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***de Novo* Protein Structure Prediction using Fragment Based Potential and Conformational Space Annealing**
Juyong Lee[1,2], Masaki Sasai[3,4], Chaok Seok[1,2], Jooyoung Lee[2,4].
[1]Department of Chemistry, Seoul National University, Seoul, Republic of Korea, [2]Center for In Silico Protein Science, KIAS, Seoul, Republic of Korea, [3]Department of Applied Physics, Nagoya University, Nagoya, Japan, [4]School of Computational Sciences, KIAS, Seoul, Republic of Korea.
De novo prediction of the protein structure, modeling the native structure of a protein from its sequence information when homologous protein structures are not available from the database, is one of the most challenging problems in biophysics. Here, we have employed a coarse-grained multibody energy function approach. A sequence-specific continuous energy function is constructed from the structural and environmental information extracted from fragments. The original algorithm[1] was coupled with Langevin molecular dynamics for searching low energy structures, and when applied to "free modeling" and hard "template-based modeling" targets from CASP7, the prediction results were quite comparable to existing methods. In this study, first, the conformational space annealing (CSA) method is implemented with the above-mentioned energy function. CSA has been quite efficient in searching diverse low-energy solutions in various multiple-minima problems. As expected, lower energy model structures are obtained by CSA over Langevin molecular dynamics approach. However, lower energy structures were not necessarily better in their structural quality. We have carried out energy function optimization by adjusting weight parameters of the function. Details of the parameter optimization as well as application of the newly obtained energy function to target proteins not included in the optimization will be provided.
1. Sasaki TN, Cetin H, Sasai M: A coarse-grained Langevin molecular dynamics approach to de novo protein structure prediction. *Biochem. Biophys. Res. Comm.* 2008, 369:500-506.

2383-Pos
Iterative Assembly of Protein Fragments
Geoffrey C. Rollins, Justin L. MacCallum, Ken A. Dill.
UCSF, San Francisco, CA, USA.
MASH (Magical Assembly of Sheets and Helices) is a computational method for iterative assembly of protein secondary structure fragments into native-like tertiary structures. For a given pair of fragments, we select a pair of hydrophobic residues (in the case of helix assembly) or an H-bond donor/acceptor pair (in the case of beta strands). We then position the two fragments so that the selected residues are in close proximity to one another. Finally, we attempt to connect the two fragments with a robotics-based loop-closure algorithm. Fragment pairs that have steric clashes or unclosable loops are discarded. We repeat the above procedure to generate an ensemble of fragment pairings, which we then score on the basis of radius of gyration and solvent accessible surface area.

2384-Pos
Template-Based Protein Modeling using Global and Local Templates
Junsu Ko[1,2], Hahnbeom Park[1,2], Chaok Seok[1,2], Jooyoung Lee[3,2].
[1]Seoul National University, Seoul, Korea, Republic of, [2]Center for In Silico Protein Science, Korea Institute for Advanced Study, Seoul, Korea, Republic of, [3]Korea Institute for Advanced Study, Seoul, Korea, Republic of.
For successful template-based protein modeling, it is important to identify relevant template proteins to the target sequence and then to generate proper multiple sequence alignment (MSA) between the target and the templates. However, in many cases, the templates obtained by global sequence search do not provide relevant structural information for local regions represented by gaps in the MSA. We have developed a method to improve the modeling accuracy of such regions by detecting unreliable local regions and utilizing local templates that can provide more reliable structural information for those regions. Our approach takes the following steps. First, a new scoring scheme that utilizes a modified information score is employed to detect unreliable local regions. Second, local templates that are aligned to the local regions more reliably are identified. Finally, the local templates are combined with the global templates to produce better 3D models. With newly obtained MSA containing global as well as local templates, protein 3D models are generate by a recently proposed model-building technique, MODELLER-CSA.

2385-Pos
Determination of the Pseudo-Atomic Structure of Nuclear Pore Complex (NPC) Components by Small Angle X-Ray Scattering (SAXS) and Computational Modeling
Seung Joong Kim[1], Jeremy Phillips[1], Anne Martel[2], Dina Schneidman[1], Michael Sauder[3], Michael P. Rout[4], Hiro Tsuruta[2], Andrej Sali[1].
[1]University of California, San Francisco (UCSF), San Francisco, CA, USA, [2]Stanford Synchrotron Radiation Laboratory, Menlo Park, CA, USA, [3]Eli Lilly, San Diego, CA, USA, [4]The Rockefeller University, New York, NY, USA.
The Nuclear Pore Complex (NPC, ~50 MDa) is the sole passageway for the transport of macromolecules across the nuclear envelope. The pore plays a key role in numerous critical cellular processes such as transcription, and many of its components are implicated in human diseases such as cancer. Previous works provided the first description of the macromolecular architecture of the yeast NPC. This structure defined the relative positions and proximities of its 456 constituent nucleoporin (nup) proteins, based on spatial restraints derived from experimental data. Further elucidation of the evolutionary origin and transport mechanism of the NPC will require higher resolution information. To help improve upon the resolution and accuracy of the NPC structure, we obtained small angle x-ray scattering (SAXS) data.
We prepared sets of single protein, protein domain, and small NPC sub-complex samples for SAXS analysis, because producing crystal structures for many of the proteins has proven difficult. We generated SAXS profiles for individual proteins or sub-complexes in solution, which provide shape information. This shape information generated by SAXS can in turn be used to improve atomic homology models for individual proteins or complexes.
We apply our Integrated Modeling Platform (IMP) software to incorporate a diverse set of experimental data, including SAXS spectra, as spatial restraints, to determine the three dimensional structures of these sub-complexes and proteins by simultaneously minimizing violations of all of the restraints.
We specifically focus on components of two sub-complexes, the 7-protein Nup84 sub-complex, and the 4-protein Nup170 sub-complex, for which complementary experimental data are available. For each SAXS profile, we utilize a score that evaluates a model structure based on the deviation between the experimental profile and a calculated profile for the model.

2386-Pos
Protein Structure Determination by Molecular Replacement using High-Accuracy Protein Structure Modeling
Keehyoung Joo[1], Mi-Sun Kim[2], Jeong Hae Han[2], Dong Hae Shin[2], Jooyoung Lee[1].
[1]Korea Inst Advanced Study, Seoul, Republic of Korea, [2]College of Pharmacy, Division of Life and Pharmaceutical Sciences, Ewha Womans University, Seoul, Republic of Korea.
Molecular replacement (MR) technique is to solve the phase problem in x-ray crystallography. Currently, many computational methods are available and they can provide MR solutions when a suitable 3D model of the target molecule is available. In practice, the success of the MR method is limited by various factors including unavailability of suitable 3D models and the ambiguity of crystallographic parameters. Accurate 3D modeling of the target molecule can provide a breakthrough in these cases. Recently, we have developed a protein 3D modeling method which can provide accurate protein 3D models both in backbones and side-chains. In addition, the method provides a variety of protein 3D models with structural variation. In recent blind tests, CASP7 and CASP8 experiments, the method produced the very top quality protein 3D models for high-accuracy template-based modeling targets. We combined this modeling method with a MR technique and successfully determined two protein structures, which could not be determined using conventional methods with available protein templates. It appears that high-accuracy protein 3D modeling for backbones as well as side-chains can boost up the success rate of molecular replacement technique allowing us to solve the phase problem in x-ray crystallography without requiring additional experiments with high cost efforts.

2387-Pos
Rosettaepr: Developing Protein Structure Prediction Methods using Sparse SDSL-EPR Data
Stephanie Hirst, Nathan Alexander, Kristian Kaufmann, Hassane Mchaourab, Jens Meiler.
Vanderbilt University, Nashville, TN, USA.
Site-Directed Spin-Labeling Electron Paramagnetic Resonance (SDSL-EPR), in combination with the Rosetta protein folding algorithm (Rohl *et al* 2004), could serve as an alternative method in structure elucidation of proteins that