

## **Current Applications of Bioinformatics In Various Fields: A Review**

**Asita Elengoe<sup>1\*</sup>, Qian Chenxi<sup>2</sup>, Luo Dagui<sup>2</sup>, Sun Zhixin<sup>2</sup>, Yuan Zhihao<sup>2</sup>**

<sup>1</sup>Department of Biotechnology, Faculty of Applied Science, Lincoln University College, 47301 Petaling Jaya, Selangor, Malaysia

<sup>2</sup>Zhejiang Chinese Medical University, 310053 Hangzhou, Zhejiang, China

*\*Corresponding Author's email:* asitaelengoe@yahoo.com

Article received on 28<sup>th</sup> August 2024

Revision received on 25<sup>th</sup> September 2024.

Accepted on 1<sup>st</sup> October 2024.

### **ABSTRACT**

The study of information gathering, processing, and analysis techniques and technology in the biological sciences is known as bioinformatics. Its goal is to develop a number of computing technologies and procedures by analyzing, storing, and transmitting data derived from several scientific fields, including genetics, cell biology, and molecular biology. The advent of bioinformatics represents a significant turning point in the advancement of computer technology and life sciences. The emergence and advancement of bioinformatics have significantly influenced contemporary biology and medical research. The advancement of molecular medicine, gene therapy, medication discovery, crop improvement, microbiology, oncology, vaccine development, food microbiology, insect resistance, forensic analysis of microbes, waste clean-up and bioenergy and biofuels, has been substantially aided by its use in molecular biology, genetics, cell biology, and other study domains.

**Keywords:** Bioinformatics, Molecular medicine, Gene therapy, Drug development, Crop improvement, Bioenergy and biofuels

### **1. Introduction**

Our comprehension and utilization of biological data have undergone a radical transformation as the area of bioinformatics has emerged as the cornerstone of contemporary biological research in recent decades. A vast amount of biological data, from protein structure to genome sequence, may be analyzed and understood through the integration of computational, statistical, and mathematical tools in bioinformatics. Numerous fields, such as molecular medicine, gene therapy, drug discovery, crop enhancement, and biotechnology, depend heavily on this multidisciplinary subject (Wani et al., 2018).

Fundamentally, bioinformatics makes use of huge data and sophisticated computing technologies to help researchers tackle intricate biological phenomena. Bioinformaticians can predict protein structures, find disease-causing mutations, and uncover molecular pathways in a range of medical disorders by analyzing genomic data. Bioinformatics aids in the development of precise genome editing techniques and improves our capacity to target genetic disorders at the molecular level in the context of gene therapy.

Furthermore, by enabling virtual compound screening, forecasting drug-target interactions, and improving therapeutic effects, bioinformatics speeds up the drug discovery process. Through genome selection and gene modification, bioinformatics aids in the cultivation of robust crops in agriculture, helping to tackle the difficulties of global food security under changing environmental conditions.

Bioinformatics supports synthetic biology, optimization of biofuel production, and environmental remediation measures, all of which foster innovation in the burgeoning field of biotechnology. As biological research expands due to technological advancements, bioinformatics is anticipated to become more crucial in determining the direction of industrial, medical, and agricultural biotechnology ((Dahiya, 2017).

Deriving useful insights from the terabytes of data generated by omics research such as proteomics, RNA-seq, genome sequencing, and others would be almost impossible without bioinformatics (Koppad et al., 2021). Drug discovery is greatly accelerated by bioinformatics tools, which mimic how possible medications interact with biological targets (such as proteins and DNA). Before starting laboratory tests, researchers can computationally evaluate thousands of drugs using molecular docking and virtual screening techniques (Supriya et al., 2021). Bioinformatics cuts the time and expense involved in introducing new pharmaceuticals to the market by reducing the pool of possible drug candidates early in the development process. Bioinformatics is used to sequence and study pathogen genomes during disease outbreaks. This makes it possible to monitor the spread of illnesses, spot changes (in viruses like SARS-CoV-2, for example), and create vaccines and therapeutics (Uddin et al., 2023).

Through the analysis of sequenced genomes and/or transcripts from environmental samples (soil, human, animal, or water), the study of a complete community of organisms is known as metagenomics, which usually leads to the discovery of species from all domains of life (Doytchinov et al., 2023). This method is typically used in monitoring and diagnostics when more focused tests, like polymerase chain reaction (PCR), don't work. Poor assay design, the development of a novel disease, or the genetic evolution of an established pathogen could all be reasons for these assays to fail. Blood, stool, cerebrospinal fluid (CSF), urine, and nasopharyngeal swabs are the most frequently used samples for metagenomic sequencing in pathogen discovery, where researchers have tried to identify the etiological agent responsible for an infection or other clinical syndrome. For example, Ruff et al. (2020) study described 454 Roche sequencing to assemble and describe the genome of a novel rhabdovirus (Bas-Congo virus, or BASV) in one of the patient's acute serum samples during a fatal 2009 epidemic of acute hemorrhagic fever in the Democratic Republic of the Congo. Using bioinformatics techniques like BEAST and IQ-TREE, disease outbreaks may be tracked through the construction of phylogenetic trees, which show the evolutionary and transmission patterns of pathogens like viruses or bacteria (Owuor et al., 2021). Understanding the global spread of COVID-19 and other infectious diseases like Zika and Ebola need knowledge of this. 16S rRNA sequencing data is analyzed in microbiome investigations using platforms such as QIIME and MetaPhlAn (Chen et al., 2024). Researchers can better understand how microbial imbalances lead to diseases like obesity, diabetes, and inflammatory bowel disease by using these bioinformatics techniques, which shed light on the function of gut microbiota in health and illness (Chen et al., 2021).

This study establishes a framework for investigating the diverse uses of bioinformatics, emphasizing its revolutionary influence on scientific research and its capacity to tackle some of the most urgent issues confronting humanity at present.

## 2. Applications of Bioinformatics

### 2.1 Molecular Medicine

Transcriptome and genetic data are analyzed and interpreted using bioinformatics techniques. In order to shed light on the connection between genes and illness, this involves processing data from genome sequencing, genome assembly, gene expression analysis, and other processes.

Proteomics uses bioinformatics to predict protein structures, annotate functions, analyze protein interaction networks, and other tasks that advance our understanding of the role proteins play in the development and course of disease.

Drug targets, drug target interactions, drug metabolic pathways, and other information can be analyzed using bioinformatics techniques to aid in the development of new medications and to maximize the efficacy of already approved ones.

By evaluating individual genomic data and clinical information, bioinformatics can offer patients individualized treatment plans that can be used to forecast a patient's response to a particular medication, their likelihood of developing a hereditary condition, etc.

By evaluating individual genomic data and clinical information, bioinformatics can offer patients individualized treatment plans that can be used to forecast a patient's response to a particular medication, their likelihood of developing a hereditary condition, etc (Tang et al., 2022).

Bioinformatics methods were helpful in detecting mutations in the EGFR (epidermal growth factor receptor) gene in non-small cell lung cancer (NSCLC). These mutations cause unchecked cell proliferation, especially in exons 19 and 21. Through the use of high-throughput sequencing technologies and bioinformatics pipelines such as GATK (Genome Analysis Toolkit) and MuTect, researchers were able to identify these particular mutations in NSCLC patients (Qureshi et al., 2022).

### 2.2 Gene therapy

In order to help physicians make precise genetic diagnoses and decide if gene therapy is appropriate, bioinformatics techniques can be used to examine patients' genomic data and find and validate particular gene mutations or variations.

Gene editing instruments like CRISPR-Cas9 are designed and optimized in large part because of bioinformatics technologies. Improved accuracy and efficiency in gene editing can lead to precise repair or regulation of patient genes by examining the sequence features, structure, and functional information of target regions (Maule et al., 2020).

Viral or plasmid vectors-two types of gene delivery vectors-can be designed and optimized using bioinformatics. The most appropriate vector type and construction technique can be chosen to increase the effectiveness and safety of gene delivery by forecasting variables including immunogenicity, safety, and the interaction between the vector and target cells (Pai and Satpathy, 2021).

After gene therapy, data can be analyzed using bioinformatics to assess treatment effectiveness, track alterations in protein levels and gene expression, and forecast any negative reactions or side effects, all of which can improve treatment regimens.

By integrating the patient's unique genetic data with their clinical features, bioinformatics can assist in creating individualized gene therapy regimens. For instance, forecasting a patient's reaction and tolerance to particular gene therapies and modifying the frequency and dosage of treatments to optimize their safety and effectiveness (Fangyan, 2019).

Overall, the use of bioinformatics in gene therapy extends beyond the creation of new technologies and data analysis; it also emphasizes the utilization of genomic data and computational techniques to achieve precise and tailored gene therapy, offering patients with gene-related illnesses more effective treatment regimens.

Mutations in the SMN1 (Survival of Motor Neuron 1) gene result in a deficiency in the SMN protein, which is essential for motor neuron survival, and cause Spinal Muscular Atrophy (SMA), a hereditary condition. Weakness and eventual muscular atrophy are the outcomes of this insufficiency. Utilizing bioinformatics techniques, the SMN1 gene mutation was found to be the root cause of SMA. Comparative genomic analyses showed that, as a result of a splicing error, the SMN protein is produced by another gene, SMN2, albeit in smaller amounts. These gene sequences were mapped, genetic variants were identified, and the ways that distinct gene mutations cause SMA of variable severity were all made clear with the aid of bioinformatics. The FDA authorized Zolgensma, a gene therapy medication, in 2019 for the treatment of SMA. It functions by employing the AAV9 vector to transfer a functional copy of the SMN1 gene to motor neurons. In order to successfully develop the therapy, analyze clinical data, and make sure the medication reached its target cells, bioinformatics was essential (Lejman et al., 2023).

## 2.3 Drug development

A shift in the pharmacological development paradigm was identified. As genomic research advances, a vast amount of data and information becomes available. Bioinformatics can swiftly analyze and choose, assist in identifying new drug targets from massive data, and construct various computer-generated models to quickly and easily validate various hypotheses and direct biological activity screening, leading to the design or discovery of safer and more effective drugs. This process produces a new drug development model that includes target identification, target confirmation, lead compound discovery, lead compound optimization, clinical evaluation, and market launch. Modern novel drug research and development is now more focused and efficient, has a shorter cycle, and requires less R&D expenditure thanks to the creation of new models.

Finding the structure of a lead chemical that binds to the target protein and can be subsequently developed into a medication is the first stage in the drug development process. Therefore, the way biological macromolecules and ligands interact as well as identification data are crucial in drug design. As the three-dimensional structures of many biological macromolecules are known, there is an increasing focus on using bioinformatics techniques to identify lead compounds due to financial and experimental constraints. Currently, a few frequently employed techniques include de novo drug design, molecular docking, and three-dimensional structure searching (Li et al., 2020).

New medications like Osimertinib were designed to target both the initial EGFR mutations and the T790M resistance mutation in Non-Small Cell Lung Cancer (NSCLC) in order to overcome resistance, based on these bioinformatics discoveries (Shaikh et al., 2021). These next-generation treatments were designed and optimized in large part thanks to bioinformatics.

## 2.4 Microbiology

Microorganisms display polymorphisms in both space and time as a result of the high frequency of variation in the expression of microbial genetic material. A problem in the study of microbes. Specifically, the study of pathogenic microorganisms, including drug-resistant superbugs, the global spread of A(H1N1), and the widespread transmission of HIV. Thus, one of the main areas of interest for life science researchers has always been the study of harmful

microbes. Bioinformatics approaches enable the rapid and accurate realization of microbial typing, identification, and traceability analysis. They also facilitate the study of microbial disease and the creation of novel vaccines (Xiao et al., 2016).

Microbial identification, particularly the identification of recently found microbes, can be accomplished through the use of bioinformatics. Multilocus sequence typing (MLST) is one of the faster and more accurate DNA sequencing techniques (Boers et al., 2012).

Analysis of microbiological traceability can be done with it. The intricate phylogenetic relationships among microorganisms are astounding. In the subject of microorganism traceability analysis, one of the key applications of scientific methodologies is the construction of a phylogenetic tree to describe the evolutionary relationship between species or molecules.

To put together and annotate microbial genomes using sequencing data, bioinformatics is essential. Prokka, MEGAHIT, and SPAdes are among the tools used to reconstruct bacterial genomes from raw data. In addition to annotating genes and predicting their functions, these techniques also discover metabolic pathways and contribute to our understanding of the function of certain microbial species in the gut (Kayani et al., 2021).

## 2.5 Vaccine development

Ever since Group B *Neisseria* provided the first illustration of a vaccine developed from microbial genome sequences. Since the discovery of meningitides (MenB), genome-wide approaches to vaccine development have shown promise in the creation of innovative vaccinations against a variety of pathogenic microbes (Maurakis and Cornelissen, 2022). The advancements in microbial genomes and bioinformatics have introduced novel approaches to vaccine research. For instance, in order to obtain pertinent antibodies, researchers employed bioinformatics analysis software to predict extramembrane proteins and open reading frames (ORFs) for *Streptococcus haemosaea* (Liu et al., 2022).

Bioinformatics methods were utilized to optimize the codon usage of the mRNA sequence encoding the spike protein for mRNA vaccines such as Moderna's mRNA-1273 and Pfizer-BioNTech's BNT162b2. This guarantees that, in human cells, the mRNA gets translated into protein efficiently, increasing the production of the spike protein that sets off an immunological response (Blenke et al., 2023).

## 2.6 Oncology

The field of oncology makes extensive use of bioinformatics, which offers strong data support and analytical tools for cancer research, diagnosis, treatment, and prognosis. The Cancer Genome Atlas (TCGA), Gene Expression Profiling Interactive Analysis (GEPIA), The Database for Annotation Visualization and Integrated Discovery (DAVID), The Cancer Genome Atlas (TCGA), Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG), Search tool for the retrieval of interacting genes/proteins (STRING), etc. are among the databases frequently used in human cancer research. They collaborate to investigate tumors in bioinformatics and store a variety of data from many oncology-related fields (Barzaman et al., 2020; Zou et al., 2020).

The diagnosis of cancer also makes extensive use of bioinformatics. Notably, there has been notable advancement in the diagnosis of colorectal cancer, pancreatic cancer, breast carcinoma, and other cancers (Chan and Buczacki, 2021; Diaz-Cano, 2012).

Furthermore, big data analysis, bioinformatics, immunology, evolution and clone analysis, biomarker identification, tailored therapy, cancer immunology, and genomes and analysis of cancer can all benefit greatly from bioinformatics (Li et al., 2021).

Bioinformatics methods are utilized to sequence the exome, or protein-encoding region of the tumor, in patients with non-small cell lung cancer (NSCLC). Scientists are able to determine the somatic mutations responsible for tumor growth by using bioinformatics pipelines such as GATK (Genome Analysis Toolkit) (Pereira et al., 2020). It has been discovered that some gene mutations, such as those in EGFR (Epidermal Growth Factor Receptor), ALK (Anaplastic Lymphoma Kinase), and KRAS, are important in NSCLC (Uras et al., 2020).

### **2.7 Crop improvement**

In agricultural genetics and breeding, bioinformatics is becoming more and more significant. First, the examination of significant crop genomes is one of the many applications of bioinformatics. For instance, by effectively analyzing the genome sequences of rice, corn, wheat, and other crops using bioinformatics techniques, scientists have discovered numerous genes linked to significant agronomic qualities including yield, disease resistance, and adaptation. These results offer fresh breeding resources and a significant theoretical foundation for crop breeding (Chaudhry et al., 2020).

Secondly, one of the main areas of interest for bioinformatics study is the possible use and difficulty of genome editing technology in crop development. With the use of genome editing technology, such as the CRISPR/CAS9 system, crops' genomes can be precisely altered to improve specific agricultural attributes. For instance, scientists have effectively added weed resistance, disease resistance, insect resistance, and other features to crops using genome editing technology (Saini et al., 2023). The accuracy of gene editing, the off-target effect, and the residue of the gene editor are some of the difficulties associated with using genome editing technologies to improve crops.

In summary, a great deal of advancements have been achieved in the use of bioinformatics in crop breeding and genomics. Scientists have effectively studied the genomes of significant crops using bioinformatics techniques, and they have also produced novel breeding resources and the theoretical framework for crop breeding. In addition, the difficulties and possible uses of genome editing technologies in crop development provide bioinformatics researchers with a fresh perspective.

Using bioinformatics tools, scientists scan the whole genomes of several maize varieties to find certain genes or genetic markers linked to desired qualities like disease resistance, drought tolerance, and high yield. This process is known as the genome-wide association study (GWAS) of maize (Sahito et al., 2024). These analyses often involve the mapping of quantitative trait loci (QTL) related to variables such as yield or stress tolerance using programs like PLINK and TASSEL (Satrio et al., 2021). Using bioinformatics techniques, scientists analyze the whole genomes of several maize varieties to find certain genes or genetic markers linked to desired features like disease resistance, drought tolerance, and high yield. This process is known as genome-wide association study (GWAS) in maize. In these analyses, it is usual practice to map quantitative trait loci (QTL) related to traits such as yield or stress tolerance (Paudel et al., 2020).

### **2.8 Insect resistance**

Insect resistance research heavily relies on bioinformatics. In order to uncover genes and signaling pathways linked to insect resistance, researchers can investigate the genomes of plants and insects using high-throughput sequencing and genomics technologies. For instance, it is possible to identify and functionally validate insect-resistant genes by comparing the variations in gene expression between susceptible and insect-resistant plants. Furthermore,

gene-to-gene interactions can be predicted using bioinformatics methods, which aids in the understanding of the intricate web of insect resistance mechanisms (Uesaka et al., 2022; Hack and Kendall, 2005).

Furthermore, gene editing-based anti-insect techniques are developed through bioinformatics. For example, target genes can be precisely altered to increase a plant's resistance to insects using CRISPR-Cas9 technology (Borrelli et al., 2018). Gene editing procedures can be designed more effectively, their efficacy assessed, and potential off-target consequences predicted with the aid of bioinformatics techniques.

In summary, bioinformatics not only speeds up the identification and functional analysis of genes that confer insect resistance, but it also offers strong technological assistance for the creation of innovative insecticides.

One type of bacteria that naturally produces insecticidal proteins is *Bacillus thuringiensis* (Bt toxins) (Yamamoto, 2022). The identification and characterization of the particular Bt toxin genes (such as cry1Ac and cry2Ab) that are effective against particular pests, like the cotton bollworm (*Helicoverpa armigera*), a significant pest in the cotton producing industry, was done using bioinformatics tools like BLAST and InterPro (Yusoff et al., 2024).

## 2.9 Food Microbiology

Bioinformatics techniques can use high-throughput sequencing technologies to examine the composition of the microbial population in dietary samples. The microbial species and quantity present in the sample can be swiftly and precisely identified using 16S rRNA gene sequencing or whole genome sequencing, which aids in assessing the microbial quality and safety of food (Patel, 2001).

Pathogenic microorganisms in food, including bacteria (such as *Salmonella* and *Escherichia coli*), molds, and fungi, can be found and identified using bioinformatics (Liyana et al., 2020). Food samples with possible food safety concerns can be rapidly identified by cross-referencing sequencing data with database entries for known pathogenic microorganism genome sequences.

Yogurt, wine, and fermented meat products are examples of fermented foods whose microbial communities can be tracked and analyzed dynamically using bioinformatics techniques. This enhances the quality of the final product, optimizes fermentation conditions, and helps to understand the roles and interactions of microorganisms during the fermentation process (Bigot et al., 2015).

Microorganisms in food can have their origins traced using bioinformatics. Possible origins and paths of contamination can be identified by comparing the genetic traits and microbial community structure of food samples from various batches or geographical areas. This provides a scientific foundation for the management of food safety.

Bioinformatics can be used to track the origins of microorganisms found in food. By comparing the genetic characteristics and microbial community structure of food samples from different batches or regions, potential sources and routes of contamination can be found.

This gives the administration of food safety a solid scientific basis.

Overall, the use of bioinformatics in food microbiology helps to advance the field's understanding of food safety, quality, and fermentation processes while also accelerating the pace and accuracy of microbial community analysis. This is crucial for preserving public health and advancing the food industry.

Bioinformatics technologies are used in yogurt production to examine the microbial population that is included in the finished product. Researchers can identify the many bacterial species involved in fermentation by sequencing the 16S rRNA gene (Hu et al., 2020). Scientists

are able to characterize the microbial makeup of yogurt by processing the sequencing data using tools such as QIIME (Quantitative Insights Into Microbial Ecology) (Sola et al., 2021).

### **2.10 Forensic analysis of microbes**

Forensic experts can swiftly and precisely analyze DNA samples from crime scenes for person identification and paternity testing thanks to high-throughput sequencing and bioinformatics techniques. A bioinformatics program can separate the genetic information of various persons, assess a variety of DNA in mixed samples, and enhance the analysis of complex instances. Create and use a genetic variation database. Bioinformatics aids in the comparison and identification of people as well as the inference of their ancestry and geography. Bioinformatics can assist in determining the location and date of a corpse's death by examining the makeup and alterations of microbial communities. The effectiveness and precision of forensic analysis are considerably increased by these applications (Valdivia-Granda et al., 2015).

Microbial fingerprints for various settings or sources (such as soil, water, or animal feces) can be produced using bioinformatics techniques. Samples can be subjected to methods such as Amplified Fragment Length Polymorphism (AFLP) and Multilocus Sequence Typing (MLST) to ascertain their provenance (Ramadan, 2022).

### **2.11 Waste clean-up**

Bioinformatics can discover and optimize the microorganisms that degrade waste and increase the degradation efficiency through metabolomics and genome sequencing. Bioinformatics can monitor and assess treatment effects by utilizing high-throughput sequencing technologies to track changes in the microbial community in landfills and wastewater treatment plants. Bioinformatics assists in the design and optimization of gene editing techniques to create more effective waste-degrading strains through the use of technologies like CRISPR-Cas9. Toxic contaminants can be biodegraded efficiently by using bioinformatics to study microbial metabolic pathways (Sadraeian and Molaei, 2019).

Using bioinformatics tools such as Prokka, genomes of discovered bacteria can have their genes annotated. Particular attention should be paid to genes encoding hydrocarbon-degrading enzymes (e.g., cytochrome P450s, alkane monooxygenases) (Wang et al., 2023).

### **2.12 Bioenergy and Biofuels**

Scientists can screen and tune microbes to increase their efficiency in producing biofuels through genome sequencing and bioinformatics analysis. Researchers can improve biomass degradation and fuel generation capacities by designing and optimizing microbial metabolic pathways with the aid of bioinformatics tools. Bioinformatics helps change microbes to make them more adept in using varied raw materials to generate more biofuels through gene editing technologies like CRISPR-Cas9. Optimizing production settings and conditions, integrating multi-omics data, and building and simulating the biofuel production process can be done using bioinformatics tools (Misra et al., 2013).

Lignocellulosic biomass is made up of cellulose, hemicellulose, and lignin and is obtained from forestry wastes, agricultural residues, and other plant materials. Analyzing the genetic and metabolic processes that convert these components into fermentable sugars is made easier with the use of bioinformatics tools (Joshi et al., 2023).



### 3. Conclusion

In the field of biomedicine, bioinformatics has emerged as a vital tool that expedites the comprehension of disease mechanisms through the analysis and interpretation of intricate biological data. It also fosters the advancement of medical care, ecology, and other fields in a manner that is both economical and efficient. Bioinformatics will continue to be more significant in these domains due to the quick collection of biological data and the ongoing development of computing technology, particularly in the areas of multi-omics data integration, precision medicine, and AI-assisted decision-making.

### 4. Future directions

Integrating data from proteomics, metabolomics, transcriptomics, and genomics will enable a more thorough knowledge of biological systems. Understanding disease mechanisms, metabolic processes, and organismal reactions to environmental changes can all be improved by this combination. Predicting protein structures, identifying possible therapeutic targets, and analyzing complicated biological datasets will all be improved by utilizing AI and machine learning methods. Additionally, these technologies can increase the precision of transcriptomics and genome investigations. Bioinformatics will be used more and more in personalized medicine to enable individualized treatment recommendations based on patient genetic profiles. This includes pharmacogenomics, which uses a person's genetic composition to anticipate how they will react to drugs. The increasing amount of biological data makes cloud computing necessary for scalable data processing and storage. This will facilitate the efficient and cooperative processing of big datasets by academics. Bioinformatics tools that help with the creation and analysis of gene constructs for synthetic biology applications will promote advancements in CRISPR and other gene-editing technologies.

### References

- Allaby RG, Woodwark M. Phylogenetics in the bioinformatics culture of understanding. *Comparative and functional genomics*. 2004 Mar;5(2):128-46.
- Barzaman K, Karami J, Zarei Z, Hosseinzadeh A, Kazemi MH, Moradi-Kalbolandi S, Safari E, Farahmand L. Breast cancer: Biology, biomarkers, and treatments. *International immunopharmacology*. 2020 Jul 1;84:106535.
- Bigot C, Meile JC, Remize F, Strub C. Applications of metagenomics to fermented foods. *Fermented Foods, Part I (Biochemistry Biotechnol)*. 2015:333-46.
- Blenke EO, Örnskov E, Schöneich C, Nilsson GA, Volkin DB, Mastrobattista E, Almarsson Ö, Crommelin DJ. The storage and in-use stability of mRNA vaccines and therapeutics: not a cold case. *Journal of pharmaceutical sciences*. 2023 Feb 1;112(2):386-403.
- Boers SA, Van der Reijden WA, Jansen R. High-throughput multilocus sequence typing: bringing molecular typing to the next level. *PloS one*. 2012 Jul 18;7(7):e39630.
- Borrelli VM, Brambilla V, Rogowsky P, Marocco A, Lanubile A. The enhancement of plant disease resistance using CRISPR/Cas9 technology. *Frontiers in plant science*. 2018 Aug 24;9:1245.
- Chan DK, Buczacki SJ. Tumour heterogeneity and evolutionary dynamics in colorectal cancer. *Oncogenesis*. 2021 Jul 16;10(7):53.
- Chaudhry SM, Ahmed R, Shafiullah M, Huynh TL. The impact of carbon emissions on country risk: Evidence from the G7 economies. *Journal of environmental management*. 2020 Jul 1;265:110533.

- Chen J, Qin Z, Jia Z. The application status of sequencing technology in global respiratory infectious disease diagnosis. *Infection*. 2024 Aug 16;1-3.
- Chen Y, Zhou J, Wang L. Role and mechanism of gut microbiota in human disease. *Frontiers in cellular and infection microbiology*. 2021 Mar 17;11:625913.
- Dahiya BP. Bioinformatics impacts on medicine, microbial genome and agriculture. *Journal of pharmacognosy and phytochemistry*. 2017;6(4):1938-42.
- Diaz-Cano SJ. Tumor heterogeneity: mechanisms and bases for a reliable application of molecular marker design. *International journal of molecular sciences*. 2012 Feb 13;13(2):1951-2011.
- Doytchinov VV, Dimov SG. Microbial community composition of the Antarctic ecosystems: Review of the bacteria, fungi, and archaea identified through an NGS-based metagenomics approach. *Life*. 2022 Jun 18;12(6):916.
- Fangyan X. Advances in the Application of Gene Editing Technology in Gene Therapy [J]. *Biological Chemical Engineering*. 2019;2:162-5.
- Hack C, Kendall G. Bioinformatics: Current practice and future challenges for life science education. *Biochemistry and Molecular Biology Education*. 2005 Mar;33(2):82-5.
- Hu N, Lei M, Zhao X, Wang Y, Zhang Y, Wang S. Analysis of microbiota in Hainan Yucha during fermentation by 16S rRNA gene high-throughput sequencing. *Journal of food processing and preservation*. 2020 Jul;44(7):e14523.
- Joshi C, Sharma S, MacKinnon N, Masakapalli SK. Efficient system wide metabolic pathway comparisons in multiple microbes using genome to KEGG orthology (G2KO) pipeline tool. *Interdisciplinary Sciences: Computational Life Sciences*. 2020 Sep;12:311-22.
- Kayani MU, Huang W, Feng R, Chen L. Genome-resolved metagenomics using environmental and clinical samples. *Briefings in bioinformatics*. 2021 Sep;22(5):bbab030.
- Koppad S, Gkoutos GV, Acharjee A. Cloud computing enabled big multi-omics data analytics. *Bioinformatics and biology insights*. 2021 Jul;15:11779322211035921.
- Lejman J, Panuciak K, Nowicka E, Mastalerczyk A, Wojciechowska K, Lejman M. Gene therapy in ALS and SMA: advances, challenges and perspectives. *International journal of molecular sciences*. 2023 Jan 6;24(2):1130.
- Li M, Zhang Z, Li L, Wang X. An algorithm to quantify intratumor heterogeneity based on alterations of gene expression profiles. *Communications biology*. 2020 Sep 11;3(1):505.
- Li K, Du Y, Li L, Wei DQ. Bioinformatics approaches for anti-cancer drug discovery. *Current drug targets*. 2020 Jan 1;21(1):3-17.
- Liu Y, Zeng S, Wu M. Novel insights into noncanonical open reading frames in cancer. *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer*. 2022 Jul 1;1877(4):188755.
- Liyan LI, Wen WA, Jianyu SU. Application of Probiotics Detection in Food Microbiology Experiment. *Agricultural engineering*. 2020;10(5):101-3.
- Maurakis SA, Cornelissen CN. Recent progress towards a gonococcal vaccine. *Frontiers in cellular and infection microbiology*. 2022 Apr 11;12:881392.
- Maule G, Arosio D, Cereseto A. Gene therapy for cystic fibrosis: progress and challenges of genome editing. *International journal of molecular sciences*. 2020 May 30;21(11):3903.
- Misra N, Panda PK, Parida BK. Agrigenomics for microalgal biofuel production: an overview of various bioinformatics resources and recent studies to link OMICS to bioenergy and bioeconomy. *Omics: a journal of integrative biology*. 2013 Nov 1;17(11):537-49.
- Owuor DC. Sequence Diversity, Evolution and Transmission of Influenza A (H1N1) pdm09 and A (H3N2) Viruses in Kenya, 2009-2018. *Open University (United Kingdom)*; 2021.
- Pai JA, Satpathy AT. High-throughput and single-cell T cell receptor sequencing technologies. *Nature methods*. 2021 Aug;18(8):881-92.

- Patel JB. 16S rRNA gene sequencing for bacterial pathogen identification in the clinical laboratory. *Molecular diagnosis*. 2001 Dec;6:313-21.
- Paudel D, Dhakal S, Parajuli S, Adhikari L, Peng Z, Qian Y, Shahi D, Avci M, Makaju SO, Kannan B. Use of quantitative trait loci to develop stress tolerance in plants. In *Plant life under changing environment* 2020 Jan 1 (pp. 917-965). Academic Press.
- Pereira R, Oliveira J, Sousa M. Bioinformatics and computational tools for next-generation sequencing analysis in clinical genetics. *Journal of clinical medicine*. 2020 Jan 3;9(1):132.
- Qureshi R, Zou B, Alam T, Wu J, Lee VH, Yan H. Computational methods for the analysis and prediction of egfr-mutated lung cancer drug resistance: Recent advances in drug design, challenges and future prospects. *IEEE/ACM Transactions on Computational Biology and Bioinformatics*. 2022 Jan 10;20(1):238-55.
- Ramadan AA. Bacterial typing methods from past to present: A comprehensive overview. *Gene Reports*. 2022 Dec 1;29:101675.
- Ruff TM, Marston EJ, Eagle JD, Sthapit SR, Hooker MA, Skinner DZ, See DR. Genotyping by multiplexed sequencing (GMS): a customizable platform for genomic selection. *PLoS One*. 2020 May 1;15(5):e0229207.
- Sadraeian M, Molaee Z. Bioinformatics analyses of *Deinococcus radiodurans* in order to waste clean up. In *2009 second international conference on environmental and computer science* 2009 Dec 28 (pp. 254-258). IEEE.
- Sahito JH, Zhang H, Gishkori ZG, Ma C, Wang Z, Ding D, Zhang X, Tang J. Advancements and prospects of genome-wide association studies (GWAS) in maize. *International Journal of Molecular Sciences*. 2024 Feb 5;25(3):1918.
- Saini H, Thakur R, Gill R, Tyagi K, Goswami M. CRISPR/Cas9-gene editing approaches in plant breeding. *GM Crops & Food*. 2023 Dec 31;14(1):1-7.
- Satrio RD, Fendiyanto MH, Supena ED, Suharsono S, Miftahudin M. Genome-wide SNP discovery, linkage mapping, and analysis of QTL for morpho-physiological traits in rice during vegetative stage under drought stress. *Physiology and Molecular Biology of Plants*. 2021 Nov;27(11):2635-50.
- Shaikh M, Shinde Y, Pawara R, Noolvi M, Surana S, Ahmad I, Patel H. Emerging approaches to overcome acquired drug resistance obstacles to osimertinib in non-small-cell lung cancer. *Journal of medicinal chemistry*. 2021 Jul 29;65(2):1008-46.
- Sola L, Quadu E, Bortolazzo E, Bertoldi L, Randazzo CL, Pizzamiglio V, Solieri L. Insights on the bacterial composition of Parmigiano Reggiano natural whey starter by a culture-dependent and 16S rRNA metabarcoding portrait. *Scientific reports*. 2022 Oct 15;12(1):17322.
- Supriya P, Marudamuthu B, Soam SK, Rao CS. Trends and application of data science in bioinformatics. *Trends of Data Science and Applications: Theory and Practices*. 2021:227-44.
- Tang A, Woldemariam S, Roger J, Sirota M. Translational bioinformatics to enable precision medicine for all: elevating equity across molecular, clinical, and digital realms. *Yearbook of medical informatics*. 2022 Aug;31(01):106-15.
- Uddin M, Mustafa F, Rizvi TA, Loney T, Al Suwaidi H, Al-Marzouqi AH, Kamal Eldin A, Alsabeeha N, Adrian TE, Stefanini C, Nowotny N. SARS-CoV-2/COVID-19: viral genomics, epidemiology, vaccines, and therapeutic interventions. *Viruses*. 2020 May 10;12(5):526.

- Uesaka K, Oka H, Kato R, Kanie K, Kojima T, Tsugawa H, Toda Y, Horinouchi T. Bioinformatics in bioscience and bioengineering: recent advances, applications, and perspectives. *Journal of bioscience and bioengineering*. 2022 Nov 1;134(5):363-73.
- Uras IZ, Moll HP, Casanova E. Targeting KRAS mutant non-small-cell lung cancer: past, present and future. *International Journal of Molecular Sciences*. 2020 Jun 17;21(12):4325.
- Valdivia-Granda WA. Bioinformatics for biodefense: challenges and opportunities. *Biosecurity and bioterrorism: biodefense strategy, practice, and science*. 2010 Mar 1;8(1):69-77.
- Wani MY, Ganie NA, Rani S, Mehraj S, Mir MR, Baqual MF, Sahaf KA, Malik FA, Dar KA. Advances and applications of Bioinformatics in various fields of life. *International journal of fauna and biological studies*. 2018;5(2):03-10.
- Wang M, Ding M, Yuan Y. Bioengineering for the microbial degradation of petroleum hydrocarbon contaminants. *Bioengineering*. 2023 Mar 10;10(3):347.
- Xiao YC, Xiong H, Xie C, Lü NH. Research Progress on the application of bioinformatics in prediction and molecular design of antimicrobial peptide. *Biotechnology bulletin*. 2016 Dec 25;32(12):23.
- Yamamoto T. Engineering of *Bacillus thuringiensis* insecticidal proteins. *Journal of Pesticide Science*. 2022 May 20;47(2):47-58.
- Yussoff MA, Hassan M, Mohd-Assaad N, Othman NW, Sulaiman S, Abidin CM, Muhammad NA. In silico prediction of effector proteins in oil palm pest, *Metisa plana*. *Journal of Asia-Pacific Entomology*. 2024 Dec 1;27(4):102308.
- Zou S, Tong Q, Liu B, Huang W, Tian Y, Fu X. Targeting STAT3 in cancer immunotherapy. *Molecular cancer*. 2020 Dec;19:1-9.