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The robustness and innovability of protein folds

Over 60% of the known folds carry out one or two enzymatic functions, while few folds, e.g. the TIM-barrel and Rossmann folds, exhibit hundreds. Are there structural features that make a fold amenable to functional innovation (innovability)? Do these features relate to robustness –the ability to readily accumulate sequence changes? I will discuss several hypotheses regarding the relationship between the architecture of a protein and its evolutionary potential. I will describe how, in a seemingly paradoxical manner, opposite properties such as high stability and rigidity vs. conformational plasticity, and respectively, structural order vs. disorder, promote robustness and/or innovability. Indeed, polarity –differentiation and low connectivity between a protein's scaffold and its active-site, is a key prerequisite for innovability.

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