JST Basic Research Programs

C R E S T

(Core Research for Evolutional Science and Technology)

Annual Report for Research Work in the fiscal year 2005

Research Area :

High Performance Computing for Multi-scale and Multi-physics Phenomena

Research Theme

A program system with hierarchical quantum chemical methods for accurate calculations of biological molecules

Name of Research Director, Belonging and Title:

Seiichiro TEN-NO, Nagoya university, Associate Professor

§1. Outline of Research Work

Based on highly accurate ab initio theory, we are developing novel computational methods for biological molecules with quantum mechanical (QM/QM) and molecular mechanical (QM/MM) hierarchies. Reliable and robust simulation techniques granted by the studies of low scaling and novel wave function methods along with the cultivation of new molecular properties will provide the bases of modern science and technology which enable us to study electronic states, dynamics, and inspections of properties transcending the limitation of a field.

§2. Content of Research Work

The project is focused around five core topics; 1) fundamental scaling, 2) novel wave function methods, 3) biological probes, 4) dynamics, and 5) installation, as explained in the following. (the name of a head in each section is underlined)

1) Fundamental Scaling [Koch, Ten-no, Sugita]

This section aims at improving the fundamental scaling of quantum chemical calculations to treat biological molecules. As the computational costs in the usual ab initio methods increase as 4-7th power in molecular size, circumventing the steep barriers is crucial in our project.

Koch has explored new aspects of the Cholesky decomposition for method specific decompositions, which are likely to open up new possibilities for large scale calculations. Dr. Jung and Ten-no (in cooperation with Choi and Sugita) have developed new hybrid QM/MM methods. As a preliminary work, the standard link-atom method was installed in the Gellan program package in the financial year. They are further constructing a reliable QM/MM method based on GHO method. These developments are going to be utilized in the calculations of excited states and QM/MM dynamics simulations under protein environments.

2) Novel wavefunction methods [Ten-no, Nakano, Hada, Koch]

Novel wavefunction methods oriented to biological molecules will play a central role in this particular project. The branch is focused around the construction of QM/QM hierarchies, multi-reference methods, and relativistic quantum chemistry.

Koch and Sanchez de Meras (Valencia) installed the AO-integral-driven coupled cluster code to the Gellan platform in the Nagoya university. This is will be the basis of QM/QM hierarchical methods in the program package.

Nakano have developed the alpha and beta string based formalism and algorithm for the contracted multiconfigurational (MC) self-consistent field (SCF) / configuration interaction (CI) method. He also coded the program of the conventional multiconfigurational quasi-degenerate perturbation theory (MC-QDPT), which will be implemented into the Gellan program in the next financial year. In addition, applying the MC-QDPT computational scheme to the Dirac-Coulomb Hamiltonian, he developed relativistic MC-QDPT that takes accounts of both the

electron-correlation and relativistic effects. The relativistic MC-QDPT well reproduced dissociation and excitation energies, i.e. usually within 0.1 eV compared to the experimental values, for the tested systems.

Hada developed a computer code which enables to calculate two-component relativistic wave-functions based on the spin-dependent infinite-order Foldy-Wouthuysen (IOFW) transformation, and he shows that it gives satisfactorily accurate results in comparison with the second- and third-order Douglas-Kroll methods which are spread recently as a most accurate two-component relativistic quantum-chemical method.

3) Biological probes [Hada, Fujii, Koch]

Spectroscopic proves useful in biological sciences are explored both from computational and experimental points of view.

Hada developed a computer code for the frequency-dependent molecular magnetizability. It was applied to a series of molecules containing heavy elements. Then, the relativistic effect on the molecular magnetizability was analyzed. The diamagnetic part in the magnetizabilities of XH_2 (X = O, S, Se, Te) was affected by the scalar relativistic hamiltonian, while the frequency-dependent part was mainly affected by the spin-orbit interaction. In addition, the circular dichroism (CD) spectra of a series of dichalcogen compounds containing the S-S, Se-Se, and Te-Te bonds, which play an important role in biological systems, were calculated by the SAC and SAC-CI methods. The calculated transition energies and the simulated CD spectra agree reasonably with the experimental ones.

Fujii and coworkers prepared their model complexes to measure structure-function relationship of cupper containing metalloproteins. The x-ray crystal study of these model complexes showed that the structures of these model complexes are very close to the active site structure of copper metalloproteins. To examine the applicability of ^{63}Cu NMR spectroscopy for studying structure and function of copper metalloproteins, we measured ^{63}Cu NMR spectra of these copper complexes. This study showed that ^{63}Cu NMR spectroscopy of copper carbonyl complexes has great potential to characterize the nature of the environment around copper in copper complex and copper metalloproteins while ^{13}C NMR spectroscopy of the copper bound carbon monoxide does not.

4) Dynamics [Nakano, Sugita, Yamato]

Interfaces between electronic structure theory and molecular simulations are constructed.

Nakano have developed a complete active space valence-bond (CASVB) based scheme for describing chemical bonds applicable even on dynamic reaction paths. He applied the scheme to a Diels-Alder reaction, and clarified that all valence-bond resonance structures could be consistently classified into a few typical bond pictures by collecting covalent and derivative ionic resonance

structures, and that these CASVB bond pictures were hold even for high-energy paths that did not proceed via the transition state structure region.

Yamato studied color tuning mechanisms of photosensory proteins using a new method, MLSCMO (Multi Layer Self Consistent Molecular Orbital), which separates the system into the FMO and the CASPT2 regions. The electronic states of these two regions are solved consistently to each other by repeating iterative calculations. This method precisely provided the optical absorption maximum of photoactive yellow protein (PYP). Yamato also studied energy transfer pathways in PYP by calculating interresidue energy conductivities. He found several pathways connecting the chromophore and the N-terminal domain involved in the signal transduction of PYP.

Sugita et al. performed classical molecular dynamics simulations of sarcoplasmic reticulum calcium pump in membrane and elucidated the molecular mechanism of the proton countertransport by the pump. He also studied the folding of an alpha-helical peptide, conformational stability of nucleotide pairs, and aggregation of amyloid peptides by performing replica-exchange molecular dynamics (REMD) simulations.

5) Installation [Ten-no, Nakano, Koch]

Computational methods developed in the research project will be collectively installed into the hierarchical quantum chemistry package, Gellan.

In addition to the above-mentioned developments, functions involving the expansion of the loop structure in inputs, free format libraries, a memory manager, and so on were equipped.

§3. Formation of Research Work

1. Nagoya university (Information Science)

Director: Seiichiro Ten-no

Items of Research:

- Supervise the development of the Gellan program package
- Hybrid coupled-cluster methods (in collaboration with the NTNU group)
- Novel QM/MM methods (with the groups in the Nagoya university (phys), the university of Tokyo, and Kyungbuk University)

2. Kyusyu university

Main Research Collaborator: Haruyuki Nakano

- The development of the contracted multiconfigurational (MC) self-consistent field (SCF) / configuration interaction (CI) method, the merit of which is that the number of electron configurations scales linearly with the system size, and highly accurate multiconfigurational

quasi-degenerate perturbation theory using the contracted MC-SCF/CI reference functions.

- The implementation of ab initio direct dynamics, especially the direct CASVB dynamics that can hold clear valence bond resonance structure picture.
- The algorism and program development of the above-mentioned (1 and 2) methods, and implementation into the Gellan program.

3. Norwegian University of Science and Technology (NTNU, Norway)

Main Research Collaborator: Henrik Koch

- Reduced scaling methods with compact representations of excitation operators in MP2/CC2/CCSD(T) making use of the scarcity of the electron repulsion integrals and the Cholesky decomposition technique.
- Development of fast linear response theories for excited states of biological molecules.

4. Tokyo Metropolitan University

Main Research Collaborator: Masahiko Hada

- Development of a new method for calculating the NMR and MCD spectra of molecules containing heavy elements, based on the relativistic IOFW theory incorporated with the energy-gradient method and the perturbation term of a magnetic field.
- The electronic and NMR spectra of metal-porphyrins in heme-proteins and various chemical environments of biological systems.
- Analysis of NMR chemical shift and metabolism reaction in a model system of metal-enzymes and especially a Cu-imidazole system.

5. Nagoya University (Physics)

Main Research Collaborator: Takehisa Yamato

- Generating statistical ensemble of photoreceptor proteins by molecular dynamics simulation.
- Study of the excited state and photochemical properties of large photoactive proteins by the multiconfigurational self-consistent field theory.

6. University of Tokyo

Main Research Collaborator: Yuji Sugita

- QM/MM methodologies for chemical reactions occurred in proteins (in collaboration with the Nagoya university group). In the method, the reaction centers of proteins are treated by quantum chemical methods, whereas the rest of the proteins and solvents are simulated by classical MD simulations.

- Simulation of a whole reaction cycle of an enzyme by the QM/MM MD simulations for better understanding of biochemical functions of enzymes.

7. Kyungbuk University (Korea)

Main Research Collaborator: Cheol H. Choi

- Acceleration of the Fock matrix engine by FMM
- Development of CGDMS and novel SCF method with a quadratic convergence.
- QM/MM and QM/QFMM methods (in collaboration with Nagoya university)

8. Natural Institute of Natural Sciences

Main Research Collaborator: Hiroshi Fujii

- The group is studying structure-function relationship of metalloproteins from multi-nuclear NMR spectroscopy to develop new NMR methodology for studying protein function.
- To get more insight into ^{63}Cu NMR spectroscopy, they prepare model complexes of copper metalloproteins and measure ^{63}Cu NMR spectra of these complexes.
- To develop new methodology, they also try to use ^{17}O NMR spectroscopy. They will apply ^{17}O NMR spectroscopy for metalloproteins and their model complexes and examine its applicability.

§4. Publication of Research Results

(4-1) Publication of Thesis (The original Work)

① Number of Publications (0 times-Domestic, 0 times-International)

(4-2) Patent Application

① Cumulative Number

1) Patent Applications in the fiscal year 2005 (Domestic- 0 Cases, Oversea- 0 Cases)
2) Cumulative number of Patent Applications for the research period of CREST
(Domestic- 0 Cases, Oversea- 0 Cases)