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Big Bang in the Protein Universe?

ScienceDaily (May 19, 2010) — Researchers at Spain's Centre for Genomic Regulation (CRG) demonstrate evidence in support of the common ancestry of life, thanks to a new computational approach to study protein evolution.

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The work, published in *Nature*, takes its inspiration from the astronomer Edwin Hubble and uses his approach to study protein evolution. The extrapolation of Hubble's approach to proteins shows that proteins that share a common ancestor billions of years ago continue to diverge in their molecular composition.

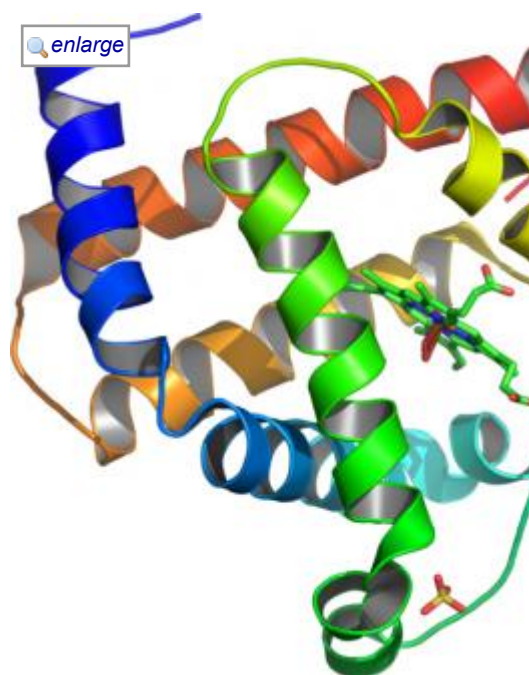
The study reveals that protein evolution has not reached its limit and it is still continuing. At the same time, it provides us new information on why this evolution is so slow and conservative, showing that protein structures are more evolutionary plastic than previously thought.

Almost 100 years ago Edwin Hubble observed that distant galaxies are moving away from Earth faster than

those that are closer. This relationship between distance and velocity is widely cited as evidence of the origin of the Universe from a Big Bang. Researchers at the Centre for Genomic Regulation used his approach to investigate the divergence between protein sequences.

"We wanted to know if the divergent evolution between proteins was still proceeding. Today, we can find proteins that are still similar after almost 3,5 billion years of evolution. Our study showed that their divergence continues with these proteins becoming more and more different despite their incredible level of conservation," said Fyodor Kondrashov, principal investigator of the project and leader of the Evolutionary Genomics group at the CRG.

The work done by Kondrashov and Inna Povolotskaya goes beyond similarity studies and discusses the evolution of proteins from the view of evolutionary dynamics, offering a new



Example of a 3-D structure of a protein (Myoglobin)
(Credit: Courtesy of Wikimedia Commons)

perspective on how protein structures are maintained in evolution. "In the same way that Hubble's observations led to an understanding of the past and the future of our universe, using his approach at a molecular level we get a similar overview that gives us the ability to analyze evolutionary dynamics and get a broad prediction of the possible changes to the proteins in the future," says Povolotskaya, first author of the work and responsible for obtaining and analyzing all data.

Proteins are formed through combinations of amino acids, with only 20 types of amino acids available to form a particular protein. To obtain the data for their study, the CRG researchers have compared proteins sequences from different species that were available in GenBank, a public database of genetic information. Comparing these sequences the authors measured the distance of proteins from each other and devised a method for measuring how fast the proteins are accumulating different changes. Thus, they could replicate Hubble's approach by correlating the distance between the proteins with the rate of their divergence. The result indicates that even the most distantly-related proteins are still accumulating differences.

The study shows how new techniques of bioinformatics and computational analysis can also expand knowledge at a molecular level. "Our work is a good example of how we can learn new and very fundamental things just by analyzing a larger volume of data that can be obtained by one experimental laboratory," says Kondrashov.

Most changes in a protein are deleterious because they somehow disrupt its structure or function. The authors observation that even very conservative proteins are still diverging challenges this view, because it implies that most amino acids in a protein can be changes without any ill effects. Their explanation is that amino acid changes that are deleterious in one combination can be benign when occurring in a different one. "Thanks to our study we now have a better understanding of protein structure dynamics," says Kondrashov. It may provide a new perspective to groups working on protein structure to find new targets for design drugs, etc.

The Povolotskaya and Kondrashov study also provides new information on how different interactions between different amino acids in the structure of proteins slows down but does not completely prevent evolution.

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Adapted from materials provided by [Centre for Genomic Regulation](#).

Journal Reference:

1. Inna S. Povolotskaya, Fyodor A. Kondrashov. **Sequence space and the ongoing expansion of the protein universe.** *Nature*, 2010; DOI: [10.1038/nature09105](https://doi.org/10.1038/nature09105)

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