RESEARCH

Tracing Bacterial Evolution Across Billions of Years

By Record Staff

Bacteria might not get the same prominent placement in the Museum of Natural History as, say, those dinosaurs on the fourth floor. They might not have their own plastic toys in the gift shop. In the arena of evolutionary staying power, however, these little guys are real champions

Bacteria appeared on Earth at the dawn of life itself, about 3.5 billion years ago. Since that time they've displayed amazing feats of evolutionary adaptation, living high in the stratosphere and many miles below the surface of Earth, in cold arctic lakes and superhot thermal vents.

But these tiny creatures are not simply passive adapters or opportunists. They played a major role in shaping our environment. Microbes created the atmospheric oxygen we breathe and are now responsible for replenishing Earth's ecosystems by degrading waste products and recycling important nutrients.

Bacteria, argues Dennis Vitkup, an associate professor at Columbia's Departments of Systems Biology and Biomedical Informatics, also have an intimate relationship with every one of us. "If you consider the total number of cells within your body, there are about 10 times more bacteria than human cells. We lead a very synergistic life with them," Vitkup says.

The contribution of bacteria to our well-being and environment is usually invisible, obscured from us due to their size. But invisible does not mean unimportant. "Life on Earth as we know it would quickly stop," says Germán Plata, a postdoctoral researcher on the Vitkup team, "if bacteria were to suddenly disappear."

BRUCE GILBERT

Researcher Germán Plata and Professor Dennis Vitkup.

Despite their omnipresence, microbial evolutionary adaptations are often challenging to study, partly due to the difficulty of growing diverse bacteria in the lab. "Probably less than a dozen bacteria are really well studied in the laboratory," Vitkup says.

Writing in the journal *Nature* this past January, Vitkup and Plata applied computational tools to investigate bacterial evolutionary adaptations by simulating metabolism for more than 300 bacterial species, covering the entire microbial tree of life.

To make sense of the puzzling nature of evolutionary adaptations over billions of years, Vitkup invokes Darwin's famous finches. Over the course of a couple million years, finches on different islands developed different forms of beaks that allowed them to pick up and eat different kinds of seeds. The differences in animal appearance, such as beak shapes or even behavior, are the external manifestations of genetic differences, what researchers usually call phenotypic differences. "But how do you compare phenotypic differences among bacteria over billions of years?" Vitkup asks.

Vitkup and Plata started with one key idea: that the crucial factor in bacterial survival is their ability to grow on different food sources. A particular bacterium's phenotype depends on its ability to convert available nutrients into the chemicals that it needs to grow and reproduce. The team then used bacterial metabolic simulations to predict phenotypes across hundreds of environments. "Bacterial metabolism serves as a kind of microscope to discern patterns of phenotypic adaptation and diversification," Plata says.

Vitkup's team discovered that long-term bacterial adaptation proceeds via two different stages. Initially, there is a relatively fast diversification lasting tens of millions of years, which is then followed by a slow divergence process continuing for billions of years.

Surprisingly, the team was able to describe

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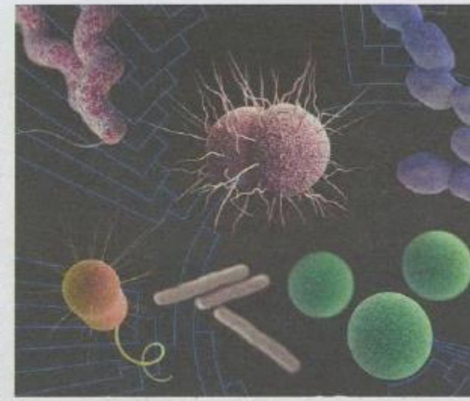
the average long-term diversification by a simple mathematical model. It shows that, on average, there is a constant rate of phenotypic change on the scale of billions of years, revealing the continuity of bacterial adaptation since the beginning of life on our planet.



MODIFIED FROM CDC/MELISSA BROWER

Professor Dennis Vitkup's composite illustration of the external manifestations of a diversity of bacteria.

Vitkup, a native of Ukraine, studied theoretical physics at the Moscow Institute of Physics and Technology. In 1992, at age 21, he moved to the U.S. to work on a Ph.D. in biophysics at Brandeis University and ended up working in the Harvard lab of Martin Karplus (the 2013 Nobel Prize winner in chemistry), using computers to simulate protein dynamics.

Vitkup arrived at Columbia in 2004 after post-doctoral fellowships at MIT and Harvard Medical School. Plata, who is Vitkup's former student, graduated with a degree in biology from Colombia's National University. He joined the graduate program here in 2008 after working as a plant biotechnology researcher in his native country.

For the last decade, the Vitkup group has been developing computer algorithms that use DNA sequences and what's known about biochemical interactions to spit out a list of metabolic reactions likely present in a given microbe. These methods could be used to fight deadly pathogens. Indeed, the algorithms have already been used to piece together the metabolism of a malaria parasite. "It allowed us to predict about 40 new therapeutic targets," Plata says. Last year Vitkup obtained a grant from the National Institutes of Health to build accurate metabolic models for all major human bacterial pathogens.

The computational algorithms developed in the Vitkup lab make it possible to analyze the hundreds of thousands of bacterial genomes which will be sequenced over the next decade. "As with simulations in the field of nuclear research," Vitkup says, "we are moving toward an era when most of this work will be done on a computer and then, in some cases, results will be experimentally investigated in the lab."

The next challenge for Vitkup and colleagues is stepping up the degree of complexity and understanding how hundreds of bacteria work together in symbiotic microbial communities. It is exciting, says Vitkup, because "we now have the tools to really understand the beauty and complexity of the invisible microbial world."