

Modeling the Human Microbiome: From Enzymes to Super-Organisms

Elhanan Borenstein

*Department of Genome Sciences, University of Washington
Department of Computer Science and Engineering, University of Washington
The Santa Fe Institute*

The human microbiome – the diverse and complex set of microorganisms that populate the human body – plays a key role in a wide range of host-related processes and has a profound impact on human health. Extensive metagenomic analyses have focused on characterizing the composition of the microbiome in health and in disease and have revealed substantial compositional changes associated with a variety of disease states. To date, however, significantly less effort has been directed at modeling the microbiome and studying it as a complex, hierarchical, and multi-scale system.

In this talk I will highlight the complexity of the human microbiome and underline the need for system-level studies of the microbiome and comprehensive modeling frameworks. I will present a number of initial attempts to model the microbiome across multiple organizational levels and demonstrate how these models can be used to obtain insights into the composition, ecology, and dynamics of the microbiome and its interaction with the host. Specifically, two such studies will be introduced: In the first study, genome-scale metabolic models of numerous gut dwelling microbial species are integrated with a ‘reverse-ecology’ framework to predict the type and extent of metabolic interactions between species and to elucidate the assembly rules of the gut microbiome. In the second study, a novel metagenomic systems biology framework, incorporating metagenomic data with systems-level analysis and community-wide network-based models, is applied to identify both gene-level and network-wide topological differences associated with obesity and with Inflammatory bowel disease. Such genome scale and metagenome scale models focus not only on the set of genes or species in the microbiome but mostly on the orchestrated activity of numerous enzymatic genes in multiple pathways and on the complex web of interactions between the species comprising the microbiome.

I will finally discuss future challenges and promising avenues for modeling the microbiome at the cellular, ecological, and supraorganismal level, ultimately providing a predictive, system-level understanding of this complex and exciting biological system.