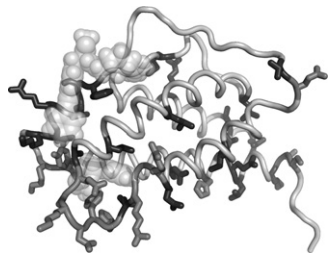
interleukin-2, two of the clusters with the strongest correlations highlight known cooperative small-molecule binding sites and show substantial correlations between these sites. We also present a newer approach based on the Kullback-Leibler divergence, an information-theory metric that quantifies population shifts and perturbations to the free energy landscape. Since these approaches identify pairs of residues with correlated conformations in an unbiased, statistically robust manner, they should be useful tools for finding novel or ''orphan'' allosteric sites in proteins of biological and therapeutic importance.



1991-Pos

Influence of Organic Solvents on the Structure and Enzymatic Activity of Haloalkane Dehalogenase DhaA

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Organisms with the ability to degrade anthropogenic chemicals are using for this purpose haloalkane dehalogenases. Hereby, a active site nucleophile attacks a carbon atom of the halogenated substrate, leading to cleavage of the carbon-halogen bond, displacement of a halide and formation of a covalent alkyl-enzyme intermediate that is subsequently hydrolyzed. The haloalkane dehalogenase DhaA from Rhodococcus rhodochrous NCIMB13064 is enzymatically active for a broad range of halogenated substrates including 1,2,3-trichloropropane (TCP) (2) and sulphur mustard (3), some of them with high hydrophobicity and low solubility in water. Improving the solubility by addition of water miscible co-solvents like dimethyl sulfoxide (DMSO) to the reaction mixture could be a way to enhance the range of potential applications for these enzymes. Therefore, in the present study we investigate effects of DMSO on structure and dynamics of DhaA using molecular dynamics (MD) simulations demonstrating that the DMSO molecules penetrate to the active site of protein and compete with the halogentaed substrate for the catalytic site histidine272. On the other hand, histidine 272 traps DMSO and thus prevents further progress of DMSO deeper into the active site. With respect to protein solubility, interactions of DMSO with the protein surface decrease the solvation energy of the protein compared to protein in pure water. However, the enzyme is clearly stable in up to 42% DMSO and we can conclude that the enzyme activity is expected to be less than in pure water, however retained.

1992-Pos

Characterizing Structure and Activity of Subtilisin Enzyme in Nonaqueous Media with Molecular Dynamics Simulations

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Structural and dynamical behaviors of enzyme are critical for determining its catalytic activity. Knowing that the enzyme activity may vary with different solvent polarity due to the changes in enzyme structure and flexibility, Subtilisin Carlsberg enzyme was subjected to investigate the structural variation upon different solvent systems by using molecular dynamics simulation with explicit solvents. Characterization of the structure and activity focusing on the hydration of the active site will be discussed with the effects of crystallographic water bound to the active site of this enzyme and with the solvent effects.

1993-Pos

Influence of dsDNA Architecture on Diffusion Properties in Networks

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DNA is an essential element for genetic disease treatments. Its application depends on the diffusive properties of DNA through tissues. Although, there are works on linear DNA diffusion in a network environment, the dependence of the diffusion coefficient on chain architecture is not completely understood.
In this work we study dsDNA molecule behavior in a network with the discrete slip-link model. We show dependence of the diffusion coefficient on the chain molecular weight and network mesh size. We compare theoretical predictions with experimental measurements of linear dsDNA thermal diffusion in agarose gels. To analyze the influence of the architecture of the DNA molecule on its diffusion properties, the theory can be applied to star-shaped molecules. However, to obtain experimental data it requires to synthesize a well characterized star-shaped dsDNA molecule.

1994-Pos

Electric Field Effects on Water and Water-Vacuum Interfaces in Molecular Dynamics Simulations

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Understanding the behavior of water in atomic-scale detail is essential to explaining the microscopic dynamics of such phenomena as electroporation, electrospinning, electrospraying, and electric-field-driven evaporation. In this study we employ molecular dynamics simulations to investigate water-vacuum systems under the influence of an externally imposed electric field. SPC and SPC/E water models are used to describe nanodroplets and interlaced water-vacuum slab configurations. The dynamics of these systems is studied in detail with respect to the strength of the applied electric field, and we note the importance of a proper representation of long-range electrostatics in the simulations. Water behavior is analyzed from both structural and energetic points of view. We discuss how such characteristics as the system geometry, local water density, and water molecular dipole orientation change as the electric field is increased. These changes are described in the context of interplay between pressure, surface tension, and electrodynamic dipole-field and dipole-dipole interactions. For example, we find that for nanodroplets containing ~900 water molecules there is a critical electric field strength above which there is a jump in the alignment between the water dipole and the field. Concomitant with the dipole alignment is a distortion of the droplet shape from a sphere to a prolate ellipsoid oriented along the electric field. We also study formation of small-scale structures at the water-vacuum interface in both droplet and slabs configurations and investigate the relationship between these structures and a subsequent creation of pore-like bridges between the water slabs in the water-vacuum-water systems.

1995-Pos

A Molecular Dynamics Simulation Study of the 9_25-11 Dnazyme

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DNAzymes (catalytic DNA) have recently attracted increased research interest with an eye towards applications as therapeutic agents and biosensors, among others. Advantages over proteins include an increased resistance to hydrolysis and cost-effective production.
Most DNAzymes recruit divalent metal ions as cofactors, however D.M. Perrin and coworkers have recently synthesised a M2+-independent, multiple turnover DNAzyme (Dz9(25)-11 by the inclusion of two kinds of modified nucleotides (8-histaminyl-dA and aminoallyl-dU in place of dA and dT, respectively) which afford enhanced catalytic rates that are attributed to the roles of electrostatic (cationic amine) catalysis as well as both general base and general acid catalysis (imidazoles). In this regard, Dz9(25)-11 functions as a sequence specific RNaseA mimic.
The use of DNAzymes in a number of applications notwithstanding, structural and dynamic information about DNAzymes in general is scarce compared to proteins. Moreover there is no X-ray structure of Dz9(25)-11, however, D.M. Perrin and coworkers have conducted a site-directed chemical study from which proximity information between specific nucleotides can be inferred.
Here, this information is incorporated into an atomistic, fully solvated model of Dz9(25)-11using the GROMOS96 biomolecular simulation package. The structure, dynamics and putative function of the DNAzyme is discussed in light of the simulation results.

1996-Pos

Oxidative Damage in Lipid Bilayers: A Reactive Molecular Dynamics Study

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Current simulations of lipid bilayers focus on their structural and compositional properties. Chemical reactivity between cell membranes and extra cellular species is an unexplored field for molecular dynamics. To explore this new area of research, we have simulated a lipid bilayer composed of 200 POPC lipids (along with 50 waters per lipid) and its reaction with a simple peroxide for 8 ns using Reactive Molecular Dynamics (Purdue Reax). The specific chemical pathways of oxidative damage can be determined from these simulations and a greater insight into the process can be achieved.