The Second Memorial Workshop for Kazuhide Mori on Computational Sciences

How Can We Speculate Chemical Reaction Mechanisms of Macromolecules Using Molecular Orbitals?

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Abstract: We consider how to use molecular orbital (MO) calculation for investigating reaction mechanism of large molecules. Since Hamiltonian becomes additive as far as an interaction term is negligibly small. We consider to find HOMO-LUMO states by dividing the system into independent parts.

Kagawa and Mori (1999) found lytic water MO in the HOMO of a model complex 1MMD in which ATP analog was replaced with ATP. 1MMD is a PDB datum of X-ray crystallography of myosin motor domain with ATP analog ADP-BeF_3 [1]. We recalculated various PDB data of myosin (PDB ids are 1MMA, 1MMD, 1MMG, 1MMN, 1VOM, 1MND, 1FMW) to investigate ATP hydrolysis mechanism in myosin. In the recent study, we used a little bit wider area of these data in the calculation than the previous study [1]. The model system contains ATP (or ATP analog), Mg, Asn127, P-loop (Ser181-gly182-Ala183-Gly184-Lys185-Thr186-Glu187-Asn197), Switch I (Asn233-Asn234-Asn235-Ser236-Ser237-Arg238), Switch II (Asp454-Ile455-Ser456-Gly457-Phe458-Glu459), and waters within volume area of 0.35 nm covering them. MO calculations were performed with MOPAC2009 [2] that uses semi-empirical method PM6 [3]. The present model system does not show reaction water MO in the HOMO of 1MMD as shown in Fig.1. We also show the LUMO of 1MMD in Fig. 2. Since HOMO and LUMO can give reaction mechanism between molecules [3], we examined HOMO and LUMO.

The results can be understood from the additive feature of Hamiltonian. This feature is easily understood with writing Hamiltonian in the following forms [5].

$$H = H_e + H_i + H_{ei}$$

$$H_e = \sum_i \frac{\vec{p}_i \cdot \vec{p}_i}{2m} + \sum_{(i,j)} V_{ee}(\vec{r}_i - \vec{r}_j)$$

$$H_i = \sum_I \frac{\vec{P}_I \cdot \vec{P}_I}{2M} + \sum_{(I,J)} V_{ii}(\vec{R}_I - \vec{R}_J)$$

$$H_{ei} = \sum_{(I,j)} V_{ei}(\vec{R}_I - \vec{r}_j)$$

In the above expressions H_{ei} is an interaction term between two atom groups. Atom grouping is carried out so that highly interacting atoms with each other belong to the same group and less interacting atoms belong to different groups. If the interaction term H_{ei} of two groups is negligible, two atom groups are considered to be independent of each other. In such a case the Hamiltonian

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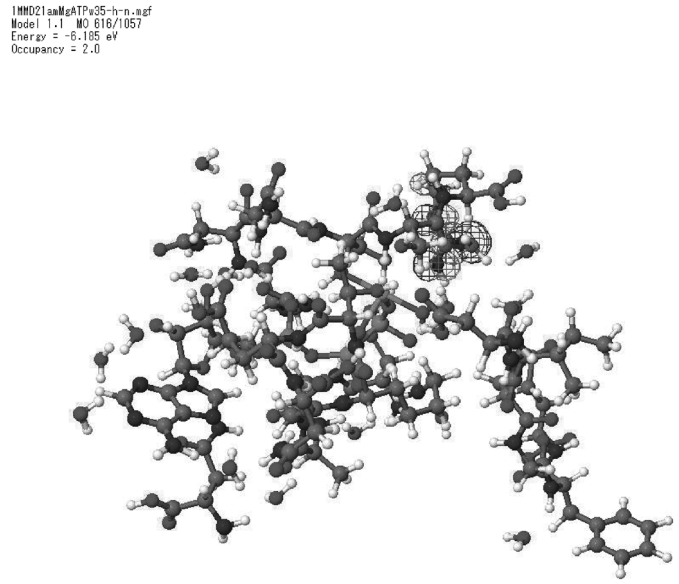

Fig. 1 HOMO of 1MMD in the present modeling (see text above)

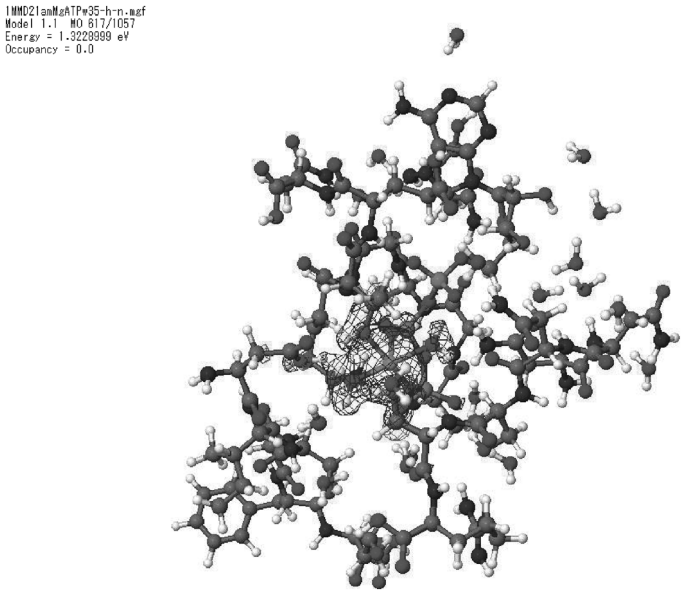

Fig. 2 LUMO of 1MMD in the present modeling (see text)

becomes additive. Since electron has a negative charge, two coupled system gives similar energy level of MO for each atom group. An inner atom interaction changes actually so that the energy level shits. If two systems interact weekly to each other, the coupled system give lower energy level MOs. Every energy level is obtained from expectation value of the above Hamiltonian using the state vec-

Table I Water MO energy levels for two kind of bond angles.

		Natural bond angle [eV]	Straightly bonded [eV]
6		6.0246	8.1126
5	LUMO	4.068	5.3841
4	HOMO	−11.89852	−13.67632
3		−14.12602	−13.67632
2		−18.95512	−23.64622
1		−30.40522	−32.17112

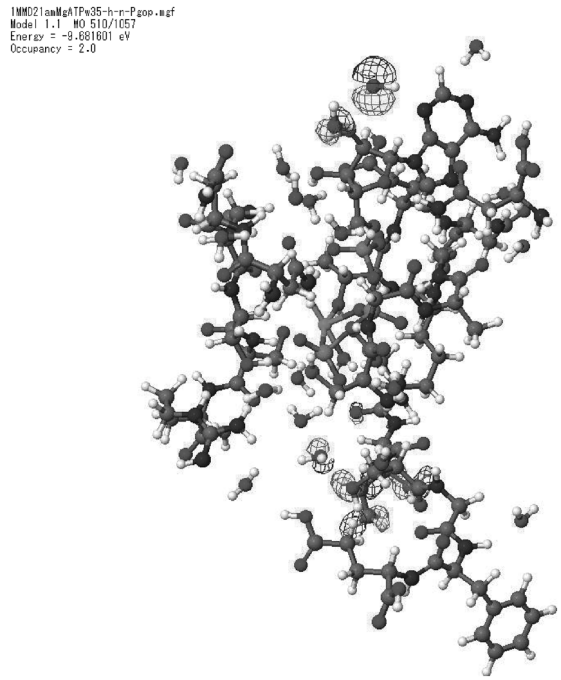

Fig. 3 Water MOs in model system

tor summing up the multiplied each atom wave function vector with appropriate coefficients satisfying canonical and normalized relations. If a state vector has independent components then energy level is the same as the one before coupled. If occupied MOs interact with each other the energy level becomes lower. Occupied and unoccupied orbitals interaction gives higher occupied energy level in the coupled system.

Following the above consideration, we investigate water MOs. Using MOPAC2009, we calculated MOs of two water conformations. One has natural bond angle, and another is straight line conformation (bond angle is 180 degree). Results are tabulated in Table I.

As seen from Table I, energy level of HOMO state changed about 2 eV. We therefore searched around the energy level of native water conformation in the MO data of 1MMD, and found clear water MOs in the model system as shown in Figs 3 and 4. These searches confirm our hypothesis

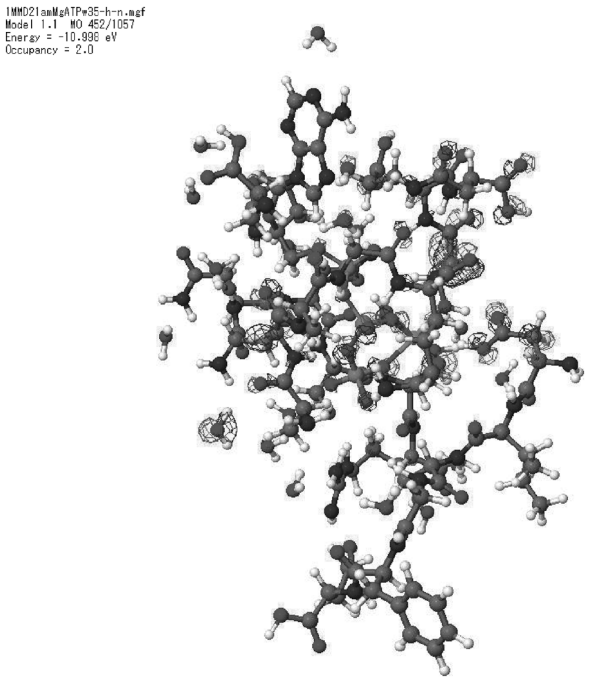

Fig. 4 Another water MO of model system

that energy level becomes lower in the occupied orbital interaction case and similar energy level in the negligibly small interaction case.

Following the hypothesis of additive feature of energy, we searched lower energy levels. We found reaction water MO of 1MMD as shown in Figs 5 and 6.

As conclusion, we found reaction water MO in 1MMD following our hypothesis that the additive property of Hamiltonian gives lower energy level for interacting occupied orbitals. The energy level was near the energy level in the model system without waters. This implies that it is difficult to conclude whether or not the reaction occures. So we should investigate carefully.

References

[1] H. Kagawa and K. Mori, ''Molecular orbital study of the interaction between MgATP and myosin motor domain.'', *J. Chem. Phys.* **B103** (1999) 7346–7352.
[2] MOPAC2009 J. J. P. Stewart http://openmopac.net/
[3] J. P. Stewart, Optimization of parameters for semiempirical method V: Modification of NDDO approximations and application to 70 elements, *J. Mol. Model* **13** (2007) 1173–1213.
[4] I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, John Wiley & Sons Ltd, 1976.
[5] A. Altland and B. Simons, *Condensed Matter Field Theory*, Cambridge Univ. Press, 2006.

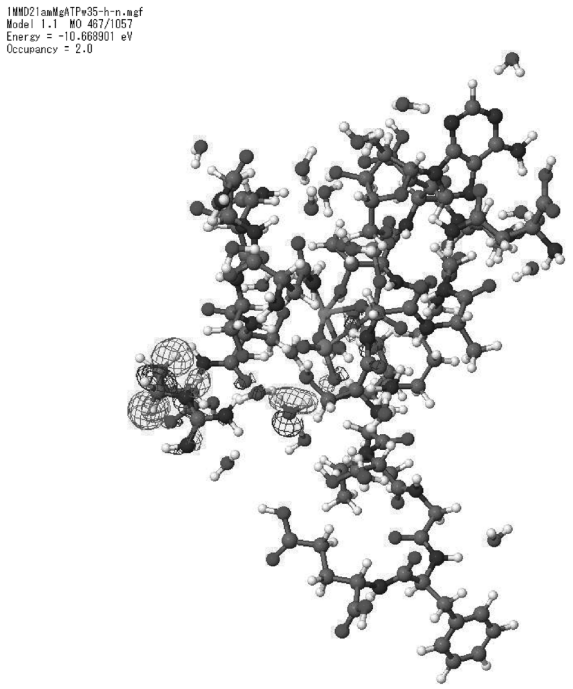

Fig. 5 Reaction water MO near gamma-phosphate in 1MMD.

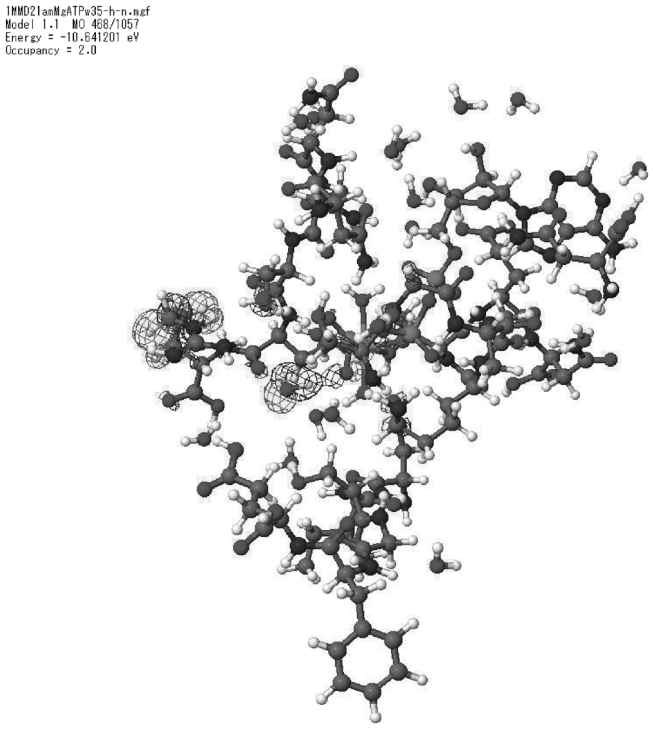

Fig. 6 Another energy level of reaction water MO in 1MMD