Complete structural characterization of flexible molecules in solution, such as sugars and peptides in aqueous environments, is demanding. Only a collection of structures with defined weights or even continuous regions of accessible phase space can describe their structural complexity. Spectroscopic techniques such as NMR and Raman appear the obvious choice for studying such systems. They are sensitive to structure, and measurements can be performed in aqueous solutions under biologically relevant conditions. Unfortunately, the obtained spectra and responses result from a weighted average of all accessible structures and are hard to deconvolute. When supported with computer simulations, one can deconvolute them and obtain an accurate description of the accessible phase space. Existing simulation protocols can perform such tasks. However, all available workflows are lengthy and require extensive human input, ultimately biasing the results. In this work, we have synthesized the experience of our developed protocols to calculate Raman and NMR spectra for saccharides into a program designed to exclude any bias by reducing human intervention. It only requires the input of the molecular structure and the corresponding experimental spectra to deliver accurate structural predictions, mainly when using spectra from different techniques simultaneously. Currently, it can handle several types of organic compounds in an aqueous solution, including biologically relevant ones (e.g., sugars and peptides). Importantly, it estimates the quality of the prediction independently for each molecular degree of freedom. The information gathered can be used to interpret the experimental spectra and develop more accurate force fields of flexible moieties. Decoding the structural complexity of organic molecules using our tool can potentially shed light on their behavior and function in aqueous environments.

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OPRLM: Orientations of proteins in realistic lipid membranes

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A new web tool and a database, OPRLM (Orientations of Proteins in Realistic Lipid Membranes), has been created based on the OPM database and the broadly used GHARMM-GUI toolset. The database provides a complete set of experimental 3D structures of integral and peripheral membrane proteins from the Protein Data Bank that are positioned in planar and curved lipid bilayers using implicit and explicit membrane representations. Membrane systems vary from single-component artificial lipid bilayers to multi-component bilayers with complex lipid composition corresponding to 18 biomembranes with either asymmetric or symmetric distribution of lipid types between two leaflets: 14 ''average'' eukaryotic cellular and organelle membranes (plasma membranes of mammals, plants, and fungi, endoplasmic reticulum and apparatus Golgi membranes of mammals and fungi, mammalian membranes of endosomes and lysosomes, mitochondrial outer and inner membranes, plant vacuole membranes, thylakoid membranes of plants and cyanobacteria), the outer and the inner membranes of Gram-negative bacteria (E. coli), and ''average'' cell membranes of Gram-positive bacteria and archaebacteria. All these membrane systems are accessible for public use in CHARMM-GUI Archive (https://www.charmm-gui.org/docs/archive/biomembrane). The web tool allows users of any level of expertise an easy setup of protein-membrane systems for atomic molecular dynamics (MD) simulations in pre-assembled realistic lipid membranes formed by mixtures of explicit lipids. OPRLM is publicly available at https://oprlm.org/.

1373-Pos

Towards the design of a conformational switchable zinc finger analogue regulating cellular behaviors

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Dynamic conformational changes in the secondary structures of proteins are essential to their functions and can regulate diverse cellular events. Herein, along with our experimental collaborators, we report the design of a synthetic polymer-based secondary structure analogue of Zinc finger (ZnF). Acting as a conformational switch between unfolded and folded states triggered by the addition of Zn^{2+} and EDTA, ZnF enables the manipulation of the accessibility of conjugated cell adhesive ligands to cell membrane receptors, by hiding or exposing the cell adhesive ligands to the transmembrane protein receptors. On the basis of the self-avoiding walk (SAW) model, we investigated the distribution of end-to-end distance of the polymer chain of ZnF and estimated the free energy barrier that the zinc coordination motif had to overcome, thereby, predicting the feasible length of the polymer chains. Our work provided valuable guidance to experimental research on the synthesis of biomimetic dynamic secondary structures to precisely control cell-biomaterial interactions and mediate the desired cellular behaviors.

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Simulating actin networks in synaptic spine heads using dynamical graph grammars

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There is a morphodynamic component to synaptic learning by which dendritic (postsynaptic) spine head size changes can strengthen or weaken the synaptic connection between two neurons, in response to signals from the axon of a presynaptic neuron. These morphological factors are in turn sculpted by the graph-like dynamics of the actin cytoskeleton. In this project, we seek to use Dynamical Graph Grammars (DGGs) [1,2] implemented within a computer algebra system to model how networks of actin filaments can dynamically grow or shrink and reshape the spine head. We designed and implemented several DGG sub-grammar mathematical models including actin network growth, isotropic/anisotropic filament forces, filament-membrane mechanical interaction, and Hessian Boltzmann sampling of random molecular displacements, to regulate the generation and deletion of graph objects. From first principles expressed in about a dozen DGG rules we simulate emergent biomechanics of a simplified network of actin polymers and its interaction with membrane, using very rough parameter estimates, all in two dimensions. We refined this model by incorporating rate constants used in previous models (e.g. [3,4,5]) in each sector, and we are currently recapitulating the previously observed sub-grammar behaviors.

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1375-Pos

The machine learning pipeline to unravel the functional effects of interactions between sodium channels

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Recent reports obtained using patch clamp approach in Na^+ channel (Na_V) pairs have suggested cooperative gating of two Na_Vs, which has been linked to their homodimerization. Yet, the existing methods of the cooperative gating analysis are not effective in unraveling alterations in kinetics of individual Na_Vs result from their interactions in dimers. To address this issue, we developed a machine learning pipeline to remove capacitance drift and noise within the signal, and detect channel activity in order to infer Markov models parameters from single and multi-channel recordings.

Cell-attached patch clamp experiments were performed in Chinese hamster ovary (CHO) cells stably expressing human $Na_V1.6$ channel. Na_V activity was elicited by step depolarizations from −120 mV to −10 mV. Capacitance currents were subtracted using the convex optimization with regularization algorithm. Next, recordings were denoised with the newly developed and validated Bayesian statistical method. This approach is based on training of hidden Markov models to separate single channel currents from noise and finding an optimal number of conductance levels in each current sweep. Further, transition probabilities of discrete time (50 μs time step) 5 states (two closed, one open, two inactivated states) Markov models were directly inferred from denoised one and two channel recordings using Markov chain Monte Carlo. The models of channel pairs assumed independent gating of identical channels. This assumption proved predictive of observed paired Na_Vs behavior. And kinetic parameters of the models inferred from single channel recordings did not differ from those inferred from two channel recordings.