information about the method run, percentage structure content, chain length and diagram of the three-state structure assignment, also provided.
(Supported by a grant from the BBSRC Bioinformatics and Biological Resources Fund, UK).

2352-Pos
An Automated Approach to Segregate and Identify Functional or Disordered Loop Regions in Protein Structures using their Ramachandran Maps
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The loops which connect or flank helices/sheets in protein structures are known to be functionally important. However, ironically they also belong to the part of protein whose structure is least accurately predicted. Here, a new method to isolate and analyze loop regions in protein structure is proposed using the spatial coordinates of the solved 3D structure. The extent of dispersion among points of successive amino acid residues in the Ramachandran map of protein region is utilized to calculate the Mean Separation between these points in the Ramachandran Plot (MSRP). Based on analysis of 2935 protein secondary structure regions obtained using DSSP software, spanning a range from 2 to 64 residues, taken from a set of 170 proteins, it is shown that helices (MSRP < 17) and strands (MSRP < 64) stand effectively demarcated from the loop regions (MSRP > 130). Analysis of 43 DNA binding and 98 ligand binding proteins revealed several loop regions with clear change in MSRP subsequent to binding. The population of such loops correlated with the magnitude of backbone displacement in the protein subsequent to binding. Can changes in MSRP quantify the temporal oscillations in dihedral angles among structured/unstructured regions in proteins? Molecular dynamics simulations (10 ns) revealed that deviations in MSRP among different snapshots in the trajectory were at least two-fold higher for unstructured proteins (PDB codes: 2SOB, 1LXL, 2HDL & 1VZS) in comparison with folded proteins (PDB codes: 1BGF & 1MUN). Additionally it was observed that deviations in MSRP were highest amongst loop regions, while it was lowest amongst alpha-helical regions. The above results validate use of MSRP parameter as a tool to identify & investigate functionally active loops and unstructured regions in protein structures.

2353-Pos
Origins of Thermophilicity in Endoglucanases
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Endoglucanases are involved in the initial stages of cellulose breakdown–an essential step in the bioprocessing of lignocellulosic plant materials into bioethanol. Although these enzymes are economically important, we currently lack a basic understanding of how some endoglucanases can sustain their ability to function at elevated temperatures needed for bioprocessing, while others with the same fold cannot. In this study, we present a detailed comparative analysis of both thermophilic and mesophilic endoglucanases in order to gain insights into origins of thermophilicity. We used the CAZy (Carbohydrate-Active enZymes) database to build our endoglucanase protein data sets and analyzed their sequences and structures. Our results demonstrate that thermophilic endoglucanases and their mesophilic counterparts differ significantly in their amino acid compositions. Strikingly, these compositional differences are specific to protein folds and enzyme families and lead to modification in hydrophobic, aromatic, and ionic interactions in a fold-dependent fashion. However, when it comes to thermophilicity, there is a caveat of applying general heuristic rules to specific proteins: although thermophilicity in endoglucanases is usually conferred through altering amino acid composition, in some cases even a single-point mutation is sufficient to convert a mesophilic protein into a thermophilic protein. Here, we provide fold-specific guidelines to control thermophilicity in endoglucanases that will make production of biofuels from plant biomass more efficient.

2354-Pos
Thermophilic Adaptation of Protein Complexes Inferred from Proteomic Homology Modeling
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What can Nature teach us about mechanisms securing unique and stable interfaces in native protein complexes and preventing aberrant assembly of their parts in misfolded conformations? As protein complexes must remain in their native conformations at physiologically relevant temperatures, thermal adaptation requires adjustment of pertinent interactions. Based on high-quality sets of structural templates and sequences of 127 complete prokaryotic proteomes with the optimal growth temperature (OGT) from 8 to 100 C°, we performed homology modeling of complexes and monomeric proteins and analyzed trends in their sequences and structures related to thermal adaptation. With model of protein stability including negative and positive components of design, we investigate compositional biases and their correlations with the habitat temperatures specific for protein complexes. Specifically, we show how positive charges work in negative design preventing aggregation and how they contribute to positive design stabilizing both the native interface and the overall structure of the complex. Aggregation propensity of interfaces is higher than the one of surfaces and increases with OGT helping to form native complexes in harsh environments. Thermophilic trends obtained in high-throughput proteomic homology modeling illuminate sequence/structure determinants of molecular mechanisms working in protein complexes. We show that these tends are generic for both obligatory and transient complexes. They can be instructive, therefore, in experimental efforts on design of protein complexes and preventing aberrant assembly.

2355-Pos
Protein-Protein Docking Using a Brownian Dynamics Simulations Approach
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A successful protein-protein docking method provides theoretical understanding of how two or more proteins combine and interact with each other at the atomic level. It involves some unsolved problems partly due to the huge sampling space. Here we present an adapted Brownian Dynamics (BD) method used to predict the structure of protein complexes. The BD protein docking approach includes two steps, 1) global BD sampling; 2) local energy minimizations. In the first step, we run thousands of independent BD simulations to explore the entire possible conformational spaces of the protein complexes. The proteins are treated as two rigid bodies, and the translational and rotational motions are simulated for one of the proteins (protein II) around the other (protein I). The intermolecular forces and torques between proteins are given by the sum of electrostatic and exclusion forces. In the second step, we conduct local energy minimizations for all protein complexes obtained from the step one, and rank them by interaction energies. To reduce the computational costs for energy evaluations, we developed a grid-based force field to represent protein I and solvation effect. The rigid-body energy minimizations of the protein complexes are based on the downhill simplex method using the newly developed force field. The prediction quality of this newly developed BD protein docking approach is evaluated on a re-docking experiment for predicting the acetylcholinesterase-fasciculin complex (PDB entry 1FSS). The result shows that 100,000 independent BD runs generated 32797 protein complexes for the subsequent local energy minimizations. The root mean square deviation (RMSD) between the predicted lowest energy and the crystal structures is 0.17 Å. In conclusion, this adapted BD protein docking approach could be used for prediction of other protein complexes, and help better understanding protein-protein interactions.

Protein Aggregates II

2356-Pos
Both the Formation and Polyphenol-Induced Dissociation of Various Amyloid Fibrils are Accompanied by ROS Formation
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Fibrillization of amyloid polypeptides is accompanied by formation of reactive oxygen species (ROS), which, in turn, is assumed to further promote amyloid-related pathologies. Different polyphenols, all of which are established antioxidants, cause dissociation of amyloid fibrils. In this study we address the latter, poorly understood process. Specifically, we have investigated the dissociation of Aβ42 fibrils by six different polyphenols, using electron microscopy and spectrofluorimetric analysis. Simultaneously, we have monitored the production of ROS using electron spin resonance (ESR) and the commercially available peroxide assay kit. Using the same methods, we found that curcumin, one of the most potent destabilizing agents of Aβ42, induces dissociation of fibrils of other amyloid polypeptides [Aβ40, Aβ42Nle35, islet amyloid polypeptide and a fragment of α-synuclein].
When the solution contained traces of transition metal, all the dissociation reactions were accompanied by ROS formation, independent of the presence of a methionine residue. Kinetic studies show that the formation of ROS lags behind dissociation, indicating that if casual relationship exists between these two processes, then ROS formation may be considered a consequence and not a cause of dissociation.
Understanding of our results and of their implications requires further research.