helix has shown that there is a sequence dependent cationic localization toward the purine-rich run within the TAR duplex. A region of high ion affinity agrees very well with the position of the X-ray determined divalent cations within a fragment from the HIV-1 TAR RNA. We show that a unique sequestration of ions within the core helix occurred independently of a nucleotide bulge and solely based on sequence of the helix. Our results suggest a high propensity toward purine dependent colocalization of one to two cations distinct from those performing phosphate backbone screening.

225-Pos

Computational Exploration of Thermodynamics and Kinetics of Mobile Ions Around RNA Duplex

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Atomically detailed distributions of ions around an A-form RNA are computed. Different mixtures of monovalent and divalent ions are considered explicitly. Studies of tightly bound and of diffusive (but bound) ions around 25 base pairs RNA are conducted in a explicit solvent. Replica exchange simulations provide detailed equilibrium distributions with moderate computing resources (20 nanoseconds of simulation using 64 replicas). Magnesium ion distributions show significant near-RNA binding while sodium ion distributions are more diffusive. Predicted binding sites of at the RNA surface are in accord with structures from crystallography. Electric field relaxation is investigated. The relaxation due to solution rearrangements relaxes in tens of picoseconds, while the contribution of RNA tumbling continues to a few nanoseconds. Negative mobile ions can be found near the RNA but must be assisted by proximate and mobile cations. At distances larger than 16Å from the RNA center, a continuum model of RNA charge density and solution becomes accurate. At shorter distances, the structure of RNA (and ions) has significant impact on the pair correlation functions.

226-Pos

Photochemistry of DNA Fragments Via Semiclassical Nonadiabatic Dynamics

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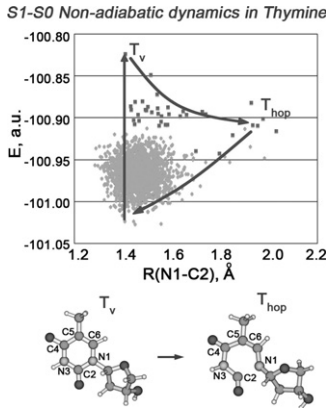
Forming upon absorption of a UV photon, excited states of DNA are subject to nonadiabatic evolution. Though photo-excited DNA mostly undergoes internal conversion back to the ground state, various routes of mutagenesis are also possible. Ultimately, the accumulation of errors in the genome can result in cancer. Here, nonadiabatic processes following the formation of the first singlet excited states, S1, in ten different small DNA fragments have been investigated: four single 4′H-nucleosides, two Watson-Crick base pairs, and four nucleotide quartets. Simulations were done via the nonadiabatic direct trajectory surface hopping semiclassical dynamics. The electronic wavefunction was obtained with configuration interaction, based on the semiempirical PM3 Hamiltonian with fractional orbital occupation numbers. The evolution of the electronic wavefunction was governed by the time-dependent Schrödinger's equation with a locally-diabatic representation, intrinsically stable near surface crossings. The nuclei evolved on adiabatic potential energy surfaces, as prescribed by classical Newtonian dynamics. The ''fewest switches'' surface hopping algorithm coupled the quantum and classical parts of the system. The dynamics simulations revealed several routes of nonadiabatic relaxation in these systems, which were not reported previously.



227-Pos

Application of Reptation Model on Brownian Dynamics for Electrophoresis of Single DNA in Polymer Solution

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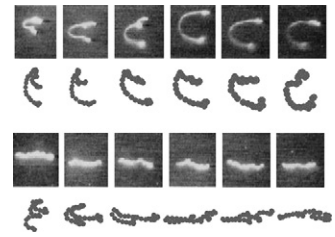
Brownian dynamcis(BD) simulation is performed to study electrophoretic motion of a single DNA moecule in polymer solution. When a DNA is forced to pass through pores in polymer solution under electrophoresis, the motion of DNA is strongly influence by surrounding entangled polymer molecules. We following the concept in the reptation model to represent the dynamics of DNA in polymer solution. Using the cubic Bezier spline, we manifest the contour of DNA to apply the constraint force from entangled polymer molecules surrounding the DNA. U-shaped, I-shaped migration, and periodic motions of DNA corresponding to each concentration of polymers solution under DC field, and the dynamics of DNA under AC field are simulated. We derive electrophoretic mobility using BD model with the constraint force to compare with experiment. We make the empirical correlation of the constraint force with concentration of polymer solution.



228-Pos

Partitioning of the Elastic Energy in Protein-Dna Chimeras

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We synthesize Protein-DNA chimeras where a DNA molecular spring mechanically perturbs the conformation of the protein. We measured the elastic energy stored in one such molecule, consisting of the enzyme Guanylate Kinase coupled to a 60 bp DNA spring. From these measurements, the response of the protein in terms of its enzymatic activity, and a mechanical model of the DNA spring we deduce that, in this case, most of the elastic energy of the molecule is stored in the DNA spring. Thus the DNA spring is ''softer'' than the protein.

229-Pos

Self-Assembly in a Model Amphiphile System

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The physical origin of the large and negative excess entropy of mixing of alcohols and water remains controversial. In contrast to standard explanations that evoke concepts of water structuring, recent work has shown that, at ambient conditions, it can be quantitatively explained in terms of molecular scale partial demixing of the two components. Here, we estimate the negative excess entropy of aqueous methanol at low temperature and high pressure using experimentally-derived structural data and a recently introduced cluster model. On cooling to 190 K the cluster sizes increase, but the change in negative excess entropy, which according to this method of calculation depends on the surface area to volume ratio of the clusters, is not significant, suggesting that the topology of the clusters must change with decreased temperature. On compression the cluster sizes also increase, and the negative excess entropy is now positive, suggesting an even more pronounced change in cluster topology with increased pressure. This work suggests that it is the amphiphilic nature of a molecule that determines aggregation and self-assembly processes in aqueous solution.
The results therefore give useful insight into the processes of cold and pressure denaturation of proteins.

230-Pos

Hydrophobic and Hydrophilic Interactions

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We are trying to understand mysteries of nature by looking at extra large (Cosmology and Astrophysics) and extra small distances (Weak/Strong interactions High energy Physics) while it can be seen in the physics of life systems. In previous presentations I developed some theoretical vision about conformational motion and non-equilibrium dancing of biological macromolecules by giving definitions of non-equilibrium entropy and geometrical motion. Those two key definitions and formulations are believed to be enough to answer the questions what is big energetic fluctuation is induced by in non-equilibrium systems and how the life system functions properly under that fluctuations. Self-organization is dynamic process where hydrophobic-hydrophilic interactions take a crucial role. Non-equilibrium dancing may induce 'hydrophobic-hydrophilic' waves which may be felt by other molecules. One may think that the suggestion about conformational motion may complicate quantitative and qualitative description of hydrophobic-hydrophilic interactions. Nevertheless, geometrical motion itself indicates changes of hydrophobicisity of the surfaces and can be completely described if it is taken into account dynamic processes of the surfaces solvent interactions. Since, in solvents, we have large number of interacting molecules statistical physics supposed to have crucial role in describing those dynamic processes but tusk is complicated by non-equilibrium nature of the processes. Fluctuation theorem guarantees reversibility of non-equilibrium processes but caries probabilistic nature so can not strictly predict whether entropy will decrees or increase in time. The problem becomes solvable in

theory of conformational motion which gives possibility to be written time evolution equation of the entropy. Up together, taking into account previously presented equation of conformational motion and non-equilibrium entropy definition, solves hydrophobic-hydrophilic interactions problem. Preliminary calculations show excellent matching with experimental data. Complete picture of hydrophobic-hydrophilic interactions and time evolution equation of the entropy will be presented.

231-Pos

In Silico Study of the Inhibition of Taq Polymerase by Fullerol C60(oh)20

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Polymerases are enzyme proteins catalyzing the polymerization of nucleic acids by the addition of nucleotides to a substrate ss-DNA (or RNA) against a template ss-DNA, making the correct Watson-Crick base pairs. *Taq*DNA polymerase (*taq*pol), a thermostable polymerase from the bacterium *thermus aquaticus*, is widely used in polymerase chain reactions (PCR) - a popular technique for the amplification of a DNA sample. Recent studies have reported that fullerol C60(OH)*n*, a water-soluabe fullerene derivative, can inhibit PCR [1, 2]. The experimental evidence suggests that fullerol inhibits PCR by interacting with the enzyme *taq* polymerase [2]. Since polymerases in all organisms use the same mechanism for the polymerization of nucleotides, fullerol may inhibit other polymerases and thus affect DNA duplication in cells.

We have used molecular dynamics (MD) and molecular docking to understand the mechanism of *taq* polymerase inhibition. The crystal structure of polymerizing domain (Klentaq) of the *taq* polymerase is obtained from [3]. Molecular docking is used to find the binding sites of fullerol on Klentaq (Autodock 4.2 [4]). MD simulation are started from the conformations obtained from docking studies. By a detailed comparison of the simulations of the protein in the presence of fullerol with simulations in the absence of fullerol, insight into the mechanism of inhibition is obtained.

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[2] J. Shang *et. al*, Nanotechnology 20, 415101 (2009)
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[4] G. M. Morris *et. al*, J. Comput. Chem., in press (2009)

232-Pos

Electrostatic Contribution to the Transition States Binding Free Energy Using Simplified Coarse Grained Model

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Simplified coarse-grained (CG) models (of the type originally developed by Levitt and Warshel (1)) can provide an effective way of evaluating the free energies of explicit protein models (2). Here we use such a reference potential strategy in evaluating the transition state electrostatic binding free energies calculations, which are essential for the rational enzyme design. The method is examined and demonstrated in studies of the effects of mutation on the transition state binding free energies of the esterase catalytic substrates (*p*-nitrophenyl acetate, *1*-and *2*-naphthyl acetates) of human carbonic anhydrase II (hCAII) and dienelactone hydrolase (DLH). These have been computed using empirical valence bond (EVB) approach in MOLARIS program (3) with and without the use of the CG model as a reference potential. The calculated electrostatic contributions to the transition state binding free energies reproduce the experimental trends (4, 5). This indicates that the method should provide a powerful tool for exploring the esterase activities of hCAII and DLH for understanding the promiscuity of these enzymes.

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(2) Messer, M. M., Roca, M., Chu, Z. T., Vicatos, S., Vardi-Kilshtain, A. and Warshel, A., Proteins, 2009, in press.
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(4) Gould, S. M. and Tawfik, D. S., Biochemistry, 2005, vol. 44, no. 14, pp. 5444-5452.
(5) Kim, H.-K., Liu, J.-W., Carr, P.D., Ollis, D.L., Acta Cryst., 2005, vol. D61, pp. 920-031.

233-Pos

Hydration Analysis on Atp Hydrolysis by Microwave Dielectric Spectroscopy

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Recent theoretical works reveiled that the hydration energies of nucleotides and inporganic phosphates are one of important factors in the ATP hydrolysis energy. Here we have measured the hydration states of the reactants and the products of ATP hydrolysis reaction by precesion microwave dielectric relaxation spectroscopy. The complex dielectric spectra of hydrated solutes, such as sodium salts of ATP^{4-}, ADP^{3-}, HPO_4^{2-}, were measured. We detected constrained water and hyper-mobile water around nucleotides and phosphates. Hydration change upon the neutralization reaction of phosphate, $H_2PO_4^- + OH^- \diamond HPO_4^{2-} + H_2O$, was investigated by measuring high-resolution complex dielectric spectra of mono- and di-sodium phosphate solutions at 20°C to understand the hydration effect on the thermodynamics of phosphate buffer reaction. From each solution spectrum the dielectric spectrum of a spherical volume containing each hydrated solute in water was derived based on a suspension theory. Each spectrum was decomposed into a bulk water ($f_{cw} \sim 17$ GHz) component and two Debye dispersion components, assigned as constrained water ($f_{c2} \sim 6.4\text{GHz} < f_{cw}$) and hyper-mobile water ($f_{c1} \sim 19.5\text{GHz} > f_{cw}$), respectively. The dielectric dispersion of hyper-mobile water was about five times stronger than the constrained one. The strengths of these two Debye dispersions decreased by 20% ($\Delta N_2 = -7$) for the constrained water number and by 10% ($\Delta N_1 = -15$) for the hyper-mobile water number upon the neutralization reaction, while those decrements were compensated by an increase of dispersion strength of bulk water. It is thought that the entropy changes corresponding to the number increases of constrained water and hyper-mobile water molecules are negative and positive, respectively. So the present result provides us a physical explanation of the small effect of hydration change on the total entropy change upon the reaction.

234-Pos

Thermodynamic Studies on the Cataract-Associated Mutant, E107a, of Human Gamma-D Crystallin: Molecular Basis for Cataract Formation

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The E107A mutation in human gammaD-crystallin (HGD) is associated with nuclear cataract. The concentration of crystallins in the lens is extremely high, approaching that within protein crystals. The composition in the lens nucleus, i.e. the central core, is such that the alpha- and gamma crystallin weight fractions are comparable. In earlier studies we showed that mutations in HGD dramatically compromised protein solubility, while maintaining the overall protein structure. In contrast, in the E107A mutation neither the structure (circular dichroism and tryptophan fluorescence emission) and stability (thermal denaturation), nor the solubility are affected significantly. However, as expected, the mutation raises the pI by ~1 pH unit, i.e. from 7.4 to 8.4. The increase in pI suggested a change in the interaction of E107A with alpha crystallin, which is negatively charged at neutral pH. To determine changes in such interaction, we compared the liquid-liquid phase boundaries in binary mixtures containing either HGD or E107A, and alpha crystallin. Our preliminary studies show that while the phase-separation temperatures of mixtures in the two cases (i.e. HGD+alpha and E107A+alpha) remain comparable, the nature of the paired compositions of the two phases in equilibrium are distinct. In particular, the tie-line slopes are altered in the direction predicted to correspond to increased alpha-gamma attraction, on the basis of molecular dynamics simulation and thermodynamic perturbation theory (1). Thus, it appears that increased attractive interactions between the E107A mutant of HGD and alpha crystallin could destabilize the crystallin mixture in the lens nucleus, and lead to increased light scattering and cataract.

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235-Pos

Urea Facilitates the Translocation of Single-Stranded DNA and RNA Through the α-Hemolysin Nanopore

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The staphylococcal α-hemolysin (αHL) protein nanopore is under investigation as a fast, cheap detector for nucleic acid analysis and sequencing. Although the discrimination of all four bases of DNA by the αHL pore has been demonstrated, the analysis of single-stranded DNAs and RNAs containing secondary structure mediated by base pairing is prevented because these nucleic acids cannot be translocated through the pore. Here, we show that a structured 95-nucleotide single-stranded DNA and its RNA equivalent are translocated through the αHL pore in the presence of 4 M urea, a concentration that denatures the secondary structure of the polynucleotides. The αHL pore is functional even in 7 M urea and therefore it is easily stable enough for the analysis of challenging DNA and RNA species.