Review on Microbial Bioinformatics: Novel and Promoting Trend for Microbiomics Research and Applications

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Abstract. The recent biotechnological advances and the rapid development of next-generation sequencing technologies accompanied by efficient computational facilities and tools have led to explosive and extensive data generation from finished complete genomes and draft genomes, because of this development, an urgent need arises for fast computing and automated approaches to analyze these bio big-data issued from microbial genomes and metagenomes in effective and a comparative way. Bioinformatics has come to play this major role via microbial bioinformatics and microbiomics which fill in the gap between just data accumulation and theoretical speculations to solution discovery and ready for use applications. In this perspective, our review gives an overview on microbial bioinformatics disciplines and subdisciplines and surveys their items, roles, influencing technologies and challenges, as well as lists the most microbial bioinformatics and metagenomics online resources, assemblers, and software, Furthermore, summarizes all the possible biotechnological applications of microbial bioinformatics and microbiomics in agriculture, food, medicine, industry, energy, and environment.

Keywords: Microbial bioinformatics · Microbiomics · Metagenomics · Biotechnological applications

1 Introduction

The sequencing technological revolution generated huge bio big data that require the harnessing of bioinformatics to archive, organize, analyze and use it to solve thorny biological problems [1]. Furthermore, the continuous development of high-throughput sequencing technologies during the last two decades, especially whole-genome sequencing (WGS), led to cumulative and extensive data issued from finished microbial genomes, draft genomes and metagenomes have irreversibly changed the way of microbial research and paved the way for microbial bioinformatics.

Since the sequencing of the first bacterial genome of *Hemophilus influenzae*, several microbial genomes, draft genomes and metagenomes, were finished and need analysis and exploitation, microbial bioinformatics via cloud computing, artificial intelligence

and machine learning provides an alternative approach that facilitates the fast treatment of this large genome dataset [2].

Table 1. Microbial bioinformatics disciplines and subdisciplines.

	No	Disciplines	Subdisciplines
Fundamental Applications	1	Informatics	Data science, cloud computing, machine learning and artificial intelligence, physical and computational infrastructures
	2	Mathematics	Numerical analysis, algorithms
	3	Statistics	Probability, statistical analysis, statistical modeling
	4	Physics	Material, laser, optics, quantum, nano, bio-radiation, spectroscopy
	5	Chemistry	Physical, material, inorganic, organic, biochemistry, analytical, quantum, photo, nano, chemistry, cheminformatics
	6	Microbiology	Agricultural, food, pharmaceutical, medical and clinical microbiology
	7	Microbial genetics	Viral, bacterial, fungal, microalgal, and protozoal genetics, microbial population genetics, microbial phylogenetics
	8	Microbial genomic	Ceramics, bacteriomics, fungomics, microbiomics, microbial population genomics, comparative microbial genomics
	9	Genomics	Microbiomics, plant, animal, rumen and human microbiomics, oncogenomic, epigenomics, pharmacogenomics, phylogenomic, microbial paleogenomics, structural, functional and comparative genomics, phylogenomic, population genomics
	10	Omics	genomic, transcriptomic, proteomic, secretomics, metabolomics, physiolomics, phenomics,
	11	Meta-Omics	Metagenomic, metatranscriptomics, metaproteomic
	12	Biology	Cellular, molecular, structural, synthetic, integrated, systems, evolution and population biology
	13	Biotechnology	Microbial, plant, animal and human biotechnology
			Environmental, industrial, agricultural, food, pharmaceutical, medical and nano biotechnology
	14	Medicine	Clinical microbiology, microbial epidemiology, health microbiomics, preventive, molecular medicine
	15	Pharmacology	Biologics, pharmacogenomics, antimicrobial drugs, pharmaceutical microbiology
	16	Veterinary sciences	Veterinary microbiology, animal and rumen microbiomics, animal breeding, animal health microbiomics
	17	Agriculture	Soil Microbiology, plant microbiology, phytopathology, terragenomics, soil microbiomics, rhizosphere microbiomics, plant microbiomics
	18	Geology	Geomicrobiology, geobiology, geomicrobiomics, micropaleontology, glacier geomicrobiomics
	19	Environment	Terrestrial, aquatic ecology, marine metagenomics, microbial diversity, marine and environmental microbiology, ecogenomics, environmental genomics and metagenomics
	20	Engineering	Electronics, electrotechnics, robotics, biorobotics, nano technology, biomimetics, bionics or biologically inspired engineering

In this review, we define microbial bioinformatics and list their disciplines and sub disciplines, roles, influencing technologies and challenges in the post-genomic era, as well as discuss the concepts of microbiomics, enumerate their computational tools, softwares and possible biotechnological applications.

2   Microbial Bioinformatics Multi-interdisciplinarity

While bioinformatics is an interdisciplinary research field that applies methodologies from computer science, mathematics and statistics to the study of biological phenomena,

Table 2. Microbial bioinformatics items, roles, influencing technologies and challenges.

Microbial bioinformatics Items	Roles	Influencing sciences and technologies	Challenges
Computational hardwar and software	Create, organize, develop, optimize and standardize, improve	High-Throughput Sequencing (HTS) Technologies	Data sharing,
Data bank	Creation, organization, classification	Next-Generation Sequencing (NGS) Technologies	Data scalability,
Data/metadata	Storage, access, organization, mining, processing, integration, visualization, binning, interpretation, management, shift the focus from data to discovery	Whole Genome Sequencing (WGS)	Data security,
Gene/multigenes	Finding, location prediction, abundance, profiling, annotation,	Whole Shotgun Metagenomic (WSM) sequencing	Data backup,
Genome/metagenome	Preprocessing, processing, binning, analysis, taxonomy, structural annotation, functional annotation, assembly, interpretation, gene prediction, novel genes discovery, recovery of more complete genomes from the metagenome	Mass Spectrometry (MS)	Integrated analytics,
Microbiome/meta microbiome	Archive, assembly, de novo assembly, visualize, binning, taxonomy, interpretation, gene prediction, novel genes discovery	Meta microbiomics/metagenomics	Accuracy and performance,
Phylogenomic/phylomicrbiomics	Analysis, phylogenomic reconstruction, phylogeny inference	Cloud computing, artificial intelligence, and machine learning	Focus on what matters

microbial bioinformatics is extremely multi-interdisciplinary, covering fundamental disciplines such as mathematics, statistics, informatics, physics, chemistry biology, microbiology and computational science, as well as applied disciplines such as agriculture, food, medicine, industry, energy and environment (Table 1).

In this review we define microbial bioinformatics and lists their disciplines, roles, influencing technologies and challenges in the post-genomic era, as well as discuss the concepts of microbiomics and their possible biotechnological applications.

3   Microbial Bioinformatics and Microbiomics

Microbial bioinformatics intersecting microbiology and bioinformatics and become to bridges the gap between data and discovery via analyzing the wealthy data gleaned from the fully sequenced microbial genomes and metagenomes to solve the complex biological problems. Microbial bioinformatics items, roles, influencing technologies, and challenges were summarized in Table 2 as well as online resources, assemblers, and software was listed in Table 3. These data banks and computational tools were very useful for promoting various kinds of analyses and meta-analysis which facilitate the discovery of hidden secrets of microbial ecosystem and microbiomic research in various fields.

The microbiome defined as the total genomes of the resident microorganisms of a particular organism [3]. Microbiomics harnessing bioinformatics to the study the microbial genes, genomes, and metagenomes via high throughput technologies accompanied by efficient computing tools which drastically changing the way of microbial DNA analysis, and revolutionized our understanding of microbial diversity, their functional roles in their environment, and association with plant, animal and human hosts. The various microbial bioinformatics applications spanning from environment, energy and agri-foods to bio-pharma- medicine fields were recapitulated in Table 4.

Table 3. Most microbial bioinformatics and metagenomics online resources, assemblers, and software

No.	Metagenomics		Computing tools or software [4]	
	Online resources	Assemblers	Major	Minor
1	Integrated Microbial Genomes and Microbiomes (IMG) [5]	IDBA_UD [6]	QIIME2(Qualitative Insights into Microbial Ecology) is an open-source bioinformatics tool for performing microbiome analysis	Explicit, Qiita, otupipe, mockrobiota, NGS preprocessor, LOTUS (Less OTUs)
2	EBI metagenomics [7]	MetaVelvet.[9]	MOTHUR: an open-source software package, a command-line computer program for analyzing sequence data from microbial communities	
3	MG-RAST: Metagenomics rapid annotation using subsystems technology [8]	MEGAHIT [10] and Ray Meta [11]	METAREP: a software tool for comparative metagenomics	

Table 4. Microbial bioinformatics and microbiomics applications

Application field	Microbiomics type	Examples/details	Ref.
Agriculture	Plant microbiomics	Microorganisms associated with plants, may exacerbate the dissemination of antibiotic resistance via the food chain, direct contact and globalization	[12]
	Plant growth-promoting microbiomics	Microbiome engineering enhance plant growth-promoting and biocontrol activities	[13]
	phylloplane microbiomics	Improve plant growth, stress resilience and health	[14]
	Rhizosphere microbiomics	Rhizosphere microbiome studies have provided tools for manipulating the environment, improving the health of crops and enabling them to reach their maximum genetic potential	[15]
	Soil microbiomics	Soil health conservation under changing climate	[16]
	Terragenomics	Soil Terragenomics (the study of the complete sequencing of all microbial genomes that inhabits the soil environment)	[17]
	Forest microbiomics	Exploring the functional diversity of fungal microbes in their various types of symbionts, decomposers, or saprophyte	[18]
Medicine	Wound microbiome	Precise and rapid identification of wound-associated microbial communities (microbiomes) for fast clinical management treatments and accelerate healing	[19]
	Personalized medicine	Human gut microbiome and xenobiotic degradation	[20]
	Respiratory microbiome	Aberrant change in the airway microbiome promote risk for the development of pulmonary allergic inflammation	[21]
	Air ways allergy and microbiomics	Study the allergic airway dysregulation in the absence of bacterial settlement	[22, 23]
	Skin microbiome	Studying skin microbial diversity for inflammatory diseases prevention and treatment	[24]
	Human probiotics and microbiomics	Next-generation therapeutic bacteria	[25]
	Human microbiomic	Understanding changes in the human microbiome in health and disease	[26]
		Characterization of the gut microbiome and studying their drug resistance genes	[27]
		Analysis of the genetic and phylogenetic diversity of gastrointestinal bacteria by metagenomic approaches	[28]
		Discovery of emerging evidence corelated the gut microbiome to neurological disorders	[29]

(*continued*)

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Application field	Microbiomics type	Examples/details	Ref.
	Human milk microbiome	Studying milk microbiome contribution to the healthy metabolism and functioning of the immune system in the infant's intestines	[30]
	Oncogenomics	Bioinformatics and oncogenes functional analysis enhanced diagnosis and treatment	[31]
	Pathogenomics and microbiomics	using meta-genomic approaches in studying host-microbe interactions involved in disease lead in rapid infectious disease diagnosis	[32]
	Cancer microbiomics	Oral cancer, colorectal cancer, head and neck squamous cell carcinomas	[33–35]
Veterinary science	Cow microbiomics	Recovery of more than 900 bacterial and archaeal genomes from cow rumen predicted to have around 69000 genes related to carbohydrate metabolism, shows great potential for biomass-degrading enzymes prospection	[36]
	Fish gut microbiomics	Improve nutrition, growth, reproduction and feeding strategies	[37]
	Animal population genomics and microbiomics	Cattle breeding to increase traits such as protein production, carcass quality, disease resistance, or even feeding efficiency, and genetic resources conservation	[38]
	Animal gut microbiomics	Metagenomic methods by analyzing animal genome sequences have greatly helped in accelerating the discovery of animal diseases and the development of appropriate vaccines for them	[25]
	Feedomics	Improve the quantity, quality, safety and functional properties of food animal products	[39]
Pharmacology	Pharmaceutical Bioinformatics	The use of bioinformatics methods in the analysis of biological and chemical-pharmaceutical processes; Enable to understand the mechanisms of xenobiotics interaction with the human body and accelerate the discovery of smart drugs	[40]
	Pharmacogenomics and metamicrobiomics	Discovering antibiotics through soil metagenomics	[41]
		Malacidin antibiotics discovery via metagenomic approaches	[42]
	Antibiotic resistome	Sequencing analysis of bacterial genomes for antibiotic resistance genes detection (resistome)	[43]
Cosmetics	Human skin microbiome	Studying the role of everyday cosmetics in altering the skin microbiome to develops personalized skin products	[44]
Food	Food quality and safety	Characterization and molecular diagnosis of foodborne bacterial pathogens via microarrays technique	[45, 46]

Table 4. (*continued*)

Application field	Microbiomics type	Examples/details	Ref.
		Allergy assessment to genetically modified foods	[47]
	Fermented foods improvement	Analyzing the microbial metabolism of desirable food microbes to develop optimal sensory properties via bioinformatics and metabolomics tools	[48]
	Milk microbiomics	Improve starter cultures and cheese making	[49]
	Personalized nutrition	Personalized nutrition by prediction of glycemic responses	[2]
	Foodomics	The application of advanced and integrated omics technologies greatly facilitated food and nutrition studies, which were reflected in improving the health and quality of life of the consumer	[50]
	Food microbial informatics	The use of comprehensive analysis of integrated omics technologies and their databases accelerated predictions and assessment of the desirable and undesirable effects of microorganisms on foods	[51]
Environment/ecology	Microbiome metagenomics	Discovery of novel enzymes and biocatalysts	[52]
	Metagenomic-based bioremediation	Petroleum hydrocarbons treatment	[53]
		Adoption of microbial metagenomic techniques has improved control and biological treatment strategies for waste and pollutants	
		Reducing the harmful impact of pollutants on ecosystems and restoring contaminated sites with metagenomic bioremediation	
	Climate change research	Mitigating climate change by microbiome engineering and synthetic biotechnology	[54–56]
	Marine microbial ecogenomics	Understanding the diversity and ecological processes involving marine archaea, bacteria and their viruses	[57]
	Water microbiomics	Detecting herbicides, pesticides and fertilizers in polluted water and devising ways to dispose of them	[58]
	Eco-microbiomics	Analysis of microbial diversity and their environment through metagenomic approaches	[59]
	Forest microbiomics	Studying forest ecosystems diversity, complexity and dynamics	[60]
	Environmental viromics	Exploration and analysis of viral communities and their diversity in the salty desert and dry valleys of Antarctica	[61]
	Biodiversity informatics	Create and design computerized taxonomic databases	[62]

(*continued*)

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Application field	Microbiomics type	Examples/details	Ref.
Energy	Bio ethanol	Potential application of omics tools comprising transcriptomics, genomics, proteomics and metabolomics in bioenergy and ethanol industry	[63]
	Biofuel	Analysis and understanding of symbiotic or cooperating microbial communities in the production of biodiesel and the decomposition of cellulose into sugars and then fermentation into ethanol	[64, 65]
	Bioenergy	Studying microbes that produce methane and hydrogen	
	Biogas	Understanding and analyzing the microbial communities involved in biogas production	[66]
Industrial	Microbial metagenomic	Bioactive compounds and antibiotics exploring and production	[67]
	Industrial enzymes	Amylase, cellulase, lipase, protease, xylanase and other enzymes	
Archaeology	Archaeogenomics and phylogenomics	Studying and exploring the completely sequenced archaeal genomes using comparative genomics analyses and functional annotation	[68]
	Microbial paleogenomics	Analysis of ancient materials of human, animal and microbial origin have provided important insights into the microbiome, resistome, dietary habits and health and disease states of ancient times and civilizations	[69, 70]
	Paleopathogen genomics	Study and analysis of DNA sequences of pathogens and parasites from archived and archaeological remains	[71]

4 Conclusion

Network-based analytical approaches in general and microbial bioinformatics specially become to transform the raw data generated by sequencers to final outputs, furthermore, have proven useful to study systems with complex interactions, such as microbial genomes, metagenomes, and ecomicrobial systems. Development of new techniques in multi-omics approaches a long with sophisticated platforms will open new future directions for the field and facilitate the microbiomic research from diverse perspectives.

Based on the recent advances in sequencing technologies accompanied with latest research findings, we conclude clearly that microbial bioinformatics will become in the 21st century, the main creative and promoting discipline for microbiome research expansion and will provide a deeper understanding for microbiomes structurally and functionally which may fill in the gaps between pure science and practice for solving the medical, agricultural and environmental challenges.

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