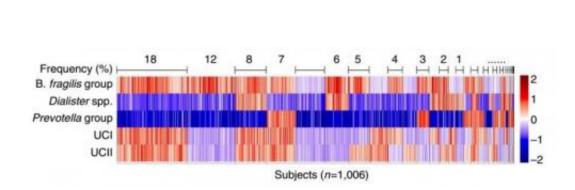


Binary bacteria "bits" in human intestines associated with health status



Five binary bacteria groups (rows) co-occur in various combinations in the 1,006 subjects (columns) in the study. The most frequent combination (18%) corresponds to the high-abundance states of the B. fragilis and two groups of uncultured Clostridiales combined with the low-abundance states of the Dialister spp. and Prevotella groups. Credit: Lahti, et al. ©2014 Nature Communications

The human gut contains hundreds of different types of bacteria, which vary widely among individuals. Understanding these variations is a complex and relatively new area of research. Now in a new study, researchers have found that some bacteria in the gut are distributed in a somewhat surprising way: they are bistable, meaning that most people either have very large numbers of these bacteria or nearly none at all. Some of these bistable bacteria groups are associated with individual factors, such as obesity, metabolic syndrome, irritable bowel syndrome, and age—making these bacteria groups potential targets for microbiomebased diagnostics and therapies.

July 17 2014, by Lisa Zyga



The researchers, Leo Lahti, et al., from universities in Finland and The Netherlands, have published their study on bistable abundance distributions of certain bacteria groups in a recent issue of *Nature Communications*.

"While we have not investigated causal relations, our findings suggest that targeted manipulation of specific bacterial groups could be used to affect health, instead of ecosystem-wide perturbations," Lahti, from the University of Helsinki and Wageningen University, told *Phys.org.* "A key impact of our work is that it simplifies the understanding of the variability in the gut ecosystem and opens up novel opportunities for research on therapeutic manipulation and diagnostics (as individuals can be categorized based on unique combinations of these bistable bacterial populations)."

In their study, the researchers analyzed fecal samples from 1,000 individuals from Europe and the United States. They found that several out of the 130 genus-like bacterial groups they studied exhibit robust bimodal abundance distributions.

As the researchers explain, bistable bacteria can be thought of as bacteria "switches" that have states of either "0" (absence) or "1" (abundance), in analogy to binary computer switches that also have states of "0" or "1." Just as the states of computer switches can be controlled, the states of bacteria "switches" might also one day be controlled by interventions in order to address related health issues.

Another interesting observation was that, when individuals had intermediate amounts of these bistable bacterial groups, the intermediate levels were unstable and tended to "flip" toward either the "0" or "1" state. In other words, the bistable states of the bacterial groups seem to be divided by tipping points, where even small fluctuations may lead to an abrupt shift to a stable state.



The researchers also observed significant associations between the bistable groups and other health factors, as well as co-occurrences among various groups. For example:

- The high-abundance states of *Bacteroides fragilis* and *Dialister* spp. groups were associated with a low gene richness and metabolic dysfunction.
- The high-abundance states of the *Prevotella* group (specifically, relatives of *P. melaninogenica* and *P. oralis*) and two groups of uncultured *Clostridiales* were associated with a high gene richness and healthy metabolic phenotytpe.
- The high-abundance states of the two uncultured *Clostridiales* groups were also associated with a low body mass index (BMI), a strong overall bacterial community diversity, as well as older age.
- The low-abundance states of the two uncultured *Clostridiales* groups were associated with <u>irritable bowel syndrome</u> and severe obesity.
- The most frequent combination of bistable bacteria groups corresponds to the high-abundance states of the two uncultured *Clostridiales* groups and *B. fragilis*, combined with the low-abundance states of the *Dialister* spp. and *Prevotella* groups.

When investigating how diet may affect the bistable bacteria states, the researchers found that, while short-term dietary interventions did cause state shifts in some individuals, the changes were not statistically significant. This was due to the fact that there was a large amount of within-state variation in other individuals, masking the strong effects of the dietary intervention in certain invidiuals. These results hint at the possibility that targeted dietary interventions could be potentially used to manipulate specific bistable groups in the future. The researchers plan to address this possibility in future research.



"Our present study was based on normal western adults across a relatively short time span of a few months," Lahti said. "Following more closely the long-term temporal dynamics of the bistable bacteria, and analyzing their behavior in different age groups, ethnic populations and disease cohorts will be useful to understand in more detail how these bacteria are associated with host factors and health. In particular, we are now investigating the effects of diet and individual variation."

More information: Leo Lahti, et al. "Tipping elements in the human intestinal ecosystem." *Nature Communications*. DOI: <u>10.1038/ncomms5344</u>

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