investigate effect of various system parameters, such as ligand density and mechanical properties of the receptor-ligand interaction, on the kinetics and mechanics of cell adhesion process. More importantly, this study provides a computational framework, with multi-scales and multi-physics, that can be extended for better controlling of cell interactions at the cell-biomaterial interface and for modeling the cell motility.

2972-Pos

A Search for Energy Minimized Sequences of Proteins

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Computational design of sequences for a given structure is generally studied by exhaustively enumerating the sequence space, which is prohibitively expensive. However, we point out that the protein topology has a wealth of information, which can be exploited to design sequences for a chosen structure. We design a computationally efficient method for ranking the residue sites in a given native-state structure, which enables us to design sequences for a chosen structure. The premise for the method is that the topology of the graph representing the energetically interacting neighbors in a protein plays an important role in the inverse-folding problem. We use edge-weighted connectivity graph for ranking the residue sites with reduced amino acid alphabet and then use continuous optimization to obtain the energy-minimizing sequences. Our methods enable the computation of a lower bound as well as a tight upper bound for the energy of a given conformation. We validate our results by using three different inter-residue energy matrices for five proteins from protein data bank (PDB), and by comparing our energy-minimizing sequences with 80 million diverse sequences that are generated based on different considerations in each case. Some of our chosen energy-minimizing sequences are similar to the sequences from non-redundant protein sequence database with an E-value of the order of 10^{-7}. In summary, we conclude that proteins show a trend towards minimizing energy in the sequence space but do not seem to adopt the global energy-minimizing sequence. The reason for this could be either that the existing energy matrices are not able to accurately represent the inter-residue interactions in the context of the protein environment or that Nature does not push the optimization in the sequence space, once it is able to perform the function.

2973-Pos

Simplified Theory for DNA Melting Maps

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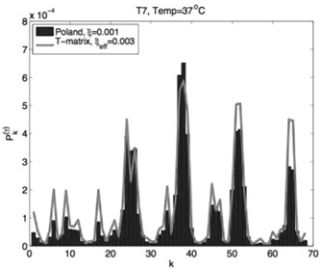
DNA melting maps on DNA stretched on surfaces or in nanochannels give a coarse grained picture of the underlying sequence with potential applications in studies of structural variations and for identification of (micro)organisms. The underlying mechanism is based on the difference in free energies associated with breaking AT and GC basepairs so that DNA melts first in AT-rich regions and only at higher temperature in GC-rich regions. With a suitable choice of dye the melted regions and the unmelted regions can readily be distinguished.

The Poland-Scheraga (PS)model is an Ising model with a long-range term due to the entropy associated with the single-stranded regions and, although computationally slow (~ square of the number of basepairs), has proven to well reproduce melting data. However, by adapting our algorithms to the resolution of the experimental melting mapping (1kbp) we can make them computationally more efficient.

We combine a transfer matrix approach and an exact Poland-type algorithm to study opening probabilities along DNA. We systematically explore different degrees of simplifications such as capping the long-range interactions or using a coarse-grained effective-medium approach. We evaluate our simplifications against exact solutions to the PS model for known sequences (figure).



2974-Pos

Testing a Hybrid Solvation Model with a Transition Layer Via Molecular Dynamics Simulation

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We previously developed a three dielectric layer hybrid solvation model for the electrostatic interactions of biomolecules in solvents using the linearized Poisson-Boltzmann equation. In this model, the interior spherical cavity contains the solute and explicit solvent molecules. Rather than employing the commonly invoked classical Kirkwood model that assumes a discontinuous change in dielectric constant from inside to outside the sphere, we introduced an intermediate buffer layer. Outside the spherical shell defines the exterior layer, where bulk solvent is modeled implicitly and characterized by a dielectric constant. Within the buffer layer, a special dielectric permittivity profile is constructed to give a continuous transition from the interior cavity to the exterior region. The purpose of the buffer layer is to remove unphysical divergence in electrostatic force at the cavity boundary. The electrostatic force within the cavity due to the reaction field of solvents with various ionic strengths is calculated using discrete image charges. Molecular dynamics simulation is performed using a recently developed simulation protocol to benchmark the effectiveness of the buffer layer, for various thickness, h, and different ionic concentration. Monitoring response functions and distributions of force and torque on molecular water facilitates relative comparisons. This work is supported by NIH 1R01 GM083600-03.

2975-Pos

Data-Driven Analysis of Cell Motility on Nanostructured Surfaces

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Experimental time series for trajectories of motile cells contains so much information that a systematic analysis yields cell-type-specific motility models. Using a range of cell types on various nanostructured surfaces we have explored how the surface type and cell type result in different motility models. This reflects the cells' different roles in the organism by showing that a cell has a memory of past velocities. They also suggest how the nanopatterns imprinted on the various surfaces affect cell motility.

2976-Pos

Development and Application of Non-Additive Force Fields for Molecular Simulations of Lipid Bilayers and Integral Membrane Proteins

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Molecular simulations today are applied across many scientific disciplines. Complementing experiment, these tools afford a molecular-level understanding and interpretation of physico-chemical processes at resolutions and timescales difficult or practically inaccessible to experiment. At the heart of such methods is the description of interactions between atoms and molecules, the force field. Traditionally, non-reactive force fields have treated electrostatic interactions using an additive, Coulomb model between fixed partial charges on atomic sites. Though quite successful, there has been conjecture as to the effects of incorporating non-additivity in classical force fields, particularly in biological systems. Over the last several decades, attempts to incorporate electrostatic non-additivity in the form of inducible dipole interactions or dynamically varying partial charges have provided a vast body of knowledge that has aided in the development of a new class of force fields attempting to explicitly account for non-additive effects. We will present our recent work in developing one such class of models, charge equilibration force fields, and applications of such models to aqueous solution interfaces, membrane bilayers and simple integral membrane peptides such as the gramicidin A bacterial channel, and recent work on modeling of protein-ligand interaction free energetics.

Imaging & Optical Microscopy III

2977-Pos

In Situ Measurements of Oligomerization State of NBCe1-A in Rat Kidneys Via Spatial Fluorescence Intensity Fluctuation Analysis

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NBCe1-A plays an important role in absorbing sodium bicarbonate across the basolateral membrane of the proximal tubule. We have previously showed that minimal functional unit of NBCe1-A is a monomer, and based on in-vitro biochemical studies in HEK293 cells, the oligomeric state of the cotransporter was shown to be predominantly dimeric with monomeric and higher oligomeric forms also present. We developed an in situ measurement methodology to determine the oligomeric state of NBCe1-A without requiring tissue disruption