New class of protein misfolding explains decades old biochemical data and offers new insight into protein folding and function

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I will present computational and experimental evidence indicating there exists a previously unrecognized, widespread class of monomeric protein misfolding that can explain decades-old biochemical data, including how synonymous mutations can alter protein function over long time scales in vivo. That this new class of misfolding involves the formation of tertiary structural motifs (non-covalent lasso entanglements) that only recently have been recognized to occur in the majority of natively folded globular proteins.

I will provide evidence that evolutionary selection pressures have enriched these non-covalent lasso entanglements in allosteric and enzymes presumably to enhance their function. Further, in terms of protein folding behavior, I will show how this new class of misfolding can give rise to stretched-exponential folding kinetics indicating they contribute to large free energy barriers between different basins on the unfolded free energy landscape. Thus, the formation of these native and non-native entangled motifs is opening up new perspectives and offering new explanations to old questions in biophysical chemistry.