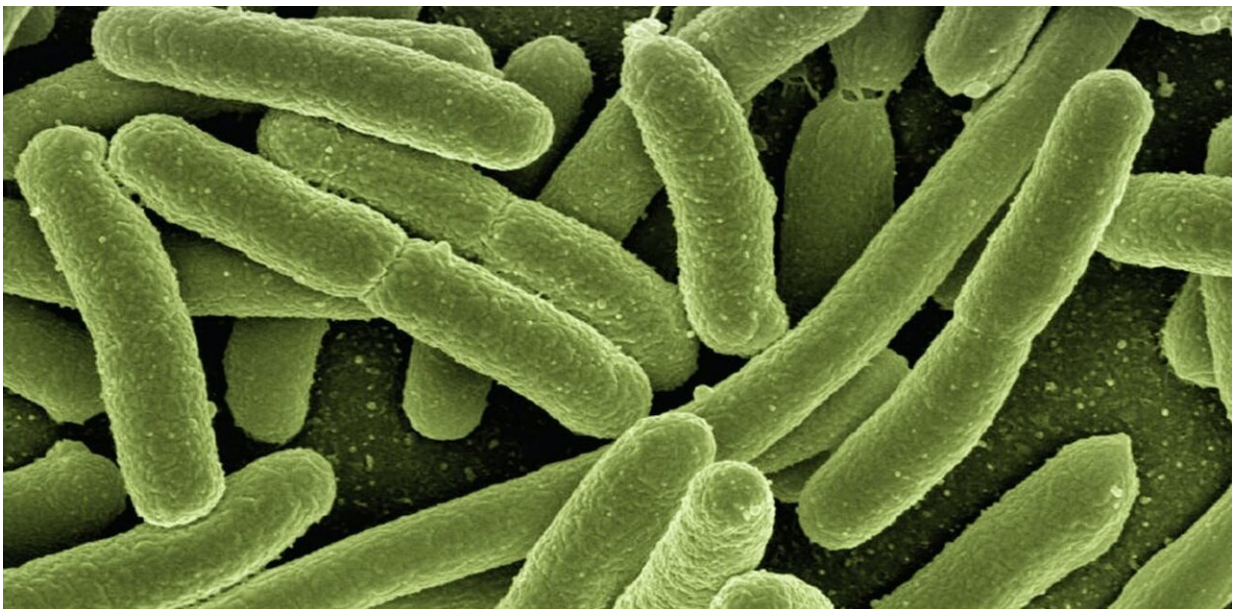


Internet of microbiota: Could synthetic probiotics help prevent our natural bacteria from going astray?

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Having a healthy E coli community in our intestinal system is essential to good human health. Credit: [Geralt/Pixabay](#)

Animals use chemical substances called [pheromones](#) to communicate with each other and attract mates, mark territory, and signal danger. Plants release volatile organic compounds to attract pollinators and repel predators. Communication using molecules, known as "molecular communication", is also useful to humans, albeit in a way that goes

unnoticed by us—it plays a critical role in the interactions between the trillions of natural bacteria that live in and on our bodies.

Indeed, the [human microbiota](#)—the natural [bacteria](#) inside the [human body](#)—use "[quorum sensing](#)" molecules to organize themselves and communicate with their human host. The microbiota is crucial for our health since it involves a wide range of physiological processes, including digestion and immune system regulation, besides producing certain hormones and other essential molecules.

Specifically, the [gut microbiota](#) directly affects the central nervous system and influences the host's moods, behavior, and cognition via the "[gut-brain axis](#)", a [complex network](#) that connects the two through signaling pathways involving molecules. This communication based on exchanges of molecules within the body is essential for maintaining [homeostasis](#) (that is, cell stability), and has been linked to many physiological processes such as [neural development](#) and dopamine metabolism. Conversely, when any failure in these [communication networks](#) occurs or when the microbiota population is not optimal, it can result in serious conditions, including [autism spectrum disorder](#) and [Parkinson's disease](#).

Despite the multiplexed benefits of gut microbiota, its population and how well they operate in the body cannot be controlled by humans since they are independent organisms that live within us. To alleviate these issues, a field of research explores human-made alternatives that could substitute for these organisms, making things more controllable and predictable. Recent research has shown that [artificial bacteria](#), also called "synthetic probiotics", could offer a promising new approach to treating gut-brain axis disorders. These artificial bacteria would use molecular communication, as it occurs naturally in living organisms, but here as a bio-inspired communication paradigm that uses molecules to transfer information.

What are artificial bacteria?

Artificial bacteria [can be designed](#) to interact with the [gut microbiome](#) and the central nervous system to modulate and interfere with communication networks within these systems. For instance, they can be programmed to produce specific molecules that [modulate the growth and activity of specific bacteria in the gut microbiome](#), or to produce neurotransmitter-like neuronal signaling molecules that can [modulate the nervous system's activity](#).

Artificial bacteria can also be designed to mimic the function of a type of natural bacteria, who are called [probiotics](#) and who have beneficial effects on the gut-brain axis: they can restore or maintain the balance of the gut microbiota, which may help to ameliorate the symptoms of gut-related disorders, such as [inflammatory bowel disease](#), [infectious diarrhea](#), and [irritable bowel syndrome](#).

The active use of artificial bacteria in the treatment of gut-brain axis-related disorders is projected to make significant breakthroughs. The ability to engineer microorganisms to perform specific functions or behaviors will be a key enabler for [preventing the proliferation of pathogens and achieving homeostasis in the body](#). For example, by developing artificial bacteria to produce antimicrobial peptides, we can target and kill harmful bacteria with greater precision, avoiding the development of antibiotic resistance. Similarly, by programming artificial bacteria to promote the growth of beneficial microorganisms in the gut, more effective communication between microorganisms can be established, [promoting the restoration of homeostasis](#).

The development of intestinal biosensors and artificial bacteria to detect disease-related biomarkers enables using them as diagnostic tools. However, the first step in developing diagnostic tools is understanding the communication between [natural bacteria](#) and the brain. Accordingly,

mimicking it via artificial counterparts might eventually help us tackle many conditions, such as mood disorders and autism, in the foreseeable future.

How to develop artificial bacteria?

Molecular communication is a bio-inspired communication paradigm that uses molecules to transfer information as it occurs naturally in living organisms, with several analogous examples in nature as exemplified throughout the article. This communication paradigm paves the way for the realization of various foreseen applications.

In the context of molecular communication, artificial bacteria refers to the development of engineered bacteria that can communicate with each other and human cells at the molecular level. This envisioned organism is nothing but a [network of systems transmitting and receiving, or, in engineering speak, "transceiving" molecules at the microscale or the nanoscale.](#)

This bacteria-based transceiver can send and receive molecular signals inside the human body to further sense and control biological processes in real time. As stated before, envisioned artificial bacteria is a perfect candidate for biomedical applications of nano-communication networks such as diagnosis and treatment of diseases, health monitoring, drug delivery, and bio-hybrid implants. Yet, the design and fabrication of these bio-compatible devices necessitate cross-disciplinary efforts that benefit from the accumulated knowledge in the fields of information and communication theory, nanotechnology, molecular science, and many others. These involve developing energy and molecule-efficient, low-complexity, and reliable communication techniques, as well as realistic molecular communication channel models validated through experiments.

These transceivers can also be designed for developing "lab-on-chip" technologies, which are miniaturized laboratory systems that can be used to perform various diagnostic and analytical tests for the gut-brain axis. Although there is a vast number of ongoing research projects and developed testbeds on this topic, no experiments in living systems have been done. Many ongoing [research projects](#) are actively working toward bringing this paradigm into reality. A notable example is the development of [a prototype molecular communication receiver using graphene](#), a nanomaterial with outstanding biochemical properties, along with the [utilization of biosensor technology](#).

These works indicate that practical devices are not too far off on the horizon, and given the pace of technological advances, we are in a good position to envision the production of these devices within a few decades. However, the main hurdle that researchers still face is conducting successful testing within living organisms such as mice, rats or any model organisms. Advancements in molecular [communication](#) and synthetic biology will pave the way for the next significant milestone for in vivo experiments that might enable diagnosis tools for many diseases, especially gut-related disorders.

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