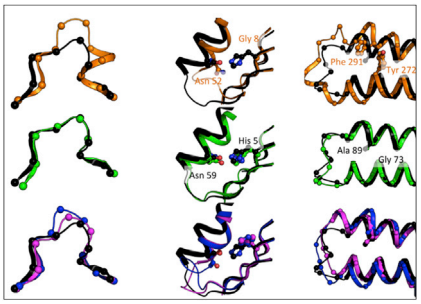
In This Issue

Technical Advance: From Fuzzy to Clear

PAGE 1725

Pfleger and Gohlke describe an approach for performing rigidity analyses of biomacromolecules on ensembles of network topologies from a single input structure. Thermal fluctuations are considered without actually sampling conformations, which significantly improves the robustness and efficiency.



Technical Advance: Comparative Modeling with Rosetta

PAGE 1735

Song et al. describe an improved method for comparative modeling, RosettaCM, which optimizes a physically realistic all-atom energy function over the conformational space defined by homologous structures and assembles topologies by recombining aligned segments and building unaligned regions in torsion space.

Regulation of the Early Stages of Microfibril Assembly

PAGE 1743

Fibrillin microfibrils are key structural and regulatory components of connective tissue, but their assembly is poorly understood. Yadin et al. report a structure of the fibrillin N-terminal domains and propose that heparan sulphate regulates end-to-end assembly.

Autoactivation of Human Mst2 Kinase

PAGE 1757

Mst1/2 are upstream kinases in the Hippo pathway that regulates organ size and suppresses tumorigenesis. Ni et al. determine the crystal structures of human Mst2 alone and bound to its regulator RASSF5. Mst1/2 autoactivation depends on SARAH-mediated homodimerization and its temporal regulation by RASSFs.

Transient Interactions, More Permanent Binding

PAGE 1769

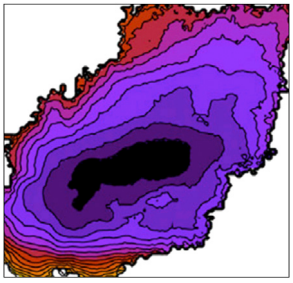
The two-domain mitotic regulator Pin1 is important in protein quality control and age-related dementia. Matena et al. studied Pin1 domain-domain interaction and binding of phosphorylated model substrates. Their results support the idea that domain interactions increase the affinity of Pin1 towards peptide ligands.

Mechanistic Divergence in Di-Domain Methyltransferases

PAGE 1778

The phosphobase methylation pathway is the major route for producing phosphocholine in plants, nematodes, and *Plasmodium*. Through structural work on a nematode di-domain phosphoethanolamine N-methyltransferases, Lee and Jez address both functional and evolutionary questions and highlight metabolic adaptability.

Conformational Analysis of NMDA Receptors



PAGE 1788

Yao et al. crystallize apo NMDA receptor ligand-binding domains (LBDs) in both open and closed cleft conformations. Free energy computations suggest GluN1, GluN2A, and GluN3A LBDs bind agonist via a conformational selection mechanism whereas the AMPA receptor GluA2 LBD binds agonist via an induced fit mechanism.

Fingers Contribute to Polyadenosine RNA Recognition

PAGE 1800

Nab2p belongs to a family of poly(A)-binding proteins and contains seven zinc finger (Zf) domains. Martínez-Lumbreras et al. report the structure of Nab2p tandem ZF12 and ZF34, and show that Nab2p Zf1-4 recognizes poly(A) RNA. The region likely cooperates with Zf5-7 to achieve full-length Nab2 RNA affinity.

Folding Mechanism of an EF-Hand

PAGE 1812

Neuronal Ca^{2+} sensors respond structurally to changes in intracellular Ca^{2+} concentrations, yet the details of their conformational dynamics are largely uncharacterized. Heidarsson et al. use single-molecule study of NCS1 to describe the complex folding network and reconstruct the energy landscape of the protein.

HIV-1 Nef: What Happens Near the Membrane

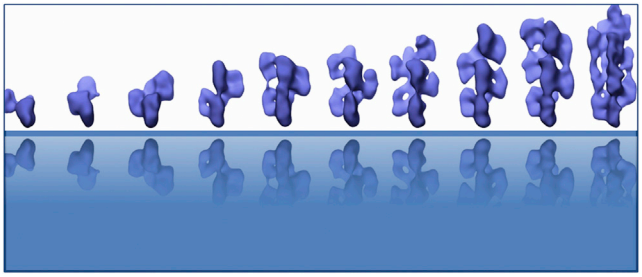
PAGE 1822

Nef is an HIV-1 accessory proteins and an essential factor in AIDS progression. Akgun et al. used neutron and X-ray reflection methods to measure the displacement of the core domain of HIV Nef from lipid membranes upon insertion of the N-terminal myristate.

Tah1 Tethers Hsp90 to R2TP Complex

PAGE 1834

What are the factors involved in the assembly of snoRNP and RNA polymerase? Back et al. show the direct interaction between Tah1 protein and Hsp90 chaperone one hand, and Tah1 and Phi1 proteins on the other hand. The high-resolution structure obtained by NMR explains how Hsp90 is recruited by the complex R2TP.



Run-On Oligomerization of a DNA Endonuclease

PAGE 1848

The coevolution between parasitic phage and host bacterium represents one of nature's most extensive struggles for survival, leading both to pursue diverse strategies of adaptation. Lyumkis et al. present the structure of a DNA endonuclease that forms large oligomers as part of an unusual host defense mechanism.

Another Way to Bind DNA

PAGE 1859

CarD-RNAP interaction is crucial for *Mycobacterium tuberculosis* (*Mtb*) viability and persistence. Gulten and Sacchettini report a crystal structure of *Mtb* CarD/RNAP β-lobe domains complex along with the uncomplexed structure of the β-lobes and explore DNA binding activity for CarD.

What It Takes to Assemble Telomerase

PAGE 1870

Telomerase is a potential drug target for cancer; approximately 90% of human cancers require telomerase activity for survival. Harkisheimer et al. identify RNA binding sites of a vertebrate RNA binding domain (TRBD) of telomerase required for telomerase ribonucleoprotein assembly and function.

Short Article: Functional Diversity in ABC Transporters

PAGE 1879

The ATP-binding cassette transporter GlnPQ is an essential uptake system for amino acids in Gram-positive bacteria. Fulyani et al. show that a small number of residues in the binding pocket of the receptor domains of GlnPQ constitute the major affinity determinants for transport.

Short Article: Mutant FGF Receptor Fools the System

PAGE 1889

Thanatophoric Dysplasia Type II is a neonatal lethal dwarfism syndrome that results from a single mutation in FGF receptor 3 (FGFR3). Huang et al. report a crystal structure of the mutant tyrosine kinase domain of FGFR3 and show that the mutation hijacks the physiological activation mechanism of the receptor.

Short Article: Peeking into an Open-Channel

PAGE 1897

Glycine receptors mediate fast inhibitory neurotransmission in the spinal cord and brain stem. Structures of the human glycine recptor-α1 transmembrane domain by Mowrey et al. reveal features potentially related to allosteric modulation of the channel function, providing templates for better understanding disease.