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of WW3 and adjacent WW domains. We speculate that while the role of the WW3 domain is to mediate binding to PPXY proteins, the primary role of the other WW domains is to modulate binding interactions through changes in the dynamics of the assembled complex.

1596-Pos  
Multiscale simulations of viruses  
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Viruses including HIV-1 and SARS-CoV-2 produce particles or virions that are a few hundred nanometers in size to infect new host cells. Viral processes at these scales have been challenging to describe using conventional molecular simulation techniques. In this work, we discuss recent advances and developments that have enabled the multiscale simulation of viruses, from the dynamics of individual capsid proteins to large-scale viral behavior, involving the concerted action of thousands of protein elements. We focus on elucidating the physical properties and molecular mechanisms of critical post-entry steps in the viral life cycle involved in capsid uncoating.

1597-Pos  
Determining the role of the coupling protein CheW in signal transduction of chemoreceptor complexes using solid-state NMR  
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How an organism senses and responds to its environment is one of the fundamental questions in nature. Chemotaxis, the ability for bacterial cells to sense their environment and control their swimming direction, has been widely studied in order to understand cell sensing. Bacterial chemoreceptor complexes are responsible for receiving signals from the environment. However, the mechanism that bacterial chemoreceptor complexes use to transmit the signal is still unknown. The chemoreceptor complexes are made up of the chemoreceptor, the histidine kinase CheA and the coupling protein CheW. The chemoreceptor binds ligands and transmits the signal across the cellular membrane to prompt CheA to switch between kinase-on and kinase-off states, which controls the swimming of the cell. The coupling protein, CheW, is essential for complex assembly, by bringing together the chemoreceptor and CheA. CheW has been proven to play a structural role in the complex, but it has also been proposed to have an additional role of transmitting the signal from the chemoreceptor to CheA. Our lab has proposed that CheA has weaker interactions with the receptor and/or CheW in the kinase-off state. We are using solid-state NMR of isotopically labeled CheW in functional complexes to identify whether CheW interactions with CheA and the chemoreceptor change between the kinase-on and kinase-off states. Changes in the CheW interactions would suggest it is important in the signaling mechanism of the complexes. This research is supported by NIH R01 GM120195 and T32 GM139789.

1598-Pos  
Cryo-electron tomography of in vivo reconstituted SARS-CoV-2 replication/transcription organelles  
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The emergence of novel coronaviruses requires new and innovative approaches in development of broad-spectrum antiviral therapeutics. Targeting and inhibiting replication machineries of pathogenic viruses is a proven and effective anti-viral strategy. Similar to other +RNA viruses, coronavirus genomic replication and transcription are moderated by an RNA replication-transcription complex (RTC) anchored in rearranged internal viral RNA synthesis. This approach will provide broad structural detail of the SARS-CoV-2 replication/transcription machinery to be leveraged for the future development of therapies targeting viral RNA replication and proliferation.

1599-Pos  
Beta-barrel models of oligomers, protofibrils, lipoproteins, and transmembrane channels formed by amyloid beta (Alzheimer’s disease), synucleins (Parkinson’s disease), and amylin (type 2 diabetes)  
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Recent findings support our hypothesis that some Amyloid beta (Aβ) oligomers and channels form β-barrels. We have now revised and expanded our Aβ models and have extended the hypothesis of concentric β-barrel amyloid assemblies to Synuclein and Amylin (IAPP). Evidence is increasing that oligomers of all three types of amyloids are more toxic than fibrils and that these amyloid oligomers bind to membranes and form toxic transmembrane channels. Symmetric β-barrels often have well defined structures composed of multiple subunits with identical conformations. Well established β-barrel theory can be used to model these structures accurately if one is able to determine the number of subunits per barrel, the number of strands per subunit, which segments comprise the β-strands, and the dimensions of the barrel. Most of our models of numerous oligomers, annular protofibrils, lipoprotein complexes, and transmembrane channels contain symmetric β-barrels with radial and sometimes P2 two-fold symmetry. These structures are consistent with molecular modeling principles and biochemical and biophysical data, including microscopic images and NMR results. Hypothetical models and concepts are vital for research because they often suggest experiments that otherwise would not be performed or funded. Our results suggest experiments to test aspects of the models, to reduce polymorphism and disorder so that specific structures can be solved experimentally, and to identify specific segments to target for drug and antibody treatments.

1600-Pos  
Unexpected control of protein self-association by translation initiation  
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Living proteomes are necessarily far from equilibrium. It is paradoxical, then, that reducing protein influx – which should promote equilibration – instead, prolongs life. We therefore reasoned that kinetic barriers to equilibration must exist and that these decrease with protein influx. We further hypothesized that the probabilistic nucleation of ordered protein assemblies such as amyloids could underlie those barriers. To investigate the effects of influx on protein self-assembly, we used our quantitative reporter of nucleation-limited protein self-assembly (termed Distributed Amphiphilic FRET or DaM FRET) to probe kinetic barriers to self-assembly of structurally diverse protein assemblies at different rates of translation initiation in living cells. We specifically reduced translation initiation just our protein of interest either by using a uORF or weak Kozak sequences. We achieved comparable total translation of the protein in each case - by reducing plasmid copy number by relaxed selection for fast translating cells. Remarkably, this manipulation dramatically reduced nucleation, even for proteins of diverse structures, and independently of changes in their expression level. Further experimentation revealed that the proteins remained fully competent for polymerization when provided with a pre-existing template, indicating that translation initiation rate specifically influences the kinetic barrier to nucleation. We additionally find that manipulations that enhance polypeptide interaction during translation, enhances nucleation. By probing the assembly of a tight dodecamer, we find that polypeptides interact in cis on the same mRNA during translation at high initiation rates. In addition, our observations are true in both yeast and mammalian cells alike, thereby underscoring the widely conserved nature of this phenomenon. We are exploring both - the factors that contribute to this phenomenon, as well as the physiological implications of this phenomenon, via approaches such as proteomics and single molecule mRNA imaging.

1601-Pos  
Relationships between RNA topology and nucleocapsid structure in a model isosahedral virus  
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We are using solid-state NMR of isotopically labeled CheW in functional complexes to identify whether CheW interactions with CheA and the chemoreceptor change between the kinase-on and kinase-off states. Changes in the CheW interactions would suggest it is important in the signaling mechanism of the complexes. This research is supported by NIH R01 GM120195 and T32 GM139789.