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The role of protein dynamics in the evolution of new enzyme function

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Enzymes must be ordered to allow the stabilization of transition states by their active sites, yet dynamic enough to adopt alternative conformations suited to other steps in their catalytic cycles. The biophysical principles that determine how specific protein dynamics evolve and how remote mutations affect catalytic activity are poorly understood. Here we examine a 'molecular fossil record' that was recently obtained during the laboratory evolution of a phosphotriesterase from Pseudomonas diminuta to an arylesterase. Analysis of the structures and dynamics of nine protein variants along this trajectory, and three rationally designed variants, reveals cycles of structural destabilization and repair, evolutionary pressure to 'freeze out' unproductive motions and sampling of distinct conformations with specific catalytic properties in bi-functional intermediates. This work establishes that changes to the conformational landscapes of proteins are an essential aspect of molecular evolution and that change in function can be achieved through enrichment of preexisting conformational sub-states.

Keywords or phrases (comma separated)

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No

Do you wish to take part in</br>the Student Poster Slam?

No

Are you an ECR? (<5 yrs</br>since PhD/Masters)

No

What is your gender?

Male

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