

Expanding the space of protein geometries by computational design of de novo fold families

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Exploring the design landscape

Protein design typically selects a protein topology and then identifies the geometries (secondary-structure lengths and orientations) that give the most stable structures. A challenge for this approach is that functional sites in natural proteins often adopt nonideal geometries. Pan *et al.* addressed this issue by exploring the diversity of geometries that can be sampled by a given topology. They developed a computational method called LUCS that systematically samples geometric variation in loop-helix-loop elements and applied it to two different topologies. This method generated families of well-folded proteins that include structures with non-native geometries. The ability to tune protein geometry may enable the custom design of new functions.

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