I-E Prediction of Protein Tertiary Structures from the First Principles

Prediction of the three-dimensional structures of protein molecules by computer simulations is a very challenging problem in theoretical molecular science. The difficulty of the problem lies in two facts: (1) the inclusion of accurate solvent effects is non-trivial and time-consuming (2) there exist huge number of local minima in the energy function, forcing conventional simulations to get trapped in states of energy local minima. We have been exploring the strategies that allow us to overcome these difficulties.

I-E-1 Classification of Low-Energy Conformations of Met-Enkephalin in the Gas Phase and in a Model Solvent Based on the Extended Scaled Particle Theory

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We employed Monte Carlo simulated annealing method to classify the low-energy conformations of Met-enkephalin in the gas phase and in aqueous solution. In order to include the free energy of cavity formation in aqueous solution, we used the method of extended scaled particle theory. This was the first attempt to combine the Monte Carlo simulated annealing method and the extended scaled particle theory. We conducted 20 Monte Carlo simulated annealing runs of 10000 Monte Carlo sweeps both in the gas phase and in aqueous solution. It was found that the obtained conformations (20 each) can be classified into 3 groups of similar structure both in the gas phase and in aqueous solution. We studied in detail the structural characteristics of the classified conformations. It was found that the cavity-formation effects of aqueous solution do not drastically change the backbone structures obtained in the gas phase. The relation between the solvent-accessible surface area and the cavity-formation free energy was studied in detail. The results show unambiguously that the cavity-formation free energy is not necessarily proportional to the accessible surface area, at least for a small peptide.

I-E-2 Temperature Dependence of Distributions of Conformations of a Small Peptide

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[*J. Mol. Graphics Modell.* **16** (1999) in press]

We have performed a multicanonical Monte Carlo simulation of Met-enkephalin in order to study its low-energy conformations in detail. The obtained conformations are classified into six groups of similar structures by the pattern of intrachain hydrogen bonds. We have identified six such groups. Several thermodynamic quantities such as the distributions of hydrogen bonds and those of backbone dihedral angles are obtained as a function of temperature. From these results, it was concluded that at least four of the six groups are well-defined local-minimum-energy states.

I-E-3 α-Helix Propensities of Homo-Oligomers in Aqueous Solution Studied by Multicanonical Algorithm

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Helix-coil transitions of homo-oligomers in aqueous solution are studied by multicanonical Monte Carlo simulations. The solvation effects are represented by the term that is proportional to the solvent-accessible surface area of the peptides. Homo-oligomers of length 10 are considered for two characteristic amino acids, alanine and glycine, which are helix former and helix breaker, respectively. It is shown that the helix-coil transition temperature for homo-alanine in water is considerably lower than in gas phase. The helix propagation parameter s and nucleation parameter σ for both alanine and glycine are calculated and shown to be in remarkable agreement with experimental results.

I-E-4 Replica-Exchange Molecular Dynamics Method for Protein Folding

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We have developed a formulation for molecular dynamics algorithm for the replica-exchange method. The effectiveness of the method for protein folding problem is tested with a penta peptide, Met-enkephalin. The method can overcome the multiple-minima problem by exchanging non-interacting replicas of the system at several temperatures. From only one simulation run, one can obtain probability distributions in canonical ensemble for a wide temperature range by the multiple-histogram reweighting techniques, which allows the calculation of any thermodynamic quantity as a function of temperature in that range.

membered ring. We then discussed the basis set dependence of geometrical parameters and concluded that the polarization functions improve the description for double and triple bond states. Ab initio parameters such as transfer integrals were calculated for DCNQI dimers and trimers and compared with formerly calculated parameters. We found that the transfer integrals correlate well with lattice parameters of the c axis.

I-L-3 Theoretical Study on Electron Correlation of 1-D $(DCNQI)_2M$ (M = Li, Ag)

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[*Chem. Phys. Lett.* **298**, 15 (1998)]

We study electronic states of the $(DCNQI)_2M$ (M = Li and Ag) salts based on the full configuration interaction (FCI) method using effective Hamiltonians derived from the ab initio molecular orbital theory. FCI results of the DCNQI tetramer and octamer models indicate that the ground state has the antiferromagnetic and charge ordering correlations. It corresponds to the 2 kF spin density wave and 4 kF charge density wave states (SDW and CDW). In the octamer model, it is also found that some low-lying excited states have similar spin-flipped CDW correlations and the antiferromagnetic correlation is weakened.Electronic and geometrical structures of DR-DCNQI molecules (R = H, Cl, Br, I, Me and OMe) were studied by performing ab initio MO calculations at the HF/DZP level. We carried out DCNQI monomer calculations and found that the optimized structures are close to experimental ones within errors of 0.04 Å in a six-membered ring. We then discussed the basis set dependence of geometrical parameters and concluded that the polarization functions improve the description for double and triple bond states. Ab initio parameters such as transfer integrals were calculated for DCNQI dimers and trimers and compared with formerly calculated parameters. We found that the transfer integrals correlate well with lattice parameters of the *c* axis.