Electrostatics free energy in guiding the functional cycle in other actin-based myosin motors.

146-Plat
Different 3D Domain-Swapped Oligomeric Cyanovirin-N Structures Suggest Trapped Folding Intermediates
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Although it has long been established that the amino acid sequence encodes the fold of a protein, how individual proteins arrive at their final conformation is still difficult to predict, especially for oligomeric structures. Here, we present a comprehensive characterization of oligomeric species of cyanovirin-N that all are formed by a polypeptide chain with the identical amino acid sequence. Structures of the oligomers were determined by X-ray crystallography, and each one is a subunit of 3D domain-swapping. One uncharacterized 3D domain-swapped structure is observed for the trimers, while for both dimer and tetramer, two different 3D domain-swapped structures were obtained. In addition to the previously identified hinge-loop region of the 3D domain-swapped dimer, which resides between strands β5 and β6 in the middle of the polypeptide sequence, another hinge-loop region is observed between strands β7 and β8 in the structures. Plasticity in these two regions allows for variability in dihedral angles and concomitant differences in chain conformation that results in the differently 3D domain-swapped multimers. Based on all of the different structures, we propose possible folding pathways for this protein. Altogether, our results illuminate the amazing ability of cyanovirin-N to proceed down different folding paths and provide general insights into oligomer formation via 3D domain swapping.

147-Plat
Structural Basis of Conformational Transitions Involved in Pseudopilus Assembly and Stability
Michael Niles1,2, Manoyarakarasi Nivaskumar1,2, Guillaume Bouvier1,2, Manuel Campos1,2, Edward H. Egelman4, Xiong Yu4, Olivera Francetic1,2, Alexandre M.J.J. Bonvin3, Tobias Restle1.
In the present study, we performed MD simulations on the hAgo2 protein in complex with mir-20a. Cell 150(1), 100-110.

149-Plat
Mechanisms of Substrate Degradation by Energy-Dependent Proteases
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Energy-dependent proteases of the AAA⁺ family catalyze the highly specific protein degradation involved in cellular protein quality control and the regulation of numerous vital processes, yet the detailed mechanisms coupling ATP hydrolysis with mechanical substrate unfolding and translocation remain poorly understood. Our cryo-EM structural studies of the eukaryotic 26S proteasome show that its heterohexameric AAA⁺ ATPase ring adopts a conformation with pronounced spiral-staircase arrangement of subunits in the absence of substrate, but transitions into a translocation-competent conformation upon substrate engagement. This substrate-engaged ring conformation is characterized by uniform interfaces between the six ATPase subunits, a widened central channel coaxially aligned with the peptidease, and a rearranged, more planar spiral orientation of ATPase subunits that suggests a highly coordinated rapid progression of ATP-hydrolysis events around the ring. This coordinated ATP hydrolysis mechanism is further supported by our optical tweezers single-molecule studies of the related bacterial protease ClpXP and may be a general feature of AAA⁺ translocases. ClpXP translocates substrate polypeptides in steps with constant frequency but variable length, depending on the number of ATP-hydrolyzing subunits.

150-Plat
Structure, Dynamics, Evolution and Function of a Major Scaffold Component in the Nuclear Pore Complex
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The Nuclear Pore Complex, composed of proteins termed Nucleoporins (Nups), is responsible for the nucleo-cytoplasmic transport in eukaryotes. NPC's form an annular structure composed of the nuclear ring, cytoplasmic ring, a membrane ring, and two inner rings. Nup192 is a major component of the NPC's inner ring. We report the crystal structure of Saccharomyces cerevisiae Nup192 residues 2 to 960 [ScNup192(2-960)], which adopts a z-helical fold with three domains (i.e., D1, D2 and D3). SAXS and EM studies reveal that ScNup192(2-960) could undergo long-range transition between an “open” and “closed” conformations. We obtained a structural model of full-length ScNup192 based on EM, structure of ScNup192(2-960), and homology modeling. Evolutionary analyses using ScNup192(2-960) structure suggest that NPC's and vesicle coating complexes are descended from a common membrane-coating ancestral complex.
We show that suppression of Nup192 expression leads to compromised nuclear transport and hypothesize a role for Nup192 in modulating the permeability of the NPC central channel.

151-Plat
Structural Gymnastics by Proteins make the Clock Mechanism go Round and Round
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Endogenous clocks regulate metabolism, physiology and behavior of most organisms in anticipation of daily swings in ambient light and temperature by