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The relationship between relative solvent accessibility and evolutionary rate in protein evolution

CLAUS WILKE, The University of Texas at Austin

Recent work with the yeast *Saccharomyces cerevisiae* shows a linear relationship between the evolutionary rate of sites and the relative solvent accessibility (RSA) of the corresponding residues in the folded protein. Here, we aim to develop a mathematical model that can reproduce this linear relationship. We first demonstrate that two models that both seem reasonable choices (a simple model in which selection strength correlates with RSA and a more complex model based on RSA-dependent amino-acid distributions) fail to reproduce the observed relationship. We then develop a model based on observed site-specific amino-acid distributions and show that this model behaves appropriately. We conclude that evolutionary rates are directly linked to the distribution of amino acids at individual sites. Because of this link, any future insight into the biophysical mechanisms that determine amino-acid distributions will improve our understanding of evolutionary rates.