Team shows how evolution can allow for large developmental leaps

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How evolution acts to bridge the chasm between two discrete physiological states is a question that's long puzzled scientists. Most evolutionary changes, after all, happen in tiny increments: an elephant grows a little larger, a giraffe's neck a little longer. If those tiny changes prove advantageous, there's a better chance of passing them to the next generation, which might then add its own mutations. And so on, and so on, until you have a huge pachyderm or the characteristic stretched neck of a giraffe.

But when it comes to traits like the number of wings on an insect, or limbs on a primate, there is no middle ground. How are these sorts of large evolutionary leaps made?

According to a team led by scientists at the California Institute of Technology (Caltech), in close collaboration with Patrick Piggot and colleagues from the Temple University School of Medicine, such changes may at least sometimes be the result of random fluctuations, or noise (nongenetic variations), working alongside a phenomenon known as partial penetrance. Their findings were recently published online in the journal *Nature*.

"Our work shows how partial penetrance can play a role in evolution by allowing a species to gradually evolve from producing 100 percent of one form to developing 100 percent of another, qualitatively different, form," says Michael Elowitz, the Caltech assistant professor of biology and applied physics, Bren Scholar, and Howard Hughes Medical Institute investigator who led the team. "The intermediate states that occur along the way are not intermediate forms, but rather changes in the fraction of individuals that develop one way or the other."

Partial penetrance is the name given by evolutionary biologists to the degree to which a single genetic mutation may have different effects on different organisms in a population.

"If you take a bunch of cells and grow them in exactly the same environment, they'll be identical twin brothers in terms of the genes they have, but they may still show substantial differences in their behavior," says Avigdor Eldar, a postdoctoral scholar in biology at Caltech and the paper's first author. These sorts of variations—or noise, as the researchers call it—can actually allow a mutation to have an effect in some organisms but not in others. For example, while some genetically variable cells will show the expected effect of the mutation, others may still behave like a normal, or wild type, cell. And still others may do something else entirely.

"These mutant cells don't only show a different morphology," Eldar notes. "They show more variability in their behavior. In a population, you can see a mixture of several different behaviors, with some cells doing one thing and others doing something else."

In their *Nature* paper, Elowitz and Eldar, along with their colleagues, studied partial penetrance in a species of bacterium known as *Bacillus subtilis*. Specifically, they looked at the spores *B. subtilis* produces as a survival mechanism when times get tough. These spores are smaller, dormant clones of their so-called "mother cell." They're attached to the mother, but are separate entities with their own DNA.

A bacterial spore is designed specifically to do nothing but survive. "It doesn't grow, it doesn't do anything," says Eldar. "It just waits for the good times to return."

The wild-type *B. subtilis* bacterium always sporulates the same way: it creates a single spore, smaller than the mother cell, but with an exact single copy of the mother's chromosome.

What the scientists looked at was a "mutant in which the sporulation process was altered," Eldar explains. "Usually, these cells talk with each other, with the small spore telling the large mother cell, 'I'm here, and I'm doing OK.' In the wild-type cell, this chatter is loud; in the mutant, it's just a whisper, and the mother can't always hear."

When this whispering sort of mutation occurs, the researchers discovered, there are four possible outcomes:

- The bacterium sporulates normally, like the wild type.
- The bacterium makes two copies of its chromosome instead of one, so that there are three chromosomes but creates only a single spore. In this case, the mother cell retains two of the chromosomes and gives the spore one.
- The bacterium makes only one copy of its chromosome, but creates two spores instead of one. In this case, each spore will have a chromosome, and the mother cell will have none. (This is a lethal mutation; neither the mother nor its spores will survive.)
- The bacterium makes two copies of its chromosome instead of one, so that there are three chromosomes. It then creates two spores. In this case, the mother and each of the twin spores will have a single chromosome.

This last possibility, notes Eldar, is something that had never been seen before in *B. subtilis*. But that doesn't mean this twinning behavior doesn't have its advantages. "In some environments, it might be better for the cell," he says. "We know that because there are other species whose wild types do the same thing that our mutant was doing only once in a while."

The scientists soon realized that this variability was their way in to understanding how evolution makes the leap from one to another phenotype. "You can't switch from 1 to 1.1 spores," Eldar points out. "But it's easy to find a mutation that simply changes the frequency of the behavior. If 10 percent of the population makes 2 spores and the rest makes 1, that works. It solves the need for a quantum jump between 1 and 2 spores."

Once they had seen this rare behavior in a small minority of the bacteria, the researchers took the process one step further, tweaking other players in the sporulation system. For instance, they looked at what would happen if, in addition to dampening the communication between mother and spore—making the mother think she hadn't yet successfully produced a spore—you also increased the volume of the signals that tell the mother to replicate its chromosome.

Perhaps not surprisingly, they found that these sorts of changes increase the percentage of *B. subtilis* individuals that decide to produce two spores rather than one. In fact, by combining mutations, Eldar says, they were able to up the percentage of bacteria that create twin spores from about 1 percent (in singly mutated bacteria) to as high as 40 percent (in multiply mutated bacteria).

"When you have only a single mutation, twinning shows very low penetrance," Eldar says. "But when you add more and more mutations, you can build up the penetrance to very high levels."

"We showed that some mutations cause a low frequency of twin spores to develop in the same cell, rather than a single spore per cell, as occurs normally," Elowitz says. "The relative frequency of this form could be tuned up to high levels by other mutations."

This study provides a concrete example of a particular scenario to explain developmental evolution. "It illustrates a somewhat unfamiliar mode in which developmental evolution might work," Elowitz adds. "Qualitative changes from one form to another can proceed through changes in the relative frequencies—or penetrance—of those forms.

"It's interesting that noise—these random fluctuations of proteins in the cell—is critical for this to work," he continues. "Noise is not just a nuisance in this system; it's a key part of the process that allows genetically identical cells to do very different things."

In addition, Elowitz notes, the work shows that "bacterial development can be a good system to enable further study of these general issues in developmental evolution."

More information: "Partial penetrance facilitates developmental evolution in bacteria," *Nature*.

Source: California Institute of Technology (news : web)