

Proteins diverge during biological evolution. At the level of sequences, different aminoacids evolve at different rates, which is a clear evidence of natural selection. We recently found that the rate of evolution of a site depends on the stress of the protein's active structure generated when it mutates, which is related to the degree of packing of the site. However, at the level of structure, even though there are preliminary, the role of natural selection has not been elucidated yet. To study this, we deeply analyzed the effect of natural selection on the structural divergence of a wide set of families of proteins. For each family, we compared a set of experimental data with two equivalent sets of simulated data: purely mutational or mutational restricted by natural selection. To simulate the mutants we generated subsequent random mutations by perturbing the oscillators coupled to the corresponding site. For the set restricted by natural selection, we selected each mutation according to its fixation probability, which depends exponentially on the packing density of the site. The profiles we analyzed were both in Cartesian coordinates and projected on the normal modes of proteins. We found that the agreement between experimental and simulated profiles is high either considering or not natural selection in the simulations. Moreover, there are no clear differences between simulated profiles. These results suggest there is no evidence of natural selection on the evolution of the structure and go against the common belief that natural selection governs molecular evolution.