Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
supported by experimental evidence, to propose a model that best-represents PSMa1 functional anayloids in solution. Candidate models were created to test how the lateral aggregation of protoflaments (1, 2, and 3 protoflaments), the length of the fiber, and the secondary structure of aggregated peptides (alpha or beta) change fiber properties. Our results compare the chemical and physical structure, diameter, and periodicity of experimental fibers to computational models to demonstrate that longer, 2-protoflament beta-sheet fibers are the best candidate. The development of such a model is critical to the progression of this study, so we intend to computationally screen our library of nanoparticle compounds for potential antibiotics. These nano-biotics will either prevent PSM aggregation or destabilize already-formed fibers. This work, however, not only advances our understanding of staphylococcal amyloids, but also demonstrates the unparalleled value of computational insight in the investigation of a myriad of amyloid complexes, ubiquitous in nature.

1496-Plat
AI-Driven prediction of binding trends of SARS-CoV-2 variants from atomistic simulations
Sara Capponi1,2, Shangying Wang1,2, Erik Navarro1,2, Simone Bianco1,2,
1IBM Almaden Research Center, San Jose, CA, USA, 2Center for Cellular Construction, San Francisco, CA, USA.
Protein-protein interactions are fundamental for cellular processes underlying functions such as signal transduction, cell regulation, or immune response activation among others. However, in silico characterization at atomic level of the binding process between two proteins can be computationally demanding due to the long timescale of typical binding/unbinding events. To address this challenge, several approaches have been developed to estimate the binding free energies between two molecules and weigh mutation effects. Here, we present a novel technique to predict binding affinity between two molecules from atomistic molecular dynamics simulations. The technique uses a neural network algorithm applied to a series of images generated by the simulation data and representing the distance between two molecules in time. The algorithm is capable of distinguishing with high accuracy low vs high binding affinity of non-hydrophobic mutations, indicating that our method excels on the inference of the binding affinity trends for charged and/or polar amino acid mutations. Moreover, it shows high accuracy in prediction using a small subset of the simulated data, therefore requiring a much shorter simulation time. We apply our algorithm to the binding between several variants of the SARS-CoV-2 spike protein and the human receptor ACE2.

1497-Plat
The functional evolution of ACE2 receptor binding of Betacoronaviruses in the past, present, and uncertain future
Gregory A. Babbitt
Department of Biological Sciences, Rochester Institute of Technology, Rochester, NY, USA.
Comparative functional analysis of the dynamic interactions between various Betacoronavirus mutant strains and broadly utilized target proteins, is crucial for a more complete understanding of zoonotic spillovers of viruses that cause COVID-19. Here, we employ machine learning to replicate sets of nanosecond scale GPU accelerated molecular dynamics simulations to statistically compare and classify atom motions of these target proteins in both the presence and absence of different endemic and emergent strains of the viral receptor binding domain of the S spike glycoprotein. We demonstrate some important recent trends in the functional evolution of viral binding to human ACE2 in both endemic and emergent human strains, including the recent delta variant of SARS-CoV-2. We compare these trends to viral target binding in its likely progenitor species (Rhinolophus bat) finding that the alpha variant, evolutionary adapted to bats and not humans, exhibits a clear pattern of strong binding interaction with 5 sites on bat ACE2 (two sites on N-terminal helices, Q325, K353, S559 and QP 388-89). The spillover to human ACE2 still shows functional binding at most of these sites, but with a less defined pattern of binding interaction, suggesting it was less stable than the bat variant dynamics. The delta variant has adapted to re-establish stronger and less transient contacts with some of these same sites observed in the bat interaction. Further analysis of the binding interface mutations in CDC variants of concern demonstrate that they have collectively increased human ACE2 binding over the last year and a half. We also analyze the effect of predicted SARS-CoV-2/ACE2 glycosylation on functional binding, finding that most sites have negligible impacts while identifying a single site on the virus with large effect at N370.

Platform: RNA Structure and Dynamics
1498-Plat
Characterizing the rugged conformational energy landscape of RNA
Sara Capponi1,2, Shangying Wang1,2, Erik Navarro1,2, Simone Bianco1,2,
1IBM Almaden Research Center, San Jose, CA, USA, 2Center for Cellular Construction, San Francisco, CA, USA.
Protein-protein interactions are fundamental for cellular processes underlying functions such as signal transduction, cell regulation, or immune response activation among others. However, in silico characterization at atomic level of the binding process between two proteins can be computationally demanding due to the long timescale of typical binding/unbinding events. To address this challenge, several approaches have been developed to estimate the binding free energies between two molecules and weigh mutation effects. Here, we present a novel technique to predict binding affinity between two molecules from atomistic molecular dynamics simulations. The technique uses a neural network algorithm applied to a series of images generated by the simulation data and representing the distance between two molecules in time. The algorithm is capable of distinguishing with high accuracy low vs high binding affinity of non-hydrophobic mutations, indicating that our method excels on the inference of the binding affinity trends for charged and/or polar amino acid mutations. Moreover, it shows high accuracy in prediction using a small subset of the simulated data, therefore requiring a much shorter simulation time. We apply our algorithm to the binding between several variants of the SARS-CoV-2 spike protein and the human receptor ACE2.

1499-Plat
Deterministic insights into co-transcriptional folding of cyclic-di-nucleotide riboswitches
Albrecht E. Voelklein1, Tom Landgraf1, Olivier Binas1, Boris Fuertig1, Christian Richter1, Harald Schwab1,
1Chemistry, Goethe University, Frankfurt, Germany, 2Goethe University, Frankfurt, Germany.
Untranslated mRNA regions called riboswitches bind messenger molecules with high affinity and influence the expression of downstream genes. Cyclic-di-nucleotide sensing riboswitches are major regulators of lifestyle changes of bacteria. Current methodology is limited to indirect structural probing of riboswitch structures inherent to the regulation mechanism. Our results show that changes in binding affinity, binding capability and refolding propensity are associated with non-overlapping transcriptional intermediates. Our results were applied in a Markov model simulating co-transcriptional unfolding, yielding a ligand sensitivity in line with in vivo concentration and the switching efficiency depending on transcription and refolding speed. The obtained detailed understanding of the transcriptional folding pathways of riboswitches could contribute to a better understanding of these systems as a whole.

1500-Plat
RNA hairpin folding dynamics in a cell
Hyejin Yoo, Caitlin Davis.
Chemistry, Yale University, New Haven, CT, USA.
RNA folding plays an essential role for temperature-dependent functions in cells. For example, RNA thermometers regulate translation of heat shock and virulence genes by folding and unfolding. Here, we employed the four-arm RNA thermometer motif of Salmonella, a hairpin—structured RNA to study in-cell folding stability of an RNA hairpin and its in vitro stability which is perturbed by crowding and sticking agents. To discover the solution environment that accounts for cellular crowding and sticking we conduct a two-dimensional scan of mixtures of artificial crowding and sticking agents, PEG10K (polyethylene glycol, 0-300 mg/ml) and M-PER buffer (Mammalian Protein Extraction Reagent, 0-80%). As anticipated, we found that the addition of artificial crowding- and sticking agents, PEG10K and M-PER buffer, leads to a stabilization and