

STRUCTURES AND FUNCTIONS OF HYPOTHETICAL PROTEINS FROM THERMUS THERMOPHILUS HB8

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We aim to determine three-dimensional structures of proteins whose functions are unknown and conserved among many organisms, and assign putative functions by obtaining the knowledge about fundamental biological phenomena from its structural information. An extreme thermophile, *Thermus thermophilus* HB8, has unknown functions as high as 40% and is the set of our target.

In order to conduct the structural analysis, a relatively large amount of highly purified samples of hypothetical proteins from *Thermus thermophilus* HB8 are synthesized. The purification of expressed proteins is being performed by means of the combination of heat treatment and various column chromatography.

The production of selenomethionine incorporated proteins for the multi-wavelength anomalous diffraction (MAD) phasing are prepared by cell-free protein expression systems and *in vivo* expression systems. Structural determination is mainly done by X-ray crystallography using the large-scale synchrotron radiation facility, SPring-8. A large fraction (about 30%) of proteins has achieved structural determinations. Molecular function is analyzed by gene disruption of *Thermus thermophilus*, by yeast two-hybrid system, and by biochemical activity measurement for each protein. Acknowledgements: We are grateful to Noriko Handa, Miki Idaka, Makoto Inoue, Miyuki Kato, Yasuhiro Katsura, Seiichiro Kishishita, Kazutaka Murayama, Naoto Ohtani, Shun-ichi Sekine, Chie Hori-Takemoto, Yumiko Terazawa, Takashi Wada, Hong-fei Wang, and Hiroto Yamaguchi for their great contributions.

Keywords: HYPOTHETICAL PROTEINS STRUCTURE AND FUNCTION

THE USE OF ACCURATE ELECTROSTATIC MODELS IN CRYSTAL STRUCTURE AND PROPERTY PREDICTION

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The initial step in the computational search for hypothetical polymorphs involves a search for all low energy minima in the potential energy. The global minimum is assumed to be the most likely observable structure and other low energy structures are possible polymorphs. However, such searches usually generate far more energetically feasible structures than are known or are likely to be observed. The hypothetical structures are ranked by lattice energy, but the energy differences are usually very small, so this sorting requires the use of as accurate a model intermolecular potential as possible. As an advance on the usual empirical, isotropic atom-atom intermolecular potentials, a distributed multipole analysis of the molecular wavefunction has been used to model the electrostatic contribution. This has been shown to significantly improve the modeling of crystal structures, lattice energies and relative energies in prediction studies.

However, even with a perfect ranking on lattice energy, other factors will influence the likelihood of observing a metastable structure. We have been exploring the usefulness of predicted crystal properties, such as growth rates of morphological dominant faces, mechanical strength, and vibrational contributions to the energy, in evaluating hypothetical structures.[1] The sensitivity of such calculations to the electrostatic model has been examined.[2] The predicted properties of low energy structures help rationalize the observed polymorphs.

References

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PREDICTION OF POLYMORPHIC STRUCTURES AND SOLID STATE TRANSFORMATIONS OF ORGANIC CRYSTALS

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While the polymorphism and phase transition phenomena are recognized to be very common to organic solids, examples of them studied systematically at atomic resolution are quite rare among a quarter of million of structure determinations published so far. This is caused by the lack of crystals of proper quality that would be available for both the initial and final states of the same phase transition, not speaking of the transient states possibly involved. To this end, it is presently evident that no further progress in the understanding of transformation phenomena can be expected without a substantial support from the computer-mediated structure-prediction techniques.

In this talk, we shall discuss the crystal structure predictions based on potential energy calculations. The global energy hypersurface defines polymorphic properties of a molecular solid: its low-energy minima represent the structure and thermodynamic stability of stable phases while stationary points connecting the minima control transformation kinetics. Its high symmetry in the multidimensional structure-parameter space is a fundamental property relevant to many aspects of the structure-prediction study. The principles and mathematical formulae used to search for the energy minima systematically as well as the programs to operate and compare crystal structures in the rigid-body parameter space will be presented. These will be illustrated by a few examples of successful crystal structure predictions.

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Keywords: POLYMORPHISM STRUCTURE PREDICTION ORGANIC CRYSTALS

SEMIEMPIRICAL QUANTUM-CHEMICAL CALCULATIONS ON THE LATTICE ENERGIES OF ORGANIC MOLECULAR CRYSTALS

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Semiempirically calculated quantities like atom-in-molecule polarizabilities, atomic charges, vertical (Koopmans) ionization potentials, and molecular orbitals have been used to evaluate the major contributions (dispersion, induction, electrostatic, and repulsion energy) to the lattice energies of organic molecular crystals. Approximations to the exact expressions derived from intermolecular perturbation theory for the single components have been employed to calculate these four components. The quantum-chemical methods used in these calculations are CNDO/2, INDO, MINDO/3, MNDO, AM1, and MSINDO. The standard versions of the corresponding Hamiltonians have been used and none of the semiempirical parameters has been reoptimized to reproduce experimental lattice energies. Results are presented for borazine, as well as for different polymorphs of both glycine and oxalic acid. Our results obtained for the carboxylic acids show that the presented method can be applied without modifications or extensions to such crystal lattices, which are highly cross-linked by hydrogen bonds.

Keywords: LATTICE ENERGIES, SEMIEMPIRICAL METHODS, CALCULATIONS