of NMP binding domain, however, is found to be more specific and may require a timescale longer than 100ns to close. The mechanical property of a hinge region is found to correlate with lid closing; residues in this region may be mutated to alter the rate of conformational change and hence enzyme catalysis. This prediction agrees well with the results of recent single molecule experiments. Using a double-well network coarse-grained model, multiple pathways of open-to-closed transition can be found. Motions of lid-domain and NMP binding domain are not concerted and may be treated as two distinct events. This picture is different from the result of using elastic network model and agrees better with atomistic simulations. In addition to open-to-closed transition, solvation structures and intrinsic mechanical properties of AKE are also characterized to identify key residues that may control the conformational change of AKE from mechanical perspectives.

2206-Pos Board B176

Inferring Maps of Forces Inside Cell Membrane Microdomains

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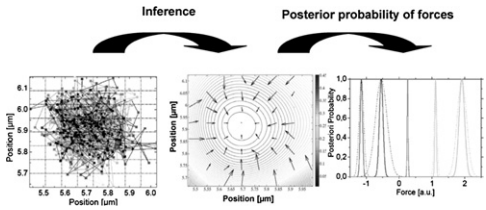
Mapping of the forces acting on biomolecules in cell membranes has spurred the development of effective labels, e.g. organic fluorophores and nanoparticles, to track trajectories of single biomolecules. Standard methods use particular statistical observables, namely the mean square displacement (MSD), to extract cues on the underlying dynamics. Yet, MSD is not an appropriate tool to access force fields and becomes easily a biased estimator in the presence of positioning noise. Here, we introduce **general inference methods** to fully exploit information hidden in the experimental trajectories, providing sharp estimates for the forces and the diffusion coefficients within membrane microdomains. Rapid and reliable convergence of the inference scheme is demonstrated on trajectories generated numerically with realistic parameters. The inference method is then applied to **infer forces and potentials** acting on the receptor of the ϵ-toxin labelled by lanthanide-ion nanoparticles. Results show a constant diffusivity inside a complex force field confining the receptor inside a specific domain, and may lead to new modelling of the membrane.
Our scheme is applicable to any labelled biomolecule and to other types of force fields, and results presented here show its general relevance to the issue of membrane compartmentation.



2207-Pos Board B177

Probe of flexibility and conformational heterogeneity in Zn-cytochrome c (Zn-cyt c) folding by Three-Pulse Photon Echo Peak Shift (3PEPS) Spectroscopy

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We investigated the dynamics and conformational heterogeneity of Zn-cyt c with 3PEPS, a type of femtosecond nonlinear spectroscopy that is used to quantify the spectrum of sub-nanosecond protein motions and the inhomogeneous broadening of the system. Wavelength-dependent measurements were performed on the Soret transitions of the folded state, the guanidine hydrochloride unfolded state (4.5 M), and the state at the midpoint (2.5 M) of the denaturant titration. The measurements resolve a substantial increase in the inhomogeneous broadening of the Soret band upon unfolding, as expected due to an increase in conformational diversity upon unfolding. Unexpectedly, the inhomogeneous broadening of the midpoint state is greater than that of the unfolded state. This observation is consistent with the Soret band spectrum, which first broadens, then attains a maximum width at the midpoint, and finally narrows, as the denaturant concentration is increased. A two-state folding model is used to quantitatively model the 3PEPS results. In this model, the homogeneous linewidth of the folded and unfolded states is identical, the piecosecond dynamics of the unfolded conformer are slightly slower, the inhomogeneous broadening of the unfolded state is 33% larger than that of the folded state, and the midpoint is a 1:1 mixture of the folded and unfolded states. Numerical results are consistent with the experimental data. Interestingly, biophysical techniques often resolve multimodal conformational distributions, whereas ultrafast spectroscopic measurements are not modeled with the functional forms of the inhomogeneous distribution function (IDF) obtained from these experiments. Our work is therefore significant because it represents the first instance in which a multimodal IDF, rather than the traditionally assumed Gaussian form, is quantitatively reconciled with a set of ultrafast spectroscopic measurements on protein conformers.

2208-Pos Board B178

Evaluation Of Three Transition Pathway Modeling Techniques In Capturing Structural Intermediates In F1 Atpase, Myosin, Kinesin, And Chaperonin Groel

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Computer modeling of conformational transitions aims to predict the order of structural events in a functioning molecular machine. Here we evaluate 3 transition pathway modeling techniques — mixed elastic network model (MENM)[1], Min-Action-Path[2] and adiabatic morphing[3]. We will assess their accuracy in capturing structural intermediates during the transitions in four ATPase-based molecular machines (F_1 ATPase, myosin, kinesin, and chaperonin GroEL), for which abundant structural data are available for validation. We will map transition pathways and experimental structures to a 2D plane spanned by two reaction coordinates that assess the progress of transition at the active site and the force-generating component, respectively. These techniques are found to perform differently in qualitatively capturing the order of structural events in agreement with the structural data (see Figure).

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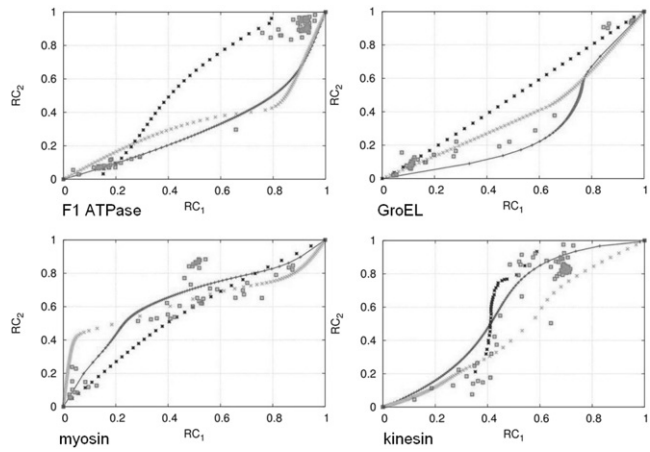

Figure. Transition pathways predicted by MENM (+), Min-Action-Path (×) and adiabatic morphing (*) compared with experimental structures (square).

2209-Pos Board B179

Self Assembly Of AOT Reverse Micelles With/without Peptides

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We are interested in understanding the dynamics and stability of proteins under confinement. To study the reverse micelle formation process and the peptide dynamics inside reverse micelle we performed molecular dynamics simulations for two AOT reverse micelle self-assembly systems, one without peptides and the other with two octa-peptides (AKAAAKA). The self-assembled systems are water-in-oil micro-emulsion systems, and each of them has a 200 ns long simulation time. The other three components of the systems are sodium ions, water and isooctane. The water to surfactant ratio for both of the systems is 6. Reverse micelles form in a quick, spontaneous way. The peptides get encapsulated during the self-assembly and are located at the inner face of the reverse micelle close to the AOT surfactants. The two peptides adopt different conformations, unfolded and alpha-helical, respectively. The peptides are encapsulated in separate reverse micelles. The encapsulated peptides have high coordination with AOT head groups and sodium ions. They experienced low hydration environment and showed much slower dynamics inside the reverse micelle. We find that the dynamics of peptides inside reverse micelle is very different from that in bulk water.

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