accurate, yet computationally more efficient_and perhaps even better suited for supramolecular assembly dynamics modeling_than standard docking algorithms. Here, the relative efficacy, merits and demerits of RDIMs for estimating protein-protein interactions examined in the context of two key binding domains, namely myosin:actin and G-actin:G-actin.

2017-Pos

Automated Protein-Insertion into Membranes for Molecular Dynamics Simulation Set-Up Using Taragrid

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Given a known membrane protein structure, a crucial and non-trivial preparation step in order to perform simulations of the protein in a lipid bilayer is the creation of the equilibrated bilayer-protein system. TaraGrid links an implicit protein force field with standard MD packages to automate this process. In the initial steps TaraGrid places the protein into the membrane and carves any water molecules out of the protein volume. It also erases as many lipids as necessary to conserve the bilayer density. In the main optimization phase TaraGrid calculates intermolecular forces between the protein and the molecules of the bilayer-solution system. Molecules that are within the protein volume are assigned a force that pushes them out of that volume. Molecules outside of the protein surface are assigned a linear combination of electrostatic and van-der-Waals forces. These forces are passed to a subsequent MD step carried out with a standard MD package, to obtain new peptide and water positions. This procedure enables creation of realistic and reproducible starting conformations for membrane-protein simulations within a reasonable time and with minimal intervention. Presently TaraGrid is tested to interact with NAMD and GROMACS, but as a standalone tool it is designed to work with any existing MD package.

2018-Pos

Coarse-Graining Electrostatics in Multiscale Molecular Simulations of Proteins

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All-atom molecular dynamics (MD) simulations are a powerful tool to investigate the structure and function of biomolecular systems. Nonetheless, within the atomistic framework it remains computationally unaffordable to thoroughly sample size and time scales that are critical to most of the biological processes both in vitro and in vivo. Coarse-grained (CG) schemes have been introduced to overcome these limitations; nonetheless, many issues, such as the lack of universality and transferability, still afflict CG models and limit in turn their general applicability to a vast class of relevant biological problems.

We introduce a reliable and robust scheme to account for the intrinsic non-radial nature of backbone-backbone interactions in CG molecular dynamics simulations of proteins. Specifically, we define a new CG potential term, which, mimicking the backbone dipole-dipole interactions, is able to naturally stabilize elementary secondary structure motifs, such as α-helices and β-sheets, and to modulate basilar transitions to super-secondary structure assemblies. Moreover, the scheme can properly describe the long-range electrostatic contributions in a multiscale MD framework, contributing to an accurate description of protein-ligand and protein-protein recognition. Thus, this novel scheme represents a promising step towards the development of a CG force field able to take into account intrinsic anisotropy of protein structures, leading to an improved description of the structural and dynamic properties of protein assemblies and networks.

2019-Pos

Polymer Translocation Through a Nanopore in an Interacting Membrane

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The translocation of polymers through nanopores in membranes occurs in many biological processes, such as proteins transporting through membrane channels, DNA and RNA translocating across nuclear pores, and drug delivery. The mechanism of the translocations has attracted a lot of attention from experiments, analytical theories and computer simulations. In a recent simulation study, the influence of pore-polymer interaction on the polymer translocations was discussed. Some experiments implied that the interaction between polymers and membranes might play an important role in the polymer translocation through membranes. In the present work, we use dynamic Monte Carlo simulations to study the effects of interaction between polymer segments and the membrane on the translocation of polymer chains through an interacting membrane from *cis* side (high concentration of chains) to *trans* side (zero concentration). Results show that there is a critical adsorption point ϵ_c of the interaction strength ϵ . We find the translocation timeτ is almost independent from ϵ for$\epsilon < \epsilon_c$ and $\tau = f(exp(\epsilon), n)$ for $\epsilon > \epsilon_c$, where n is the length of polymer chains. We estimate the value of the critical adsorption point ϵ_c is about -0.3, which is in good agreement with previous results in many literatures studying the adsorptions of polymers on surfaces.

2020-Pos

Conservative Algorithm for an Adaptive Change of Resolution in Mixed Atomistic / Coarse-Grained Multiscale Simulations

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Understanding complex materials often requires investigating multiple, tightly coupled time and length scales. Neither atomistic nor coarse-grained simulations are often able to adequately capture all the relevant scales. To combine the efficiency of coarse-grained models with the accuracy of atomistic models for systems that require atomistic resolution only locally, for example at an interface, mixed-resolution models have been developed. These models use a coarse-grained description for the part of the system distant from an active site and atomistic description for the active site and its direct environment. Since the active zone may diffuse during a simulation, the simulation algorithm needs to permit an on-the-fly reclassication of atoms as they transition between the high- and low-resolution regimes. In this paper, we derive a conservative Hamiltonian and present an explicit symplectic integrator for mixed-resolution systems that allows for such a change in resolution of selected groups of atoms during a MD simulation.

2021-Pos

Hydrogen-Bonding Strengths in Pyrrolidinyl Peptide Nucleic Acid and DNA Base Pairs: A Density Functional Theory (DFT) Study

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The H-bond strengths of the single base pair formed from Pyrrolidinyl Peptide Nucleic Acid (PNA) and charged as well as neutral Deoxyribonucleic Acid (DNA) were studied using the density functional theory. The B3LYP/6-31+G(d,p) level of theory was employed for evaluating the binding energies and structural parameters of heterogeneous and homogeneous base pairs. The strongest H-bond strengths were obtained from the heterogeneous base pairs, yielding the binding energies of -29.9 and -18.9 kcal/mol for the PNA-GC-DNA and PNA-AT-DNA base pairs, respectively. In contrast, a dramatic change on the H-bond strengths was observed from the charged homogenous base pairs with the binding energies of -6.2 and $+10.2$ kcal/mol for the DNA-GC-DNA and DNA-AT-DNA base pairs, respectively. With the neutralization of negative charges in the DNA backbone, the corresponding values of -29.1 and -11.7 kcal/mol were elucidated from the Na-DNA-GC-DNA-Na and Na-DNA-AT-DNA-Na base pairs, respectively, proving that the repulsion between two negative charges in the phosphate backbone plays a significant role to the H-bond interactions in base pairs. In addition, a high specificity and preferential binding between the pyrrolidinyl PNA and DNA base pairs were also observed.

2022-Pos

Protein Classification Based on Physicochemical Descriptors

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ystematic and efficient analysis of proteins on the proteome scale requires their classification into meaningful sub groups. Approaches to the problem are either top-down, following the evolutionary pathways (SCOP, CATH) and bottom-up, where structures are compared pairwise and aggregated to clusters (DALI). Here we present a novel way of protein classification based on physicochemical descriptors. Atomistic structures are for classification purpose overly rich in information and we distilled biologically relevant features by projecting from the structure space into a lower dimensional descriptor space. Chosen descriptors fall into three groups, sequence dependent, topology, and overall structure and consist of amino acid distribution, charge, hydrophobicity, average path length, cluster coefficient, helix content, sheet content, solvent accessible surface area, radius of gyration, besides others. All descriptors were corrected for chain length and normalized by the standard deviation.

Over 3000 representative and non-redundant structures from the pdb Cluster90 were mapped to descriptor space and clustered. The identified clusters coincide to large extend with those from existing classification methods. Our method provides, unlike others, a direct measure for the distance between any two proteins and is easily expandable by for instance descriptors for molecular dynamics.