difference between the ensemble of configurations they sample in the presence and in the absence of Ephrin-B2. These ensembles were generated using molecular dynamics simulations. Rank-ordering and then mapping the residues that undergo the greatest change in motion on to the 3-d structure of the G-protein reveals that they are clustered primarily on a single contiguous facet of the protein, and include the set that is known experimentally to play a vital role in regulating viral fusion.

2583-Pos Board B602

Precise Normal Mode Analysis and Frequency Prediction of DNA Nanostructure through Mass-Weighted Chemical Elastic Network Model

Soojin Jo, Min Hyeok Kim, Junyoung Son, Sung Ha Park, Moon Ki Kim.
Sungkyunkwan University, Suwon, Korea, Republic of.

In our previous study on self-assembly mechanism of DNA nanostructures, using elastic network model (ENM) based normal mode analysis (NMA), we successfully explained the reason why planar DNA tiles were self-assembled as a helical nanotube, which was totally contrast to our preconception such that they could form a planar lattice nanostructure. Although this traditional ENM based NMA is very useful to catch collective motions of biomolecules in a timely fashion, it is impossible to predict vibration frequency due to its dimensionless uniform mass and spring constants.

We propose a mass-weighted chemical elastic network model (MWCENM) which takes inertia effect and chemical bond information into account. For example, lumped masses are assigned to the representative atoms and different spring constants are given to bonded and non-bonded interactions including covalent bond, hydrogen bond, and van der Waals interaction.

Several comparison studies convince us that MWCENM is able to catch DNA dynamics more precisely and more effectively. It is also expected that one can use MWCENM based NMA results, which include both predicted frequencies and corresponding mode shapes, as a fingerprint to characterize molecular dynamics by a comparison with vibration spectrum data.

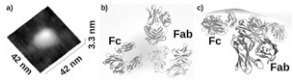
2584-Pos Board B603

Multiscale Protein Reconstruction using Atomic Force Microscopy

Rui C. Chaves[1], Michael Odorico[1], Jean-Marie Teulon[1], Pierre Parot[1], Shu-wen W. Chen[1,2], Jean-Luc Pellequer[1].
[1]CEA, iBEB, Department of Biochemistry and Nuclear Toxicology, Bagnols sur Ceze, France, [2]13 Avenue de la Mayre, 30200 Bagnols sur Ceze, France.

Recent discovered protein structures are made of folds that have been previously determined. The discovery of new folds is currently at a pause and there is a giant gap in the 3D knowledge of large proteins (> 600 residues) compared to the knowledge of protein sequences.

We have recently proposed a multiscale integrative structural biology method for the reconstruction of large macromolecular proteins based on the assembly of their individual constituents [Trinh et al., Structure 20, 113 (2012)]. The protocol is based on real-space docking of macromolecular constituents beneath an experimental topographic surface such as AFM images and the assembly of the molecular constituents is performed using a combinatorial approach. Preliminary results were obtained with simulated data. Here, an antibody structure was reconstructed using its Fab and Fc constituents: the air AFM Multimode III topographic image (32^2 pixels) [Figure a] was deconvoluted from the tip shape and used as envelop surface. The top scored result from the reconstruction of 2000^3 solutions out of 10^{11} docking orientations (computation time 3h30, 30 CPUs) is represented in Figure b (top) and c (side view). The protocol efficiency will be evaluated, advantages and drawbacks will be discussed.



2585-Pos Board B604

Are Hot-Spots Occluded from Water?

Irina S. Moreira, João M. Martins, Rui M. Ramos, Pedro A. Fernandes, Maria J. Ramos.
REQUIMTE, Porto, Portugal.

Protein-protein interactions are the basis of many biological processes and are governed by focused regions with high binding affinities, the hot-spots (HS).(Martins *et al.*, 2013, Moreira, Martins, *et al.*, 2012) It was proposed that these regions are surrounded by areas with higher packing density leading to solvent exclusion around them - ''the O-ring theory''.(Bogan & Thorn, 1998) This important inference still lacks sufficient demonstration. We have used Molecular Dynamics (MD) simulations to investigate the validity of the O-ring theory in the context of the conformational flexibility of the proteins, which is critical for function in general and for interaction with water, in particular. For a database of 160 residues in 9 complexes the MD results were analyzed for a variety of solvent accessible surface area features, radial distribution functions, protein-water distances and water residence times. The measurement of the average Solvent Accessible Surface Area features for the HS and null-spots (NS), as well as data for corresponding radial distribution functions, identify distinct properties for these two sets of residues. HS are found to be occluded from the solvent. This study provides strong evidence in support of the O-ring theory.(Moreira, Ramos, *et al.*, 2012)

Bogan, A. A. & Thorn, K. S. (1998). *Journal of Molecular Biology* **280**, 1-9.
Martins, J., Ramos, R. & Moreira, I. (2013). *Communications in computational physics* **13**, 238-255.
Moreira, I. S., Martins, J. M., Ramos, M. J., Fernandes, P. A. & Ramos, M. J. (2012). *Biochem. Biophys. Acta*, Available online.
Moreira, I. S., Ramos, R. M., Martins, J. M., Fernandes, P. A. & Ramos, M. J. (2012). In submission.

2586-Pos Board B605

Protein-Protein Interaction Prediction by using Amino Acids Interaction Pattern in Rigid-Body Docking Process

Nobuyuki Uchikoga[1], Takatsugu Hirokawa[2].
[1]Chuo University, Tokyo, Japan, [2]CBRC, AIST, Tokyo, Japan.

We approached to prediction of protein-protein interactions using rigid-body docking algorithm, generating many decoys including false positives. To search near-native decoys from a decoy set generated by a docking process, cluster analysis is useful with calculating similarities between decoys. However, this analysis goes well only in the case that a decoy set includes near-native decoys. Actually, there are some cases of protein pairs with no near-native decoys after an initial docking process.

This problem is related with a size of docking search spaces. When a size of search space is small, near-native decoys cannot be obtained after a rigid-body docking process. We then applied a profile method to obtain a region including native interacting residue pairs for re-docking process by using Profile of Interaction FingerPrints (P-IFP).

Interaction FingerPrints (IFP) has been developed for the post-docking analysis of protein-protein rigid-body docking. IFP is composed of binary states of interacting amino acid residues of each interacting proteins, as a scale for measuring unique similarities between the complex structures. Then, IFP can be used more easily to evaluate similarities between decoys than RMSD method, which depends on methods of superposing their structures. Additionally, IFP can be useful to assemble interaction profiles from various decoys.

In this work, we examined re-docking process after generating P-IFP for rigid-body docking decoys. As results, we could obtain a set of decoys with higher similarities than that of decoys generated in the initial docking process. Re-docking method using the IFP method is expected to improve cases without near-native decoys in an initial docking process.

2587-Pos Board B606

Small Druglike Molecules with Specific Binding to Plk1 Or LYN Kinases

D.S. Dalafave.
The College of New Jersey, Newtown, PA, USA.

The research addresses computational design of small druglike molecules for possible anticancer applications. Polo-like kinase 1 (Plk1) is a main regulator of mitosis. Its inhibition can lead to apoptosis of cancer cells. Most kinases interact with inhibitors via their highly conserved ATP sites. This makes the design of Plk1-specific inhibitors challenging. However, Plk1 also has the polo-box domain (PBD) that is absent from other kinases. Previously, we designed several molecules that interacted with the PBD of Plk1 and with only one other kinase, LYN. The LYN kinase regulates hematopoietic cells from which cellular blood components are derived. Yet, LYN's greatly elevated activity in glioblastoma tumors suggests that it promotes the malignancy in these cells. In light of their respective cellular roles, it is important to design inhibitors that are either Plk1- or LYN-specific. This is not trivial because of their very similar binding sites. Physicochemical differences between the sites were analyzed in the DeepView program. Relevant atomic distances within the PBD of Plk1 were found greater than those within LYN. Thus, a larger molecule could potentially fit into the PBD and would be excluded from the LYN's smaller and less flexible site. Previously designed molecules that bonded both Plk1 and LYN were used as templates to design more specific inhibitors. Designed molecules with no indicated toxicities and optimal values of other drug-related properties were used for docking in ArgusLab. Molecules that made stable complexes specifically with either Plk1 or LYN, but with no other kinases, were identified. Drugs based on these molecules could be useful against tumors with overexpressed Plk1 or LYN. Such drugs could selectively bind one of the kinases and lead to fewer side effects than a less selective drug.