Evolution by mistake

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Just like erasing misspellings on a whiteboard, organisms have evolved mechanisms to deal with errors that pop up when genetic information is translated into proteins. Joanna Masel (left) and Etienne Rajon discovered that such errors help organisms adapt to evolutionary challenges. Here, they write "GATTACA" on a whiteboard, for the 1997 movie spelled with letters of the genetic alphabet. (Photo by Beatriz Verdugo/UANews)

(PhysOrg.com) -- A major driving force of evolution comes from mistakes made by cells and how organisms cope with the consequences, University of Arizona biologists have found. Their discoveries offer lessons for creating innovation in economics and society.

Charles Darwin based his groundbreaking theory of natural selection on the realization that genetic variation among organisms is the key to evolution.

Some individuals are better adapted to a given environment than others, making them more likely to survive and pass on their genes to future generations. But exactly how nature creates variation in the first place still poses somewhat of a puzzle to evolutionary biologists.

Now, Joanna Masel, associate professor in the UA's department of ecology and evolutionary biology, and postdoctoral fellow Etienne Rajon discovered the ways organisms deal with mistakes that occur while the genetic code in their cells is being interpreted greatly influences their ability to adapt to new environmental conditions – in other words, their ability to evolve.

"Evolution needs a playground in order to try things out," Masel said. "It's like in competitive business: New products and ideas have to be tested to see whether they can live up to the challenge."

The finding is reportered in a paper published in the journal *Proceedings of the National Academy of Sciences*.

In nature, it turns out, many new traits that, for example, enable their bearers to conquer new habitats, start out as blunders: mistakes made by cells that result in altered proteins with changed properties or functions that are new altogether, even when there is nothing wrong with the gene itself. Sometime later, one of these mistakes can get into the gene and become more permanent.

"If the mechanisms interpreting genetic information were completely flawless, organisms would stay the same all the time and be unable to adapt to new situations or changes in their environment," said Masel, who is also a member of the UA's BIO5 Institute.

Living beings face two options of handling the dangers posed by errors, Masel and Rajon wrote. One is to avoid making errors in the first place, for example by having a proofreading mechanism to spot and fix errors as they arise. The authors call this a global solution, since it is not specific to any particular mistake, but instead watches over the entire process.

The alternative is to allow errors to happen, but evolve robustness to the effects of each of them. Masel and Rajon call this strategy a local solution, because in the absence of a global proofreading mechanism, it requires an organism to be resilient to each and every mistake that pops up.

"We discovered that extremely small populations will evolve global solutions, while very large populations will evolve local solutions," Masel said. "Most realistically sized populations can go either direction but will gravitate toward one or the other. But once they do, they rarely switch, even over the course of evolutionary time."

Using what is known about yeast, a popular model organism in basic biological research, Masel and Rajon formulated a mathematical model and ran computer simulations of genetic change in populations.

Avoiding or fixing errors comes at a cost, they pointed out. If it didn't, organisms would have evolved nearly error-free accuracy in translating genetic information into proteins. Instead, there is a trade-off between the cost of keeping proteins free of errors and the risk of allowing potentially deleterious mistakes.

In previous publications, Masel's group introduced the idea of variation within a population producing "hopeful and hopeless monsters" – organisms with genetic changes whose consequences can be either mostly harmless or deadly, but rarely in between.

In the present paper, Masel and Rajon report that natural variation comes in two flavors: regular variation, which is generally bad most of the time, since the odds of a genetic mutation leading to something useful or even better are pretty slim, and what they call cryptic variation, which is less likely to be deadly, and more likely to be mostly harmless.

So how does cryptic variation work and why is it so important for understanding evolution?

By allowing for a certain amount of mistakes to occur instead of quenching them with global proofreading machinery, organisms gain the advantage of allowing for what Masel calls pre-selection: It provides an opportunity for natural selection to act on sequences even before mutations occur.

"There is evidence that cryptic gene sequences still get translated into protein," Masel explained, "at least occasionally."

"When those proteins are bad enough, the sequences that produce them can be selected against. For example, if we imagine a protein with an altered amino acid sequence causing it to not fold correctly and pile up inside the cell, that would be very toxic to the organism."

"In this case of a misfolded protein, selection would favor mutations causing that genetic sequence to not be translated into protein or it would favor sequences in which there is a change so that even if that protein is made by accident, the altered sequence would be harmless."

"Pre-selection puts that cryptic variation in a state of readiness," Masel said. "One could think of local solutions as natural selection going on behind the scenes, weeding out variations that are going to be catastrophic, and enriching others that are only slightly bad or even harmless."

"Whatever is left after this process of pre-selection has to be better," she pointed out. "Therefore, populations relying on this strategy have a greater capability to evolve in response to new challenges. With too much proofreading, that pre-selection can't happen."

"Most populations are fairly well adapted and from an evolutionary perspective get no benefit from lots of variation. Having variation in a cryptic form gets around that because the organism doesn't pay a large cost for it, but it's still there if it needs it."

According to Masel, studying how nature creates innovation holds clues for human society as well.

"We find that biology has a clever solution. It lets lots of ideas flourish, but only in a cryptic form and even while it's cryptic, it weeds out the worst ideas. This is an extremely powerful and successful strategy. I think companies, governments, economics in general can learn a lot on how to foster innovation from understanding how biological innovation works."

More information: *PNAS* paper online: www.pnas.org/content/early/201 … /1012918108.abstract

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