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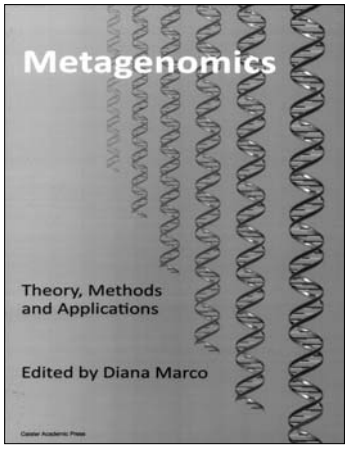

Metagenomics. Theory, Methods and Applications

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Metagenomics emerged in the late 1990s as a means for studying the collective microbial genetic material in the environment. Crucial insights into microbial communities have come by way of recent innovative breakthroughs in genotypic profiling, genome pyrosequencing, metatranscriptomics, metaproteomics, metabolomics, metagenomics itself, as well as through the tools of bioinformatics.

The book *Metagenomics*. *Theory, methods and applications* is composed of two main thematic blocks. The five chapters in the first block provide a general background on the concepts and tools used within metagenomics, from sampling to the development of integrated and global resources for data management, as well as current methods for identifying horizontal gene transfer. The six chapters comprising the second block focus on the application of metagenomic approaches to the study of interactions between microbes and other organisms, ranging from plants to the humans, and on bioprospecting novel genes and bioproducts with environmental and/or industrial applications.

Microbes interact with plants at several different levels, from pathogenesis to mutualism. They are inhabitants of the rhizosphere (directly surrounding the root), the phyllosphere (on the surface of above-ground leaves and shoots), or the plant itself, as endophytes. Interactions between plants and microbes involve complex chemical signaling. While a potential use of metagenomics is the characterization of plant microbiota communities, this has not yet been applied directly to plant-microbe interactions. Studies of this type would be a driving force towards greater microbial community functionality, plant health, and productivity. Particular attention has been paid in *Metagenomics* to those microorganisms with beneficial effects on plant growth, such as those microbes that often reside in the rhizosphere (Chapter 6).

Through metagenomics, the genetic diversity of environmentally relevant microorganisms can be investigated and new functional genes, for example, those involved in the catabolism of hazardous pollutants, identified. Metagenomic libraries can also be screened for functional and/or genetic diversity. In the search for new catabolic genes encoding enzymes that degrade pollutants, a "functional" approach, in which clones that express a desired trait are screened on appropriate media, is preferable. Growth measurements could then identify those clones bearing the catabolic genes of interest. Metagenomics also offers the possibility of retrieving unknown sequences or functions from the environment. However, the main limitation of this method is the low recovery of active clones because the desired function is not always expressed in the host cell, especially when not all the genes required for the function are clustered together. As a favorable outcome in bioremediation involves microbial communities with complex interactions, it is necessary to attain a comprehensive understanding of which community features are associated with successful biodegradation (Chapter 7).

The diversity of the microbial universe provides an unlimited resource for the exploration and development of new products and bioprocesses with substantial industrial and biotechnological impact. Selection based on function rather than on sequence homology could lead to the isolation of truly novel genes. Metagenomic technology has recently detected new compounds, such as the antibiotics terragines, violacein, indirubin, and the turbomycins, through the cloning and expression of genomic DNA of uncultured soil microorganisms. There are other areas ripe for potential exploration through metagenomics: (i) Organotriles and their conversion products, amides and carboxylic acids, are of industrial importance due to their wide spectrum of application in the production of plastics, synthetic fibers, and fumigants, as well as their role as intermediates in the synthesis of fine chemicals, pharmaceuticals, and agrochemicals. (ii) Lipases, which catalyze the hydrolysis of acylglycerides to fatty acids and glycerol, are used commercially in laundry detergents for stain removal, in the manufacture of food ingredients and pulp, and in paper processing. (iii) Proteases are also used in detergents as well as in leather processing and food manufacture (meat tenderizing, brewing and, with protein hydrolysates such as chymosin or rennin, cheese processing). (iv) Archaea, specifically, their enzymes that remain catalytically active under extremes of temperature, salinity, and pH conditions, are expected to have a wide range of biotechnological applications (Chapters 8, 9).

The Human Microbiome Project (HMP), recently launched by the National Institutes of Health [http://nihroadmap.nih.gov/hmp], is using metagenomic but also traditional approaches to genomic DNA sequencing both of which are expected to lay the foundation for further studies of human-associated microbial communities. Broadly, the project has the following goals: determining whether individuals share a core human microbiome, understanding whether changes in the human microbiome can be correlated with changes in human health, and developing the technological and bioinformatic tools needed to support these goals (Chapter 10).

It is becoming increasingly accepted that many of the fundamental questions about life on this planet will only find their answers through advances in understanding microbial communities in global environments. Sergei Winogradsky discussed the role of microbes in the cycle of life: "due to [these extensive microbial associations], we perceive living matter as a single whole, as a single giant organism… which governs all the processes of [its life cycle]" (Chapter 11).

According to GOLD [http://www.genomesonline.org], there are currently 207 ongoing metagenomic projects from different environmental samples and simulated communities, all within various stages of sequencing. Given the volumes of data produced—and the fact that many of the sequences generated have the potential to be novel and/or previously uncharacterized—the opportunity to "shop" for genes of interest is enormous.

Metagenomics has begun to address all of the above-discussed issues and to offer preliminary, tentative solutions. The metagenomic approach has the potential to elucidate the ways by which environments acquire genomes (microorganisms) and how those genomes work. DNA can be obtained from microbes whether or not they are viable and independent of our ability to cultivate them; metagenomics provides a powerful way to determine an organism's presence as well as its genetic relatedness to other organisms. Equipped with the tools to identify the genes carried by a particular species or strain of microbes we will be able to understand the capabilities demanded of organisms by particular types of environments or lifestyles in order to allow their adaptation to unusual habitats or behaviors. As very competently described in *Metagenomics*, many of these tools are already or will in the near future be available to us.

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