as the experimental. Potential energy map of the phase transition between form I and II is also evaluated to demonstrate the dynamical behaviors of aspirin polymorph. It is indicated that activation energy required for the polymorphic transition is small enough to be able to overcome the energy barrier at room temperature.

[1] C. Ouvrard, S. L. Price, Cryst. Growth Des. 2004, 4, 1119.
[2] P. Vishweshwar, J. A. McMahon, M. Oliveira, M. L. Peterson, M. J. Zaworotko, J. Am. Chem. Soc. 2005, 127, 16802
[3] A. D. Bond, R. Boese, G. R. Desiraju, Angew. Chem. Int. Ed. 2007, 46, 615, 618

Keywords: drug polymorphism, crystal structure analysis, phase transitions

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Effects of initial conformations of small ligands on computational docking accuracies

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Computational ligand docking is one of the most important techniques of Structure-Based Drug Design, which makes the most of 3D-structures of drug target proteins determined by experimental studies, such as NMR or crystallographic analyses for the drug discovery and development. In this study, the effects of initial conformations of ligands on computational docking were investigated, and appropriate settings of conditions for computational docking were determined. Five types of initial conformations were prepared, and docking calculations were carried out by using each conformation as inputs. Furthermore, several settings of docking parameters were used (default, accurate, high throughput, etc), and robust settings for various initial structures were investigated. GOLD and eHiTS were used as docking software, and structurally known protein-ligand complexes were used as test set. Root mean square deviations between computational and experimental structures (RMSD) were adopted for criteria for evaluations, and the docking pose with RMSD < 2.0 Å were defined as “reasonable poses”. When at least one of the generated poses by a docking trial was reasonable, the trial was defined as “success”, and when the top ranked pose, i.e. the pose with the lowest binding free energy, was reasonable, the trial was defined as “top pose success”. The search abilities of docking were evaluated by “success rate” and “top pose success rate”. As the results, bad initial conformations, which were much different from crystal ligand structures, cause the worst success rate and the worst top pose success rate in all initial conformations. Comparing GOLD and eHiTS, eHiTS was better than GOLD to obtain reasonable poses regardless of rankings, but GOLD was better to obtain reasonable top poses.

Keywords: computer-aided drug design, conformational analysis, protein-ligand complexes

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Trypanosoma cruzi DHOD structure-based design of 5-halogen and 5-alkyl orotate derivatives

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Trypanosoma cruzi (*T. cruzi*) is the pathogen of Chagas’ disease and affects approximately 16 to 18 million people in Latin America. *T. cruzi* produces succinate as the main end product of respiration, even though it uses the TCA cycle and the aerobic respiratory chain. Fumarate reductase (FRD), which catalyzes the last step in succinate fermentation, is the key enzyme in the energy metabolism and a promising drug target for some parasites such as Ascaris suum, Leishmania donovani and *T. cruzi*, because human hosts do not possess FRD. It has been noted that FRD in mitochondria and glycosomes of T. brucei and *T. cruzi* uses NADH as the electron donor. On the other hand, we identified a novel type of FRD in the cytoplasm of T. cruzi that uses dihydroorotate as the electron donor, and characterized this enzyme as the dihydroorotate dehydrogenase (DHOD). Since DHOD is the fourth enzyme of de novo pyrimidine biosynthetic pathway, the enzyme may play an important role not only in succinate fermentation but also in de novo pyrimidine biosynthesis. In this study, we have determined the first complete set of structures of TcDHOD in the native form and in complexes with all physiological substrates and products. In addition, we found a parasite-specific pocket near the 5th carbon of the bound orotate. In order to design specific inhibitors, 5-halogen (Cl, Br and I) and 5-alkyl (vinyl and 3,3-dimethyl-but-1-enyl) orotate derivatives, whose substituent groups were aimed for filling the pocket, were synthesized and the structures of DHOD complexed with these compounds were also determined.

Keywords: *trypanosoma cruzi*, energy metabolism, fumarate reductase, dihydroorotate dehydrogenase, drug design, parasite

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First principles study of composition fluctuation and residual strain in InGaN/GaN MQW

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The quantitative relations between mechanical properties and the composition fluctuation in InGaN films are studied theoretically. In the ternary alloy InGaN, the indium composition has been known to show spatial inhomogeneity in various growth conditions. This composition fluctuation has been considered to form the quantum disk structures in InGaN quantum wells those influence the spontaneous emission rate in light emitting devices. To investigate the mechanical properties of the structures theoretically, a new method based on first principles calculation was used in this study. The simulation models of InGaN films contain triangular pillar-shaped cells, where the composition ratio, the strain and the stress in the each cell follow an equation of state which has been determined by ab initio electronic structure calculations. The quantitative

relations between the spatial variations of the indium composition and those of the residual strain in InGaN films in InGaN/GaN multiple quantum wells (MQW) were simulated theoretically by this new method. The residual strains were found being able to be controlled significantly by selecting the pattern of composition fluctuation. The relation of the difference of the spatial pattern of the composition fluctuation to the dislocation density in InGaN/GaN MQW has been also discussed. In a typical case, $In_{0.5}Ga_{0.5}N$/GaN MQW structure with periodic composition fluctuation with period length less than 68 nm in InGaN layers seems to be able to be grown with no dislocation. In addition, the difference of the type of the short-range chemical ordering of the indium and gallium atoms, which must depend on the type of growth mode, was found to have a considerable influence on the stress distribution in InGaN films.

Keywords: *ab-initio* calculations, multilayer structures, residual stress strain

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Simulation of the para to ferroelectric phase transition in $BaTiO_3$: The role of domains

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$BaTiO_3$ - one of the most extensively technologically used ferroelectric material - undergoes successive phase transitions on lowering temperature, form cubic, to tetragonal, to orthorhombic, to rhombohedral. Different mechanistic models have been invoked over the years, among them the displacive model and the oder-disorder model, both suffering from some important disagreement with experiments [1]. To shed light on the microscopic mechanisms, we have performed molecular dynamics simulations on the para-to-ferroelectric phase transition in $BaTiO_3$ as well as subsequent transitions that involve polarization rotation. Therein, all degree of freedom are treated explicitly, including positions, cell geometry and temperature. For an unbiased mechanistic analysis, we employ the path sampling scheme, designed for activated processes and successfully applied in many previous works. Two main results are obtained: first, a detailed picture of microscopic displacements leading to domains, which do sum up to the correct macroscopic polarization and correspond very well with experiments. Second, the relevance and even the necessity of antiferroelectric arrangements [1], that naturally derive from nucleating the ferroelectric phase within the paraelectric phase and outlast in the orthorhombic one. Combination of ferro and antiferro regions results in far-from-obvious domain structures [2]. Simulation under the effect of an external field allow assessing the response of the material from multidomain to single domain, whereby antiferro arrangements play a key role. [1] Q. Zhang, T. Cagin, W. A. Goddard III, PNAS 103, 14695 (2006), [2] M. Pasciak, S. Leoni, Mater. Res. Soc. Symp. Proc. 1034E (2007), in press, [3] M. Pasciak, S. Leoni, in preparation.

Keywords: ferroelectric physics, ferroelectric phase transitions, molecular dynamics simulations

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Exploration of structures of phosphorus and calcium at high pressure using metadynamics simulation

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We predicted the structure of the phosphorus and calcium at high pressure which had been left unidentified after their powder X-ray diffraction patterns were reported. The X-ray experiment reported that the phosphorus has a new phase (P-IV) above the sc phase in the pressure region of 107GPa and 137GPa. After that some theoretical studies were made but they were not successful in predicting the structures of phosphorus which satisfactorily fit the X-ray pattern. We tried the first principles metadynamics simulation, which is a new theoretical method of finding the structures of local free energy minima. The structure of the P-IV we predicted was an incommensurately modulated structure[1] which was confirmed by an experimental group[2]. We then studied the calcium (Ca-IV and Ca-V) and found the structures of zigzag and helical modulations[3]. Both of the modulation periods were commensurate and the space groups of the structures are identified to be $P4_12_12$ and *Cmca*. These results will accelerate the study of the superconductivity of calcium in the phase V, of which the highest superconducting Tc in elements has been reported. We report the details of our studies of the exploration for those structures with some results of the studies for the origin of these modulated structures.

References:
[1]T. Ishikawa, H. Nagara, K. Kusakabe, and N. Suzuki, Phys. Rev. Lett. 96(2006), 095502.
[2]H. Fujihisa, Y. Akahama, H. Kawamura, Y. Ohishi, Y. Gotoh, H. Yamawaki, M. Sakashita, S. Tateya, and K. Honda, Phys. Rev. Lett. 98 (2007), 175501.
[3]T. Ishikawa, A. Ichikawa, H. Nagara, K. Kusakabe, M. Geshi, and N. Suzuki, Phys. Rev. B77, 020101(R), 2008.

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Cluster models for decagonal quasicrystals

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The model clusters specifying the sites for the constituent transition metals in the decagonal Al-Co-Ni and Al-Co-Cu quasicrystals have been proposed by comparing their electronic structures obtained by the x-ray emission and photoemission spectroscopic measurements [1] with those calculated by the discrete variational Xa potential (DV-Xa) method [2] on the basis of the reported electron microscopic data [3]. The experimentally observed electronic structures can be well explained by those of the model clusters. Their electronic structures show the pseudogap across the Fermi level in the Al partial density of states, which agrees well with a band structure calculation for the