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КОМПЬЮТЕРНЫЕ ТЕХНОЛОГИИ ФИЗИКИ

COHERENT SIGNAL AMPLIFICATION IN RHODOPSIN MEDIA

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A quantum optics model that explains the sensitivity of the dark-adapted rhodopsin to a single photon is presented. We describe the absorption of photons by rhodopsin molecules using the three level Λ-type model for its retinal chromofore, with 3 states being the all-trans, 11-cis and the photoexcited S_1 state. The *ab-initio* calculations have been performed to estimate the parameters of the model.

Предложена квантово-механическая модель, объясняющая высокую чувствительность родопсина в темновом состоянии к одиночным фотонам. Поглощение фотонов молекулами родопсина описано с помощью трехуровневой модели Λ-типа для ретиналь-хромофора. Тремя состояниями являются all-trans, 11-cis и фотовозбужденное S_1-состояние. Для оценки параметров модели проведены расчеты методами *ab-initio*.

INTRODUCTION

The G protein-coupled receptors (GPCR), that form a large family of signaling molecules, are involved in practically all processes of information perception and transmission in living systems. The absorption of a single photon by the rhodopsin molecule induces the activation of transducin protein, amplifying the light signal to a chemical signal [1–3]. The activation of the GPCR is the key problem in studying visual perception and in understanding the functioning of the entire nervous system. The protein rhodopsin (see Fig. 1) consists of seven transmembrane helices. Its chromophore, the 11-cis retinal, is covalently attached to the Lys296 residue of helix VII via the formation of a Schiff base.

The energy of the absorbed photon is used for the isomerization of the 11-cis retinal isomer to the all-trans one (see Fig. 2), that affects the geometry of the rhodopsin protein and causes the activation of transducin.

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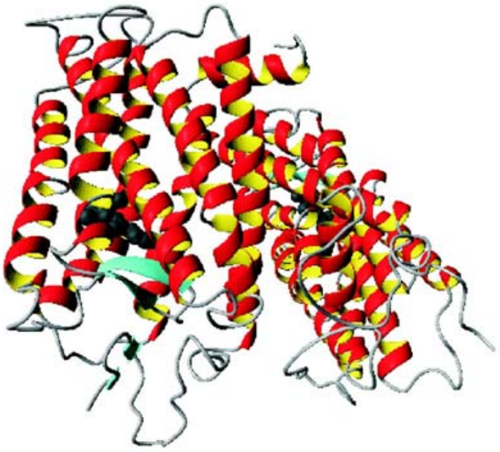

Fig. 1. Rhodopsin protein with 11-cis retinal chromophore. Retinal is shown in balls

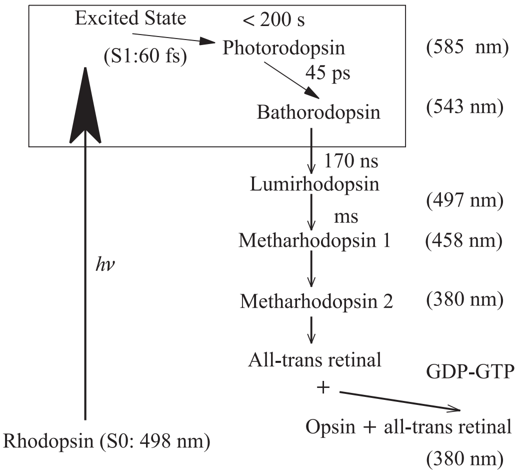

Fig. 2. Rhodopsin photocycle. Isomerization of 11-cis retinal into all-trans retinal takes place after absorption of one photon. The photoexcited state S_1 lives about 60 fs [4, 5], and decays within 200 fs into the first intermediate, the photorhodopsin

1. RHODOPSIN STRUCTURE AND PHOTOCYCLE

The rhodopsin photoreceptors are tightly stacked in the outer segments of the rod. The surface area (4.8×3.7 nm) of the unit cell houses two rhodopsin molecules [6] and the mean distance between rhodopsin molecules in the dimer is about 4 nm.

After optical excitation, the retinal chromophore relaxes to the all-trans configuration of the photorhodopsin – the first of the intermediates, which is formed in 200 fs after excitation (see Fig. 2). The process is rather complicated and involves the interaction of the prosthetic group of the retinal with the rhodopsin helices. The energy of the photo-transition to the excited state S_1 corresponds to the wavelength of 490–570 nm [4]. The formation of the primary all-trans photorhodopsin, that is, further decayed in bathorhodopsin, stable in picoseconds time scale (see Fig. 2), initiates the chain of the photoinduced chemical transformations of rhodopsin.

2. *AB-INITIO* CALCULATIONS

Theoretical calculations of the ground state geometries and IR eigenfrequencies of the retinal chromophore have been performed by many authors [7–9]. For our simplistic model we restrict ourselves to *ab-initio* quantum chemistry calculations of the retinal ground state energy and dipole momenta in vacuum, for both all-trans and 11-cis configurations.

Calculations have been performed with the B3LYP hybrid functional of Becke [10] and the Pople-type 6-31G(d,p) basis set [11] as implemented in the *Gaussian'03* software package [12]. The initial coordinates of retinal molecule were obtained from the crystal structure of Rhodopsin [13], PDB reference code 1F88.

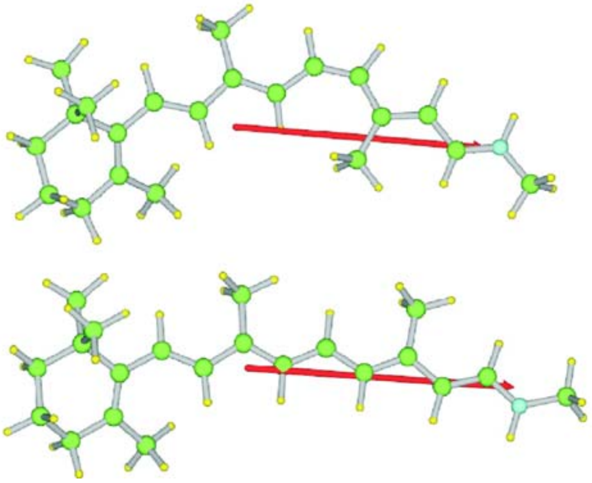

Fig. 3. Molecular geometries of 11-cis and all-trans retinal isomers as optimized at the B3LYP/6-31G(d,p) level of theory. The dipole moment vectors are shown by arrows

The Schiff base of the retinal was truncated with a terminal methyl group and the singly-charged (1+) singlet state was considered for both 11-cis and all-trans configurations. The results of our electronic structure calculations are presented in the Table below:

Conformation	Energy	Dipole moment	Method
11-cis	–874.058 Hartree	14.56 Debye	B3LYP, 6-31G(d,p)
all-trans	–874.066 Hartree	15.58 Debye	B3LYP, 6-31G(d,p)

3. MODEL AND EQUATIONS

We consider each retinal chromophore in the rhodopsin environment as a Λ-type system, see Fig. 4. The ground state $|0\rangle$ of the system corresponds to the all-trans state of the retinal chromophore. The state $|1\rangle$ corresponds to the 11-cis configuration of retinal. The energy difference (calculated in vacuum) corresponds to about 0.008 Hartrees. However, the dark-adapted rhodopsin keeps its chromophores in the 11-cis configuration by means of the hydrophobic interaction of the retinal with the rhodopsin helices. The $|2\rangle$ is the short-living photoexcited state. To study the behavior of the retinal-rhodopsin three-level system we use the transfer equation formalism [14], which enables to describe the propagation of light through the rhodopsin environment. We consider the Hamiltonian with local field operators. In dipole approximation it takes the form

$$H = i\hbar\vartheta,$$

$$\vartheta = \sum_{m,l} \sqrt{\frac{\hbar\omega_m}{2\epsilon_0\epsilon a^3}} A_{ml} \exp\left(-i\omega_m t + i\mathbf{ml}) d_l\right) - \text{h.c.} \tag{1}$$

The field operators A_{ml} stand for the packets of plain waves

$$A_{ml} = \frac{1}{\sqrt{M}} \sum_{k\sim m} a_k \exp\left(-i(\omega_k - \omega_m)t + i(\mathbf{k} - \mathbf{m})l\right),$$

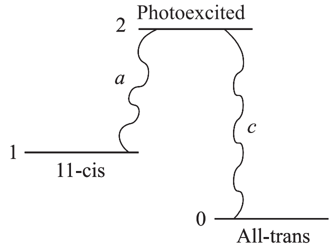

Fig. 4. Model for three-level states of retinal. Here $|0\rangle$ and $|1\rangle$ are the all-trans and 11-cis states, $|2\rangle$ is the photoexcited state

whose wave vectors $\mathbf{k} \sim \mathbf{m}$ are within the band $m_s - \pi/a \leqslant k_s < m_s + \pi/a, \Delta k_s = 2\pi/L, s = x, y, z$, with L^3 being a normalized volume for the modes $a_k, a_k^\dagger$, $[a_k, a_{k'}^\dagger] = \delta_{kk'}$. The waves are localized in a cell of $a^3 = (L^3/M)$ centered at $\mathbf{l}$. The local field creation and annihilation operators satisfy commutation relations $[A_{ml}; A_{m'l'}] = \delta_{mm'}\delta_{ll'}$.

For simplicity, we assume that there is only one molecule in each of the M normalization cell and take into account only modes close to resonance interaction. Our approximation results in one-dimensional problem, with $\mathbf{l} \rightarrow l_z = z$ and two local field operators A_{az}, A_{cz} with frequencies $\omega_a \approx \omega_{21}$ and $\omega_c \approx \omega_{20}$, where ω_{mn} is atomic transition frequency between levels m and n. Doing so, we get

$$\vartheta = \sum_z \vartheta_z, \quad \vartheta_z = g(s_{21}(z)a(z) - s_{12}(z)a^\dagger(z)) + f(s_{20}(z)c(z) - s_{02}(z)c(z)^\dagger), \tag{2}$$

where $d_z = \sum_{nm} d_{nm}s_{nm}(z)$, $s_{nm}(z) = |n\rangle_z\langle m|$, $n, m = 0, 1, 2$ and g, f are coupling constants dependent on the dipole moment $d_{mn} = \langle m|e_k d_z|n\rangle, k = a, c$,

$$g = \epsilon_a \frac{d_{12}}{\hbar}, \quad f = \epsilon_c \frac{d_{20}}{\hbar}, \tag{3}$$

with $\epsilon_q = \sqrt{\hbar\omega_q/2\epsilon\epsilon_0 a^3}$, $q = a, c$, $\epsilon_0 = 8.854 \cdot 10^{-12} F/m$ being the vacuum permittivity, ϵ being the rhodopsin media permittivity and the local field operators being denoted as $a(z) = A_{az}$, $c(z) = A_{cz}$.

The evolution of the density matrix of electromagnetic field and the retinal chromophores is governed by the master equation:

$$\left[\frac{\partial}{\partial t} + v\frac{\partial}{\partial z}\right]\rho = [\vartheta, \rho] + R\rho, \tag{4}$$

where v is the speed of light in media and R is the relaxation operator. The Eq. (4) describes the propagation of two quantized modes in the rhodopsin media represented by a chain of M independent molecules. The problem can be solved perturbatively $\rho = \rho^0 + \rho^1 + \rho^2 + \ldots$ We assume that before the interaction at $t \leqslant 0$ all retinal molecules are in the 11-cis state and that there are no correlations between incident photons and any of the molecules: $\rho^0(z,t) = (\rho_{11})^{\otimes M} \otimes \rho_f(z=0,t)$, where $\rho_f(z=0,t)$ is the density matrix of incident photons. This assumption reduces the multiparticle problem to a single particle one, when considering the evolution of the density matrix $r = \mathrm{Sp}_{M-1}\rho$ of a molecule and two quantized modes

$$\left[\frac{\partial}{\partial t} + v\frac{\partial}{\partial z}\right] r^k = [\vartheta, r^{k-1}] + R' r^k, \tag{5}$$

where $\mathrm{Sp}\,\{r^k\} = 0, r^k(z=0,t) = 0, k = 1,2,\ldots$ and R' is a relaxation operator of a molecule:

$$\begin{aligned} \dot{r}_{11} &= \Gamma_{21} r_{22}, \\ \dot{r}_{22} &= -\Gamma_{21} r_{22} - \Gamma_{20} r_{22} \equiv -\gamma_{22} r_{22}, \\ \dot{r}_{ik} &= -\Gamma_{ik} r_{ik}, i \neq k, \\ \dot{r}_{00} &= -\Gamma_{20} r_{00}. \end{aligned} \tag{6}$$

The evolution of the average number of secondary (virtual) photons is derived in the fourth order of the perturbation expansion, using the equality

$$\begin{aligned} \left[\frac{\partial}{\partial t} + v\frac{\partial}{\partial z}\right] X(z,t) = -\mathrm{Sp}\left\{ X \sum_{k=0,1,2} \left[\frac{\partial}{\partial t} + v\frac{\partial}{\partial z}\right] r^4_{kk}(z,t) \right\} = \\ = -g\langle [X, a^\dagger] r^3_{21}\rangle + g\langle [X, a)] r^3_{12}\rangle - f\langle [X, c^\dagger] r^3_{20}\rangle + f\langle [X, c)] r^3_{02}\rangle, \end{aligned}$$

where X is a field-dependent operator, and $a = a(z=0), c = c(z=0)$ are operators at $z = 0$. Next, we are interested in the number of photons $n_b(z) = \mathrm{Sp}\,(b^\dagger(0) b(0) r(z,t)^4)$, $b = a, c$. Taking into account that

$$r^3_{02}(z,t) = -g^2 f c^\dagger (a^\dagger a \rho_f + \rho_f a^\dagger a) K_{02}(z),$$

$$K_{02} = \frac{(\Gamma_{21} - \gamma_2)^2 + \mathrm{e}^{-\Gamma_{21}\frac{z}{v}} \left[-\gamma_2^2 \Gamma_{21}\dfrac{z}{v} + \gamma_2 \Gamma_{21}^2 \dfrac{z}{v} - \gamma_2^2 + 2\gamma_2\Gamma_{21}\right] - \Gamma_{21}^2\,\mathrm{e}^{-\gamma_2\frac{z}{v}}}{\Gamma_{21}^2 \gamma_2 (\Gamma_{21} - \gamma_2)^2},$$

we get for the number of photons

$$\left[\frac{\partial}{\partial t} + v\frac{\partial}{\partial z}\right] n_c(z) = (n_c(0) + 1) n_a(0) Q(z), \qquad Q(z) = 4Mg^2 f^2 K_{02}(z). \tag{7}$$

The Eq. (7) states that secondary photons c are emitted as a result of absorption of incident photons a.

For qualitative estimation of the effect we take $\gamma_2^{-1} = 45$ ps, $\Gamma_{21}^{-1} = 60$ fs, $\omega_a = \omega_c = \dfrac{2\pi c}{510 \text{ nm}}$ with the maximum concentration of molecules $n_m = a^{-3}$ with $a = 4$ nm and $n_c(0) = 0$, then $Q(z) \approx 4g^2 f^2 (\gamma_2 \Gamma_{21}^2)^{-1}$ and one finds

$$T = \frac{n_c(z)}{n_a(0)} = Q\frac{z}{v} = \frac{d_{12}^2 d_{20}^2 \omega_a \omega_c z n_m}{\hbar^2 \gamma_2 \Gamma_{21}^2 \epsilon^2 \epsilon_0^2 v a^3}, \tag{8}$$

where n_m is the concentration of molecules. For $d_{12} = d_{20} = 15$ Debye and $z = 30$ μm this gives an amplification $T = 4 \cdot 10^{12}$.

The reasons for high value of the gain $T \gg 1$ are short relaxation times and large values of dipole moments. Indeed, let the rod be illuminated by one photon per second and all photons c are transformed into the electron current. Then, the found gain may result in photocurrent about 0.1 μA, that is already a significant macroscopic signal.

CONCLUSION

The structure of the outer segment of the rod seems to be specially designed for detecting single photons. The typical wavelength of incident photon rods are sensible to about 500 nm. The distance between retinals packed in rhodopsin media in the outer segment of the rod is of the order of a few nm. Since the number of retinal chromophores interacting with the same quantum of light is large, and there may be entanglement effects between the photon field and the quantum ensemble of retinal chromophores, a collective behavior of retinal chromophores is expected. The strength of this collective interaction may depend on many factors: on the energy dissipation within rhodopsin, on the interaction with the solvent, and on the external forces changing the thermodynamic state of the rhodopsin. It is impossible to describe all these processes taking place *in vivo*. However, we can estimate the coherence length of the collective interaction. If the dipole–dipole interaction between the retinal chromophores is responsible for the collective behavior, the classical energy of the dipole–dipole interaction is

$$V \approx -\frac{1}{4\pi\epsilon_0}\frac{2d_1 d_2}{r^3} \approx 1.0 \cdot 10^{-3} \text{ Hartree} = 4.5 \cdot 10^{-14} \text{ erg}$$

for $d_1 = d_2 = 15$ Debye and the distance between retinals in atomic units $a_0 = 0.529$ Å taken as $r = 40$ Å$/a_0 = 76$. This corresponds to the wavelength $\lambda = c/\nu = 22$ μm, corresponding to the possible formation of a coherent structure. But the rod size is about 30 μm! Therfore, the rod can be regarded as a resonator used for the amplification of electronic density waves.

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