Design and Engineering of Nanopores with Emergent Functions
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interaction partners. How difficult, then, is it for a protein to discriminate its correct interaction partner(s) from the possibly large set of other proteins it may encounter in the cell?

An important ingredient of recognition is shape complementarity. The ensemble of protein shapes should be constrained by the need for maintaining functional interactions while avoiding spurious ones.

To address this aspect of protein recognition, we consider the ensemble of proteins in terms of their three-dimensional shapes, more precisely in terms of their solvent-excluded surfaces. We take into account the high-resolution structures from E. coli non-DNA-binding cytoplasmic proteins that can be retrieved from the Protein Data Bank. We aim to characterize the statistical properties of the protein surfaces at two levels: First, we study the intrinsic dimensionality at the level of the ensemble of the surface objects. Second, at the level of the individual surfaces, we determine the scale of shape variation. We further discuss how the dimensionality of the space of protein surfaces is linked to the statistical properties of individual protein surfaces.

2642-Pos Board B19
A Novel In Silico 4D Geometrical Measure of the Active Site Correlates with the Enzymatic Activity of HCV NS3 Protease; Implications in Catalysis and Drug Design
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We have previously developed and improved on a 4D computational methodology, based on 3D structural modeling coupled with molecular dynamics simulations, to analyze, pan-genotypic, the active sites of the NS3 proteases of HCV, in relation to their catalytic activity and drug susceptibility. The 4D analysis of the interactions between the catalytic triad residues (His57, Asp81, and Ser139) yielded a divergent, gradual and genotype-dependent, 4D conformational instability measures, which correlate well with the known altered catalytic activities. Here, we present the correlation of our 4D instability measures to known intra-genotypic alterations in NS3 protease activity, due to sequence variations in the NS4A cofactor. The correlation is qualitatively evident, which further validates our methodology, paving the way to building an accurate quantitative metric to predict protease activity in Silico. In addition, the results suggest a plausible “information” pathway from the activation subunit (the NS4 cofactor binding site) to the catalytic subunit (the catalytic triad region). The results strongly suggest that the structural dynamics behaviour, more than the rigid structure, is related to the altered catalytic activity and possibly drug susceptibility seen in HCV NS3 proteases.

2643-Pos Board B20
Tensile Mechanics of Coiled Coil Protein Structures
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A coiled-coil protein structure consists of two or more interacting z-helical strands that together form a supercoil structure. Coiled-coil structures entail unique mechanical properties that are critical to the function and integrity of various motor proteins, cytoskeletal filaments and extra-cellular matrix proteins. Here we present a thermodynamic model to predict the mechanical properties of a given coiled-coil structural motif. Within the proposed model we identify and quantify various energetic and entropic effects, responsible for dimerization of two helical poly-peptides into a coiled coil structure. We determine our model parameters by examining a large body of solved protein structures that contain coiled coil motifs. This would allow us to develop a thermodynamic model for predicting the propensity of given amino acid sequence to form a coiled coil structure. Further incorporation of the above model into our previously developed sequence to form a coiled coil structure. Further incorporation of the above model into our previously developed sequence to form a coiled coil structure. Further incorporation of the above model into our previously developed sequence to form a coiled coil structure. Further incorporation of the above model into our previously developed sequence to form a coiled coil structure. Further incorporation of the above model into our previously developed sequence to form a coiled coil structure.