分子系の構造と電子状態—『生物物質科学』を目指して
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Quantum Chemistry for Photo Biology and Giant Molecular System

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理論化学の３つの目標

○ 正確な予言能

正確な予言学としての量子化学の確立

○ 大きな系への適用性

化学的に面白い系を kcal/mol の精度で

○ 多様な電子状態を対象に

基底状態だけでなく励起状態やイオン化状態も

○ 正確な予言学

Schrödinger 方程式を解析的に解く一般的な方法を確立すること。

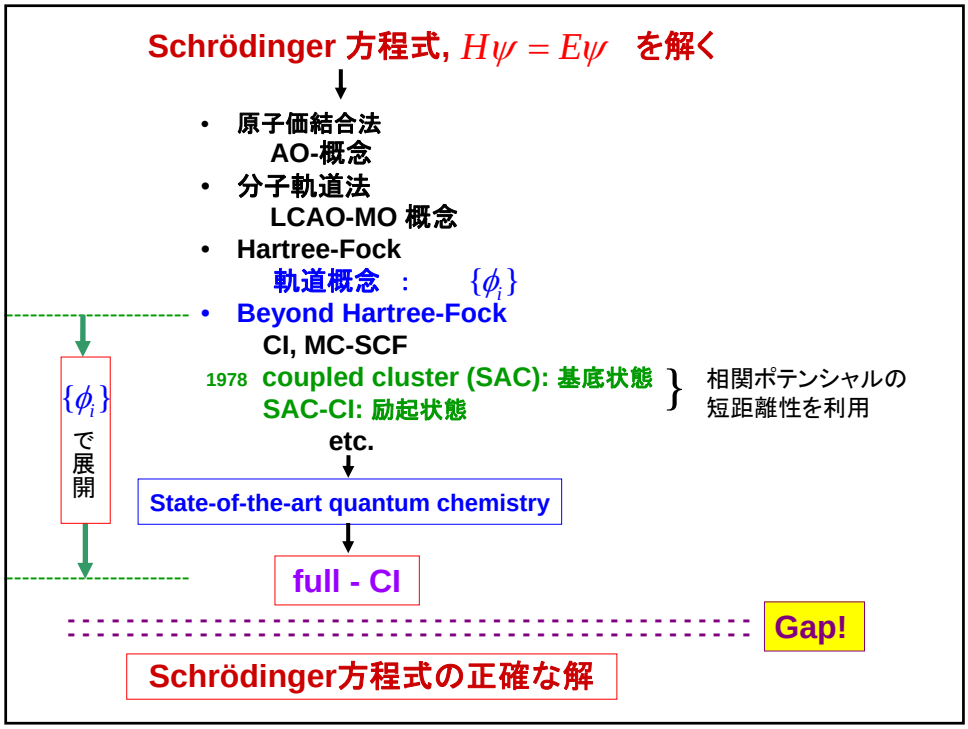
H. Nakatsuji, Phys. Rev. Lett., 93, 030403 (2004).
H. Nakatsuji, H. Nakashima, Phys. Rev. Lett, 95, 050407 (2005).
H. Nakatsuji, Phys. Rev. A 72, 062110 (2005).
Y. Kurokawa, H. Nakashima, H. Nakatsuji, Phys. Rev. A 72, 062502 (2005).
H. Nakatsuji, Bull. Chem. Soc. Jap. 78, 1705 (2005).

○ 大きな系

巨大系の電子状態理論の開発
- Giant SAC/SAC-CI 法の提案 -

○ 多様な電子状態

いずれの方法も、基底・励起両状態を対象



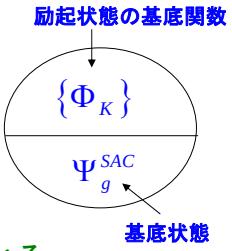
SAC/SAC-CI method

- **SAC:** $\Psi_g^{SAC} = \exp\left[\sum_I C_I S_I^\dagger\right]\Phi_0,$

  Φ_0 : Hartree-Fock ➡ correlation: short-range force

  ➡ exp 形が、短距離型相関ポテンシャルの記述にベスト。

  $S_I^\dagger$: symmetry adapted operator (singles & doubles)
  - otherwise mixed-symmetry -



- **SAC-CI:** $\langle\Phi_K|\Psi_g^{SAC}\rangle = 0, \quad \langle\Phi_K|H|\Psi_g^{SAC}\rangle = 0$

  $\{\Phi_K\}$: 励起状態の空間を張っている。

  従って、この関数で励起状態を記述する。

  $\Psi_e^{SAC-CI} = \sum_K d_K \Phi_K$

  ➡ **SAC-CI theory : SACと同程度のaccuracy**
  exact when SAC is exact.

SAC-CI on GAUSSIAN 03

SAC-CI理論: 分子のあらゆる電子状態を記述できる**電子相関理論(1978)**

SAC-CI Gaussian

SAC法 一重項閉殻分子系(基底状態)

SAC-CI法

- 一重項励起状態
- 三重項基底・励起状態
- イオン化状態(二重項基底・励起状態)
- 電子付加状態(二重項基底・励起状態)
- 四重項～七重項基底・励起状態

エネルギー・グラジエント(原子核に働く力)
励起状態の反応ダイナミクス

対象: これらの状態が関与する化学と物理

➡ **Size-extensive な理論**

SAC/SAC-CI topics

1. Fine Spectroscopy
   very fine spectroscopy of small molecules
2. Photo-functional material design
3. Photo-biology
   Photo-functions and biological mechanisms
4. Surface Photochemistry & catalysis
   Dipped Adcluster Model (DAM) applied to surface catalysis
5. Molecular Crystal
   - size-extensive, size-intensive
   - potential curves of ground and excited states

Chemical Theory に発展

Photobiology : Quantum principle & Life

Role of Light in Life

- Energy : Conversion of photon energy into chemical energy
  Electron & proton transfers
  Photosynthesis: Reaction center, PS I, PS II
  Proton& ion pumps: Bacteriorhodopsin, Halorodopsin
- Information : Absorption and emission of light of specific wave length
  Vision: Rhodopsin
  Photo-sensor in plants and bacteria : phytochrome, sensoryrhdopsin
  Communication: firefly luciferase?, green fluorescent proteins

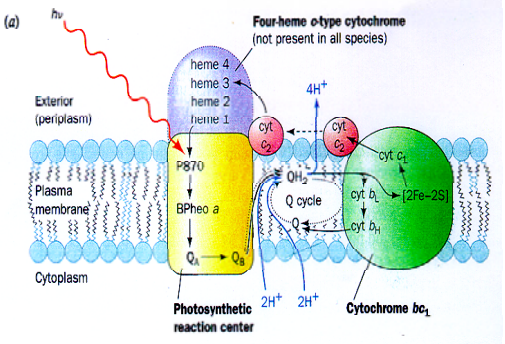
Quantum chemistry can clarify quantum principles behind these photo-biological phenomena.

Photobiology with the SAC-CI method

- Today's Topics -

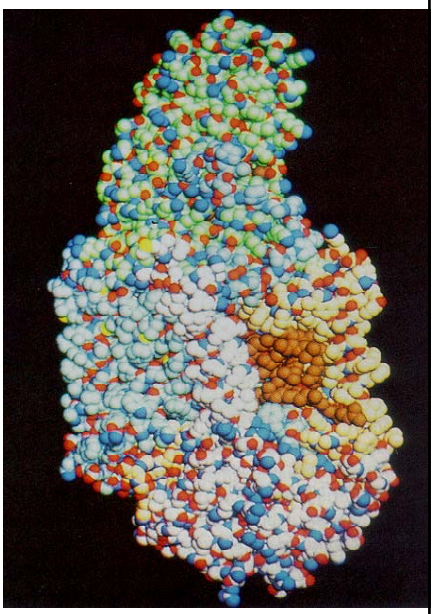
- **Photosynthetic reaction center**
  - Excited states & electron transfer
- **Retinal proteins**
  - Color-tuning mechanism
    - Rhodopsin, Bacteriorhodopsin, and Sensoryrhdopsin II
    - Human blue
- **Firefly luciferine**
  - Source of the yellow-green emission

SAC-CI Theory applied to Photosynthetic Bacteria



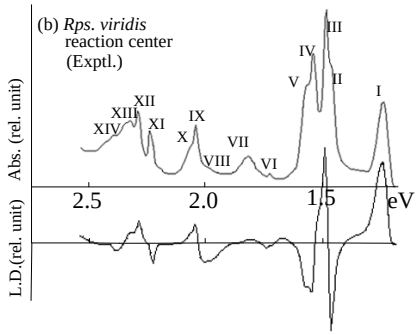
SAC-CI study

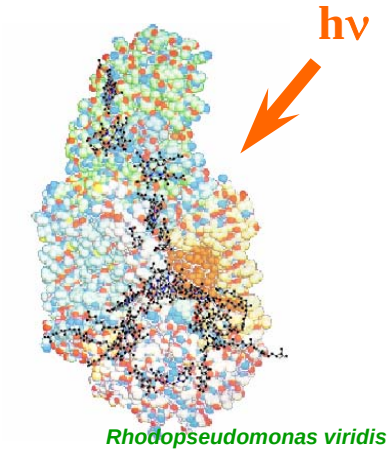
- ***Rhodopseudomonas viridis***
  1998 - 2002
- ***Rhodobactor sphaeroides***
  2005 - 2006



Reaction center of *Rps. viridis*

Absorption spectra of photosynthetic reaction center





Rhodopseudomonas viridis

SAC-CI study

- **Absorption spectra of all chromopheres were calculated.**
- **Proteins were approximated by the point-charge model.**

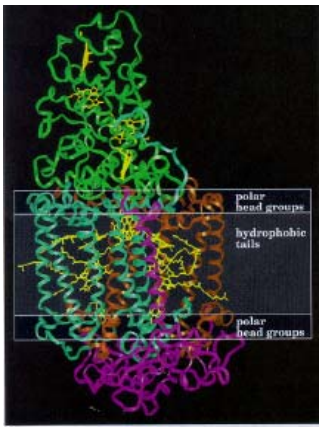
H. Nakatsuji, J. Hasegawa, and K. Ohkawa, Chem. Phys. Lett., 296, 499 (1998).

J. Hasegawa, K. Ohkawa, and H. Nakatsuji, J. Phys. Chem. B, 102 10410 (1998).

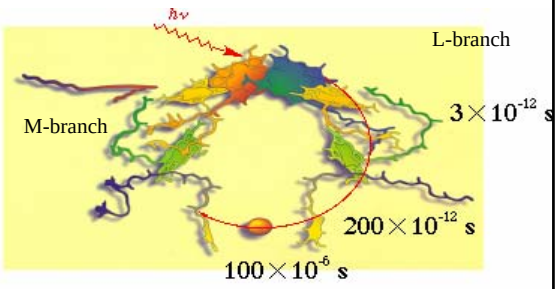
Mechanism and Unidirectionality of Electron Transfer

Four Questions?

1. **Why electron transfer occurs only in L-branch?**
2. **Why electron transfer is so efficient?**
3. **Why charge recombination does not occur?**
4. **What is the effect of protein?**



Rhodopseudomonas viridis



Rhodobactor sphaeroides

Electron Transfer and Unidirectionality

H. Nakatsuji, J. Hasegawa, and K. Ohkawa, Chem. Phys. Lett., 296, 499 (1998).

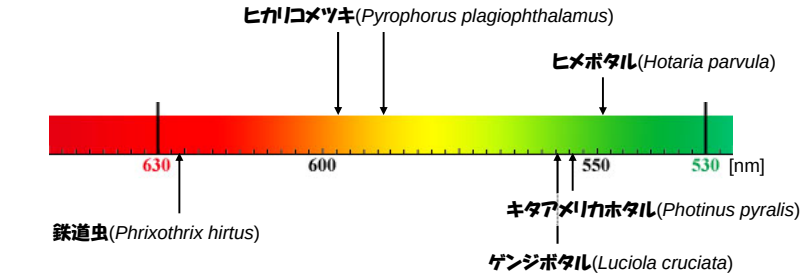
J. Hasegawa and H. Nakatsuji, J. Phys. Chem. B, 102, 10420 (1998).

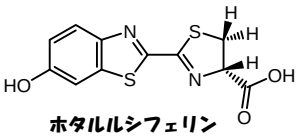
J. Hasegawa and H. Nakatsuji, Chemistry Letters. 34, 1242-1243 (2005).

Emitting State of Firefly Luciferase

Yellow-green bioluminescence
from Firefly, *Photynus pyralis*

Emitting Color of Firefly





ホタルルシフェリン
(D-Firefly luciferin)

Common pigment for all fireflies

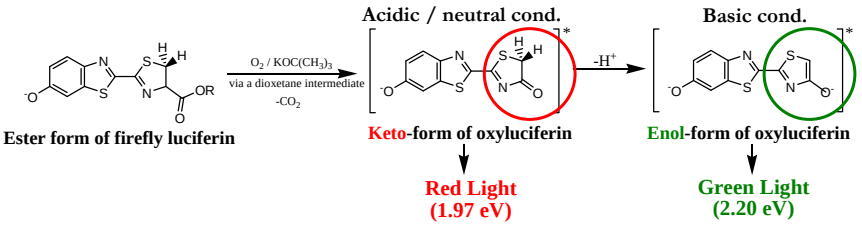
Color origin – Structure of luciferase protein?

Origin of Different Color?

Chemiluminescence:

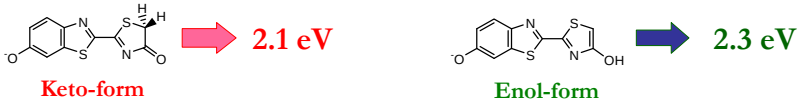
Emission energy from keto-enol tautomers

Confirmed color [1]



[1] White, E. H., Rapaport, E., Seliger, H. H., and Hopkins, T. A. *Bioorg. Chem.* 1971, ***1***, 92

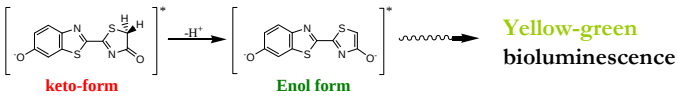
SAC-CI Calculation also confirmed. SAC-CI/D95(d) // CIS/D95(d) with PCM



Bioluminescence:

What is the emitting state?

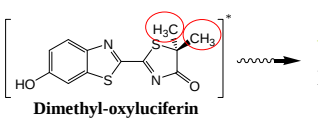
1970 ~: Chemiluminescence-based reasoning



Chemiluminescence			Bioluminescene in the firefly
Keto-form	Red (1.97 eV)	Similarity	
Enol-form	Green (2.20 eV)	⟷	Green (2.23 eV)

(Keto-form is energetically more stable.)

2002: keto-constrained luciferin emits yellow-green light in Luciferase

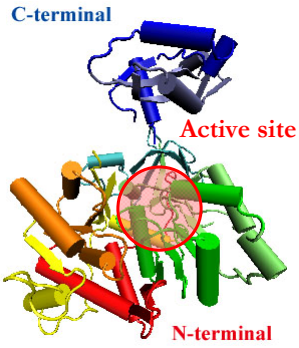


Keto-constrained in Luciferase

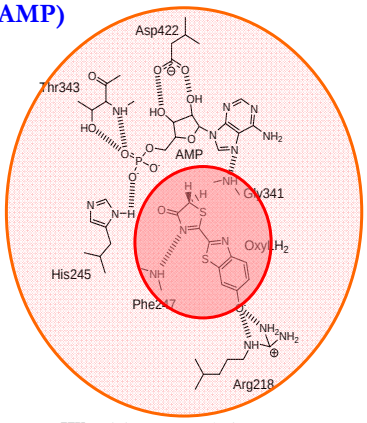
[1] Branchini, B. R., Murtiachaw, M. H., Magyar, R. A., Portier, N. C., Ruggiero, M. C., and Stroh, J. G. (2002) ***J. Am. Chem. Soc.*** **124**, 2112

Structure of Luciferase including Luciferin

Existing X-ray structure for Luciferase (*Photinus pyralis*) contains no substrates (no $OxyLH_2$, no AMP)



X-ray structure(1LCI)
(1996 Conti et al.)



Working model
in the experimental study[1]

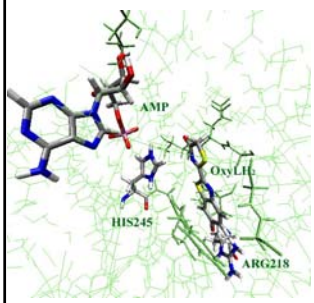
⇒MD, MM (AMBER) & QM Calculations (CIS)

Geometry optimization of excited state

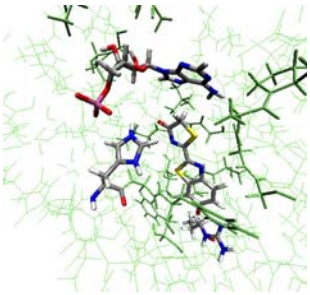
[1]Branchini, B. R., Southworth, T. L., Murtiashaw, M. H., Magyer, R. A., Gonzalez, S. A., Ruggiero, M. C., Stroh, J. G. *Biochemistry* **2004**, *43*, 7255.

Optimized structures for the first excited state

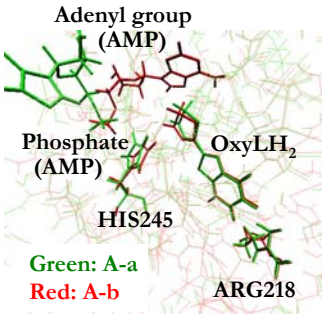
- available only with calculations -



A-a: $OxyLH_2$(A), AMP(a)



A-b: $OxyLH_2$(A), AMP(b)



A-a (Green) & A-b (Red) superimposed

Two stable structures of the 1st excited states

$OxyLH_2$ and phosphate locate similar position.
Position of the Adenyl group is different.

$OxyLH_2$, ARG218, HIS245, and Phosphate group of AMP are included in the QM part of the SAC-CI calculations.

⇒ Both structures A-a and A-b are used for SAC-CI calculations for excited state.

SAC-CI results for the emission energy from the keto-form of $OxyLH_2$

Calc.	Environment	QM region	Geometry[a]	Emission energy / eV	
				SAC-CI[b]	Exptl.
1	in Gas phase	$OxyLH_2$	Gas	1.84 (0.0)	1.97[c]
2		$OxyLH_2$	A-a	1.73(-0.11)	
			A-b	1.58(-0.26)	
3	in Protein	$OxyLH_2$	A-a	2.02 (+0.18)	
			A-b	1.82 (-0.02)	
6		$OxyLH_2$ + ARG218 + HIS245 + Phosphate	A-a	2.33 (+0.49)	

Structural effect (-0.11,-0.26eV)

Protein electrostaic Interaction between $OxyLH_2$ and protein (-0.29,+0.24eV)

Interaction from quantum effect (+0.60,+0.55eV)

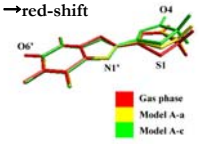
Red shift

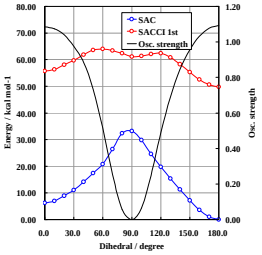
Blue shift

Blue shift

The calculated emission energy of l
is close to the yellow-gree
⇒Emission energy of the keto forn

Not co-planner
→red-shift





Structural effect causes Red shift.

Protein-$OxyLH_2$ interaction contrib

- Protein electrostatic interaction.
- Interaction from protein residues by quantum calculations.

electrostatic effect

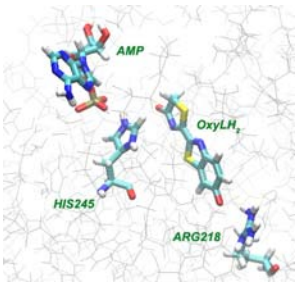
$$\Delta E = \sum_{M}^{\text{Residues}} \left\{ \sum_{A}^{OxyLH_2} \sum_{B \in M}^{\text{Others}} \frac{Q_A^{Ex} Q_B}{r_{AB}} - \sum_{A}^{OxyLH_2} \sum_{B \in M}^{\text{Others}} \frac{Q_A^{G} Q_B}{r_{AB}} \right\}$$

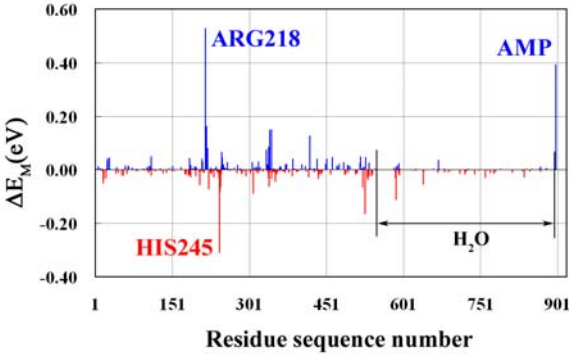
excited ground

$$= \sum_{M}^{\text{Residues}} \left\{ E_M^{Ex} - E_M^{G} \right\}$$

$$= \sum_{M}^{\text{Residues}} \Delta E_M$$

shift by residue





Blue shift

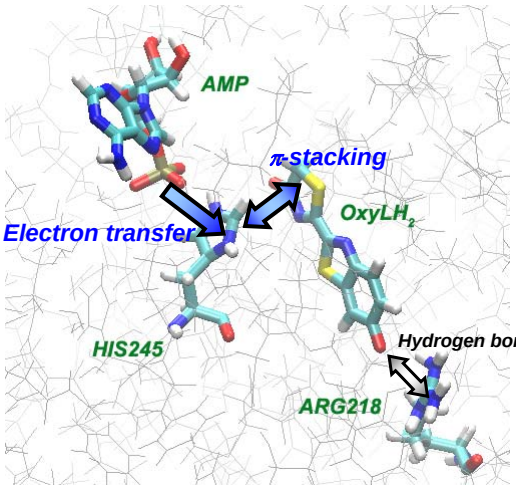
ARG218 : stabilize ground

AMP : destabilize excited

Red shift

HIS245 : stabilize excited

Quantum effect



Quantum effect by

$OxyLH_2$ only — 2.02 eV

↓ 0.05 eV

+ ARG218 — 2.07 eV

↓ 0.15 eV

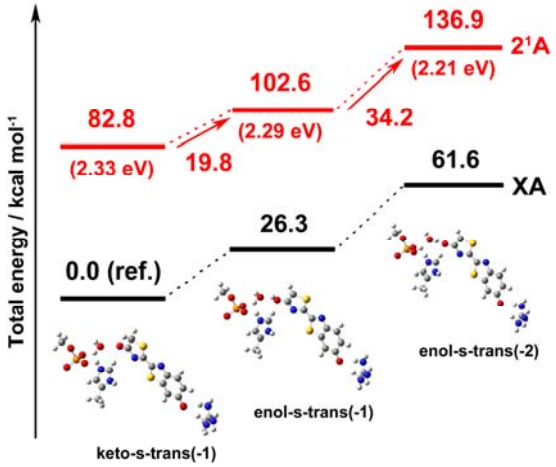
+ HIS245 — 2.22 eV

↓ 0.11 eV

+ AMP — 2.33 eV

π–stacking with HIS245 and CT from AMP stabilize the ground state of $OxyLH_2$

How about enol forms?



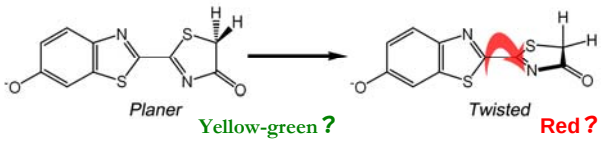
Exptl. 2.23 eV

Fig. Potential energy profile at RHF/CIS level. The number in parenthesis is emission energy calculated by the SAC-CI method.

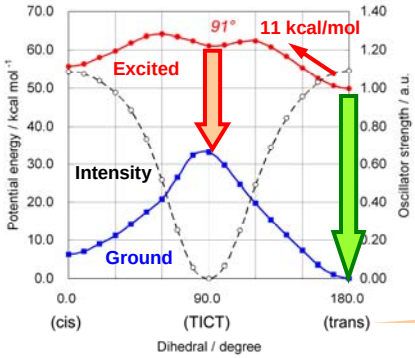
- Emission energies of the enol forms (2.29, 2.21eV) are close to that of the keto form (2.33 eV) and experiment (2.23 eV).
- **However, the enol form is energetically unfavorable.**

Twist rotation of oxyluciferin

Twisted Intramolecular Charge Transfer (TICT) exited state



Yellow-green ? Red ?



Twisted structure

Energetically unstable

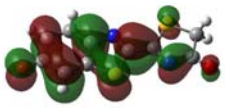
Essentially zero intensity

TICT mechanism is unfavorable

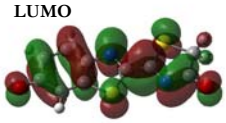
Electronic structure of $OxyLH_2$ in the 1st excited state in relation to the blue-shift of the emission peak

- SAC-CI wave function : (HOMO)→(LUMO)

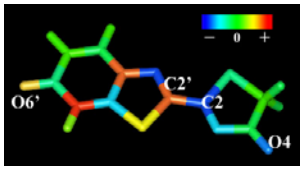
HOMO



LUMO

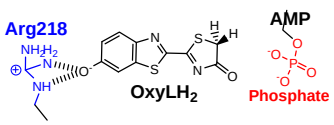


- Difference of the atomic charge between the ground and excited state



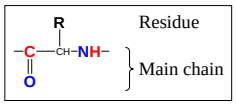
$\Delta q = q(\text{Excited}) - q(\text{Ground})$

- Protein environment and phosphate group unstabilize the excited state



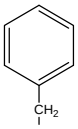
⇒Blue-shift of the emission

主要なアミノ酸の構造と名称

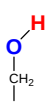
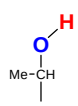
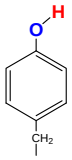
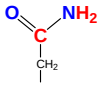
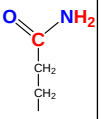


Color of Atoms
X : **Positively** charged
X : **Negatively** charged

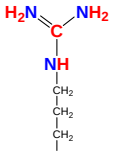
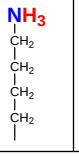
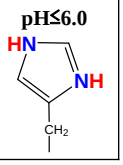
(1) 中性の無極性アミノ酸

Glycine (Gly, G)	Alanine (Ala, A)	Phenylalanine (Phe, F)
		

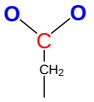
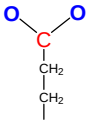
(2) 中性の極性アミノ酸

Serine (Ser, S)	Threonine (Thr, T)	Tyrosine (Tyr, Y)	Asparagine (Asn, N)	Glutamine (Gln, Q)	Histidine (His, H)
					

(3) 正の電荷を持つ極性荷電アミノ酸

Arginine (Arg, R)	Lysine (Lys, K)	Histidine (His, H)
		

(4) 負の電荷を持つ極性荷電アミノ酸

Aspartic acid (Asp, D)	Glutamic acid (Glu, E)
	

Conclusion

Both chemi- and bio-luminescence were reproduced by the SAC-CI method

⟹ *Bio-luminescence is yellow-green from Keto-form*

Quantum effect from nearby amino-residues and electrostatic effect from protein environment cause blue shift of keto-form

π-stacking with HIS245 and CT between AMP-HIS

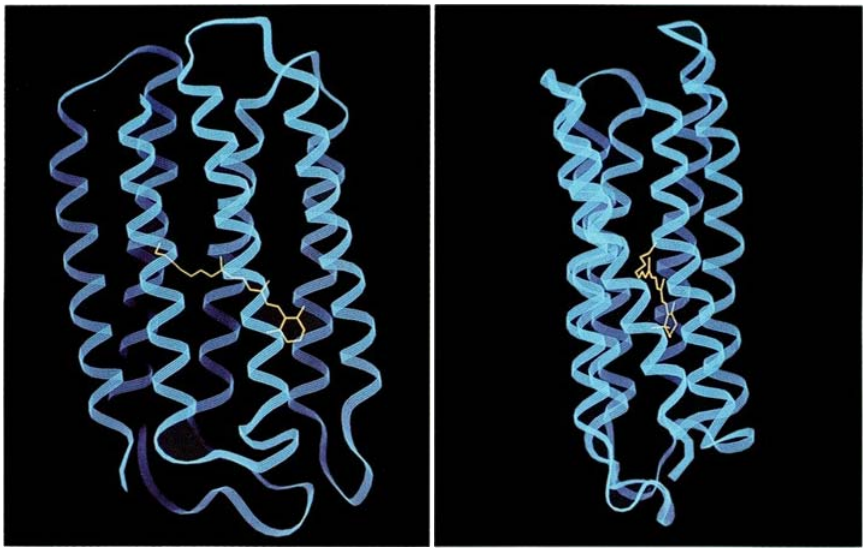
Electrostatic effect from ARG218、HIS245、and phosphate part of AMP

Mechanism of Color-tuning in retinal proteins

SAC-CI and QM/MM study

K. Fujimoto, J. Hasegawa, S. Hayashi, S. Kato, H. Nakatsuji,
Chem. Phys. Lett. 414, 239 (2005).
K. Fujimoto, J. Hasegawa, S. Hayashi, and H. Nakatsuji,
Chem. Phys. Lett. 432, 252 (2006).

Bacteriorhodopsin: light-driven proton pump vision



Retinal

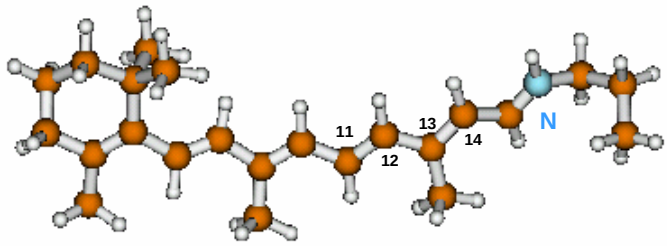
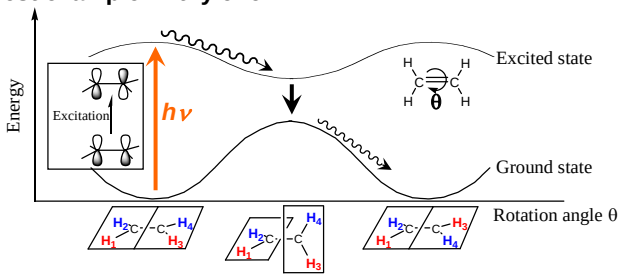
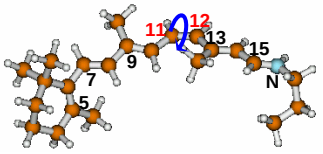


Photo-isomerization of the retinal proteins

(1) A simplest example : Ethylene

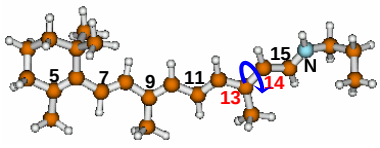


(2) Rhodopsin : Vision



Rotation around C_{11}-C_{12} bond

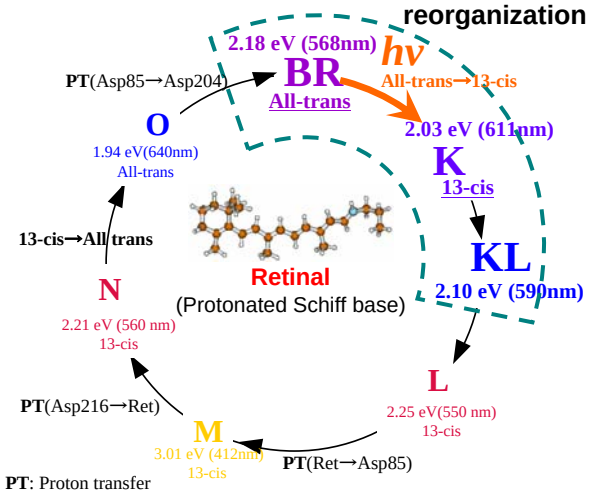
(3) Bacteriorhodopsin : Proton pump



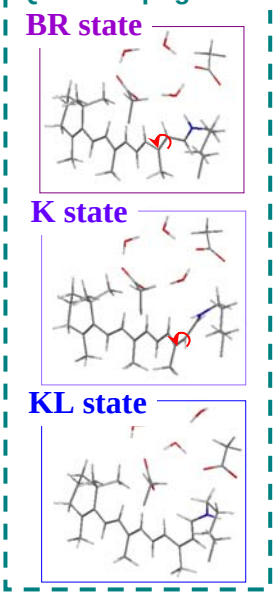
Rotation around C_{13}-C_{14} bond

Retinal protein as light-driven proton pump : Bacteriorhodopsin

Photo-reaction cycle:
photo-isomerization, protein structure reorganization



QM/MM Opt geometry



Retinal protein as photo-receptor : Vision

(1) Rhodopsin in Retina

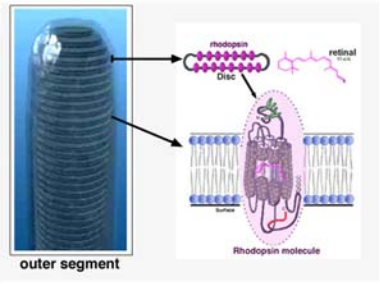


Fig 8. Schematic diagram of Rhodopsin in the outer segment discs.

(2) Absorption peaks of the photorescepters

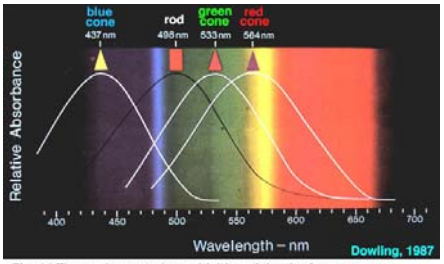
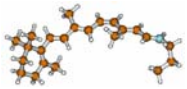


Fig. 14.The peak spectral sensitivities of the the 3 cone types and the the rods in the primate retina (Brown and Wald, 1963). From Dowling's book (1987).

From "Web vision", H. Kolb, E. Fernandez, R. Nelson, Univ. Utah

➢Retinal protein = **Retinal (chromophore) + Opsin (Protein environment)**



➢**Common chromophore, but large spectral shift in the absorption peak**

⇒ **Protein environments may regulate the color-tuning.**

K. Fujimoto, J. Hasegawa, S. Hayashi, S. Kato, H. Nakatsuji, Chem. Phys. Lett., 414, 239 (2005).
K. Fujimoto, J. Hasegawa, S. Hayashi, and H. Nakatsuji, Chem. Phys. Lett. 432, 252 (2006).

- **SAC-CI reproduced well the excitation energies of all retinal proteins under study.**
  promising approach for studying color-tuning mechanism in retinal proteins
- **X-ray geometry did not reproduce the excitation energy**
  used as initial quess for calculating
- **QM/MM optimized geometry is more reliable.**
- **Mechanism of Color-tuning**
  Distortion of retinal : Rhodopsin
  amino-acid residues close to retinal
  Protein electrostatic effects

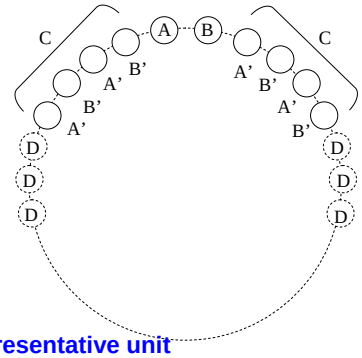
Quantum Chemistry for Giant Molecular System

- Giant electron-correlation theory within singles & doubles
- can handle excited states → Photo properties-design
- must be size-extensive

→ SAC/SAC-CI 法

H. Nakatsuji, T. Miyahara, R Fukuda, J. Chem. Phys. 126, 084104 (2007).

SAC/SAC-CI method applied to molecular crystal
- Ring crystal composed of same molecule A -



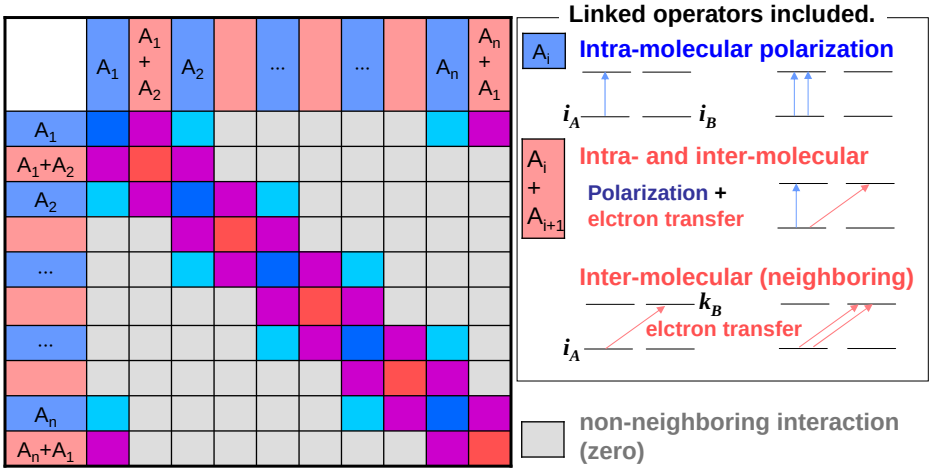
Nature of interactions

1. Two neighboring monomers A-B : representative unit
2. C-region is connected electronically to A-B
3. The effect of D-region on C-AB-C can be approximated by electrostatic potential

→ 1. Hartree-Fock calculation for $_{DD}$C-AB-C$_{DD}$ region ($_{DD}$: electrostatic D)
2. electron correlation (short range) effect for A-B region

Linked Hamiltonian Matrix

only four distinct blocks, independent of the size of the crystal (very fast integral evaluation)

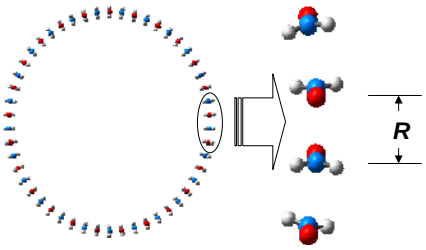


Application

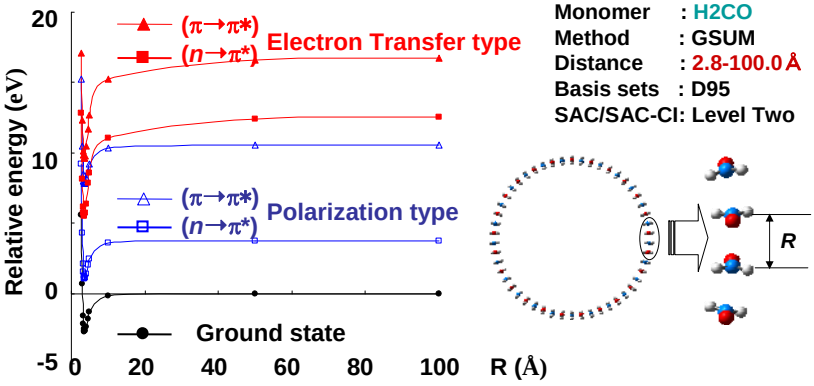
Potential energy curve for ground and excited states

H_2CO-ring crystal

50-mers
Inter-monomer distance : *R* = 2.8-100.0Å
basis set : double zeta (D95)
Perturbation selection : Level Two



***H_2CO Ring 50-mer Crystal :* Excitation energy**

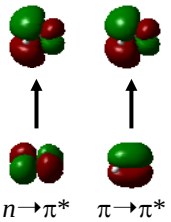


new absorption !

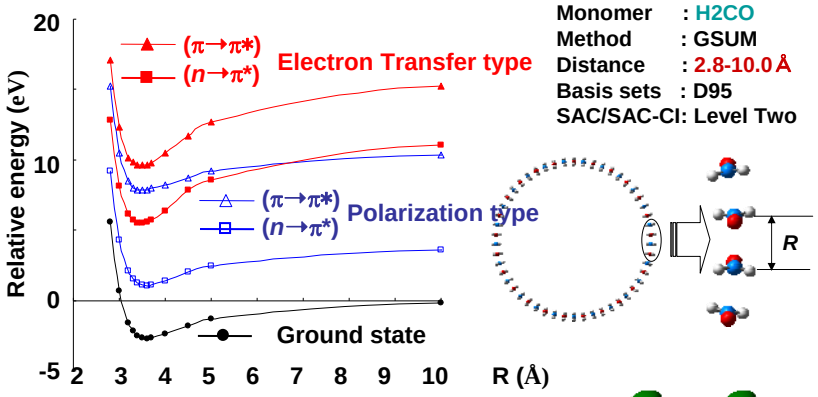
Excitation energy (eV)

R(Å)	Polarization		ET	
	n→π*	π→π*	n→π*	π→π*
3.60	3.76	10.61	8.26	12.35
100.0	3.76	10.52	12.53	16.71
monomer	3.79	10.58	12.41	16.65
expl.	4.1	10.7	------	------

R-dependence: no change big change

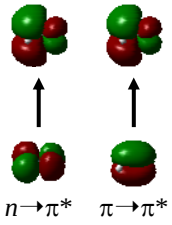


H_2CO Ring 50-mer Crystal : equilibrium distance, vibrational frequency, depth

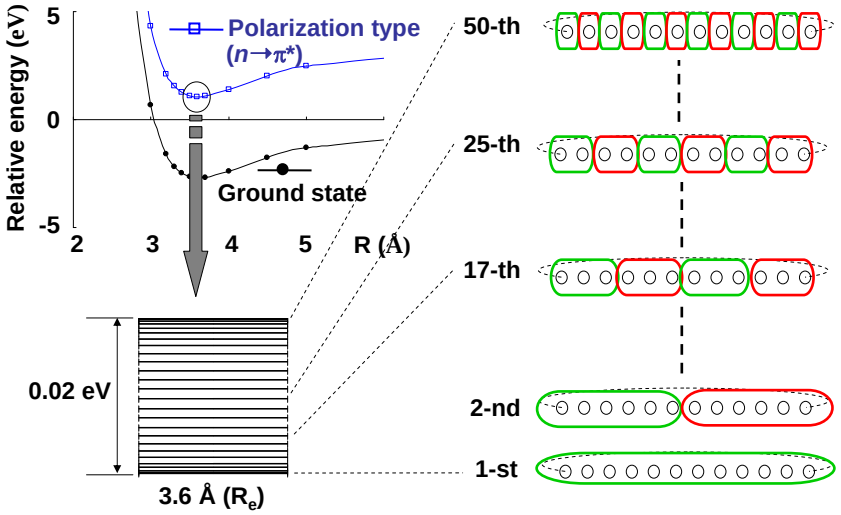


Potential property

H_2CO	Ground	Excited state: Polarization		Excited state: ET	
		$n\rightarrow\pi^*$	$\pi\rightarrow\pi^*$	$n\rightarrow\pi^*$	$\pi\rightarrow\pi^*$
Re (Å)	3.60	3.59	3.45	3.48	3.47
ωe (cm^{-1})	295	297	343	387	388
depth (eV)	2.69	2.70	2.68	7.04	7.14

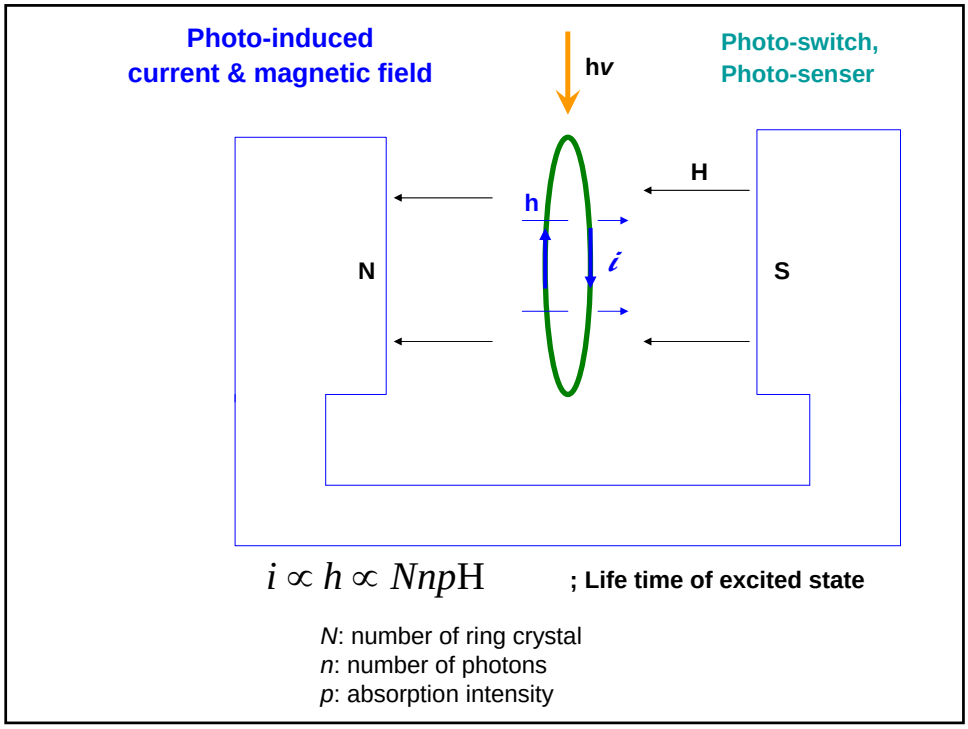


H_2CO Ring 50-mer Crystal : 50 polarization $n\rightarrow\pi^*$ excited states



50 states are within 0.02 eV.
Wannir localized states are easily realized. → interesting implication to molecular engineering

e.g. induced ring current when magnetic field is applied.

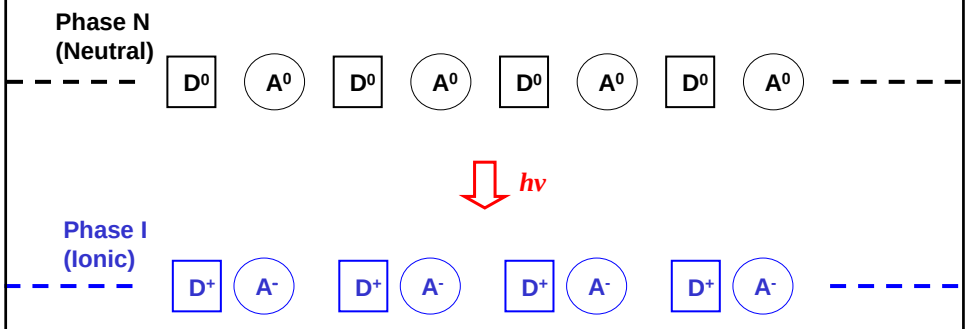


$i \propto h \propto NnpH$; Life time of excited state

N: number of ring crystal
n: number of photons
p: absorption intensity

光誘起相転移

Photo-Induced Phase Transition (PIPT)

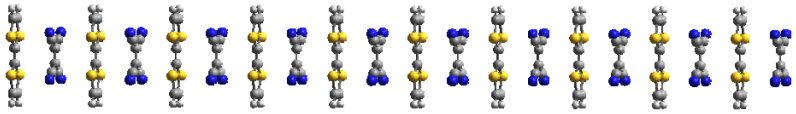


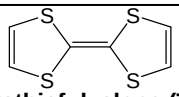
1. 光励起によって等間隔に並んでいた 分子が変化し、2量体化が起こり、中性からイオン性へと変化する。
2. 新しい光センサー・光スイッチなどへの応用。

TTF (Tetrathiafulvalene) – CA (p-chloranil) : E. Collet, Science, 300 (2003) 612

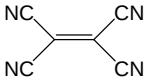
光誘起相転移のモデル

Tetrathiafulvalene - Tetracyanoethylene (TTF-TCNE)





Tetrathiafulvalene (TTF)



Tetracyanoethylene (TCNE)

1. 現実には存在しない結晶であるが、TTFは電子供与体、TCNEは電子受容体である。
2. 計算コストが小さい。

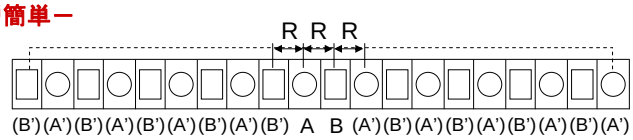
計算方法

- 単量体で最適化した構造を直線状に並べた。
- 下図は一次元結晶のモデル。

モデル：TTF-TCNE
$(TTF\text{-}TCNE)_{1,2}$: Standard
$(TTF\text{-}TCNE)_{10}$: Giant
Localization : ml-CMO
Distance *(R)* : 下図
Basis sets : D95
SAC/SAC-CI : Level One

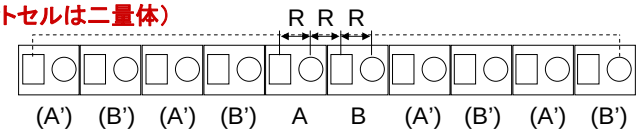
単量体近似 （ユニットセルは単量体）
ー計算はより簡単ー

(1) R=3.61Å

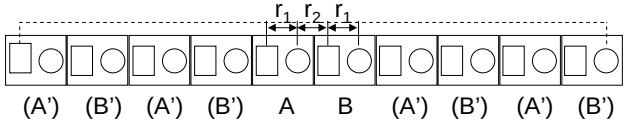


2量体近似 （ユニットセルは二量体）

(2-1) R=3.61Å



(2-2) r_1=3.58Å
r_2=3.64Å
($2R=r_1+r_2$)



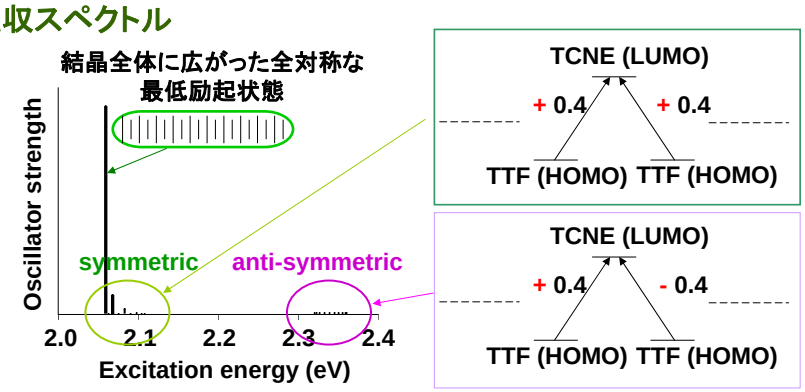
TTF-TCNEの励起状態 (単量体近似)

State	Starndard SAC/SAC-CI						Giant SAC/SAC-CI	
	TTF		$(TTF\text{-}TCNE)_1$		$(TTF\text{-}TCNE)_2$		$(TTF\text{-}TCNE)_{10}$	
	EE (eV)	Osc strength	EE (eV)	Osc strength	EE (eV)	Osc strength	EE (eV)	Osc strength
TTF→TCNE (CT型)	-----	---------	1.79	0.0003	1.86	0.0003	2.06	0.0808
					1.91	0.0002	⋮	
					2.11	0.0002	2.36	0.0000
TTF (Pol型)	3.33	0.0000	3.31	0.0118	3.29	0.2317	3.20	0.0009
							⋮	
					3.32	0.0006	3.28	0.0000
Cpu time	42m4s		7h49m42s		11d21h57m54s		2d6h49m41s	

1. TTF→TCNE(CT)の励起エネルギーは多くの相転移物質の励起エネルギーの範囲内(1.0~2.5 eV)にある。(J. G. Torrance, Phys. Rev. Lett. 26 (1981) 253)
2. Giantの計算時間は非常に速い。

CT excited states の Band 構造と吸収強度

吸収スペクトル



Oscillator strength は結晶全体に広がった、全対称な最低励起状態のみ大きな値を持つ。

↓

Concerted Mechanism の可能性：将棋倒し(ドミノ)でなく。

今後の課題

1. TTFとTCNEとの距離にTTF-CAの実験値を用いているので、TTF-TCNEの距離を、基底状態、励起状態のNー，Iー状態両方について最適化し、より詳細なメカニズム解析を行う。
2. 現実系の計算。
3. ・・・

- Giant SAC/SAC-CI Method -

- ring crystal

  J. Chem. Phys. 126 084104 (2007).

- three-dimensional crystal
- polymer
- DNA
- protein

→ Future subjects

- 高速化
- パラレル化

Importance of Reliability for the Theory of Complex Molecular Systems

For complex systems, theory must be reliable. Otherwise, no clear conclusion is possible.

- **SAC-CI mehod: reliable even for biological and molecular-engineering subjects**
- **Theory with large error:**

  no reliable mechanism analysis
  prediction: completely impossible

Acknowledgements

Photo Biology

- **Dr. J. Hasegawa**
- **Dr. K. Fujimoto**
- **Mr. N. Nakatani**

Giant SAC/SAC-CI

- **Dr. T. Miyahara**
- **Dr. R. Fukuda**

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