Redefining adaptation, the study of how populations grow and survive

June 28 2013, by Marlene Cimons

These vials contain frozen evolved populations. Credit: Christopher J. Marx, Harvard University

(Phys.org) —How do organisms adapt over time? Do they evolve through a series of small beneficial steps as envisioned by Charles Darwin, or through a series of rare but large jumps? Or through a combination of both?

For example, "did a giraffe's neck get longer because there were thousands of mutations each resulting in a millimeter increase?" asks Christopher Marx, associate professor of organismic and evolutionary biology at Harvard University. "Or were there three or four changes over time that changed the size of the vertebrae dramatically?"

Marx's research focuses on adaptation, the process by which populations improve in their ability to grow and survive. "One of the major questions that we are trying to address is: What is the relative proportion of small beneficial mutations to big beneficial mutations?" he says. "And how does this outcome differ with the size of the population?"

Understanding how adaptation works in smaller populations is important because many scenarios—from new infections to cancer—involve small numbers of cells.

"Many current therapeutic approaches aim to reduce population sizes of pathogens in order to thwart their eventual success," Marx says. "This would work very well if these shrunken populations struggle to find beneficial mutations, but would be much less effective if big benefit mutations—to the pathogen or cancer—are actually fairly easy to achieve."

Until recently, many scientists held the classic Darwinian view that adaptation occurs gradually through a series of small changes, he says. Furthermore, they believed that it is extremely rare that a random mutation would actually benefit an organism in a given environment, he says.

"One consequence of the rarity of beneficial mutations would be that any improvement that arose would have a chance to take over before another beneficial mutation would arise, and would thus proceed unchallenged," Marx says. "This would lead to a series of rare, step-like jumps in performance. It would also mean that the mutations that won—rising to 100 percent of the population—would give a fairly clear picture of what is biologically possible for that organism."

In order to study adaptation, including how organisms can improve, Marx's laboratory grows hundreds of bacterial populations in the laboratory. Scientists can preserve live bacteria in an ultra-cold freezer, allowing them to revive and directly study their common ancestor, the one they used to initiate succeeding generations over time.

"Despite the diminutive physical size of these populations, each of which were grown in 1/50th of an ounce of liquid, the final population size could reach as high as 100 million cells," Marx says.

Recent work from a number of laboratories, including Marx's, has shown that beneficial mutations actually can occur much more readily than previously thought. "This changes adaptation dramatically because many innovations can arise at once and they cannot all win," he says.

He compares this competition between rival genetic innovations to what happens in a market economy when, for example, a new field opens and "many companies enter the race and, over time, the better ones beat out the weaker ones," he says.

"Because of the potential for having many new inventions present at once, the population size itself has a profound effect on adaptation," he adds. "The intuition has been that really amazing solutions to a problem are much less common than mediocre ones. Thus, the current theory is that small populations improve via little steps and big populations take big steps."

Marx is conducting his research under a National Science Foundation (NSF) Faculty Early Career Development (CAREER) award, which he received in 2009 as part of NSF's American Recovery and Reinvestment Act. The award supports junior faculty who exemplify the role of teacher-scholars through outstanding research, excellent education and the integration of education and research within the context of the mission of their organization. NSF is funding his work with $702,452 over five years.

The educational component of his grant includes a project-based lab course built around experimental evolution, and a website where scientists who work in microbial evolution can freely share educational materials.

Specifically, Marx has been studying Methylobacterium, a common microbe that lives on the surface of leaves and eats such things as methanol. "It's also the main cause of that pink scum in your shower," he says.

Based upon ongoing work evolving Methylobacterium in the laboratory, Marx and his graduate student, Nigel Delaney, have both confirmed and begun to question current beliefs.

"If you change the population size, three things are supposed to happen," he says. "The first is that big populations should adapt faster than small ones, which turns out to be true. The second is that big populations should have more infighting than little populations, which is also true. The third is that big populations will move by big steps, and small populations will move by small steps."

Their work is ongoing; however, their current data suggest that the third point might not necessarily be true. "Our small and big populations both took big steps," he says. "Big mutations can happen easily. We've seen that in our bug, and it completely changes the picture."

The experiments conducted by Marx and others using populations of microbes in the laboratory that they can control allows them to learn about the range of adaptation possibilities in a way that is difficult when directly studying infectious diseases or cancer, where there will be confounding differences in environments, starting strains or host genetics, and medical treatments.

"The recent use of sequencing to discover cancer variants within a polyp, for example, has re-discovered what researchers in the lab had already shown: many beneficial mutants tend to rise simultaneously, rather than sequentially," he says.

Marx's lab also has begun to examine the outcome of combining more than one beneficial mutation. "Do they stay equally valuable?" he says.

Last year, in a paper his team published in the journal *Science*, they reported on a general trend of diminishing returns. "It turns out that beneficial mutations become less valuable when combined with each other," he says.

Similarly, a University of Houston group led by Marx's friend and colleague, Tim Cooper, an assistant professor of biology, found this identical trend in the evolution of Escherichia coli.

"We had given presentations right after each other at a conference the year before and were shocked by the similarity in our work," Marx says. "That the same trend emerged in two very different systems hinted that it might be a much more widespread finding. Indeed, later papers with viruses and yeast have seen the same."

Ultimately, Marx and Cooper decided to submit their papers at the same time, because "unlike the mutations we studied, we felt our work was more valuable when combined."

Provided by National Science Foundation