All biological organisms compete for limited resources. The successful ones reproduce, and their species survive to another generation. And when species are in direct competition, the one that wins is the one that reproduces fastest – according to the traditional rules of population genetics.

But recent research indicates that rapid reproduction may not always be the winning evolutionary ticket. When mutation rates are low, says Chris Adami of the California Institute of Technology (Caltech), the standard rule applies. But when mutation rates are high, a different principle applies, which Adami and his colleagues call "survival of the flattest."

Adami hasn’t come to this conclusion by studying biological organisms, however. The organisms that he and his colleagues study are digital.

Researchers at Caltech’s Digital Life Laboratory and Michigan State University’s Center for Biological Modeling use a software program called Avida, to create their digital creatures. The organisms exist as sequences of self–replicating computer code. The code determines how the organisms reproduce and how they utilize the available resources: memory and processor cycles. To survive, the organisms have to find a way to increase, or at least to maintain, their share control over these resources. Built–in to their code is the ability to change, or mutate. The code, says Adami, is their genome. Adami believes that valuable lessons about evolution can be learned by studying how digital organisms adapt and survive.
The still−frames depict a competition for resources between two strains of digital organism. Species A (green) replicates twice as fast as Species B (blue), but Species B is more robust. In the top series, which represents a mutation rate of 0.5 mutations per generation, the faster−replicating Species A easily wins out over Species B. In the bottom frame, which represents a mutation rate of 1.5 mutations per generation, the more−robust Species B triumphs.

Credit: courtesy of C.O. Wilke

Humans create the digital creatures by writing their initial computer code. But, says Adami, "they usually shed that coding after a few tens of generations, basically because it’s inane as far as they’re concerned. They just throw it away immediately and come up with something that is much more adapted to the kind of conditions that they live in."

The researchers had found that organisms exposed to high mutation rates, over time, developed a "robustness," or tolerance to mutation. And they suspected that in a high−mutation environment these robust organisms would beat out more−prolific but less−robust competitors.

By adjusting mutation rates, they evolved 40 pairs of species, from which they used 12 to test their theory. Each pair began as a single species. But one organism in the pair evolved under low mutation, the other under high mutation. After many generations, two distinct species had descended from the original one.

In each of the 12 selected pairs, one species (the one evolved under low mutation) was at least 1.5 times as fast at replication, while the other (evolved under high mutation) was slower but more robust.
The researchers then let each pair of species compete. When the competition took place with a low mutation rate, the fast replicator won, as predicted by population genetics. But when faced with a high mutation rate, being fast didn’t help: Even though the faster replicator produced more offspring, most of them couldn’t survive. The more robust species ultimately won out. The results of the research were published in the July 19, 2001, issue of the journal Nature, in an article co-authored by Adami, Claus Wilke and Jialan Wang (Caltech); and Richard Lenski and Charles Ofria (MSU).

How the robust species manage to prevail is a bit of a mystery, says Adami. "We believe they do it by rearranging their code, in a sense spreading it out over the genome so that they are less vulnerable to mutations. However, we haven’t done an extensive study of it, so we have to say that right now we don’t know how they do it."

**Taking the Low Road**

An "artificial petri−dish" studied by Adami and his colleagues. 
*Credit: caltech.edu*

Scientists sometimes represent competition among species within an ecosystem as a landscape with peaks of different heights. Each species is shown as inhabiting a "fitness peak" that sticks up above the baseline, much as a mountain rises above a plain. Species well adapted to survival under low mutation rates – this is the typical state of affairs in nature – appear as tall, thin peaks.

But for such a species, change can be disastrous. If the mutation rate suddenly increases due to some environmental stress, many organisms become ill adapted and fail to reproduce. In terms of the fitness landscape, they are seen as falling off their peak. If the mutation rate gets high enough, the entire species can be threatened. So many offspring in each generation become unfit for reproduction that the remaining offspring can’t reproduce quickly enough to maintain a viable population.

Recall, though, that a species exposed to a high mutation rate – assuming the species survives – responds over time by developing resistance to damaging mutations. While any individual organism might not survive any particular mutation, the "cloud" of organisms that make up the population will contain some individuals that can survive. Adami refers to this cloud as a "quasi−species" because no one organism contains the genome for the species. Rather, a range of genomes exists, and it is this variety that enables the quasi−species to survive in the face of harmful mutations.

On a fitness landscape, such species are represented by lower, flatter peaks. Hence the concept of survival of the flattest.
But Are They Alive?

These digital experiments may be interesting, but can code strings really be considered alive? Can they tell us anything useful about the way evolution works in organisms with RNA and DNA?

Benton Clark, an astrobiologist with the University of Colorado and Lockheed Martin, isn’t so sure. "The nomenclature ´digital organisms´ might be somewhat confusing or misleading," says Clark. "I consider such things as potentially being ´artificial, simulated organisms´ or ´virtual organisms.´" He doesn’t think digital organisms qualify as true life forms because they "do not have physical essence and physical entities are neither reproduced nor created."

"These organisms are in no way simulated," Adami counters. "While it´s true that we simulate a world, we certainly do not simulate the population that actually exists and has to fight in order to survive. The information that is the genetic sequence of these digital organisms is coded in a physical manner in voltage differences in the memory of the computer. And, as such, they are as physical as the information coded in a nucleic acid sequence."

Moreover, Adami adds, "Darwinian evolution is a process that does not refer to nucleic acid bases [DNA] for the very obvious reason that Darwin didn´t know about nucleic acids, since they hadn´t been discovered yet." And because the process of evolution doesn´t depend on "whether it happens in nucleic acids or bit strings, the type of dynamics we observe will be predictive of other types of organisms also."

Viruses, for example, exhibit the kind of quasi−species behavior that the more robust of his digital organisms do, says Adami.

"In virus evolution, you clearly have mutation rates on the order of those that we have played around with. It is clear that a virus is not one particular sequence. Viruses are not pure species. They are, in fact, this cloud, this mutational cloud, that lives on flat peaks. They present many, many, many different genotypes." Adami suggests that this understanding could be useful in designing effective anti−viral treatments.
What’s Next?

Adami believes that his research may also prove useful in the search for extraterrestrial life. One of the difficult questions that astrobiologists struggle with is how they will be able to recognize the biosignature of life forms on other worlds that may have a different chemical foundation than life on Earth.

Adami thinks his digital organisms can help. As he points out, "We’re the only ones who have an alien form of life at our disposal." He has found, for example, that digital organisms that have evolved through many generations display a curious pattern of instructions. "Some instructions are used much more often and some other instructions are used much, much, much less than their random occurrence."

A similar pattern can be seen among amino acids on Earth. Wherever life is at work, the amino acids favored by biological organisms appear in much higher concentrations than they do in the absence of life. Even if you knew nothing about the chemistry of life on Earth, Adami suggests, seeing an atypical abundance of some amino acids, regardless of their specific chemistry, could signal that some type of life was present.

Adami, who is working with Ken Nealson at JPL’s Center for Life Detection and Evan Dorn at Caltech, believes that understanding life’s patterns in this generalized, abstract way can help researchers develop a non–Earth–centric approach to the search for life on other worlds.

"If you are interested in discovering life on other planets, then clearly you would like to be as non–specific as you can about how you go about it," Adami says. "Because you can’t assume that life [elsewhere] is coded in nucleic acids and proteins just as it is on Earth."

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