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Scale-free Evolution: From Proteins to Organisms. Nikolay V. Dokholyan, Dept. Biochemistry & Biophysics, U. North Carolina-Chapel Hill, CB 7260, Chapel Hill, NC 27599, dokh@med.unc.edu; Web: <http://dokhlab.unc.edu/>.

The bottom-up approach to understanding the evolution of organisms is by studying molecular evolution. We have discovered peculiar patterns that nature imprints on protein structural space in the course of evolution. In particular, we have found that the universe of protein structures is organized hierarchically into a scale-free network. We propose a model that explains the hierarchical organization of proteins in fold families. The model, which is based on the evolutionary selection of proteins by their native state stability, reproduces patterns of amino acids conserved across protein families. Due to its dynamic nature, the model sheds light on the evolutionary time-scales. By studying the relaxation of the correlation function between consecutive mutations at given position in proteins, we observe separation of the evolutionary time-scales: at short time intervals families of proteins with similar sequences and structures are formed, while at long time intervals the families of structurally similar proteins that have low sequence similarity are formed.

[1] N. V. Dokholyan and E. I. Shakhnovich, *J. Mol. Biol.* 312: 289-307 (2001)

[2] N. V. Dokholyan et al., *Proc. Natl. Acad. Sci. USA* 99: 14132-14136 (2002).