for times shorter than a characteristic time that depends on the sequence and length of polypeptides. Deviation from exponentiality cannot be simply explained with the non-Markovian polymer dynamics at very short times, but appears to be characteristic of polypeptides with either specific or non-specific attractive interactions. Our results agree with recent experimental measurements and offer a comprehensive interpretation for them.

1325-Pos Board B55
Suppression of Picosecond Dynamics in β-Casein upon Calcium Binding
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Understanding the relationships between proteins secondary structure, dynamics and function is a key question in molecular biophysics. In a recent study1 we suggested an intriguing relationship between protein’s structure, rigidity and low-frequency collective vibrations (the boson peak): proteins containing only α-helices are significantly softer than those with β-structure. The current contribution extends this study to an intrinsically disordered protein, β-casein. It is a flexible natively unfolded protein in its functional state, and binds as trivalent Ca2+ ions in the form of protein-bound nano-clusters. We compared rigidity and dynamics of β-casein to those of Green Fluorescent Protein (GFP), a well-folded rigid β-barrel, investigating dry and hydrated powders at T=170K and T=295K with neutron and depolarized light scattering techniques. Our results show that β-casein is softer than GFP at both temperatures and hydration levels. This is consistent with previous findings1. In the sub-nanosecond-picosecond time range β-casein presents the same types of motions exhibited by GFP, such as methyl groups rotations, localized diffusion relaxations (which are enhanced in presence of water) and boson peak collective vibrations2. We also analyzed β-casein samples containing CaCl2 in order to monitor the effects of ion-binding and partial folding on the rigidity and dynamics of a natively unfolded protein. The presence of Ca2+ stiffens the system and largely decreases the localized picosecond dynamics of β-casein. The latter effect is particularly strong in the hydrated case. The cations bind the negatively charged β-casein, stabilize a more folded structure of the protein and interact with hydration water. We conclude that β-casein dynamics are strongly influenced by electrostatic forces, in addition to the interactions with the water molecules.


1326-Pos Board B56
Partial Folding and Unique ATP Function in Protein Phosphatase 2A Latency and Activation
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The function of metalloenzyme protein phosphatase 2A (PP2A) relies on proper formation of diverse heterotrimERIC PP2A holoenzymes, comprising catalytic (PP2Ac) and regulatory (PP2Aa) subunits. Holoenzyme assembly is highly regulated by carboxymethylation of PP2Ac. Our recent study demonstrated that the enzymatic reaction of PP2A methylation is highly responsive to PP2A activation via a direct binding of PP2A methyltransferase to the dynamic PP2A active site (Mol. Cell. 2011, 41(3):331-42). Interestingly, the entire protein fold of PP2Ac is highly dynamic and tends to partially unfold, which renders α4-binding that involves the inner structure of PP2Ac near the active site. α4-binding leads to an allosteric relay of conformational changes that perturbs the scaffold subunit binding site at the opposite surface. This unique mode of α4-binding underlies important mechanisms for stability latency of PP2Ac as well as dissociation of PP2A holoenzymes and recycling of PP2Ac in response to cell signaling. We further showed that PP2A phosphatase activator makes broad contacts with the structural elements surrounding the PP2A active site, which stabilizes the protein fold of apo-PP2Ac required for activation. PTPA-binding also defines a combined ATP-binding pocket that orients ATP phosphoryl groups to bind directly to the PP2A active site. This allows ATP to modulate the metal-binding preferences of the PP2A active site and drastically enhances binding of Mg2+ by 10,000-fold, which is crucial for acquisition of pSer/Thr-specific phosphatase activity. Consistent with the activation chaperone function of PTPA and activation-dependent PP2A methylation, PTPA stimulates both PP2A phosphatase activity and methylation. Collectively, our studies revealed a linear pathway for the biogenesis of PP2A holoenzymes, including stable latency, activation, methylation, and holoenzyme assembly, which is elegantly controlled by the protein dynamics and conformational switches of PP2Ac.