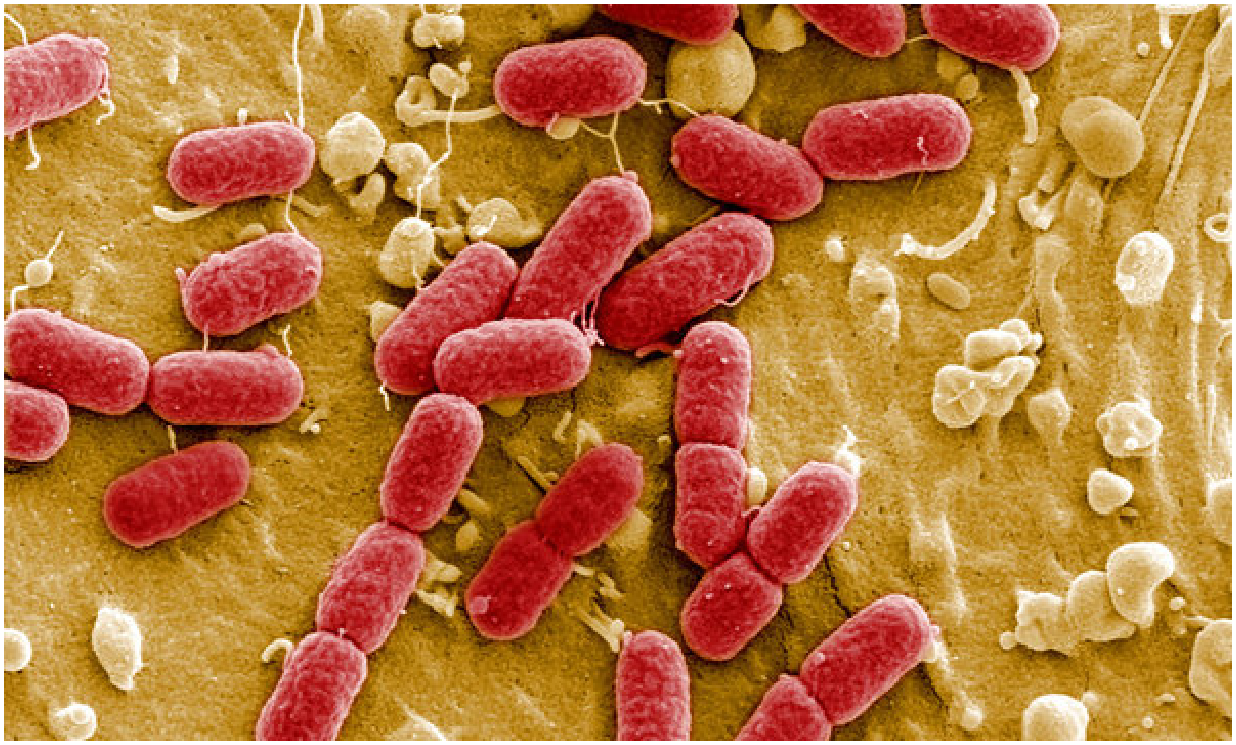
How Simple Can Life Get? It's Complicated



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The microbe Escherichia coli has just 4,100 protein-coding genes. Scientist have found, by systematically shutting those genes off one at a time, that only 302 are absolutely essential to its survival.

In the pageant of life, we are genetically bloated. The human genome contains around 20,000 protein-coding genes. Many other species get by with a lot less. The gut microbe Escherichia coli, for example, has just 4,100 genes.

Scientists have long wondered how much further life can be stripped down and still remain alive. Is there a genetic essence of life? The answer seems to be that the true essence of life is not some handful of genes, but coexistence.

E. coli has fewer genes than we do, in part because it has a lot fewer things to do. It doesn't have to build a brain or a stomach, for example. But E. coli is a versatile organism in its own right, with genes allowing it to feed on many different kinds of sugar, as well as to withstand stresses like starvation and heat.

In recent years, scientists have systematically shut down each of E. coli's genes to see which it can live without. Most of its genes turn out to be dispensable. Only 302 have proved to be absolutely essential.

Those essential genes carry out the same fundamental tasks that take place in our own cells, like copying DNA and building proteins from genes. And yet the 302 genes that are essential to E. coli turn out not to be life's minimal genome. Scientists have come up with lists of essential genes in other microbes, and while the lists overlap, they are not identical.

Scientists can also look to nature for species that are closer to the minimal genome.

In 1969, they first recognized that a group of disease-causing bacteria called Mycoplasma had remarkably tiny genomes. One species, Mycoplasma genitalium, turned out to have a mere 475 genes — one-fiftieth the number in our own set.

For years, M. genitalium held the record for the smallest genome. (Scientists don't allow viruses into this contest, since viruses can't grow and reproduce on their own.) But in recent years, M. genitalium has lost its minimalist crown. Today, the record-holder is a microbe called Tremblaya princeps, which contains only 120 protein-coding genes.

Have we found the minimal genome at last? The answer, once again, is no. But the reason for that reveals something else intriguing about life.

Tremblaya lives in one particular place: the body of a mealybug. And the mealybug, in turn, depends on Tremblaya for its survival.

The insect's only source of food is the sap that it drinks from trees. On its own, the mealybug couldn't survive on this meager diet. Tremblaya transforms the sap into vitamins and amino acids, which the mealybug can then use to build proteins. In exchange for this biological alchemy, mealybugs provide Tremblaya with a steady source of food and shelter.

It's not precisely accurate to say that Tremblaya provides this service. It needs help. Scientists have long known that Tremblaya contains mysterious blobs, but it wasn't until 2001 that Carol D. von Dohlen of the University of Utah and her colleagues discovered that those blobs were a second species of bacteria, living within Tremblaya.

The bacteria, named Moranella endobia, have a genome of their own. It's a tiny genome, with just 406 genes, but it's more than twice as big as Tremblaya's.

Last month in the journal Cell, John McCutcheon of the University of Montana and his colleagues dissected the genes of both Tremblaya and Moranella to get a better sense of what each one does. The two species split up the work involved in building amino acids and assembling them into proteins. Just as the mealybug cannot live without its microbes, the microbes can't live without each other.

Dr. McCutcheon's research reveals a baroque history. At some point in the distant past, the ancestors of Tremblaya infected the ancestors of mealybugs. The microbes gave the insects new metabolic powers, allowing them to feed on an abundant substance — sap — that most other insects couldn't touch. In its comfortable environment, Tremblaya cast off most of its genes.

Only later did Moranella invade the mealybug, and then Tremblaya. It took over some of Tremblaya's work, opening the way for Tremblaya to lose even more of its DNA, until it was stripped down to a mere 120 genes.

Tremblaya and Moranella are the only bacteria found in a healthy mealybug. But Dr. McCutcheon and his colleagues also found vestiges of vanished microbes — in the mealybug's own DNA. Some of its genes are more closely related to genes found in bacteria than genes found in any animal.

This strange resemblance means that mealybugs were once host to other species of bacteria, and some of the genes from those mystery microbes accidentally ended up incorporated into their own DNA.

Six separate species apparently donated genes to the insects. Dr. McCutcheon and his colleagues suspect that the insect uses some of these genes to manage its microbial residents — perhaps using bacteria proteins to extract amino acids from them, for example.

Studies like Dr. McCutcheon's show that the concept of a minimal genome, while provocative, is ultimately a dead end. Life does not exist in a laboratory vacuum, where scientists can pare away genes to some Platonic purity. Life exists in a tapestry, and the species with the smallest genomes in the world survive only because they are nestled in life's net.