

(Protein) Networking and Dating

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Biological redox reactions are a crucial component of planetary biogeochemical cycles. The ability to get, use, and store energy is a pre-requisite for life. Thus, biological electron transfer, likely facilitated by metal-containing ligands, must have been one of the earliest functionalities acquired by living organisms. The original metal-ligand binding folds would, arguably, have been simple and small. These were “decorated” with additional features in the process of evolution.

We extracted the regions in 3D structures of existing proteins that contain the likely original folds and used a newly developed computational method to estimate their functional similarities. We further built a network of these folds (nodes) and their similarities (edges) and annotated it with metadata (ligand, metal, enzymatic activity) and, where available, evolutionary information. Our results reveal that folds in our set have similar structural geometry of binding, regardless of the ligand specifics, suggesting that metal-ligand binding may thus have a limited number of common origins. Moreover, we find that the localization (centrality) of ligands within the fold-network is in line with the coarse biomarkers of evolutionary eras. These results suggest that further exploration could outline evolutionary history of biological redox even more precisely.