Mutations: When benefits level off

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Beneficial mutations within a bacterial population accumulate during evolution, but performance tends to reach a plateau. Consequently, theoretical evolutionary models need to take into account a "braking effect" in expected benefits on the survival and the reproduction of organisms. This phenomenon (known as negative epistasis) has, for the first time, been demonstrated experimentally by a French-American collaboration, including a team from CNRS. The results are published in *Science* on 3 June 2011.

This study was made possible thanks to a unique experiment in the world, conducted in a laboratory of Michigan State University for over twenty years. Escherichia coli bacteria are cultivated in the laboratory night and day, 365 days a year, and researchers take samples of the populations at regular intervals in order to analyze their evolution. In the course of this long experiment, it has been demonstrated that some bacteria – the best adapted to the environment – gain the upper hand over the rest of the population as generations go by. In other words, natural selection is at work. Conserving bacterial strains through freezing enables researchers to track the memory of this evolution. Better still, they can “revive” at will the ancestral strain and all the strains isolated over the course of the evolution in order to compare bacteria at the end of, for example, 50,000 generations (which, on the human scale, corresponds to nearly two million years). In this way, they are able to quantify the adaptation of bacteria to their environment over time, by evaluating the reproduction rate (or “fitness”) of recent strains compared to that of the oldest strains.

The person in charge of this study, Richard Lenski, initiated collaborations with several international laboratories, including Dominique Schneider's team. The use of modern genomics techniques – the analysis of entire genomes as opposed to just several genes as was previously the case – makes it possible to thoroughly characterize the mutations that occur during bacterial evolution and in particular those that have a beneficial effect, responsible for an increase in the selective value of the population. Here, the researchers focused on the interactions between some of these mutations. After having identified the first five beneficial mutations combined successively and spontaneously in the bacterial population, the scientists generated, from the ancestral bacterial strain, 32 mutant strains exhibiting all of the possible combinations of each of these five mutations. They then noted that the benefit linked to the simultaneous presence of five mutations was less than the sum of the individual benefits conferred by each mutation individually. Epistasis thus tends to reduce the benefit conferred by new beneficial mutations, as they appear in increasingly better-adapted individuals, a phenomenon that explains the slowdown in the adaptive value, observed as organisms continue to adapt.

Thus, beneficial mutations build up during evolution but on the other hand, the performance of the bacterial population tends to level off. Theoretical evolutionary models, which are used to predict results, therefore need to take account of a "braking effect" linked to negative epistasis in the expected benefit on the survival and reproductive potential of organisms. Moreover, this work demonstrates the existence of networks of interconnected genes and suggests that it may be possible to map them so as to better understand and anticipate their interactions.

More information: Negative Epistasis Between Beneficial Mutations in an Evolving Bacterial Population, Aisha I. Khan, Duy M. Dinh, Dominique Schneider, Richard E. Lenski and Tim F. Cooper - Science, 3 June 2011

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