

# Biotechnological Applications Of Bioinformatics In The Post Genomic ERA

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**Abstract**— The huge data gleaned from genomes sequencing including (DNA, RNA, protein sequences, structures and interactions, genes, chromosomal maps, pathways, networks, biological signals and images) has led to explosive and diverse growth in biological data that presents the urgent need for intensive computing and big data analysis techniques potential for their storage, organization, analysis and integration. Bioinformatics has come to play this major role and the pursuit for future biological discoveries. It is widely accepted that bioinformatics coupled with the high throughput sequencing technologies has paved the way for the post-genomic era and will become an essential and indispensable part of the future of life sciences and molecular medicine.

This review discusses and surveys the concepts and progress of bioinformatics and highlights their recent biotechnological applications in post genomics era, in many fields starting with basic and applied future life sciences where the philosophy and style of both research and knowledge has changed. Furthermore, discusses their related applications in molecular medicine and microbial genome, as well as summarizes all their possible biotechnological applications in agriculture, energy and environment.

**Key words:** *bioinformatics, genome, post genomics, sequencing, biotechnological applications*

## I." INTRODUCTION

During the early 1960s, computer sciences emerged as important tools in studying molecular biology. In 1970 Bioinformatics term was coined by Paulien Hogeweg and Ben Hesper for "the study of informatics processes in biotic systems" (1).

While bioresearchers collect and submit a high amount of different scientific data, including Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA), and amino acid sequences, protein structures and biological pathways, and biological signals from diverse origin, bioinformaticians use mathematical, statistical and computing methods to store, visualize, and analyze these wealthy data to solve complex biological problems. (2).

With the fully sequenced genomes including Human Genome Project, the biological data increased tremendously.

This led to the explosive growth of bioinformatics of post- and meta genomic era which will become an indispensable part of the future of life sciences and genomic medicine. In this review we define bioinformatics in pre and post genomic era, and discuss the impact of next-generation sequencing on their progress, Furthermore, we highlight their recent biotechnological applications in different areas of life.

## II." BIOINFORMATICS IN PRE AND POST- GENOMIC ERA

Bioinformatics in the pre genomic era was very classical and deal primarily with nucleotides and amino acids sequence analysis ,and defined according Fredj Tekaia as "The mathematical, statistical and computing methods that aim to solve biological problems using DNA and amino acid sequences and related information." (3)

While Post-genomic bioinformatics began in the 1990s with the dramatic increase in the number of fully sequenced genomes, including the Human Genome Project (HGP) coupled with the advent of high throughput sequencing technologies and platforms has led to explosive and diverse growth in biological data that presents the urgent need for intensive computing techniques potential for their storage, organization, analysis and integration. Bioinformatics has come to play this major role and the pursuit of future biological discoveries.

By recent biotechnological advances accompanied by huge data diversity (like DNA and protein sequences, genes and chromosomal maps , protein structures, pathways, networks, and biological signals) and development in genomics technologies, bioinformatics continues to be a new concept, generating different but related areas of research such as transcriptomics, proteomics, metabolomics, metagenomic and pharmacogenomics , it is widely accepted that bioinformatics and NGS has paved the way for the post-genomic era and will become an essential and indispensable part of the future of life sciences and genomics medicine. (4)

### A. next-generation sequencing platforms

In recent past years several platforms of next-generation sequencing (NGS) with varied features and clear advantages have been developed for multiple applications (5) Fig.1

### III.<sup>o</sup> BIOTECHNOLOGICAL APPLICATIONS OF BIOINFORMATICS

Diverse applications ranging from biomedical field to food, agriculture, energy and environment, were summarized in table 1

TABLE 1. BIOTECHNOLOGICAL APPLICATIONS OF BIOINFORMATICS

Application Field		Examples / details	Ref.
Major	Minor		
Biology	microbiomics	studying microbial genome sequences to search for virulence and antibiotic resistance genes	(25)
		Identification and characterization of microbes	
	viromics	Studying viral community and diversity in saline desert and in Antarctic dry valleys	(8,9)
	genomics	Gene prediction and genome annotation	
	metagenomics	analysis of DNA sequences recovered from environmental samples	(32 )
	Metatranscriptomics	provides information on the regulation and expression profiles of complex communities	( 23)
	glycomics	integrated genomic, transcriptomic and proteomic data to detect glycosylated proteins and glycosylation enzyme and there alterations implicated in development of cancer and autoimmunity disorders	(26,27 ,28 )
	Evolutionary Biology	Studying evolutionary relationships between organisms via comparative genomics and phylogenetic analysis	(51 )
Biotechnol ogy	Biodiversity protection	Application of informatics techniques to biodiversity information for improved management, presentation, discovery, exploration and analysis. It typically builds on a foundation of taxonomic, biogeographic, or ecological information stored in digital form	(52 )
	Microbial biotechnology	discovery of new genes, enzymes, and natural products via metagenomic	(13 )
		development of fine chemicals, agrochemicals and pharmaceuticals	(14 )
	Human,animal, plant, and microbial biotechnology	metagenomic data bioprospecting	(15)
Medicine	Molecular medicine	Or clinical genomics that solving clinical problems using molecular biology information and bioinformatics approaches	(50 )
	Personal genomics	or consumer genetics branch of genomics concerned with the sequencing, analysis and interpretation of the genome of an individual	(48 )
	Personalised medicine	Medical method that targets patient's genes, proteins, and environment as the primarily factors analyzed to prevent,	

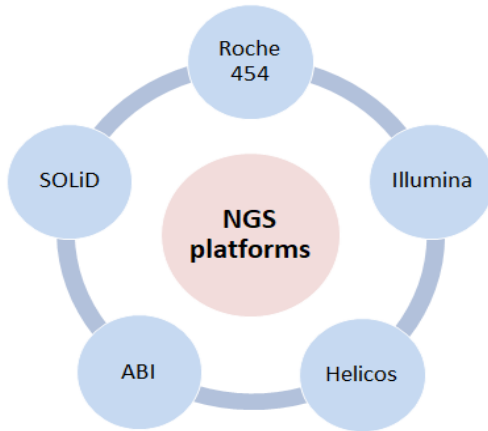


Fig.1 the most famous NGS platforms

#### B. Bioinformatics for NGS big data

While high throughput sequencing technologies opens many challenges for bioinformatics to store, organize, and analyze, the huge raw big data generated, poses also a problematic for information mining and interpretation, for example , the average NGS experiment generates terabytes of raw data. Furthermore, the bio big data generated through NGS across the world in research laboratories were characterized by their ‘Volume , Variety ,Velocity, Veracity, visualization and Value’ (6) Fig.2.

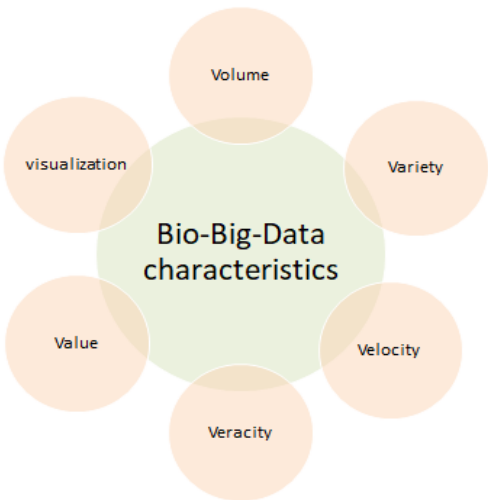


Fig.2 Bio-Big-Data characteristics

Application Field		Examples / details	Ref.
Major	Minor		
		diagnose, and treat disease.	(49 )
	Predictive medicine	field of medicine that utilizes information, often obtained through personal genomics techniques, to both predict the possibility of disease, and institute preventative measures for a particular individual	
	Preventative medicine	an emerging medical discipline that involves using genomic information about an individual as part of their clinical care (e.g., for diagnostic or therapeutic decision-making)	
	Genomic medicine	development and optimization of success personalized gene therapies via multi-omic tools and systems biology	(64 )
	Gene therapy	Processing different types of epigenetic data, prediction of chromatin states, and study of protein dynamics via computational methods to avoid serious pathologies, such as neurological disorders affecting brain development, neurodegeneration, and intellectual disability	(59 )
	Epigenomic	understand human microbiome changes that can be correlated with human health and diseases	(47,60 )
	Human microbiomic	human gut resistome ,Gut microbe characterization	(20 )
		phylogenetic diversity analysis of gastrointestinal bacteria through metagenomic techniques	(8 )
		Emerging evidence linking the gut microbiome to neurologic disorders	(21 )
		Bioinformatics and functional analysis of oncogenes which improve prognosis, diagnosis, and therapy	(63 )
	oncogenomics	integrated genomics, transcriptomics and proteomics to understand the molecular mechanisms that underlie the cancer development	(61 )
	Operomics	Studying host-microbe interactions involved in disease Infectious disease diagnosis via metagenomic techniques	(62 )
	Pathogenomics	Person's , gender and parentage identification	(22 )
	Legal and forensic medicine	Animal genetics, and genomic approaches for animal breeding ,conservation and genetic resources management	(24 )
	Animal diversity conservation	metagenomic approaches improve livestock disease detection and vaccine development from genomes sequencing	(57 )
	Animal health		(56 )
Application Field		Examples / details	Ref.
Major	Minor		
Pharmacology	Pharmaceutical Bioinformatics	Studying biological and chemical processes in the pharmaceutical area; to understand how xenobiotics interact with the human body and the drug discovery process.	( 55 )
	pharmacogenomics	Pharmacogenomics involves using an individual's genome to determine whether or not a particular therapy, or dose of therapy, will be effective	(16 )
		malacidin antibiotics drug discovery using metagenomic	
	Antibiotic resistance	Studying bacterial genome Sequences to search for antibiotic resistance genes (resistome).	(7 )
Food	Food processing	functional genomics, proteomics and metabolomics is providing precisely the knowledge necessary to readdress food processing using bimolecular activities	(41 )
	food quality and safety	predict the behavior of normal organisms or GMOs	(34 )
		molecular characterization of bacterial food borne pathogens using microarrays	(33,38 )
		evaluating allergenicity for genetically modified foods	(35,36 )
	nutritional quality	Improve the nutritional quality by selecting the best nutritional crop varieties via comparative genomics	(43 )
	fermented foods improvement	understanding microbial metabolism of food desirable microbes to develop the best organoleptic properties via bioinformatics approaches specially metabolomics	(44 )
	Food flavour	Comparative genomics of enzymes in flavor-forming pathways from amino acids in lactic acid bacteria.	( 37 )
	Food taste	Identifying the molecular and genetic basis of the taste receptors(sweet, salt, sour, better, and umami)	( 39,40 )
	Foodomics	studying Food and Nutrition domains through the application and integration of advanced - omics technologies to improve consumer's well-being, health, and knowledge	( 46 )
	Food microbial informatics	predicting and assessing the desired and undesired effects of microorganisms on food using panomic analysis tools and data bases	(45 )
Agriculture	Terragenome	The complete sequencing of a soil metagenome (i.e., the genomes of all microorganisms inhabiting the soil environment)	(31 )
	Drought resistant crops	Selecting the drought resistant crop varieties via comparative genomics	( 42 )
	Insect resistance crops	Selecting and developing insect and pest resistant crop varieties	( 58 )

Application Field		Examples / details	Ref.
Major	Minor		
		via integrated comparative genomics and <i>Bacillus thuringiensis</i> genome mapping	
	Crop health improvement	Functional metagenomic explore plants microbes interactions	( 18 )
		Plant genomics and metagenomic approaches improve crops disease detection	(19 )
	Crop nutritional quality improvement	genetically modified rice contains more Vitamin A	(58 )
	horticulture	Plant genetic amelioration via comparative genomics	
	agricultural biowarfare and bioterrorism	Strong phytopathogens creation via virulence genomics	(66)
Environment/ecology	Bioremediation /Waste cleanup	Enhance the success of bioaugmentation or biostimulation trials	(12)
		improve monitoring and cleaning up strategies via microbial metagenomic	
		Reduce the impact of pollutants on ecosystems and recovery of contaminated environments	
	Climate change Studies	study the genomes of microbes utilizing CO <sub>2</sub> as sole carbon source	( 53,54)
		Multiplex data from genomic, transcriptomic, proteomic, and metabolomics studies on cyanobacteria	
	Water/air analysis	Water, debris of filtered air, and dirt metagenomic analyses can establish the range of invasive and endangered species, and track seasonal populations.	(17)
	Metagenomic/ environmental genomics/ ecogenomics	Studying the genetic material recovered directly from environmental samples	( 29 )
	microbial ecology	Studying microbial biodiversity and ecology via metagenomic techniques	(30)
Energy	Biodiversity Informatics	construction of computerized taxonomic databases	(52 )
	Biofuel	Studying microbial consortia (association) that produce biodiesel and transform the cellulose into sugars and fermented into ethanol.	(10 )
		Studying microbes that produce methane and hydrogen.	
	Biogas	Studying biogas fermenting microbial communities	(11)
Military	Bio-weapon creation	design and development of new bioweapons via genomics research	(67)
Archaeology	Archaeogenomics and phylogeny	comparative genomics analyses and functional annotation of the completely sequenced archaeal genomes	(68)
	Computational archaeology	Computational approaches were used to elucidate the molecular	(70)

Application Field		Examples / details	Ref.
Major	Minor		
		archaeology of the E. coli genome, this involved the identification of foreign DNA introduced by horizontal gene transfer (HGT).	
	Paleogenomics	Studying human evolution via comparative archaic paleogenomics	(69)
	Biomolecular archaeology	The study of ancient DNA, recovered primarily from fossilized bones and teeth.	(71)
	Paleopathogen genomics	sequencing of pathogen and parasite DNA from archived and archaeological remains	(72)

#### IV." CONCLUSION

We hope that this review will assist bioinformaticians and biologists for better understanding the crucial roles of bioinformatics in present and future biological discoveries which will find there expanding applications in all life sectors.

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#### REFERENCES

- [1] S. A. Sousa, J. H. Leitão, R. C. Martins, J. M. Sanches, J. S. Suri, and A. Giorgetti , Bioinformatics Applications in Life Sciences and Technologies, Biomed Res Int.,vol 2016,pp 3603827,2016.
- [2] S.Gupta, Bioinformatics—Research Applications. In: Fulekar M.H. (eds) Bioinformatics: Applications in Life and Environmental Sciences. Springer, Dordrecht,2009
- [3] D.Mende, R., Alison , S. Waller, S. Shinichi ,I. Aino ,M. Järvelin, M. Chan; A.Manimozhiyan ,R. Jeroen ,and B. Peer , "Assessment of Metagenomic Assembly Using Simulated Next Generation Sequencing Data". PLoS ONE. Vol. 7 ,2,pp e31386K,2012.
- [4] RR. Gullapalli, KV. Desai, L Santana-Santos, JA Kant,and MJ. Becich , Next generation sequencing in clinical medicine: challenges and lessons for pathology and biomedical informatics. J Pathol Inform.,vol. 3,pp 40,2012.
- [5] SK. Shivakumar, 2013. Big Data – a big game changer. CSI Communications, - csi-india.org
- [6] GD. Wright, "The antibiotic resistome: the nexus of chemical and genetic diversity". Nature Reviews Microbiology.vol. 5, 3, pp175–186, March 2007.
- [7] S.Willem van , The human gut resistome, Philos Trans R Soc Lond B Biol Sci.,vol.370,1670,pp20140087. Jun 2015.
- [8] C.Kerepesi, and V. Grolmusz , "Giant Viruses of the Kutch Desert". Archives of Virology. Vol.161 ,3,pp 721–724, 2016.
- [9] C.Kerepesi, and V. Grolmusz, "The "Giant Virus Finder" Discovers an Abundance of Giant Viruses in the Antarctic Dry Valleys". Archives of Virology. Vol.162 ,6,pp 1671–1676,2017.
- [10] Li, Luen-Luen, S. R McCorkle, S. Monchy, S. Taghavi,and D. van der Lelie (18). "Bioprospecting metagenomes: glycosyl hydrolases for converting biomass". Biotechnology for Biofuels.vol. 2,pp 10. May 2009.
- [11] S. Jaenicke, A. Christina ,B Thomas ,B. Regina ,D. Marcus ,G. Karl-Heinz Gartemann, S.Jünemann,K.Olaf ,K. Lutz ,T. Felix , M.

- Zakrzewski, A. Pühler, A. Schlüter, A. Goesmann (26). K. Aziz, Ramy K, ed. "Comparative and Joint Analysis of Two Metagenomic Datasets from a Biogas Fermenter Obtained by 454-Pyrosequencing". *PLoS ONE*. vol. 6, 1, pp e14519, January 2011.
- [12] I. George, et al. "Application of Metagenomics to Bioremediation". *Metagenomics: Theory, Methods and Applications*. Caister Academic Press. 2010, ISBN 978-1-904455-54-7.
  - [13] C. Simon, and R. Daniel, "Metagenomic Analyses: Past and Future Trends". *Applied and Environmental Microbiology*. Vol. 77, 4, pp 1153–1161, 2010.
  - [14] D. Wong, "Applications of Metagenomics for Industrial Bioproducts". *Metagenomics: Theory, Methods and Applications*. Caister Academic Press. 2010, ISBN 978-1-904455-54-7.
  - [15] N.P. Skorupa, F. Marie, and G. Grauslund, "Isolation of xylose isomerases by sequence- and function-based screening from a soil metagenomic library". *Biotechnology for Biofuels*. vol. 4, 1, pp 9, 2011
  - [16] B.M. Hover, S. Kim, M. Katz, Z. Charlop-Powers, J.G. Owen, M.A. Ternei, et al. "Culture-independent discovery of the malacidins as calcium-dependent antibiotics with activity against multidrug-resistant Gram-positive pathogens". *Nature Microbiology*. vol. 3, 4, pp 415–422, Feb. 2018.
  - [17] What's Swimming In The River? Just Look For DNA". [www.npr.org](http://www.npr.org). 24 July 2013. Retrieved 10 October 2014.
  - [18] T. Charles, "The Potential for Investigation of Plant-microbe Interactions Using Metagenomics Methods". *Metagenomics: Theory, Methods and Applications*. Caister Academic Press. 2010. ISBN 978-1-904455-54-7.
  - [19] Committee on Metagenomics: Challenges and Functional Applications, National Research Council (2007). *The New Science of Metagenomics: Revealing the Secrets of Our Microbial Planet*. Washington, D.C.: The National Academies Press. 2007. ISBN 978-0-309-10676-4.
  - [20] K.E. Nelson, and B.A. White "Metagenomics and Its Applications to the Study of the Human Microbiome". *Metagenomics: Theory, Methods and Applications*. Caister Academic Press. 2010, ISBN 978-1-904455-54-7.
  - [21] G. Suen, J. Jarrod, F. Scott, O. Aylward, M. Sandra, S. Adams, G. Tringe, A. Adrián, T. Pinto, E. Clifton, Foster, P. Markus, P. J. Weimer, W. Kerrie, L. Barry, A. Goodwin, P. Bouffard, L. Lewyn, Jolene Osterberger, T. T. Harkins, C. Steven, Slater, Timothy J. Donohue, Cameron R. Currie. Sonnenburg, Justin, ed. "An insect herbivore microbiome with high plant biomass-degrading capacity". *PLoS Genetics*. Vol. 6, 9, pp e1001129, 2010.
  - [22] M. J. Pallen, and B.W. Wren, "Bacterial Pathogenomics". *Nature*. Vol. 449, 7164, pp 835–842, 2007.
  - [23] C. Simon, and R. Daniel, "Metagenomic Analyses: Past and Future Trends". *Applied and Environmental Microbiology*. Vol. 77, 4, pp 1153–1161, 2010.
  - [24] M. sidra tul muntaha, U. mirza jawad, K. waqas ahmad, R. fahad, M. tariq pervez and H. tanveer, role of bioinformatics in forensic science, *fuust j. biol.*, vol. 8, 1, pp 133 – 138, 2018.
  - [25] D. Golemboski, Application of Bioinformatic Tools for the Identification and Characterization of Microbes in the Medical Microbiology Laboratory, *Clin Lab Sci*, vol. 28, 1, pp 19, 2015.
  - [26] B.J. Campbell, L.G. Yu, and J.M. Rhodes, Altered glycosylation in inflammatory bowel disease: a possible role in cancer development. *Glycoconj J*, vol. 18, 11–12, pp 851–8, 2001.
  - [27] A. Varki, R. Kannagi, and B.P. Toole, Glycosylation Changes in Cancer, in *Essentials of Glycobiology*, A. Varki, et al., Editors. Cold Spring Harbor (NY). 2009.
  - [28] G. Lauc, A. Vojta, and V. Zoldos, Epigenetic regulation of glycosylation is the quantum mechanics of biology. *Biochim Biophys Acta*, vol. 1840, 1, pp 65–70, 2014.
  - [29] J. Raes, I. Letunic, T. Yamada, L. Jensen, and P. Bork, "Toward molecular trait-based ecology through integration of biogeochemical, geographical and metagenomic data". *Molecular Systems Biology*. vol. 7, pp 473, 2011.
  - [30] T.M. Vogel, P. Simonet, J. Jansson, K. Hirsch, P. R. Tiedje, J. M.; Van Elsas, J. D.; Bailey, M. J. Nalin, R., and L. Philippot. "TerraGenome: A consortium for the sequencing of a soil metagenome". *Nature Reviews Microbiology*. vol. 7, 4, pp 252, 2009.
  - [31] <http://www.terragenome.org/>
  - [32] N. Segata, D. Boernigen, L. Timothy, T. Xochitl, C. Morgan, S. Wendy Garrett, and H. Curtis, "Computational meta'omics for microbial community studies". *Molecular Systems Biology*. vol. 9, 666, pp 666, 2013.
  - [33] H. Fang, J. Xu, D. Ding, S.A. Jackson, I.R. Patel, et al. An FDA bioinformatics tool for microbial genomics research on molecular characterization of bacterial foodborne pathogens using microarrays. *BMC Bioinformatics*, vol. 11, pp S4, 2010.
  - [34] J.A. Jenkins, S. Griffiths-Jones, P.R. Shewry, H. Breiteneder, and E.C. Mills, Structural relatedness of plant food allergens with specific reference to cross-reactive allergens: an in silico analysis. *J Allergy Clin Immunol*, vol. 115, pp 163–170, 2005.
  - [35] M.W. Fiers, G.A. Kleter, H. Nijland, A.A. Peijnenburg, J.P. Nap, et al., Allermatch, a webtool for the prediction of potential allergenicity according to current FAO/WHO Codex alimentarius guidelines. *BMC Bioinformatics*, vol. 5, pp 133, 2004.
  - [36] A. Mari, E. Scala, P. Palazzo, S. Ridolfi, D. Zennaro, et al., Bioinformatics applied to allergy: allergen databases, from collecting sequence information to data integration. The Allergome platform as a model. *Cellular immunol*, vol. 244, pp 97–100, 2006.
  - [37] M. Liu, A. Nauta, C. Francke, and R.J. Siezen, Comparative genomics of enzymes in flavor-forming pathways from amino acids in lactic acid bacteria. *Appl Environ Microbiol*. vol. 74, pp 4590–4600, 2008.
  - [38] S. Brul, F. Schuren, R. Montijn, B.J. Keijser, H. Van Der Spek, et al. (2006) The impact of functional genomics on microbiological food quality and safety. *Int J Food Microbiol*, vol. 112, pp 195–199, 2006.
  - [39] H. Matsunami, J.P. Montmayeur, and L.B. Buck, A family of candidate taste receptors in human and mouse. *Nature*, vol. 404, pp 601–604, 2000.
  - [40] M. Max, Y.G. Shanker, L. Huang, M. Rong, Z. Liu, et al. Tas1r3, encoding a new candidate taste receptor, is allelic to the sweet responsiveness locus Sac. *Nature genetics*, vol. 28, pp. 58–63, 2001.
  - [41] F. Desiere, B. German, H. Watzke, A. Pfeifer, S. Saguy, S. Bioinformatics and data knowledge: the new frontiers for nutrition and foods. *Trends Food Sci Technol*, vol. 12, pp 215–229, 2001.
  - [42] K. S. Mochida, Genomics and bioinformatics resources for crop improvement. *Plant and Cell Physiol.*, vol. 51, pp 497–523, 2010.
  - [43] R.D. Pridmore, D. Crouzillat, C. Walker, S. Foley, R. Zink, et al. Genomics, molecular genetics and the food industry. *J Biotechnol*. vol. 78, pp 251–258, 2000.
  - [44] K.M. Waidha, N. Jabalia, D. Singh, A. Jha, and R. Kaur, (2015) Bioinformatics Approaches in Food Industry: An Overview, PP1–4, 2015.
  - [45] W. Alkema, J. Boekhorst, M. Wels, and S.A. van Hijum, Microbial bioinformatics for food safety and production. *Brief Bioinform*, vol. 17, pp 283–292, 2016.
  - [46] A. Cifuentes, "Food analysis and Foodomics". *J. Chromatogr. A*. vol. 1216, 43, pp 7109, 2009.
  - [47] B.E. Bernstein, A. Meissner, and E.S. Lander, "The mammalian epigenome". *Cell*. Vol. 128, 4, pp 669–81. Feb 2007.
  - [48] NCI Dictionary of Cancer Terms". National Cancer Institute. 2011-02-02. Retrieved 5 December 2016.
  - [49] Predictive medicine - Latest research and news | Nature". [www.nature.com](http://www.nature.com). Retrieved 5 December 2016.
  - [50] R. B. Altman, Bioinformatics in support of molecular medicine. *Proc AMIA Symp*. pp 53–61, 1998.
  - [51] R. Lyons, M. Settles, S. Iyer, and L. Forney, Initiative for Bioinformatics and Evolutionary Studies Core Laboratories: A Multidisciplinary Resource for High-Throughput Biomedical Studies, *J Biomol Tech*, vol. 21, 3 Suppl, pp S75–S76, Sep 2010.
  - [52] OECD Megascience Forum Working Group on Biological Informatics (1999). Final Report of the OECD Megascience Forum Working Group on Biological Informatics, January 1999. pp. 1–74.
  - [53] S. Subrata, Role of Bioinformatics in Climate Change Studies, *Journal Of Science*, Vol. 1, 1, 2015.

- [54] C. Gupta, D. Prakash, and S. Gupta, Role of microbes in combating global warming. *Int. J. Pharm. Sci. Lett.*, vol. 4,2, pp359-363,2014.
- [55] Introduction to Pharmaceutical Bioinformatics, (ISBN 978-91-979403-0-6), Oakleaf Academic, 2015
- [56] O. Kehinde, Soetan, and E. A.J. Awosanya, Bioinformatics and its application in animal health: a review, *Tropical Veterinarian*, vol.33,pp1-2,2015
- [57] WE. Johnson, and K. Koepfli , The role of genomics in conservation and reproductive sciences. *Adv Exp Med Biol. Vol.753*,pp71-96,2014.
- [58] S. Shouche ,and S. Rahangadale , Bioinformatics and horticulture. *Horticult Int J.* ,vol.2,1,pp15,2015.
- [59] F. Mac Gabhann, B. H. Annex, and S. Aleksander ,Gene Therapy from the perspective of Systems Biology ,*Curr Opin Mol Ther. Vol.12*,1,pp. 570–577. Oct 2010.
- [60] VE. Angarica, and A.Del Sol, Bioinformatics Tools for Genome-Wide Epigenetic Research. *Adv Exp Med Biol.*,vol.978,pp 489-512, 2017.
- [61] A. Gonzalez-Perez, V. Mustonen,B. Reva,GR. Ritchie,P. Creixell, P.Karchin , et al. , "Computational approaches to identify functional genetic variants in cancer genomes". *Nat. Methods. Vol.10* ,8,pp 723–9, August 2013.
- [62] SM. Hanash, "Operomics: molecular analysis of tissues from DNA to RNA to protein". *Clin. Chem. Lab. Med. Vol.38* ,9, 805–13 , Sept.2000
- [63] A. J. Griffiths, and K. S. Mazmanian, Emerging evidence linking the gut microbiome to neurologic disorders ,*Genome Medicine*,vol.10,pp 98, 2018.
- [64] LA. Hindorff, P. Sethupathy, HA. Junkins, et al. Potential etiologic and functional implications of genome-wide association loci for human diseases and traits. *Proc Natl Acad Sci USA. Vol.106*,pp9362–7,2009.
- [65] <https://www.genome.gov/27552451/what-is-genomic-medicine/>
- [66] M.L. Wheelis, The threat of agricultural biowarfare and bioterrorism: an analytical framework, (in preparation)
- [67] M . Claire. Fraser, and R. Dando ,Malcolm,Genomics and future biological weapons: the need for preventive action by the biomedical community , *Nature Genetics* ,vol. 29, pp 253–256 ,2001.
- [68] J.Thijs ,G. Ettema, M. de Vos Willem ,and J. van der Oost ,Discovering novel biology by in silico archaeology ,*Nature Reviews Microbiology* vol. 3, pp 859–869 ,2005.
- [69] C.Lalueza-Fox, and MT. Gilbert, Paleogenomics of archaic hominins. *Curr Biol.* , vol.21,24, pp R1002-9. Dec 2011 .
- [70] JG. Lawrence, and H. Ochman, Molecular archaeology of the *Escherichia coli* genome. *Proc Natl Acad Sci USA.*,vol. 95 ,16,pp 9413-9417. 1998.
- [71] P. Hunter, ,Dig this. Biomolecular archaeology provides new insights into past civilizations, cultures and practices., *EMBO Reports; Heidelberg Vol. 8* ,3,pp 215-7 ,Mar 2007.
- [72] KM. Harkins, and AC. Stone , Ancient pathogen genomics: insights into timing and adaptation. ,*J Hum Evol.* 79,pp137-49, Feb 2015.