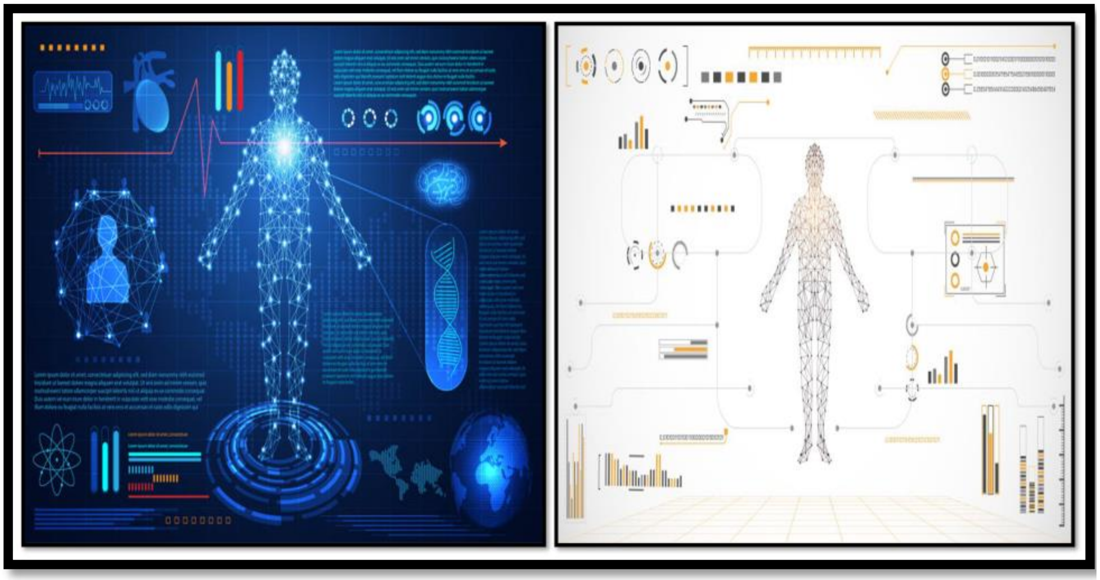

Figure 5: A Visualization of Future Healthcare (Experimental)

Regenerative medicine encompasses four main areas: cell transplantation, tissue engineering, drug research, and gene therapy, all of which rely on highly active cells. Enhancing cell activity through scientific methodologies is crucial for advancing regenerative medicine. However, beyond the interaction between biomaterials and targeted cells, the interplay between biomaterials and immune cells near the targeted cells is equally significant, as it can trigger immune responses. For example, immune cells like neutrophils and macrophages, with their M1 (pro-inflammatory) and M2 (anti-inflammatory) phenotypes, respond to local environmental conditions. Modifications induced by biomaterials in M1 macrophages, for instance, may hinder tissue regeneration. Recent research has also explored the intricate relationship between nanomaterials and immune cells, shedding light on processes like bio-corona formation, immune sensing, immune evasion, and degradation. Thus, in the ongoing development of biomaterials-based regenerative medicine, considering the reactions of immune cells is crucial to ensure overall therapy success. This holistic approach, addressing both enhanced cell activity and immune response modulation, is key to the future of regenerative medicine. Tissue engineering is a promising field poised to revolutionize healthcare by providing innovative solutions for tissue restoration, replacement, and rejuvenation. By integrating principles from biology, engineering, and medicine, tissue engineering enables the creation of functional, living tissues capable of restoring or improving damaged or ailing bodily tissues. Despite persistent hurdles and complexities, ongoing research and technological advancements are steadily advancing the development of increasingly sophisticated and clinically relevant tissue-engineered products. With this continuous progress, tissue engineering is set to play a pivotal role in shaping the future medical landscape, ultimately improving the quality of life for countless patients worldwide. Ethical considerations are significant in tissue engineering, particularly regarding the use of human cells or embryos.

Researchers must adhere to rigorous ethical guidelines and regulations to ensure the ethical acquisition and application of cells and tissues, while respecting the autonomy and dignity of donors involved in this groundbreaking field of medical science. Organ-on-a-chip (OoC) technology has made significant strides in biomedical research, offering insights into various medical applications from disease modeling to drug testing. While single-organ-on-a-chip models exist for most organs, the field is advancing towards interconnected multiple OoC devices, enabling revolutionary discoveries. Integrating sensors into these chips simplifies monitoring critical physiological parameters, enhancing their utility. The ultimate goal is to develop a human-body-on-a-chip, a comprehensive model of interconnected OoCs that could potentially replace animal testing and accelerate pharmaceutical research. Innovative biomaterials and fabrication techniques, including 3D printing and bioprinting, are driving advancements in OoC technology, making it more cost-effective and efficient. Ultimately, these developments may lead to automated medical procedures and improved patient care, marking a significant step forward in biomedical research and healthcare. To provide an overall understanding, Table 2 presents a graphical view of the context.

Tissues/Organs	Cell types	Types of hydrogels	Applications	References
Bone	Osteoblasts	Poly(ethylene glycol) (PEG), poly(ethylene glycol) poly (lactic acid) (PEG-PLA)	Drug delivery, cell encapsulation, scaffold for bone regeneration	[20] [21]
Heart	Bone marrow cells, embryonic stem cells, cardiomyocytes	Fibrin, PEG, alginate, hyaluronic acid (HA), superabsorbent polymer (SAP)	Scaffold for heart tissue engineering	[22] [23]
Cartilage	Chondrocytes	Fibrin, PEG, SAP	Drug delivery, cell encapsulation, scaffold for cartilage regeneration	[24] [25] [26]
Eye	-	HA	Corneal transplantation	[27]
Skin	Fibroblast	Collagen, fibrin, HA	Abdominal wall, ear, nose and throat reconstruction, grafting	[28] [29]
Blood vessels	Stem cells, endothelial cells	PEG, alginate, HA	Vascular grafting	[30] [31]

Table 2: Selection of Biomaterials within Research and Development for Regenerative Medicine Applications

7. Discussions and Future Directions

Research in the field of AI and healthcare has been crucial in developing the technology we have today. It has led to breakthroughs in areas such as medical imaging, drug development, and personalized medicine. AI algorithms can analyze vast amounts of data, including patient records and clinical trials, to identify patterns and make accurate predictions, enhancing diagnoses and treatment plans. The development of natural language processing algorithms has enabled the analysis of unstructured data, such as doctor's notes and patient records, to extract vital information and trends, further improving medical decisions. Wearable devices are another outcome of AI research in healthcare. These devices can monitor a patient's health remotely, collecting data on vital signs and transmitting it to healthcare professionals in real-time. This facilitates early intervention and improves patient outcomes significantly. AI has the potential to revolutionize healthcare by providing faster and more accurate diagnoses, enhancing treatment plans, and improving patient care and safety. Ongoing research in the field of AI and healthcare will continue to push the boundaries, leading to further advancements and a healthier world. The future of AI in healthcare looks promising, and its applications are poised to make a significant positive impact on the industry.

The future of tissue engineering and regenerative medicine holds immense promise as advancements in additive manufacturing, medical imaging, biomaterials, and cellular engineering converge to enable the fabrication of patient-specific vascular tissue constructs. While significant progress has been achieved, substantial challenges remain, including defining precise cell and material requirements, achieving tissue maturation and functionality, and ensuring proper vascularization and innervation. Nonetheless, ongoing multidisciplinary research and development efforts are poised to drive transformative innovations in these fields, offering groundbreaking applications in personalized medicine and regenerative therapies. Oral routes of drug administration offer significant advantages in terms of patient compliance and convenience, making them an attractive option for delivering immunotherapeutic. However, the efficacy of many orally delivered drugs is hindered by factors like degradation and biological barriers such as mucosal and epithelial layers. Innovative particulate systems employing mucoadhesive and permeabilizing technologies have shown promise in improving drug bioavailability and are gradually advancing in clinical translation.

8. Conclusions

Accelerated Computing has completely changed the way how we humans view and visualize particulars to an overwhelming level of superiority. In spite of all the advancements and rapid development and deployment of data device peripherals and AI integration there is still a huge concern in the relation towards human health. The better the system the more complexify the scenario and outcome becomes. As a civilization, we are constantly evolving with time and the computing technicality continues to grow our interest to dive higher into the unknown. But we cannot ignore the matter when it revolves around and concerns between life and death. Proper Ethics and Moral Integrity are very crucial for a context like human health. If not checked properly and without authentic guidelines and instructions even the greatest of systems can produce an unimaginable error. When that level of hierarchy concerns around health it is a matter of life and death and to beyond. The COVID-19 Pandemic was a prime example of how devastating the consequences can shape out to be and impact human lives to a scale of unimaginable heights.

In the context of today and in the near future and in the following years to come the whole world will go through a wide range of shift in terms of both engineering and medical science to a great degree and will change the way how humans deal with machinery and technicality to a great extent. True, remarkable and great innovations and extraordinary achievements will be applicable but in the midst of all the betterment we must not lose sight of what is truly needed and required in terms of health. The way the prospect is moving towards perhaps when at its peak even the most unorthodox matter and issue might rise in terms of human mortality and how there can a path beyond that line of scaling and a situation alternate can be made possible.

So, there is a lot of matter and concern to consider from diversity of backgrounds. One thing must be understood above everything else; Every Human Being is Liable to Error and I will finish this retrospect upon that and leave the rest to time and human civilization society. To effectively apply these approaches in immune engineering, it is crucial to ensure they do not disrupt the natural immune function of the gastrointestinal tract and that they are transient yet efficient in design. Sublingual and buccal routes, which bypass first-pass metabolism and offer rapid onset of effects, are also worth considering for immunotherapeutic delivery, although few formulations have received U.S. FDA approval. Overall, research in these systems is expected to focus on immunoengineering, constructing biomaterials targeting various immune cells and organs while preserving gastrointestinal tract integrity. The convenience of sustained administration and high patient compliance makes oral routes a promising avenue for future developments in immunotherapy delivery.

While biologics are recognized as a pivotal component of the future pharmaceutical landscape, particularly in addressing challenging diseases like cancer, autoimmune disorders, and genetic conditions, small molecules are far from becoming obsolete in the industry. Recent discoveries have renewed interest in small molecules, especially those capable of modulating protein-protein interactions, offering versatile treatment options for various diseases. Small molecules' ability to penetrate cell membranes, coupled with their cost-effective production, ensures their enduring significance in treating chronic conditions where long-term affordability is crucial. In essence, the future of medicine envisions a harmonious coexistence of both small molecules and biologics, ensuring a diverse and complementary therapeutic arsenal.

Declarations

- Funding

No Funding was provided for the conduction of this research.

- Conflict of interest/Competing interests

There are no Conflict of Interest or any type of Competing Interests for this research.

- Ethics approval

The author declares no competing interests for this research.

- Consent to participate

The author has read and approved the manuscript and have agreed to its publication.

- Consent for publication

The author has read and approved the manuscript and have agreed to its publication.

- Availability of data and materials

The original imaging and clinical data are not publicly available, because they contain various types of private information. The provided data sources, visualizations, illustrations, representations that support the findings and information of the research investigations are mentioned and referenced where appropriate.

- Code availability

Mentioned in details within the Acknowledgements section.

- Authors' contributions

Described in details within the Acknowledgements section.

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References

1. Johnson, A. T., & Phillips, W. M. (1995). Philosophical foundations of biological engineering. *Journal of Engineering Education, 84*(4), 311-318.
2. Vincent, J. F., Bogatyreva, O. A., Bogatyrev, N. R., Bowyer, A., & Pahl, A. K. (2006). Biomimetics: its practice and theory. *Journal of the Royal Society Interface, 3*(9), 471-482.
3. "Systems biology | Britannica". www.britannica.com. Retrieved 2023-02-15.
4. World Health Organization. (2003). *Medical device*

regulations: global overview and guiding principles. World Health Organization.

5. Duda, R. O., & Shortliffe, E. H. (1983). Expert systems research. *Science, 220*(4594), 261-268.
6. Miller, R. A. (1994). Medical diagnostic decision support systems—past, present, and future: a threaded bibliography and brief commentary. *Journal of the American Medical Informatics Association, 1*(1), 8-27.
7. Chan, S., Reddy, V., Myers, B., Thibodeaux, Q., Brownstone, N., & Liao, W. (2020). Machine learning in dermatology: current applications, opportunities, and limitations. *Dermatology and therapy, 10*, 365-386.
8. "Convention on Biological Diversity". 13 May 2016. Retrieved 27 April 2018.
9. Akhtar, Z. B., & Rozario, V. S. (2020, June). The Design Approach of an Artificial Human Brain in Digitized Formulation based on Machine Learning and Neural Mapping. In *2020 International Conference for Emerging Technology (INCET)* (pp. 1-7). IEEE.
10. Fagette Jr, P. H., & Horner, P. I. (2004). Celebrating 35 years of Biomedical Engineering: An Historical Perspective (PDF). *Landover, MD: Biomedical Engineering Society,* 4.
11. Kassab, G. S. (2004). YC" Bert"Fung: The Father of Modern Biomechanics. *Molecular & Cellular Biomechanics, 1*(1), 5.
12. Gallo, J., Holinka, M., & Moucha, C. S. (2014). Antibacterial surface treatment for orthopaedic implants. *International journal of molecular sciences, 15*(8), 13849-13880.
13. Huang, J., Su, L., Kowalski, J. A., Barton, J. L., Ferrandon, M., Burrell, A. K., ... & Zhang, L. (2015). A subtractive approach to molecular engineering of dimethoxybenzene-based redox materials for non-aqueous flow batteries. *Journal of materials chemistry A, 3*(29), 14971-14976.
14. Mingyan, W., Xingcheng, X., Nenad, V., Shidi, X., Xiangyun, S., Paul, O. V., ... & Gao, L. (2013). Toward an Ideal Polymer Binder Design for High-Capacity Battery Anodes. *Journal of the American Chemical Society, 135* (32), 12048–12056.
15. Choi, J., Kim, K., Jeong, J., Cho, K. Y., Ryou, M. H., & Lee, Y. M. (2015). Highly adhesive and soluble copolyimide binder: improving the long-term cycle life of silicon anodes in lithium-ion batteries. *ACS applied materials & interfaces, 7*(27), 14851-14858.
16. Tan, S., Ji, Y. J., Zhang, Z. R., & Yang, Y. (2014). Recent progress in research on high-voltage electrolytes for lithium-ion batteries. *ChemPhysChem, 15*(10), 1956-1969.
17. Zhu, Y., Li, Y., Bettge, M., & Abraham, D. P. (2012). Positive electrode passivation by LiDFOB electrolyte additive in high-capacity lithium-ion cells. *Journal of the Electrochemical Society, 159*(12), A2109.
18. Liang, Y., Chen, Z., Jing, Y., Rong, Y., Facchetti, A., & Yao, Y. (2015). Heavily n-dopable π-conjugated redox polymers with ultrafast energy storage capability. *Journal of the American Chemical Society, 137*(15), 4956-4959.
19. Surwade, S. P., Smirnov, S. N., Vlassiouk, I. V., Unocic, R. R., Veith, G. M., Dai, S., & Mahurin, S. M. (2015). Water desalination using nanoporous single-layer graphene. *Nature nanotechnology, 10*(5), 459-464.
20. Yan, Q., Xiao, L. Q., Tan, L., Sun, W., Wu, T., Chen, L. W., ... & Shi, B. (2015). Controlled release of simvastatin-loaded thermo-sensitive PLGA-PEG-PLGA hydrogel for bone tissue regeneration: in vitro and in vivo characteristics. *Journal of Biomedical Materials Research Part A, 103*(11), 3580-3589.
21. Vinay, R., & KusumDevi, V. (2016). Potential of targeted drug delivery system for the treatment of bone metastasis. *Drug Delivery, 23*(1), 21-29.
22. Hasan, A., Khattab, A., Islam, M. A., Hweij, K. A., Zeitouny, J., Waters, R., ... & Paul, A. (2015). Injectable hydrogels for cardiac tissue repair after myocardial infarction. *Advanced Science, 2*(11), 1500122.
23. Sun, X., & Nunes, S. S. (2015). Overview of hydrogel-based strategies for application in cardiac tissue regeneration. *Biomedical Materials, 10*(3), 034005.
24. Chen, W., Chen, S., Morsi, Y., El-Hamshary, H., El-Newhy, M., Fan, C., & Mo, X. (2016). Superabsorbent 3D scaffold based on electrospun nanofibers for cartilage tissue engineering. *ACS applied materials & interfaces, 8*(37), 24415-24425.
25. Wang, J., Zhang, F., Tsang, W. P., Wan, C., & Wu, C. (2017). Fabrication of injectable high strength hydrogel based on 4-arm star PEG for cartilage tissue engineering. *Biomaterials, 120*, 11-21.
26. Rahman, R. A., Sukri, N. M., Nazir, N. M., Radzi, M. A. Z. A., Zulkifly, A. H., Ahmad, A. C., ... & Sha'ban, M. (2015). The potential of 3-dimensional construct engineered from poly (lactic-co-glycolic acid)/fibrin hybrid scaffold seeded with bone marrow mesenchymal stem cells for in vitro cartilage tissue engineering. *Tissue and Cell, 47*(4), 420-430.
27. Xu, W., Wang, Z., Liu, Y., Wang, L., Jiang, Z., Li, T., ... & Liang, Y. (2018). Carboxymethyl chitosan/gelatin/hyaluronic acid blended-membranes as epithelia transplanting scaffold for corneal wound healing. *Carbohydrate polymers, 192*, 240-250.
28. Bencherif, S. A., Gsib, O., & Egles, C. (2017). Fibrin: An underrated biopolymer for skin tissue engineering. *J. Mol. Biol. Biotech, 2*(1).
29. Monteiro, I. P., Shukla, A., Marques, A. P., Reis, R. L., & Hammond, P. T. (2015). Spray-assisted layer-by-layer assembly on hyaluronic acid scaffolds for skin tissue engineering. *Journal of Biomedical Materials Research Part A, 103*(1), 330-340.
30. Tresoldi, C., PENEDA PACHECO, D. P., Formenti, E., Gentilini, R., Mantero, S., & Petrini, P. (2017). Alginate/gelatin hydrogels to coat porous tubular scaffolds for vascular tissue engineering. *European Cells & Materials, 33*.
31. Rouwkema, J., & Khademhosseini, A. (2016). Vascularization and angiogenesis in tissue engineering: beyond creating static networks. *Trends in biotechnology, 34*(9), 733-745.
32. Ewart, L., Apostolou, A., Briggs, S. A., Carman, C. V., Chaff, J. T., Heng, A. R., ... & Levner, D. (2022). Performance assessment and economic analysis of a human Liver-Chip for predictive toxicology. *Communications medicine, 2*(1), 154.
33. Acar, H., Ting, J. M., Srivastava, S., LaBelle, J. L., & Tirrell, M. V. (2017). Molecular engineering solutions for therapeutic

peptide delivery. *Chemical Society Reviews, 46*(21), 6553-6569.

34. Lequieu, J., Córdoba, A., Hinckley, D., & de Pablo, J. J. (2016). Mechanical response of DNA–nanoparticle crystals to controlled deformation. *ACS central science, 2*(9), 614-620.
35. Orive, G., Anitua, E., Pedraz, J. L., & Emerich, D. F. (2009). Biomaterials for promoting brain protection, repair and regeneration. *Nature Reviews Neuroscience, 10*(9), 682-692.
36. Singelyn, J. M., DeQuach, J. A., Seif-Naraghi, S. B., Littlefield, R. B., Schup-Magoffin, P. J., & Christman, K. L. (2009). Naturally derived myocardial matrix as an injectable scaffold for cardiac tissue engineering. *Biomaterials, 30*(29), 5409-5416.
37. Hernandez, M. J., Gaetani, R., Pieters, V. M., Ng, N. W., Chang, A. E., Martin, T. R., ... & Christman, K. L. (2018). Decellularized extracellular matrix hydrogels as a delivery platform for MicroRNA and extracellular vesicle therapeutics. *Advanced therapeutics, 1*(3), 1800032.
38. López-Gallego, F., & Benítez-Mateos, A. I. (2020). Manufacturing of protein-based biomaterials coupling cell-free protein synthesis with protein immobilization. *Immobilization of Enzymes and Cells: Methods and Protocols*, 335-343.
39. Ounkaew, A., Kasemsiri, P., Jetsrisuparb, K., Uyama, H., Hsu, Y. I., Boonmars, T., ... & Chindaprasirt, P. (2020). Synthesis of nanocomposite hydrogel based carboxymethyl starch/polyvinyl alcohol/nanosilver for biomedical materials. *Carbohydrate polymers, 248*, 116767.
40. Cao, H., Duan, L., Zhang, Y., Cao, J., & Zhang, K. (2021). Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity. *Signal transduction and targeted therapy, 6*(1), 426.
41. Abdul Khalil, H. P. S., Yahya, E. B., Tajarudin, H. A., Balakrishnan, V., & Nasution, H. (2022). Insights into the role of biopolymer-based xerogels in biomedical applications. *Gels, 8*(6), 334.
42. Vinchhi, P., Rawal, S. U., & Patel, M. M. (2021). Biodegradable hydrogels. In *Drug delivery devices and therapeutic systems* (pp. 395-419). Academic Press.
43. Crosby, C. O., Stern, B., Kalkunte, N., Pedahzur, S., Ramesh, S., & Zoldan, J. (2022). Interpenetrating polymer network hydrogels as bioactive scaffolds for tissue engineering. *Reviews in chemical engineering, 38*(3), 347-361.
44. Enderle, J., & Bronzino, J. (2011). *Introduction to biomedical engineering*. Academic press.
45. Hatze, H. (1974). The meaning of the term" biomechanics". *Journal of biomechanics, 7*(2), 189-190.
46. Couvreur, P., & Vauthier, C. (2006). Nanotechnology: intelligent design to treat complex disease. *Pharmaceutical research, 23*, 1417-1450.
47. Curtis, A. S., Dalby, M., & Gadegaard, N. (2006). Cell signaling arising from nanotopography: implications for nanomedical devices.
48. Jacobson, L. E., Olayan, M., Williams, J. M., Schultz, J. F., Wise, H. M., Singh, A., ... & Kirby, D. F. (2019). Feasibility and safety of a novel electromagnetic device for small-bore feeding tube placement. *Trauma Surgery & Acute Care Open, 4*(1), e000330.
49. Goyal, M. R. (2018). *Scientific and Technical Terms in Bioengineering and Biological Engineering*. CRC Press.
50. "Biomedical Engineering - Electrical and Computer Eng. Ryerson". (2011). Ee.ryerson.ca. 2011-08-04. Archived from the original on September 27, 2011.
51. "Ryerson Biomedical Engineering Students Invent Brain-Controlled Prosthetic Arm". (2011). STUDY Magazine.
52. Gallegos, E. (2011). Alfred E. Mann Foundation for Scientific Research (AMF). *Aemf. org. Retrieved,* 09-24.
53. Pasotti, L., & Zucca, S. (2014). Advances and computational tools towards predictable design in biological engineering. *Computational and mathematical methods in medicine, 2014*(1), 369681.
54. Cuello, J. C. (2005). 'Engineering to biology'and'biology to engineering': The bi-directional connection between engineering and biology in biological engineering design. *Int J Engng Ed, 21*, 1-7.
55. Graur, D., Zheng, Y., Price, N., Azevedo, R. B., Zufall, R. A., & Elhaik, E. (2013). On the immortality of television sets:"function" in the human genome according to the evolution-free gospel of ENCODE. *Genome biology and evolution, 5*(3), 578-590.
56. Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., ... & Mesirov, J. P. (2005). Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proceedings of the National Academy of Sciences, 102*(43), 15545-15550.
57. Wang, H., Mayhew, D., Chen, X., Johnston, M., & Mitra, R. D. (2011). Calling Cards enable multiplexed identification of the genomic targets of DNA-binding proteins. *Genome research, 21*(5), 748-755.
58. Kwasnieski, J. C., Fiore, C., Chaudhari, H. G., & Cohen, B. A. (2014). High-throughput functional testing of ENCODE segmentation predictions. *Genome research, 24*(10), 1595-1602.
59. Arnold, C. D., Gerlach, D., Stelzer, C., Boryń, Ł. M., Rath, M., & Stark, A. (2013). Genome-wide quantitative enhancer activity maps identified by STARR-seq. *Science, 339*(6123), 1074-1077.
60. Fields, S., & Song, O. K. (1989). A novel genetic system to detect protein–protein interactions. *Nature, 340*(6230), 245-246.
61. Hart, T., Chandrashekhar, M., Aregger, M., Steinhart, Z., Brown, K. R., MacLeod, G., ... & Moffat, J. (2015). High-resolution CRISPR screens reveal fitness genes and genotype-specific cancer liabilities. *Cell, 163*(6), 1515-1526.
62. Gilbert, L. A., Horlbeck, M. A., Adamson, B., Villalta, J. E., Chen, Y., Whitehead, E. H., ... & Weissman, J. S. (2014). Genome-scale CRISPR-mediated control of gene repression and activation. *Cell, 159*(3), 647-661.
63. Laboratory, D. A., Fund, N. C., Site—NDRI, B. C. S., Site—RPCI, B. C. S., Resource—VARI, B. C., of Miami, B. B. R. U., ... & Statistical Methods groups—Analysis Working Group. (2017). Genetic effects on gene expression across human tissues. *Nature, 550*(7675), 204-213.

64. "GTEx Creates a Reference Data Set to Study Genetic Changes and Gene Expression". National Institutes of Health : Office of Strategic Coordination - The Common Fund. 8 February 2018. Retrieved 2022-01-13.
65. Li, Y., Shi, W., & Wasserman, W. W. (2018). Genome-wide prediction of cis-regulatory regions using supervised deep learning methods. *BMC bioinformatics, 19*, 1-14.
66. Diss, G., & Lehner, B. (2018). The genetic landscape of a physical interaction. *Elife, 7*, e32472.
67. Mardis, E. R. (2008). Next-generation DNA sequencing methods. *Annu. Rev. Genomics Hum. Genet., 9*, 387-402.
68. Nirenberg, M., Leder, P., Bernfield, M., Brimacombe, R., Trupin, J., Rottman, F., & O'neal, C. (1965). RNA codewords and protein synthesis, VII. On the general nature of the RNA code. *Proceedings of the National Academy of Sciences, 53*(5), 1161-1168.
69. Fiers, W., Contreras, R., Haegeman, G., Rogiers, R., Van De Voorde, A., Van Heuverswyn, H., ... & Ysebaert, M. (1978). Complete nucleotide sequence of SV40 DNA. *Nature, 273*(5658), 113-120.
70. Buchanan, B. G., & Shortliffe, E. H. (1984). *Rule based expert systems: the mycin experiments of the stanford heuristic programming project (the Addison-Wesley series in artificial intelligence)*. Addison-Wesley Longman Publishing Co., Inc..
71. Baxt, W. G. (1991). Use of an artificial neural network for the diagnosis of myocardial infarction. *Annals of internal medicine, 115*(11), 843-848.
72. Koomey, J., Berard, S., Sanchez, M., & Wong, H. (2010). Implications of historical trends in the electrical efficiency of computing. *IEEE Annals of the History of Computing, 33*(3), 46-54.
73. Jha, A. K., DesRoches, C. M., Campbell, E. G., Donelan, K., Rao, S. R., Ferris, T. G., ... & Blumenthal, D. (2009). Use of electronic health records in US hospitals. *New England Journal of Medicine, 360*(16), 1628-1638.
74. Dougherty, G. (2009). *Digital image processing for medical applications*. Cambridge University Press.
75. "Artificial Intelligence and Machine Learning for Healthcare". Sigmoidal. 21 December 2017. Archived from the original on 17 August 2020. Retrieved 26 March 2018.
76. Power, B. (2015). Artificial intelligence is almost ready for business. *Harvard Business Review.*
77. Bahl, M., Barzilay, R., Yedidia, A. B., Locascio, N. J., Yu, L., & Lehman, C. D. (2018). High-risk breast lesions: a machine learning model to predict pathologic upgrade and reduce unnecessary surgical excision. *Radiology, 286*(3), 810-818.
78. Bloch-Budzier, S. (2016). NHS using Google technology to treat patients. *BBC News, 22*.
79. Wang, H., Zu, Q., Chen, J., Yang, Z., & Ahmed, M. A. (2021). Application of artificial intelligence in acute coronary syndrome: a brief literature review. *Advances in Therapy*, 1-9.
80. Infante, T., Cavaliere, C., Punzo, B., Grimaldi, V., Salvatore, M., & Napoli, C. (2021). Radiogenomics and artificial intelligence approaches applied to cardiac computed tomography angiography and cardiac magnetic resonance for precision medicine in coronary heart disease: a systematic review. *Circulation: Cardiovascular Imaging, 14*(12), 1133-1146.
81. Sotirakos, S., Fouda, B., Mohamed Razif, N. A., Cribben, N., Mulhall, C., O'Byrne, A., ... & Connolly, R. (2021). Harnessing artificial intelligence in cardiac rehabilitation, a systematic review. *Future cardiology, 18*(2), 154-164.
82. Chen, W., Sun, Q., Chen, X., Xie, G., Wu, H., & Xu, C. (2021). Deep learning methods for heart sounds classification: A systematic review. *Entropy, 23*(6), 667.
83. "COVID-19 Pandemic Impact: Global R&D Spend for AI in Healthcare and Pharmaceuticals Will Increase US$1.5 Billion By 2025". Medical Letter on the CDC & FDA. May 3, 2020 – via Gale Academic OneFile.
84. Akhtar, Z. B. (2024). The design approach of an artificial intelligent (AI) medical system based on electronical health records (EHR) and priority segmentations. *The Journal of Engineering, 2024*(4), e12381.
85. Akhtar, Z. B., & Gupta, A. D. (2024). Integrative approaches for advancing organoid engineering: from mechanobiology to personalized therapeutics. *Journal of Applied Artificial Intelligence, 5*(1), 1-27.