

#### Article

# **Bioinformation metaverse: Current status, challenges, and future research themes**

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https://creativecommons.org/licenses/ by/4.0/ Abstract: The bioinformation metaverse proposed in this paper is founded on bioinformatics, which takes the big data of biology to collect, filter, display the visual, calculate, merge, simulate, and optimize the big biology problem during the analysis process with the application of high-end information-processing technologies to solve the high-dimension, high-complexity problem for the bioinformation metaverse field. It can realize multi-scale traversal from atomic layers and molecules to proteins and complete biological systems. They are important for bioinformation metaverse construction and development. Multi-source data fusion and analytics methods are important in efficiently interpreting high-dimensional and high-complexity biological systems from atomic layers to molecules. In this paper, the application of the metaverse in six aspects (molecular manipulation, biological perception, protein structure study, decentralized technology, interactive simulation, and visualization) is analyzed further, highlighting the significance of the bioinformation metaverse for bioinformatics research and development. The multi-layered and closely connected biological information system can be built up to make life-science study and technology research more efficient.

**Keywords:** bioinformation metaverse; molecular manipulation; protein structure analysis; biological perception

## **1. Introduction**

The metaverse of bioinformatics is defined as the next generation of virtual environments that reflect and integrate biological data at multiple scales, including atomic, molecular, protein, cellular, and organismal levels. It enables real-time interaction, simulation, and visualization through immersive technologies such as virtual reality (VR), augmented reality (AR), and biosensing interfaces. Key features of the concept include multi-scale biodata fusion, interdisciplinary interoperability, and dynamic virtual-physical feedback mechanisms.

Unlike traditional paradigms such as digital twins, which primarily focus on creating virtual copies of physical systems with real-time data synchronization, the metaverse of biological information goes beyond passive replication. It combines interactive simulations, gamified problem-solving environments, and crowdsourced collaboration to allow observation, intervention, hypothesis testing, and educational exploration in a fully immersive space. In addition, it integrates technologies such as blockchain for data integrity and privacy and AI for intelligent data mining and pattern recognition.

In the era of the big explosion of biological information, computer technology, biological conceptual principles, and high-precision sensors are integrated to help data be presented, analyzed, modified, and predicted to realize the construction of a biological information metaverse. To this end, based on the key areas of bioinformation metaverse molecular manipulation, biosensors, protein structure, decentralization, interactive simulation, and data visualization, the author elaborated on the powerful advantages of bioinformation metaverse.

Molecular manipulation: The current literature focuses on genome editing and gene therapy [1] for molecular manipulation, focusing on precise genome repair and disease treatment [2]. Based on the biological information metaverse discussion, this paper proposes a molecular virtual editing environment. It uses virtual reality technology for molecular editing, providing a molecular virtual editing environment for researchers to edit, observe, and test molecules in this environment.

Biological perception: Previous studies on biological perception have mainly focused on physiology, neurology, and psychology [3], but a working platform could not integrate the above information [4]. Different from other research work in this field, this paper combines biosensing technologies such as MojoLens, EEG head ring, EMG armband, etc., with the metaverse to form a multi-level virtual biosensing platform, which provides more extensive possibilities for bioinformatics research and bioinformatics experiments.

Protein structure analysis: Current research on protein structure prediction mainly focuses on methods and technologies for protein structure prediction [5], and few generative artificial intelligence technologies for protein design and prediction have been applied to the bioinformation metaverse [6]. This paper proposes a freer and more intuitive method for protein prediction based on the visualization and intelligence characteristics of the bioinformation metaverse, which provides a new idea for research on protein prediction.

Decentralized technology: Currently, research on decentralized technology focuses on blockchain technology [7] and decentralized applications [8], and less attention is paid to its combination with bioinformatics applications. In this paper, we propose to start with decentralized technology and use blockchain technology to protect the privacy of biological data and ensure data transparency, supporting an open and secure platform.

Interactive simulation: Most current interactive simulations involve gamification learning [9] and simulation training [10], and there is no biological research on gamification. This paper proposes an interactive simulation element to realize the educational research of metaverse + gamification and the knowledge transfer and skill cultivation of gamification of metaverse + research in the metaverse of biological information.

Visualization: Although some scholars have studied the visualization tools of biological information [11], biological information visualization in the metaverse has just started. In this paper, VR (virtual reality) technology is combined to provide a more immersive and intuitive biological information visualization method, which is convenient for researchers to interpret and analyze data.

# 2. Interaction

#### 2.1. Molecular manipulation

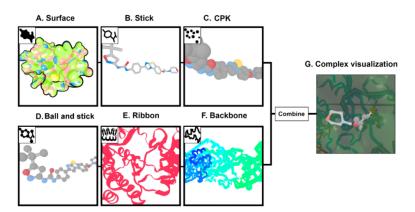
In the metaverse virtual field, molecular spectroscopy technology is applied to generate the virtual scene in the metaverse of molecular structure, simulate the intermolecular forces such as van der Waals forces, and analyze the intermolecular interactions in different states and the changes of the interactions [12]. In the bioinformation metaverse, in addition to the above methods, high-precision sensors are also implanted in the molecules to build a molecular network composed of sensors to capture, collect, and integrate the state of molecules while transferring dynamic information such as molecular vibration to the virtual field to achieve the effect of synchronizing the real molecular state with the virtual field. In addition, in terms of three-dimensional reconstruction of molecular structure, compared with traditional manual construction, SFM (Structure from Motion) [13] can grasp molecular structure through movement. With a high-precision molecular microscope or camera, molecular images can be taken from multiple directions and analyzed for accurate molecular model reconstruction. Combined with the molecular visualization [14] technology processed by computer technology, the efficiency of molecular modeling is improved.

The real molecules in MioT (Molecular Internet of Things) can be mapped into two worlds: the virtual molecules in the bioinformation metaverse and the physical molecular model of the real world.

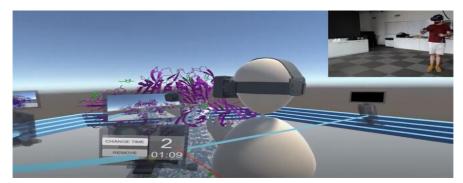
Molecular structures in the real world are represented in virtual reality, i.e., virtual molecules. The virtual molecule is the digitization of molecular structure. This step uses structural, physical, and chemical data to model molecular structure for molecular virtual reality and explore molecular structure function through virtual reality (VR) or augmented reality (AR) technology. Virtual molecules in the metaverse can be simulated and calculated through molecular dynamics simulation tools [15]; that is, the process of drug interaction or chemical reaction with the target is dynamically simulated with the molecular structure as the medium, which provides a visual and intuitive scientific observation window for research and development to accelerate biomedical work such as drug design and toxicology research.

The physical molecular model presents the molecular model more intuitively, and the 3D printing technology is used to solidify the physical, virtual three-dimensional molecular model [16] and truly present the specific arrangement of molecules and atoms and the composition of molecular chemical bonds so that the abstract molecular knowledge is more solid and interactive. Such molecular models are also suitable for educational AIDS and scientific experiences for students and audiences. In addition, scanning tunneling microscopes (STMs) [17] and atomic force microscopes (AFMs) [18] are used to scan molecular atoms accurately, obtain the arrangement of atoms and the form of chemical bonds inside the molecules, and further precise them into 3D printing models so that the molecular model not only presents a static molecular state but also presents a static molecular state. It can also carry out structural interaction changes of other processes, such as chemical reactions, so that users can get a complete and deep sense of interaction and a more in-depth and intuitive understanding of the structure and efficacy of molecules.

Figure 1 is a visualization of drug-protein binding molecules [19]; MINT's VR interface embraces a range of visualization techniques to improve the understanding of a 3D environment, e.g., the binding of a drug to a protein, in a versatile and robust way. As shown in Figure 1A, protein structures are rendered with a surface model and dynamic shadows. Different types of atoms are marked in the diagram in different colors. Figure 1B–D are diagrams of different ligand structure forms, enabling users to perform molecular operations. Figure 1E,F are specific renderings of ribbon protein structure and main chain, respectively, enabling users to understand biomolecular structure better [20]. Users can choose visual panels to dynamically customize virtual environments and freely combine editing options to create unique and complex visualizations. In the bioinformatics metaverse, users of various platforms may conduct collaborative high-precision editing of multiple cells, share knowledge, increase the efficiency of editorial analysis, and even build supramolecules. As shown in Figure 2 [21], wearable devices enable viewing the molecular environment in the metaverse. At the same time, with the assistance of 3D printing technology, the modified molecular model can also be transformed into a physical form by printing the virtual model to achieve a more accurate presentation of the molecular model.



**Figure 1.** Molecule visualization options using MINT and combining these options to make complex and interactive renderings of 3D molecule models: (**A**) Surface models of molecular structures; (**B**–**D**) Represent the molecular structure of the stick, CPK, and ball-stick models, respectively; (**E**,**F**) The structure and skeleton representation of the protein in the band diagram; (**G**) A combination of the above options where the surface model is presented transparently.



**Figure 2.** In a screenshot from the VRdeo tool, users observe molecules in the Metaverse through a VR device.

### 2.2. Biological perception

MojoLens is a smart contact lens application of continuous blood glucose detection (CGM, Continuous Glucose Monitoring) [22] technology; the embedded microsensor can sense blood sugar; these sensors can be radio-linked to a subcutaneously implantable sensor or patch sensor to sense glucose levels in the blood. Figure 3A shows the sensor's operating mechanism to detect glucose concentration in tears. Google designed a smart contact lens to monitor glucose concentration in eye fluid (Figure 3B). In addition, Yao et al. fabricated contact lenses with glucose sensors to detect glucose concentration (Figure 3C), which has the advantage of regular, accurate, and long-term wear comfort detection of glucose concentration. Park et al. have also designed a glucose-sensor contact lens to detect the physical health of diabetic patients. Figure 3D(a,b) shows the image of the contact lens embedded with LED pixels and a schematic of the contact lens's sections, respectively [23]. When the information enters the biometric universe, the user's blood sugar can be displayed to directly observe the self-blood sugar value in the real world through AR display, or it can be uploaded to the biometric universe for virtual body state observation-intuitive understanding between self-status and physiological health indicators in the virtual world. In addition, the physiological indicators of the body can be connected with muscle activity through the EMG bracelet and other bracelets. As shown in Figure 4, the EMG signal can be transmitted to the computer [24] to understand further and control one's health.

Suppose users upload information about their physiological state into the metaverse. In that case, it can be processed with the help of the blockchain's datadecentralized ledger and hash function, and each piece of data will be accompanied by a timestamp and authenticity verification through the consensus mechanism so that the data is not easily tampered with. In addition, the smart contract can automatically input the data into the verification process. The encryption technology and public/private key mechanisms achieve access rights and other data integrity and security protection.

MojoLens can also use implantable neural sensors to decode and detect neural signals and synchronize the neural information of the organism to the bioinformation universe in real time, improving the ability of neural decoding and enhancing the organism's function. For example, the brain nerves are connected to the exoskeleton to improve flexibility. The optic nerve is connected to the electronic eye to optimize the cooperation of the artificial vision system. MojoLens has a screen and speaker, which can provide an immersive experience. However, when combined with VR gloves and other auxiliary devices, users' immersive experience can be further enhanced. As shown in Figure 5 [25], after MojoLens detects an increase in heart rate, VR gloves can apply a slight tightening or vibration to specific parts of the user's wrist to prompt the user to relax or rest. Similarly, when MojoLens detects a decrease in blood oxygen levels, the VR glove can stimulate the user at different resistance points to prompt the user to take a deep breath or rest. In this way, users can always know their physical condition to ensure a healthy condition; the multi-sensory feedback system integrates visual, auditory, and tactile feedback to provide complete health feedback and uses virtual reality to provide interactive, safe, and more immersive sensory.

The use of EEG technology in collaboration with the bioinformation metaverse can not only realize the function of comprehensive detection and evaluation of user perception, psychology, emotion, and other states but also provide cognitive status detection and judgment and the prediction of conscious activity content by brain wave content, which is conducive to neuroscience research [26]. **Figure 6** shows a mind-controlled virtual reality game system from neurotech company MindMaze. Two players are playing against each other with mind control. Moreover, it can be expanded to medical health, brain-computer interface interaction, intelligent rehabilitation training, and other application fields so that the human-computer interfaction of the biological information metaverse becomes more innovative, intelligent, and personalized.

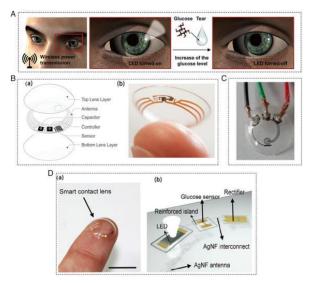


Figure 3. Operation and different designs of contact lenses to monitor glucose concentration: (A) Operation process of the contact lens sensor for detecting glucose levels in tears; (B) (a) Google's three-layer contact lens with an integrated sensor; (b) view of the contact lens sensor. Reproduced with permission; (C) A glucose contact lens sensor with a wired power supply. Reproduced with permission; (D) (a) Image of a smart contact lens with an LED pixel displaying the glucose level; (b) schematic of all integrated sections in the contact lens.



Figure 4. Users transfer their own EMG information to a database.



Figure 5. VR gloves applied to virtual reality.



**Figure 6.** Controlling virtual reality activities through brain waves in the game, there is a stretchable magic ball on each side of the screen and a small ball in the center. The players' mental focus controls the magic balls, wearing headbands with sensors implanted on their foreheads. The game's objective is to use bursts of energy to expand the central ball and push back the opponent's magic ball. The larger the central ball expands, the stronger the player's mental power is demonstrated to be.

## 3. Feature

#### **Protein structure analysis**

As the most basic constituent of life, protein depends on the folding state of its amino acid sequence in terms of functional structure and conformation [27]. This process, in turn, determines its secondary, tertiary, and quaternary structure. However, at the same time, because of the complexity of the folding structure, it is difficult to predict the function, which has been a difficulty in bioinformatics research. However, combined with AI and a virtualized metaverse, data on the structure of these proteins can be processed much more quickly. Combining bioinformatics and artificial intelligence can increase the speed and accuracy of data analysis and create new ways to explore complex biological problems. AI algorithms can efficiently process large amounts of biological data, enabling more accurate and detailed biological simulations. The prediction model's accuracy, specificity, and sensitivity have also improved effectively. AI can accurately mine hidden models and deep information in biological data. Based on AI technology, more accurate, stable, and reliable prediction models can be developed [28]. In addition, using the computing power of the metaverse, protein prediction can be further transferred from laboratory calculation to the simulation and analysis of proteins in the virtual environment, and the three-dimensional structure and function of proteins can be predicted from the amino acid sequence, which is convenient for researchers to quickly verify the biological activities of proteins, significantly shorten the research time, and improve the reliability of prediction.

Finally, 3D visualization in the metaverse can be used to explore protein structures. People can dynamically understand and study protein folding dynamics and change processes at any time through the metaverse visualization software. The intuitive and vivid visual 3D interface is conducive to further understanding the molecular structure of proteins, analyzing the microscopic changes within proteins, and carrying out environmental changes of different degrees of proteins. For drug research and development applications, the 3D molecular structure of drugs can be more clearly displayed, which helps to identify molecular targets of new drugs and verify the effects of new drugs.

More critically, in the metaverse, computing resources and analysis software are packaged and connected to a virtual collaboration platform, allowing scholars from different disciplines to collaborate on protein structure prediction in a virtual environment, speeding up the prediction work, and achieving the integration of multidisciplinary knowledge to improve the accuracy and reliability of the prediction structure. For example, the prediction of protein-protein interaction simulations can help researchers analyze potential protein complexes for drug design. At the same time, proteins are modified and optimized in the platform to understand the regulatory mechanisms of biological signals and potential therapeutic strategies.

The metaverse platform combines machine learning prediction methods with 3D virtual protein modeling techniques. Machine learning methods are learning protein folding models to achieve accurate predictions. 3D Virtual Protein Modeling: This method allows users to combine 3D virtual protein modeling techniques with machine learning techniques, using computational methods to predict the possible folded structure of a protein based on the interaction patterns of neighboring amino acids. To accelerate the speed and efficiency of the computing process, the computing unit can be sent to one or more computer processing nodes to achieve distributed computing of tasks. For example, database collaboration enables any two or more people or groups of people to share data content online or perform collaborative analysis of project data files. For researchers, information encryption protects private or sensitive data or materials to some extent. Users can easily incorporate 3D simulation and visualization of proteins into protein structure studies. With the help of the virtual platform, the computational study of protein structure can analyze the form and composition of the protein as well as its properties.

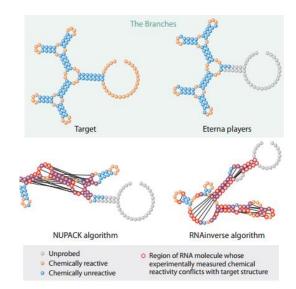
In large-scale protein databases, researchers can identify proteins and study their morphology, composition, folding patterns, and function [29]. **Figure 7** shows the user-designed RNA sequence [30]. The user-designed RNA sequence can be tested and analyzed in the virtual environment, and the user's feedback can determine whether the design conforms to the expected structure. Compared with the existing computational prediction methods, the user-designed target secondary structure sequence in the metaverse environment performs better. The bioinformation

metaverse can also design 3D visual models of protein interactions, allowing researchers to analyze the relationships between proteins, search for potential protein complexes, and provide structural references for new drug development. All researchers participate in the prediction process on a collaborative platform, providing interaction between researchers, exchanging research ideas, and improving research methods to improve protein functional prediction results. At the same time, users can modify protein composition in the environment, design corresponding protein enzymes to control biological signals, or search for potential therapies.

The application of generative AI can increase the speed of protein prediction by several times. Understanding the protein's amino acid sequence can analyze the protein's function so that users of the metaverse can accurately analyze the potential function of different amino acids and further understand the protein's biological activity. In addition, efficient protein structure predictions are made. The visualization and intelligence of generative AI make it easier for scientists to predict the primary structure, secondary structure, tertiary structure, and quaternary structure of proteins, making the prediction of protein structure more "easy to operate", and generative AI can also identify and learn protein form, structure, folding pattern, and protein function and make predictions in the protein data of large-scale databases. Possible protein structures are predicted by analyzing the interaction of adjacent amino acids. At the same time, generative AI can also be applied to protein interaction prediction. In the bioinformation metaverse, users can draw and present three-dimensional models of protein interactions, infer the structure of candidate protein complexes, and contribute to developing innovative new drugs and life science applications. In the bioinformation metaverse, all aspects of the drug development lifecycle (from drug design to validation, raw materials to marketing) can be applied. Combining AI and VR can improve the ability to analyze and predict drug behavior. Through drug sensors, microliquid sensors, and other technologies, it is possible to evaluate the molecular structure, pharmacokinetics, administration regimen and route, drug release method and speed, movement mode in the body, and the change of drug concentration in the blood over time, and accelerate the visualization of the way to analyze and predict drug response. Metaverse bioinformation research can observe the multidimensional association between drugs and diseases, diseases and proteins, predict new indications and drug reactions, simplify the selection of drug indications, and accelerate the clinical reuse of existing drugs. At the same time, it can observe the effects of drugs in the human body, their side effects, and other information, and on this basis, it can conduct the simulation of drug clinical research and shorten the test cycle.

Phase I and Phase II clinical trials are avoided, and the efficiency and safety of drug therapy are improved. In the bioinformation metaverse, the purchase of raw materials and the sale of drugs are managed by the metaverse financial management system, and the ownership of assets is guaranteed by blockchain technology. Financial records can be safely recorded and protected through the untampered and unforgeable blockchain. In addition, Smart Contracts [31] protect the rights of both parties to a transaction and provide an automated tool for data access management. Blockchain-based smart contracts enable data to be modified or verified only by authorized users, improve the efficiency of data sharing and transmission in team collaboration, and

provide a reliable audit trail for data changes so that every update can be verified and traced.



**Figure 7.** The RNA sequences designed by players in Eterna, achieving secondary structures, are called "the branches".

## 4. Technology

#### 4.1. Decentralized technology/NFT

Decentralized technology focuses on the future development of the Internet and pays more attention to the application of distributed, decentralized, and blockchain technology [32]. Blockchain technology has the characteristics of decentralization, traceability, encryption algorithms, and tamper-proof characteristics, making it a subversive technology in bioinformatics and providing a feasible solution to protect and monitor sensitive personal genetic data effectively [33]. The bioinformation metaverse contains vast amounts of genetic information and life science data, which can be dispersed and stored on different nodes to prevent data loss or tampering. In addition, data access and changes can be traced through blockchain technology, which is conducive to medical and scientific research compliance. Distributed technologies can also enable smart contracts-computer programs that run automatically when certain conditions are met, as agreed in advance. In the life metaverse, smart contracts can deal with the interactions between living beings in the metaverse ecosystem, such as simulating the process of competition, cooperation, and evolution between living beings, which can create a more realistic virtual ecosystem. One of the key points of bioinformation metaverse decentralization technology is to achieve cross-platform operability of different platforms, in other words, to make these platforms have interoperability, that is, interoperability of data, resources, and information. The diversity of virtual ecosystems enables virtual life, virtual ecosystems, and virtual applications to interact and collaborate, thus building a more complex and rich virtual world.

NFT (non-fungible token) is an irreplaceable, trustworthy, and unique digital property certificate on the blockchain that can record and manage complex multi-

dimensional attributes [34]. In the biological metaverse, identity authentication and digital identity management achieved through decentralized technology can be integrated with NFT to ensure that the ID numbers of virtual life forms, researchers, and users are unique, which can improve the security of the virtual life world and avoid the theft and abuse of virtual life.

The organic combination of decentralized technology, NFT, and bioinformatics technology can form a safe, fair, and diverse biological information metaverse, providing new opportunities to expand the boundaries of bioinformatics digitally and commercially. With subsequent integration and development, these new technologies will promote the emergence of virtual life and the subsequent development of virtual ecosystems. The virtual life managed by NFT in the biological information metaverse can use NFT to verify the uniqueness and immutability of its biological information based on the biological information recorded on the blockchain. Through smart contracts, the different behavioral patterns, genetic genes, appearance characteristics, and other data information of biological individuals in the biological information metaverse platforms, supporting transactions and interactions between different metaverse platforms.

In NFT, problems such as data storage, transaction costs, and interoperability among different platforms can be solved through Off-Chain Storage and On-Chain Verification storage solutions. Storage of data using high-performance services such as IPFS Reduce expenses using lower-cost blockchains and expanding blockchain technologies such as Layer [35]; Use common NFT standards such as ERC-721 [36] or ERC-1155 [37] to make the NFT compatible across different metaverse platforms and conform to standardized processes. The optimization of NFT technology can realize more levels of virtual life management in the bioinformation metaverse to support the progress of bioinformation digitization.

#### 4.2. Interactive simulation

Interactive simulations will continue to evolve into increasingly complex and detailed forms in the metaverse of biological information. Providing solutions to realistic problems in the biological information-related new path, in the case of users gathering global users to solve the same problem jointly through immersive use and entertainment, improving the accessibility of biometric information content and problem-solving efficiency, and reducing repetitive labor.

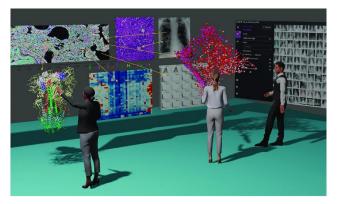
In the fields of molecular design, protein prediction [38], biosensing, drug detection, etc., we can embed processes in interactive simulations, crowdsourcing the world's players through the power of the metaverse [39]; for example, neural decoding can be designed as an interactive simulation game, in which players guess what psychological reactions and emotional changes are likely to occur based on neural changes in the brain, thus providing a new method for related psychological research and neuroscience research.

**Figure 8** illustrates scientists conducting molecular analysis and manipulating proteins in the metaverse [40]. After solving a set of problems, the simulation platform can take advantage of different settings, increasingly interesting problems, and more

and more different problems to support motivated players in continuing to focus and improve their abilities and knowledge.

In addition, the metaverse also offers rich possibilities for biological information education [41], especially for adolescent students. Bioinformatics games can be customized for young students to learn in, such as the adventure metaverse game of medical education, which allows students to experience the role of molecules, physiology, and drug design on patients in the virtual environment through interactive levels of the game to ignite students' interest in exploring medicine and life science.

To sum up, interactive simulation is an important part of the biological information metaverse, a helping hand to solve professional problems, and a vivid teaching presentation.



**Figure 8.** The example shows a multidisciplinary group analyzing a fictitious COVID-19 spatial omics and single-cell data set projected in a 3D scatterplot. From left to right, molecular imaging (with colored marker overlay), H and E stain, and patient cohort *x*-ray imaging are shown. Heatmaps derived from spatial analysis allow cellular phenotyping in conjunction with the location of the scatterplot and imaging. Meanwhile, a structural biologist manipulates the COVID spike protein in an XR protein viewer, looking for variations in the patient's genetic background that change binding affinities.

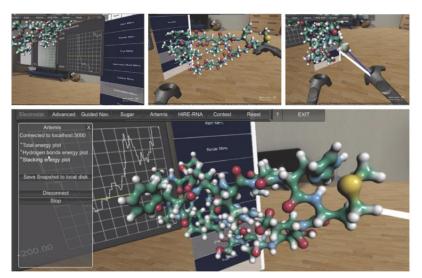
### 4.3. Visualization

Data visualization technology is the key technique of the universe, making data presentation and problem-solving into 3D visualization and immersion [42]. 3D data visualization means making biological information data vivid, more interactive, and immersive, giving users a better understanding of this data to make intelligent decisions.

First, in terms of data visualization, data visualization plays a significant role in the analysis and interpretation of biological data for data analysis and understanding. Biological information has many complex genetic, genomic, and molecular structure data. Three-dimensional visual analysis of biological information using threedimensional data visualization means can map biological information data from a twodimensional plane structure to a three-dimensional spatial structure so that the data's pattern, trend, and anomaly can be more precise and more information can be obtained. For example, when using biomolecular three-dimensional visualization technology to study protein structure, I will integrate myself into it, directly observe and compare with human beings through the perspective, intuitively and graphically understand the protein, and understand the mutual relationship between protein function and molecules.

Secondly, it is also important for scientific and medical education. In research, the bioinformatics metaverse should envisage highly interactive and engaging 3D data visualization teaching tools so that students can better understand the life sciences. For example, the Virtual Biology Lab allows students to immerse themselves in a virtual, three-dimensional environment to experience the basic concepts of molecular biology and genetics rather than just learning from books and two-dimensional pictures [43]. In addition, data visualization enhances collaboration and communication between professionals, and research groups using the bioinformatics metaverse can access and edit 3D data visualization work in a collaborative project to share their findings and insights, enabling faster scientific exploration and drug development and improving their collaborative communication. Figure 9 shows the implementation of the same interactive simulation approach in a VR environment [44]. The picture illustrates a sequence of molecular dynamics interactions, showing how energy changes as the molecule changes, and the molecule has features such as hydrogen bonding. Users in a virtual environment can use a controller to bring molecules closer together, use a laser pointer to select, and use visual feedback to feel the forces being applied. Finally, the image shows how the molecule is stretched [45].

Data visualization technology expanded from two-dimensional data information analysis and display towards more three-dimensional and immersive areas in the data analysis and information representation within the bioinformatics metaverse. This will drive interdisciplinary cooperation among scholars and researchers to allow human beings to understand data better and further develop scientific and medical education. With the growth of the metaverse, there will be even larger space for data visualization of biological data, more applications for future inventions in the life sciences field, and more interesting and creative applications for teaching and knowledge exchange.



**Figure 9.** Interactive molecular dynamics in virtual reality. The top row shows the sequential steps of displaying simulation properties such as energy and hydrogen bonding, approaching the molecule with the controllers for manipulation, selecting by a laser pointer metaphor (blue beam), and providing visual feedback on the applied force (white rectangular block). The last image shows how the molecule is stretched due to this manipulation.

#### 4.4. Privacy risks and ethical governance

The research context where genetic data are employed is currently witnessing a transition. Previously, the scientist would produce a small number of 'markers' of the genome-(say) particular DNA sequences with a known role in disease pathophysiology-they now (often) employ many thousands, these markers being scattered throughout the genome. These innovations have significantly broadened our appreciation of the human genome and its relevance to many important problems, especially human disease. However, in some ways, more complicated concerns have emerged due to these technological advances. Individuals who personally consent to supply genomic samples (or contribute genome samples through family members) suffer the possibility of involuntary disclosure of their data and being subjected to genetic discrimination. The scenario in the bioinformatics metaverse becomes particularly worrisome since it is in virtual worlds that people can be immersed, exist persistently, and create voluminous amounts of data. Biomedical data such as physiological signals, behavioral data and genetic information are gathered, shared, and stored in virtual environments that enforce data encryption, access control, and user consent.

Lastly, there are ethical issues with the stewardship of virtual biological entities: within immersive systems, virtual content like virtual avatars (i.e., not always human in form), virtual animals, or AI-enhanced bioculture products may become greatly dependent on the underlying system; the situation is symbiotic between content producers and content hosts. As a result, there have been some unsettled controversies regarding data sovereignty, intellectual property, and control of individuals over their virtual biological data. Given solving these problems, Arunkumar et al. [46] devise a new scheme based on two emerging techniques: zero-knowledge proof and blockchain technology. The central aim of the scheme is to strengthen the security of the DNA STR profile, ensuring its privacy and the integrity of the genetic information. Park et al. [47] presented a private genomic data management system relying on blockchain and local differential privacy (LDP). They utilize two kinds of storage: private storage for internal employees and semi-private storage for external users. Only internal employees can access the data in private storage since encrypted genetic data are stored there. On the other hand, in semi-private storage, genetic data is transformed by LDP that cannot be reverted anymore. Bohua et al. [48] suggest the following ethical governance framework that should be considered to achieve innovation and reduce risk. Their framework is based on the precautionary principle and balances interests among stakeholders before developing and commercializing the project. Zeng et al. [49] suggested three approaches to establishing a responsible "metaverse" governance framework: collective responsibility, realism, and co-governance. Such works guide the development of bioinformatics cyberspace's fair, safe, open-source, and basic algorithm infrastructure.

#### 5. Current situation, challenges and future development

The bioinformatics metaverse is a new concept based on the research of the metaverse and bioinformatics. It is a virtual space based on biological information that coexists with reality, links with each other, and mirrors the real world. It solves the

multi-scale biological information problem of atomic, molecular, protein, neuron, and biological body layers. It virtualizes with digital twins, artificial general intelligence, the Internet of Things, and blockchain, enabling a mirror of the physical world to merge with the physical world and become a mirror of the parallel real world. With the intervention of these new technologies, biometrics enhance and improve the ability to collect, filter, visualize, calculate, integrate, simulate, and analyze large biological data sets. Artificial intelligence can help create an ecosystem of bioinformation metaverse resource exploitation, using modern computer technologies such as virtual reality and digital twins to integrate biological principles such as light, sound, and biosensing as biological data becomes increasingly important. Advanced ultraprecision sensors make multi-dimensional bioinformation data research possible to achieve visual design, adjustment, and predictive development and to build a comprehensive bioinformation metaverse.

Some challenges are facing the development of the bioinformation metaverse. (1) The bioinformatics metaverse needs to process a large amount of data, which has a wealth of information from the top down at the atomic, molecular, protein, and genome levels [50]. Therefore, data collection, integration, processing, and storage have higher requirements but also need enough computing power. (2) Data security and privacy challenges [51] due to the large amount of personal information involved, including sensitive information such as genetic and personal physiological data. This is to ensure the security of this data and that this sensitive information can be used appropriately by regulations. (3) Data quality and standardization [52]: Data on the same issue may vary between different laboratories or institutions, and it is necessary to make data comparable according to the same standards and methods. At the same time, bioinformatics also involves multidisciplinary cooperation and knowledge integration [53] because bioinformatics requires applying knowledge and technology in multiple disciplines, such as biology, computer science, AI, and other disciplines. (4) Visualization of the bioinformation metaverse, user interaction experience [54], and how to visualize data so that users can understand and use bioinformation data more intuitively and simply.

Given the above problems, a reasonable research and development roadmap for the bioinformation metaverse should consider computer technology. First, the high performance of computing hardware is needed because computing large-scale data from the atomic and molecular level to protein structure or genome level is timeconsuming. Scalable and cost-efficient architectures like cloud computing and edge computing architectures can minimize the physical footprints locally for a large system while facilitating real-time or near real-time data access and data analysis capability. In addition, the modular AI inference models will be leveraged to minimize the amount of needed GPUs and decrease the total cost of deploying them decentralized.

Secondly, blockchain technology can solve data security and privacy issues and guarantee data immutability and traceability. Some scholars have already conducted systematic reviews on the role of blockchain in the healthcare sector. For example, Xie et al. [55] conducted a systematic review of blockchain technology's current applications and prospects in the healthcare sector, highlighting its decentralized, tamper-proof, transparent, and secure characteristics, which can effectively improve the quality of medical services and data management. Ratta et al. [56] systematically

explored the integrated application of the Internet of Things (IoT) and blockchain in healthcare systems, pointing out that IoT enables remote diagnosis and treatment through wearable devices and body sensor networks. In contrast, blockchain ensures data security and privacy through its decentralized, immutable, and highly transparent features. Siyal et al. [57] reviewed the latest developments in blockchain technology in the healthcare field and emphasized its great potential in enhancing the security and reliability of medical data management. The study stressed that blockchain facilitates the development of personalized medicine by enabling real-time integration and sharing of clinical data. Haleem et al. [58] examined the advantages of blockchain technology in healthcare, identifying its significant role in improving the performance, security, and transparency of medical data sharing. The authors summarized fourteen key application scenarios of blockchain in the healthcare domain, asserting that blockchain not only enhances the analytical capacity of medical records but also effectively prevents data manipulation, ensures the confidentiality and traceability of health records, and supports the construction of a safer and more efficient healthcare data ecosystem. In conclusion, the application of blockchain technology in the healthcare field can significantly enhance data security, transparency, and reliability; promote the development of personalized medicine; and lay the foundation for building a more efficient and secure healthcare data ecosystem.

Third, solving the data quality and standardization issues requires establishing a unified and open bioinformatics standard framework to unify data-collecting processes in different institutes. Establishing standard data models and ontologies can make integrated multi-source data interoperable. Meanwhile, interdisciplinary collaboration mechanisms should also be advocated, e.g., constructing common digital laboratories or simulation platforms to continually promote data quality and update the evaluation index system.

Last but not least, regarding the visualization and the use experience problems, it might be helpful if low-latency AR/VR rendering engines are used, combined with clever UI/UX design, to make biological data more attractive to users. Adaptive visualization engines, in particular, i.e., those able to show information depending on the user's roles (researcher, physician, student, etc.), might be exploited by users to access bio information at various levels of abstraction. Rendering cost, as well as hardware accessibility, is further mitigated through lightweight visualization libraries and previously rendered molecular datasets.

In the short term, creating bioinformatics meta-worlds will improve users' ability to collect biological data and view their physiological signals in real time. Since MojoLens, AR glasses, and myoelectric wristbands can be achieved on current devices (e.g., wearable devices) and cloud-computing architecture, this can help users view and interact with their physiological signals (e.g., blood glucose, muscle activities) in the virtual world. In combination with VR gloves and interactive health management apps, users can join in rehabilitation training and intuitive biological experiments that enable interactive and immersive education, healthcare, and lifestyle improvement.

In the long run, protein structure modeling will be combined with globally distributed protein databases, smart contracts, and blockchain technology to form a self-evolving, open, global scientific research ecosystem. Establishing a complete bioinformation metaverse will facilitate open global decentralized research, artificial

intelligence drug research simulation, and complete cycle digital management of pharmaceutical molecules (from molecule to market). However, these visions will also enable scientists to model the protein interactions, forecast the responses to a drug, and oversee bioethics and data governance in a secure, transparent, and scalable way. Advanced computing power, standardized data models, and robust multidisciplinary collaboration are key requirements to satisfy these visions.

In conclusion, although implementing the bioinformation metaverse requires a large scale of technologies and infrastructures, it is possible by balancing robust computing solutions, privacy-preserving solutions, data harmonization processes, and user-centric user interfaces. With this in mind, we move from a vision of the metaverse to its deployment in life sciences and personalized health.

## 6. Conclusion

This paper proposes six directions for constructing a bioinformation metaverse: molecular manipulation, biosensors, protein modeling, blockchain, interactive simulation, and data visualization. Through the collaborative solution of intelligent information mining technology, the collection, calculation, integration, and analysis of a large number of large-scale biological data are optimized, thus solving some of the more complex problems in bioinformatics. The system has also driven advances in bioinformatics, enabling new research and application techniques that can connect and collaborate more closely with different levels of biological data. It is believed that under the influence of the subsequent development of various technologies, the bioinformation metaverse will be reflected in more fields, such as the medical field, drug research and development field, and precision medicine. It will also bring more support to life science research and technology.

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# References

- 1. Saha SK, Saikot FK, Rahman MdS, et al. Programmable Molecular Scissors: Applications of a New Tool for Genome Editing in Biotech. Molecular Therapy-Nucleic Acids. 2019; 14: 212-238. doi: 10.1016/j.omtn.2018.11.016
- Gillyard T, Davis J. DNA double-strand break repair in cancer: A path to achieving precision medicine. Chromatin and Genomic Instability in Cancer; 2021. doi: 10.1016/bs.ircmb.2021.06.003
- Peng W, Cracco E, Troje NF, et al. Does anxiety induced by social interaction influence the perception of bistable biological motion?. Acta Psychologica. 2021; 215: 103277. doi: 10.1016/j.actpsy.2021.103277
- 4. Wu X, Li E, Liu Y, et al. Artificial multisensory integration nervous system with haptic and iconic perception behaviors. Nano Energy. 2021; 85: 106000.
- Kuhlman B, Bradley P. Advances in protein structure prediction and design. Nature Reviews Molecular Cell Biology. 2019; 20(11): 681-697. doi: 10.1038/s41580-019-0163-x
- 6. Chen Y, Wang Z, Wang L, et al. Deep generative model for drug design from protein target sequence. Journal of Cheminformatics. 2023; 15(1). doi: 10.1186/s13321-023-00702-2

- 7. Petcu A, Pahontu B, Frunzete M, et al. A Secure and Decentralized Authentication Mechanism Based on Web 3.0 and Ethereum Blockchain Technology. Applied Sciences. 2023; 13(4): 2231. doi: 10.3390/app13042231
- 8. Korpal G, Scott D. Decentralization and web3 technologies. Authorea Preprints; 2022. doi: 10.36227/techrxiv.19727734.v1
- García-Redondo P, García T, Areces D, et al. Serious Games and Their Effect Improving Attention in Students with Learning Disabilities. International Journal of Environmental Research and Public Health. 2019; 16(14): 2480. doi: 10.3390/ijerph16142480
- 10. DeFalco JA, Rowe JP, Paquette L, et al. Detecting and Addressing Frustration in a Serious Game for Military Training. International Journal of Artificial Intelligence in Education. 2017; 28(2): 152-193. doi: 10.1007/s40593-017-0152-1
- 11. Zhao Y, Jiang J, Chen Y, et al. Metaverse: Perspectives from graphics, interactions and visualization. Visual Informatics. 2022; 6(1): 56-67.
- Chen CT, Chen SY, Liao CH, et al. An interactive nanomanipulation visualization based on molecular dynamics simulation and virtual reality. Transactions of the Canadian Society for Mechanical Engineering. 2013; 37(3): 991-1000. doi: 10.1139/tcsme-2013-0085
- 13. Trexler CC, Morelan AE, Oskin ME, et al. Surface Slip From the 2014 South Napa Earthquake Measured with Structure From Motion and 3-D Virtual Reality. Geophysical Research Letters. 2018; 45(12): 5985-5991. doi: 10.1029/2018gl078012
- Chavent M, Vanel A, Tek A, et al. GPU-accelerated atom and dynamic bond visualization using hyperballs: A unified algorithm for balls, sticks, and hyperboloids. Journal of Computational Chemistry. 2011; 32(13): 2924-2935. doi: 10.1002/jcc.21861
- Baaden M, Burgard M, Wipff G. TBP at the Water-Oil Interface: The Effect of TBP Concentration and Water Acidity Investigated by Molecular Dynamics Simulations. The Journal of Physical Chemistry B. 2001; 105(45): 11131-11141. doi: 10.1021/jp011890n
- Baillif B, Cole J, McCabe P, Bender, A. Deep generative models for 3D molecular structure. Current Opinion in Structural Biology. 2023; 80: 102566.
- 17. Binnig G, Rohrer H. Scanning tunnelling microscopy. Helvetica Physica Acta; 1982.
- 18. Sivarajah I. Atomic Force Microscopy: General Principles and Applications. Azo Optics; 2021.
- 19. Zhang W, Fine JA, Sculley C, et al. Molecular Interactions Using New Technology: A Virtual Reality Gaming Platform to Visualize and Manipulate Molecules. Biological and Medicinal Chemistry. 2019. doi: 10.26434/chemrxiv.9889994.v1
- Axen SD, Huang XP, Cáceres EL, et al. A Simple Representation of Three-Dimensional Molecular Structure. Journal of Medicinal Chemistry. 2017; 60(17): 7393-7409. doi: 10.1021/acs.jmedchem.7b00696
- Kuťák D, Vázquez P, Isenberg T, et al. State of the Art of Molecular Visualization in Immersive Virtual Environments. Computer Graphics Forum. 2023; 42(6). doi: 10.1111/cgf.14738
- 22. Bender C, Vestergaard P, Cichosz SL. The History, Evolution and Future of Continuous Glucose Monitoring (CGM). Diabetology. 2025; 6(3): 17.
- Ma X, Ahadian S, Liu S, et al. Smart Contact Lenses for Biosensing Applications. Advanced Intelligent Systems. 2021; 3(5). doi: 10.1002/aisy.202000263
- 24. Said S, Karar AS, Beyrouthy T, et al. Biometrics Verification Modality Using Multi-Channel sEMG Wearable Bracelet. Applied Sciences. 2020; 10(19): 6960. doi: 10.3390/app10196960
- 25. Glowacki BR, Freire R, Thomas LM, et al. An open source Etextile VR glove for real-time manipulation of molecular simulations. arXiv; 2019.
- Amores J, Richer R, Zhao N, et al. Promoting relaxation using virtual reality, olfactory interfaces and wearable EEG. In: Proceedings of the 2018 IEEE 15th International Conference on Wearable and Implantable Body Sensor Networks (BSN); 2018. doi: 10.1109/bsn.2018.8329668
- 27. Baaden M, Marrink SJ. Coarse-grain modelling of protein-protein interactions. Current Opinion in Structural Biology. 2013; 23(6): 878-886. doi: 10.1016/j.sbi.2013.09.004
- 28. Jamialahmadi H, Khalili-Tanha G, Nazari E, Rezaei-Tavirani M. Artificial intelligence and bioinformatics: a journey from traditional techniques to innovative approaches. Gastroenterology and Hepatology from Bed to Bench; 2024.
- 29. Gligorijević V, Renfrew PD, Kosciolek T, et al. Structure-based protein function prediction using graph convolutional networks. Nature Communications. 2021; 12(1). doi: 10.1038/s41467-021-23303-9
- 30. Das R, Keep B, Washington P, et al. Scientific Discovery Games for Biomedical Research. Annual Review of Biomedical Data Science. 2019; 2(1): 253-279. doi: 10.1146/annurev-biodatasci-072018-021139

- 31. Buterin V. A next-generation smart contract and decentralized application platform. White Paper; 2014.
- 32. Zarrin J, Wen Phang H, Babu Saheer L, et al. Blockchain for decentralization of internet: prospects, trends, and challenges. Cluster Computing. 2021; 24(4): 2841-2866. doi: 10.1007/s10586-021-03301-8
- Balakrishnan A, Jaglan P, Selly S, et al. Emerging trends of blockchain in bioinformatics: A revolution in health care. Distributed Computing to Blockchain; 2023. doi: 10.1016/b978-0-323-96146-2.00018-8
- 34. Stefanović M, Pržulj Đ, Stefanović D, et al. The proposal of new Ethereum request for comments for supporting fractional ownership of non-fungible tokens. Computer Science and Information Systems. 2023; 20(3): 1133-1155.
- 35. Poon J, Buterin V. Plasma: Scalable autonomous smart contracts. White paper; 2017.
- Cabot-Nadal MÀ, Payeras-Capellà MM, Mut-Puigserver M, et al. Improving the token ERC-721 implementation for selective receipt: rejectable NFTs. In 2022 6th International conference on system reliability and safety (ICSRS). IEEE; 2022. pp. 243-250.
- Marin O, Cioara T, Anghel I. Blockchain Solution for Buildings' Multi-Energy Flexibility Trading Using Multi-Token Standards. Future Internet. 2023; 15(5): 177. doi: 10.3390/fi15050177
- 38. Senior AW, Evans R, Jumper J, et al. Improved protein structure prediction using potentials from deep learning. Nature. 2020; 577(7792): 706-710.
- 39. Baid SK, Bandyopadhyay A, Srivastava P, Swain S. Metaverse Using Game Theory in Healthcare. In Healthcare Services in the Metaverse. CRC Press; 2024. pp. 134-153.
- 40. Taylor S, Soneji S. Bioinformatics and the Metaverse: Are We Ready?. Frontiers in Bioinformatics; 2022. doi: 10.3389/fbinf.2022.863676
- 41. Lin H, Wan S, Gan W, et al. Metaverse in education: Vision, opportunities, and challenges. In 2022 IEEE International Conference on Big Data (Big Data). IEEE; 2022. pp. 2857-2866.
- 42. Xu H, Berres A, Shao Y, et al. Toward a smart metaverse city: Immersive realism and 3d visualization of digital twin cities. Advances in Scalable and Intelligent Geospatial Analytics. 2023; 245-257.
- 43. Ghanbarzadeh R, Ghapanchi AH. Uncovering educational outcomes deriving from students' acceptance and involvement with 3D virtual worlds. Education and Information Technologies. 2020; 26(1): 311-337. doi: 10.1007/s10639-020-10272-7
- 44. Baaden M. Deep inside molecules—digital twins at the nanoscale. Virtual Reality & Intelligent Hardware. 2022; 4(4): 324-341. doi: 10.1016/j.vrih.2022.03.001
- 45. Choi J, Lee EJ, Jang WB, Kwon SM. Development of biocompatible 3D-printed artificial blood vessels through multidimensional approaches. Journal of Functional Biomaterials. 2023; 14(10): 497.
- 46. Arunkumar P, Surendiran B, Suresh S, Sankaranarayanan V. Zero-Knowledge Proof Approach for DNA STR Profile Security using Blockchain: A Framework for Enhancing Genetic Privacy. NFSU—Journal of Cyber Security and Digital Forensics; 2024.
- 47. Park YH, Kim Y, Shim J. Blockchain-Based Privacy-Preserving System for Genomic Data Management Using Local Differential Privacy. Electronics. 2021; 10(23): 3019. doi: 10.3390/electronics10233019
- 48. Bohua L, Yuexin W, Yakun O, et al. Ethical framework on risk governance of synthetic biology. Journal of Biosafety and Biosecurity. 2023; 5(2): 45-56. doi: 10.1016/j.jobb.2023.03.002
- 49. Zeng Y, Bao A. From Virtual Reality to Metaverse: Ethical Risks and the Co-governance of Real and Virtual Worlds. International Research Center for AI Ethics and Governance; 2022.
- 50. Corringer PJ, Baaden M, Bocquet N, et al. Atomic structure and dynamics of pentameric ligand-gated ion channels: new insight from bacterial homologues. The Journal of Physiology. 2010; 588(4): 565-572. doi: 10.1113/jphysiol.2009.183160
- 51. Thomson L L, Peabody Jr A E. Privacy and security challenges in bioinformatics//Bioinformatics, Medical Informatics and the Law. Edward Elgar Publishing, 2022: 205-247.
- 52. Zhang Z, Bajic VB, Yu J, et al. Data integration in bioinformatics: current efforts and challenges. Bioinformatics-Trends and Methodologies. 2011; 41-56.
- 53. Valdivia-Granda W. The next meta-challenge for Bioinformatics. Bioinformation. 2008; 2(8): 358-362. doi: 10.6026/97320630002358
- 54. O'Donoghue S I. Grand challenges in bioinformatics data visualization. Frontiers in Bioinformatics. 2021; 1: 669186.
- 55. Xie Y, Zhang J, Wang H, et al. Applications of Blockchain in the Medical Field: Narrative Review. Journal of Medical Internet Research. 2021; 23(10): e28613. doi: 10.2196/28613

- Ratta P, Kaur A, Sharma S, et al. Application of Blockchain and Internet of Things in Healthcare and Medical Sector: Applications, Challenges, and Future Perspectives. Khan R, ed. Journal of Food Quality. 2021; 2021: 1-20. doi: 10.1155/2021/7608296
- 57. Siyal AA, Junejo AZ, Zawish M, et al. Applications of Blockchain Technology in Medicine and Healthcare: Challenges and Future Perspectives. Cryptography. 2019; 3(1): 3. doi: 10.3390/cryptography3010003
- 58. Haleem A, Javaid M, Singh RP, et al. Blockchain technology applications in healthcare: An overview. International Journal of Intelligent Networks. 2021; 2: 130-139. doi: 10.1016/j.ijin.2021.09.005