

A journey through ecosystems: the complexity of interaction networks in the gut microbiome

Adrián Aguirre-Tamaral¹, Sandra Ferreiro¹, and Jaime Iranzo¹

¹Centro de Biotecnología y Genómica de Plantas (CBGP, UPM-INIA)

Microbial communities, known as microbiomes, are everywhere in nature: in the environment, in our food and even in our bodies. They play an important role in ecosystems and also influence our health. Understanding the physical and chemical interaction network of microbiomes under different conditions is therefore a key objective for academic and medical reasons.

A perfect example is the human gut microbiome, as the intricate competitive and cooperative interactions between its microbial inhabitants play a crucial role in maintaining host health (Fig. 1, A). Indeed, several studies have correlated alterations of the gut microbiome (dysbiosis) with diseases such as inflammatory bowel diseases (e.g. Crohn's disease), colorectal cancer or type 2 diabetes [1, 2]. However, the causes underlying sudden changes in microbiome composition under pathological conditions still have several open questions, such as the effect of microbial order of cooperation on health.

Consequently, to better understand the intestinal cooperative network in different environments and pathological conditions, we reconstructed metabolic models from a longitudinal study of the human intestinal microbiome in patients with inflammatory bowel disease (HMP2, [3]), incorporating the diverse metabolic capabilities of individual species and simulating their potential interactions. Finally, we used flux balance analysis to compute the cooperation of reconstructed and curated [4, 5] metabolic models of microbial communities.

Our results indicate that there is a remarkable prevalence of cooperative interactions of higher order than two, which are also essential in certain environments (Fig. 1, B). These results provide insights into the composition of the microbiome in different media and contribute to a deeper understanding between health and microbial interactions in the gut ecosystem.

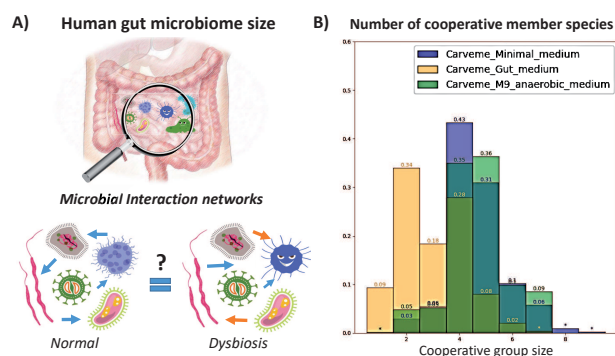


Fig. 1. The human gut microbiome: A) Schematic view of the microbial interaction networks under normal and dysbiosis conditions. B) Size of the cooperative community in different environments.

-
- [1] J. Sung, et. al, *Global metabolic interaction network of the human gut microbiota for context-specific community-scale analysis*, Nature **8**, 15393 (2016).
 - [2] J. Lloyd-Price, et. al, *Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases*, Nat. Commun. **569**, 655662 (2019).
 - [3] <http://ibdmdb.org/>
 - [4] S. Magnsdottir, et. al, *Generation of genome-scale metabolic reconstructions for 773 members of the human gut microbiota*, Nat. Biotech. **35**, 8189 (2017).
 - [5] T. Blasco, et. al, *An extended reconstruction of human gut microbiota metabolism of dietary compounds*, Nat. Commun. **12**, 4728 (2021).