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.

397-Pos
Development and Evaluation of the Silcs Methodology for Targeting RNA with Small Molecules
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RNAs can act as potential drug targets in different diseases as their dysregulated expression or misfolding can alter various cellular processes. Non-coding RNAs account for ~70% of the human genome and can have complex tertiary structures that present a great opportunity to be targeted by small molecules. Until recently, the majority of structure-based drug discovery efforts have been focused on targeting proteins; however, with greater understanding of RNA structures and functions, it is now within our reach to transfer and apply computer-aided drug design methods from protein targets to RNA targets. Site Identification by Ligand Competitive Saturation (SILCS) is a unique computational approach that provides a comprehensive 3D characterization of a target macromolecule in the form of functional group affinity maps, termed grid free energy (GFE) FragMaps obtained through enhanced sampling simulations of the macromolecule in an aqueous solution containing a range of chemical probes. The GFE FragMaps can be used to dock small molecule ligands using SILCS-MC, a Monte-Carlo based algorithm, and predict their binding conformation as well as approximate binding affinities for the target. Here we report development of SILCS and SILCS-MC protocols to be applied to RNA targets, including 5 different RNA targets and their reported small molecule binding partners. As the ion-atmosphere is critical towards the structure and dynamics of RNA tertiary structures, 100mM NaCl was added to SILCS simulations. Additionally, it is important that the Mg^{2+} ions bound to the RNA be included in the simulations. To facilitate this, we integrated a feature in SILCS to determine potential Mg^{2+} binding sites in the starting structure of the target RNA if not experimentally captured. Promising initial results indicate that the SILCS-RNA approach may significantly enhance drug discovery efforts targeting RNAs with small molecules.

398-Pos
Automated Localization and Quantification of RNA Transcripts from RNA-Fish Image Data
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The ability to resolve the spatiotemporal localization of individual RNA molecules in single cells with high detail is important for studying the dynamics of gene regulation. RNA fluorescent in situ hybridization (RNA-FISH) is a frequently used technique for visualizing RNA in fixed cells using fluorescent probes. Automated processing of the resulting images is essential for large datasets that may include many different transcripts and timepoints. Here we demonstrate that our MATLAB based RNA-FISH image processing pipeline is a useful tool for automatically detecting the 3D locations of cell boundaries and RNA transcripts at single molecule resolution in an RNA-FISH image stack. In particular, this tool is effective for facilitating quantitative analyses of FISH data such as determining the colocalization of multiple transcripts or the relative amount of RNA in various subcellular compartments. Our spot detection approach using gaussian filtering and background image data for threshold calibration provides an additional software-based method of conducting batch FISH data analysis complementary to existing image processing tools.

399-Pos
Prediction of Membrane Permeation of Small Drug Molecules using Silcs Energy Profile with Machine Learning
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The membrane permeability of drug molecules imparts a significant role in designing potential drugs in medicinal chemistry. The approaches for designing drug molecules span from experimental trial-and-error methods to a well-structured quantitative structure-activity relationship, and nowadays complemented with data-driven machine learning techniques. In this work, we present a deep neural network (DNN) based machine learning method to predict membrane permeabilities of small drug-like molecules. The DNN models used in our work were the standard fully connected multilayer perceptron with 37 input nodes with four hidden layer. The primary dataset used in this study consists of 219 molecules with an available experimental permeability coefficient (logPm). The input feature vector, used to train the proposed prediction model, includes a ligand Grid free energy (LGFE) profile obtained from Site identification by ligand competitive saturation (SILCS) method. The LGFE profiles were obtained for three different membrane systems, including DPPC, POPC-cholesterol and PAMPA (DOPC + DOPS + cholesterol). We further used an independent data set to validate the proposed model.

400-Pos
The Effect of Point Mutations on Structure and Dynamics of SARS-CoV-2 Main Protease Mutants
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The SARS-CoV-2 main protease (M^{pro}) is a serine-type protease with catalytic residues His-41 and Cys-145. These residues cleave highly specific protein sequences, making M^{pro} a vital part of the viral replication process and an attractive target for inhibitor design. As the virus spreads across the globe, sequence mutations occur, creating an additional challenge for robust inhibitor design. In previous work we have reported results from sequence analysis, structure prediction, and molecular modeling of the first seventy-nine M^{pro} variants, which revealed patterns in residue substitutions and a distribution of cohesion and constraint in the active site due to mutations. Here, we expand the analyses to our current set of 368 M^{pro} variants, which includes all clinically relevant variants of the protein as of October 1, 2020. Substituted residues continue to tend towards increased hydrophobicity and size. Analysis of structural cohesion and dynamics using protein structure networks and molecular models of the monomer and dimer conformations shows a difference between the monomer and dimer simulations, as well as differences across variants. Further analysis is done to determine effects of specific mutations on active site dynamics, as well as the functional independence of the two active sites present in the dimer conformation.

401-Pos
Structure Prediction and Molecular Phylogenetic Analysis of Membrane Interactions in Synaptotagmin-Like Proteins
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Membrane trafficking and exocytosis are evolutionarily conserved throughout eukaryotes and involve many interactions between proteins and membrane surfaces. In vertebrates, synaptotagmin-like proteins (Slp) play key roles in trafficking of large dense-core secretory vesicles. Slp family proteins promote secretory vesicle docking to the plasma membrane through their N-terminal Slp homology domains, which bind to vesicular Rab proteins, and their tandem C-terminal C2 domains (C2A and C2B), which bind plasma membrane lipids independently of calcium. Our previous experimental and computational studies showed that the C2A domain of Slp-4 (also called granuphilin) binds with high affinity to membrane surfaces containing phosphatidylinositol-(4,5)-bisphosphate (PIP2) and phosphatidylserine (PS). A conserved PIP2 binding site centered on three lysine residues in the beta3-beta4 region specifically anchors the domain to PIP2 lipids, while many other basic residues surrounding the Lys-cluster enhance interactions with PS. We hypothesize that the positive electrostatic potential of the membrane binding surface is a key determinant of its membrane affinity and function, and therefore the net charge on the protein surface is likely to be evolutionarily conserved. To test this hypothesis, the C2A domain sequences for Slp-4 and Slp-2 in vertebrates were compared to assess the evolution of their respective polybasic surfaces. Using a molecular phylogenetic approach, clades were identified and the net charges of individual and consensus sequences were calculated. Structural homology models were generated using a crystal structure of Slp-4 C2A, and Poisson-Boltzmann calculations were carried out to quantify the positive electrostatic surfaces. This approach may help characterize electrostatic interactions with charged membrane surfaces and identify conserved differences that govern affinity and function of membrane-binding proteins.

402-Pos
Extracting Protein Recruitment Kinetics to DNA Damage using qFADD.py
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