Team proposes stochastic model to explain microbiome composition

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Dr Michael Sieber (left) and professor Arne Traulsen, Max-Planck-Institute for Evolutionary Biology, developed the Neutral Model together with researchers of the CRC 1182. Credit: Christian Urban, Kiel University

All living things—from the simplest animal and plant organisms to the

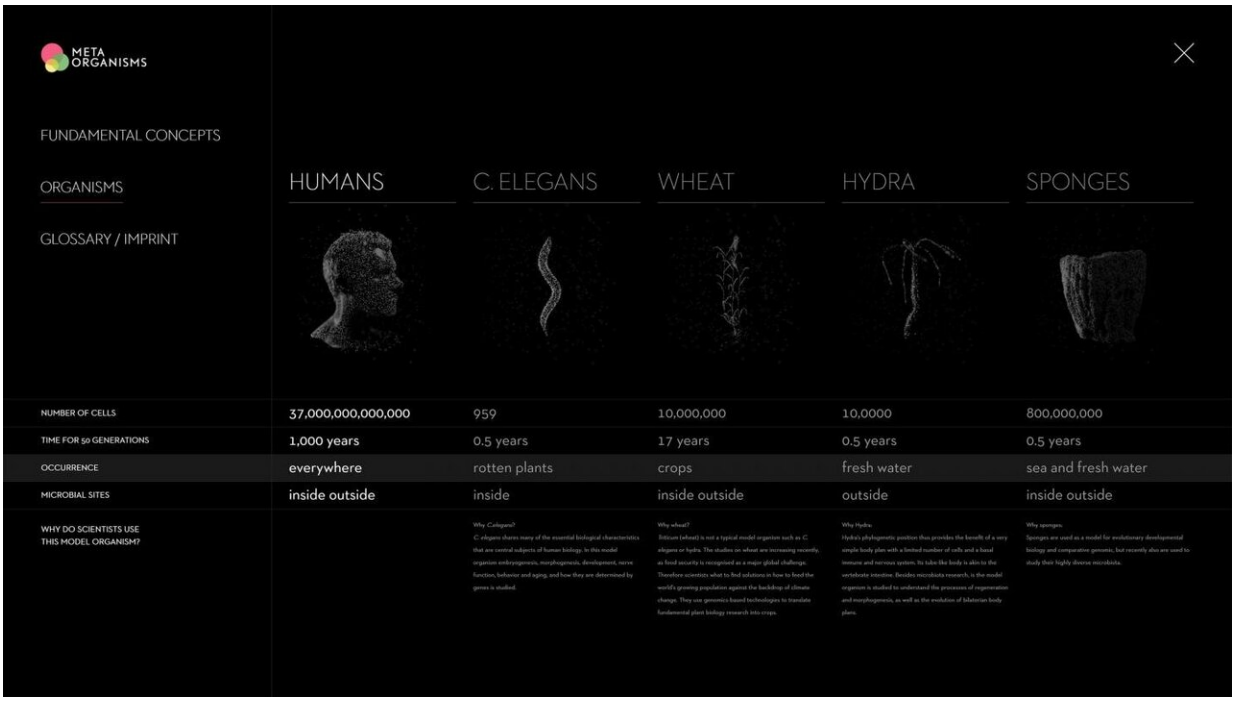
human body—live closely together with an enormous abundance of microbial symbionts, which colonise the insides and outsides of their tissues. The functional collaboration of host and microorganisms, which scientists refer to as a metaorganism, has only recently come into the focus of life science research. Today we know that we can only understand many of life's processes in connection with the interactions between organism and symbionts. The Collaborative Research Centre (CRC) 1182 "Origin and Function of Metaorganisms" at Kiel University (CAU) aims to understand the communication and the functional consequences of host-microbe relationships.

A key issue for the researchers at the CRC 1182 is how the composition of an organism's microbiome forms during its individual development. It is still unclear as to whether the microbial community composition is more governed by a functional selection process or if random processes dominate. In order to examine the microbiome composition, a research team from the CAU's CRC 1182 and the Max Planck Institute for Evolutionary Biology in Plön (MPI-EB) has now applied the theory of the so-called "neutral metaorganism" to an entire spectrum of model organisms, from very simple creatures to complex vertebrates. The scientists from Kiel and Plön published their findings yesterday in the journal *PLOS Biology*.

The null model of evolutionary theory

Theoretical models offer one way to make the highly complex, individual microbiome composition manageable. A fundamental model in evolutionary research is the so-called neutral null model. This is used to predict how populations would develop without any selection pressure whatsoever. The research team at the CRC 1182 has now applied this model to several model organisms from threadworms to house mice and compared the predictions with experimentally collected data. "Theory and experimental data match surprisingly well for many organisms. The

predicted composition in the house mouse, for example, is found in the actual microbial species community," summarised Dr. Michael Sieber, research associate at the MPI-EB and member of the CRC 1182. "It is possible that selection plays a lesser role in the microbiome's composition than we previously assumed, while this does not mean that the microbiome has no important functions for the organism, it could be an indication that many different compositions of the microbiome can perform these functions equally well. And which specific composition actually forms in a single organism is then driven by chance."



The scientists applied the new theoretical approach to a range of model organisms, e.g. threadworms or mice, which are investigated in the CRC 1182 at Kiel University. Credit: Science Communication Lab

A map for further exploration of the microbiome

The researchers did notice some significant deviations between the neutral model and the real compositions of the microbiome, however. For example, individual bacterial species in the mouse microbiome did not match the neutral prediction. And the microbial species composition of the Caenorhabditis elegans thread worm did not match the neutral model at all.

"We assume that these deviations between model and reality could indicate specific functions of certain microorganisms," Sieber emphasised. Investigating the systematic deviations from the neutral model therefore holds the potential to discover key functions of certain bacterial species within the microbiome.

First explanations for the deviations from the neutral model are already being discussed. Some non-neutral bacteria in the mouse microbiome, for example, are involved in digestion and their presence may therefore be the result of a targeted selection process. On the other hand, Caenorhabditis elegans, with its very fast generational change, might not live long enough to develop a stable, mainly neutral composition of its microbiome. "The model of the neutral metaorganism therefore provides an important theoretical basis for further functional analyses of microbiome compositions across the entire spectrum of the model organisms investigated in our Collaborative Research Centre," said CRC 1182 spokesperson Prof. Thomas Bosch.

More information: Michael Sieber et al, Neutrality in the Metaorganism, *PLOS Biology* (2019). DOI: 10.1371/journal.pbio.3000298

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