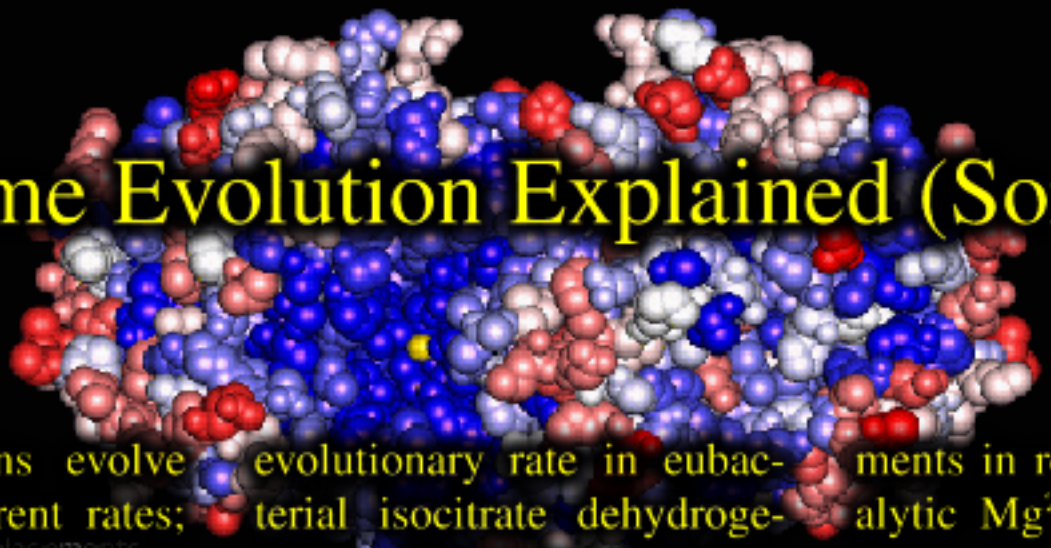
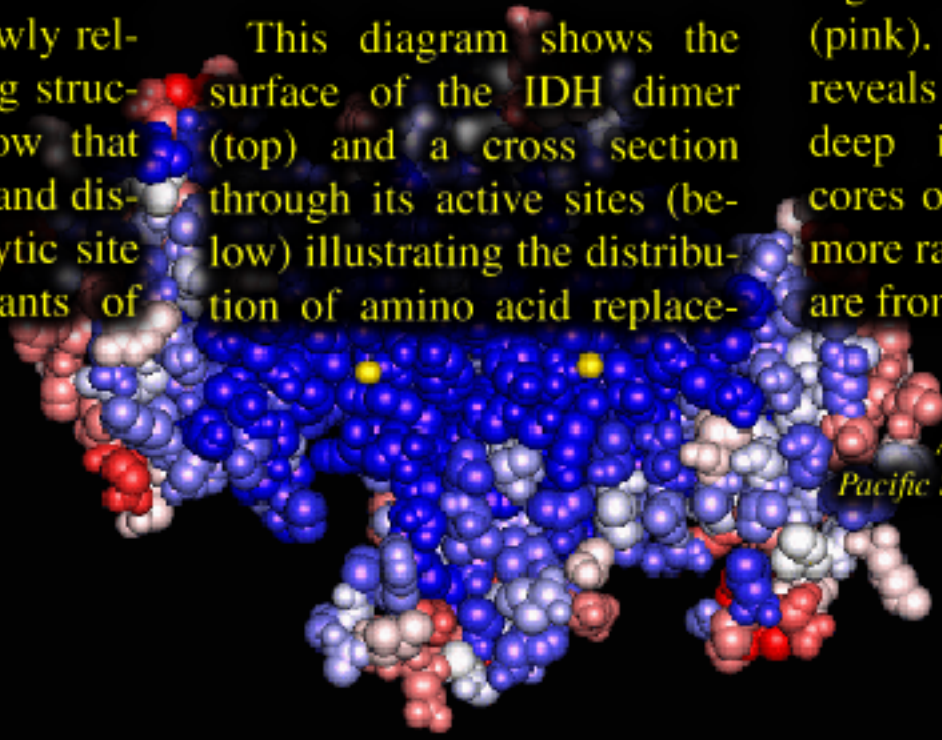
Enzyme Evolution Explained (Sort Of)



Sites in proteins evolve at markedly different rates; some are highly conserved, others change rapidly. We have developed a maximum likelihood method to identify regions of a protein that evolve rapidly or slowly relative to the remaining structure. We also show that solvent accessibility and distance from the catalytic site are major determinants of evolutionary rate in eubacterial isocitrate dehydrogenases. These two variables account for most of the rate heterogeneity not ascribable to stochastic effects.

This diagram shows the surface of the IDH dimer (top) and a cross section through its active sites (below) illustrating the distribution of amino acid replacements in relation to the catalytic Mg^{2+}'s (yellow). It needs no statistical test to confirm that the active sites are highly conserved (dark blue), whereas the remaining surfaces evolve rapidly (pink). The cross section reveals that residues buried deep in the hydrophobic cores of the domains evolve more rapidly the further they are from the catalytic Mg^{2+}.



A.M. Dean and G.B. Golding
Pacific Symposium on Biocomputing
2000. pp 6-17.