many globular proteins. For example, a simple mutation can produce marked effects at distal sites via undefined pathways for a conventionally non-allosteric protein. There are reconciling evidences on allostery mechanisms for the 'induced-fit' scheme and the 'population-shift' theory, where dynamics plays an essential role in allosteric regulations. We develop a dynamics criterion to determine possible allostery in general proteins: Given two distinctive conformational states, dynamical fluctuations and correlations, either amongst the distant functional motifs or different subunits, can be accounted for by the conformational transitions between them. If the dynamics correlations result in both correlated and anti-correlated modes of motions (Figure 1), allosteric cooperativity will occur simultaneously.

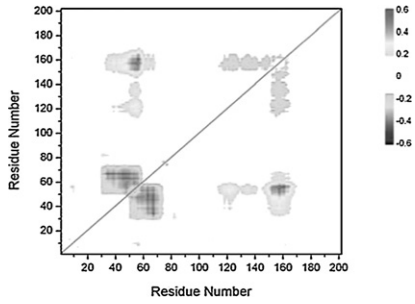
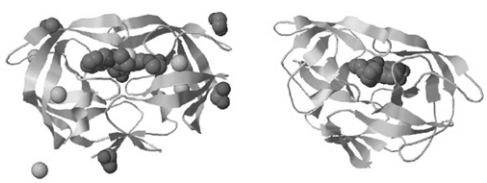


Figure 1. Difference matrix of dynamic correlations in protein - the *Aquifex* AdK case: red, a correlated motion; blue, an anti-correlated motion; and red (blue) regions correspond to same (opposite) direction distortions. The presence of both positive and negative correlations indicates the existence of an allosteric cooperativity during conformational changes, as was proved by NMR experiments.

2201-Pos Board B171
Dynamics of Intra- and Inter-Helix Contact Formation
Ronan D. Murphy, Cathal Leahy, **Nicolae-Viorel Buchete**.
University College Dublin, School of Physics, Belfield, Dublin 4, Ireland.
The ubiquitous nature of the helical fold and its characteristic physical properties make it one of the first candidates for studies of secondary structure formation in polypeptides, and the thermodynamics of helix formation is a common topic in many classical biophysics textbooks. However, though there is general agreement on the features of the equilibrium properties of the coil-to-helix transition, both experimental and theoretical studies have provided widely varying estimates of helix formation rates from tens of picoseconds to microseconds. We present results of recent molecular simulations of several helix-forming peptides that permit the quantitative study of both intra- and inter-helical contacts in polypeptides. This analysis of local, site-specific formation of intra- and inter-chain interactions is necessary for any quantitative modeling of the elementary steps of secondary and tertiary structure formation in protein folding, and it allows direct comparison to data from recent infrared vibrational spectroscopy studies.

2202-Pos Board B172
Dr. Joseph Zhou
Joseph X. Zhou.
Max Planck Institute for the Physics of Complex Systems, Dresden, Germany.
HIV-1 protease is a crucial protein during HIV infection. Protease inhibitors bind to a ''Pocket'' of this dimer and prevent its further activity, thus reducing the spread of HIV virus. However, HIV-1 protease has a high genetic variability, which generates diversity of the virus and often causes a serious problem of the emergence of drug-resistant mutants. In this research, instead of using a traditional measure of ''genetic distance'', the structural dynamic changes due to mutation is built to associated with the drug resistance of the HIV-1 protease. Traditional normal-mode analysis for biomolecules is the linear dynamic analysis near their equilibrium. However, the transition of protein state is usually highly nonlinear. Here we employ an amino acid specific GO model to investigate the nonlinear molecular dynamics changes due to the protease sequence mutations. The current results show that the mutations have obvious effects on the soft modes of the HIV protease. The reason for the drug-resistance can be clarified from our further analysis of the relationship between the soft modes change and the drug-resistance.



2203-Pos Board B173
Force Spectroscopy of the Iron Atom in Heme Proteins
J. Timothy Sage[1], Bogdan M. Leu[2], Tom H. Ching[1], Yong Zhang[3], John E. Straub[3], Jiyong Zhao[2], Wolfgang Sturhahn[2], E. Ercan Alp[2].
[1]Northeastern University, Boston, MA, USA, [2]Argonne National Laboratory, Argonne, IL, USA, [3]Boston University, Boston, MA, USA.
Nuclear resonance vibrational spectroscopy (NRVS) selectively reveals the complete vibrational density of states (VDOS) of a Mössbauer probe nucleus within a protein. Frequency moments of the VDOS determine effective force constants for ^{57}Fe at the active sites of cytochrome c (cyt *c*) and deoxymyoglobin (Mb). The *stiffness* measures the force needed to displace the Fe with the other atoms fixed, and probes the nearest neighbor interactions with the Fe. The stiffness of the low spin Fe environment in cyt *c* greatly exceeds that for the high spin Fe in Mb, reflecting the shorter Fe–N bonds to the heme. Moreover, a significant stiffness decrease upon oxidation of cyt *c* tracks the longer Fe–S bond to Met 80 in the oxidized protein. Quantitative comparison with ^{57}Fe/^{54}Fe frequency shifts suggests that Fe-L vibrations contribute to the Raman signal of cyt *c* recorded in resonance with the heme Soret band. The *resilience* measures the force needed to displace the Fe with the surrounding atoms free to respond, and determines the magnitude of the thermal fluctuations of the Fe on a time scale determined by the experimental energy resolution (ca. 4 ps for the results reported here). Quantitative agreement with the temperature-dependent mean squared displacement determined from independent Mössbauer measurements confirms longstanding assumptions that vibrational motion dominates thermal fluctuations of the heme Fe below the well-known dynamical transition at ca. 200 K and identifies THz frequencies below 100 cm^{-1} as the dominant contribution. The resilience increases significantly for cyt *c* with respect to Mb, which we attribute to the increased number of covalent links between heme and peptide in the former protein. Molecular dynamics simulations reproduce the increased resilience of cyt *c*, but find no significant change with oxidation state.

2204-Pos Board B174
Extracting Non-Gaussian Modes of Motion from the Principal Components of Gramicidin A
Martin Kurylowicz, Régis Pomé.
University of Toronto, Toronto, ON, Canada.
We have performed principal component analysis (PCA) on the trans-membrane channel gramicidin A in a membrane environment using atomistic molecular dynamics simulations. A systematic examination of all the principal components reveals a clear power law structure across the entire eigenvalue spectrum, with distinct scaling regimes for both the heavy-atom backbone as well as the side chains. Deviations from the scaling trends reveal groups of components which have symmetric but non-Gaussian distributions over the trajectory, and these correspond to anomalous diffusion in the mean square deviation over six orders of magnitude in time. The largest PCs are super-diffusive while certain groups of short PCs are sub-diffusive. We quantify the directions of collective displacement for many of the long and short PCs, and propose an extension of PCA which yields a set of apparently functional modes where many atoms move together in a uniform direction. The dominant super-diffusive mode exhibits coherent motion of the (lipid-bound) hydrophobic turns at the junction of the monomers, moving out of phase with the outermost (surface-bound) hydrophilic turns and preserving the conductive connection along the water wire at the centre of the channel. In the second super-diffusive mode, the two innermost hydrophobic turns of each monomer move out of phase with each other at the monomer junction, possibly gating the channel. The sub-diffusive modes at shorter spatial scales are associated with hydrogen-bonded groups. Our results suggest that there is information relevant to the description of protein dynamics and statistical mechanics in the entire PCA spectrum, and not just the largest few PCs as conventionally analyzed.

2205-Pos Board B175
Modeling the Open-to-closed Transition of Adenylate Kinase: All-atom Molecular Dynamics Simulations and a Double-Well Network Model
Jhih-Wei Chu.
University of California, Berkeley, Berkeley, CA, USA.
An intrinsic property of protein is the ability to undergo conformational changes upon ligand binding. In this work, we study Adenylate Kinase (AKE), an important enzyme controlling the balance of ATP in prokaryotic cells. X-ray crystallography indicates that AKE has two distinct conformations, open and closed, depending on whether it is bound with substrates (ATP and AMP). Conformation difference in AKE can be determined by the relative position of two separate domains, the lid domain and the NMP binding domain, to the core. In this work, all-atom molecular dynamics (MD) simulations and coarse-grained modeling are used to elucidate the effects of ligand binding on AKE conformation. Results based on four 100ns all-atom trajectories indicate that ATP binding induced the closing of lid domain and suggest that the relative population between closed to open structure is increased. The closing