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Title of Doctoral Dissertation

Study on energy landscape approach revealing the potential
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(炎症性腸疾患の発展に寄与する可能性のある主要細菌を明らかにするエネルギー地形図方法研究)

The dysbiosis of microbiota has been reported to be associated with numerous human pathophysiological processes, including inflammatory bowel disease (IBD). With advancements in high-throughput sequencing, various methods have been developed to study the alteration of microbiota in the development and progression of diseases. However, a suitable approach to assess the global stability of the microbiota in disease states through time-series microbiome data is yet to be established. In this study, we have introduced a novel Energy Landscape construction method, which incorporates the Latent Dirichlet Allocation (LDA) model and the pairwise Maximum Entropy (MaxEnt) model for their complementary advantages and demonstrate its utility by applying it to an IBD time-series dataset. Through this approach, we obtained the microbial assemblages' energy profile of the whole microbiota under the IBD condition and uncovered the hidden stable stages of microbiota structure during the disease development with time-series microbiome data. The Bacteroides-dominated assemblages presenting in multiple stable states suggest the potential contribution of Bacteroides and interactions with other microbial genera, like Alistipes, and Faecalibacterium, to the development of IBD.

Our proposed method provides a novel and insightful tool for understanding the alteration and stability of the microbiota under disease states and offers a more holistic view of the complex dynamics at play in microbiota-mediated diseases.