Quantum theory on protein folding

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Quantum theory on protein folding[†]

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The conformational change of biological macromolecule is investigated from the point of quantum transition. A quantum theory on protein folding is proposed. Compared with other dynamical variables such as mobile electrons, chemical bonds and stretching-bending vibrations the molecular torsion has the lowest energy and can be looked as the slow variable of the system. Simultaneously, from the multi-minima property of torsion potential the local conformational states are well defined. Following the idea that the slow variables slave the fast ones and using the nonadiabaticity operator method we deduce the Hamiltonian describing conformational change. It is shown that the influence of fast variables on the macromolecule can fully be taken into account through a phase transformation of slow variable wave function. Starting from the conformation-transition Hamiltonian the nonradiative matrix element was calculated and a general formulas for protein folding rate was deduced. The analytical form of the formula was utilized to study the temperature dependence of protein folding rate and the curious non-Arrhenius temperature relation was interpreted. By using temperature dependence data the multi-torsion correlation was studied. The decoherence time of quantum torsion state is estimated. The proposed folding rate formula gives a unifying approach for the study of a large class problems of biological conformational change.

conformational change of macromolecule, quantum transition, torsion potential, slow variable, nonadiabaticity operator, Berry's phase, quantum decoherence time, protein folding

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1 Introduction: molecular torsion as slow variable in protein folding

The prediction of how proteins fold has confounded researchers in the areas of biosciences as well as in physics. The correct three-dimensional structure is essential to function. It was proposed that the evolutionarily selected proteins are generally thought to have globally funneled energy landscapes that are largely directed toward the native state. This folding funnel landscape allows the protein to fold to the native state quickly through any of a large number of pathways and intermediates [1] Recently, by using massively parallel supercomputer Anton, the atomic-level mo-

lecular dynamics simulations were performed for 12 fast-folding proteins [2]. The results provide remarkable views of the folding process and addressed basic problems, such as whether proteins fold along pathways [3]. In fact, the problem of folding pathway is closely related to the folding mechanism. Although the molecular dynamics simulations are a powerful theoretical tool to model the protein folding process in atomistic details under natural conditions [4], because of the large computational cost the limited results currently obtained are still inadequate for giving a clear answer on the basic folding mechanism. In a recent work Garbuzynskiy et al. [5] reported that the measured protein folding rates fall within a narrow triangle (termed Golden triangle). On the other hand, the temperature dependence of the protein folding rate always exhibits the curious non-Arrhenius characteristics (the logarithm folding

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rate is not a decreasing linear function of $1/T$ [6]. To explain these longstanding problems such as the Levinthal's paradox [5] and the non-Arrhenius temperature dependence of the folding rate it seems that a novel physical model on the folding mechanism is required. Here we will propose a quantum model on the conformational change of macromolecule and deduce a formulas of protein folding rate which provides a method for calculating the folding rate of any two-state protein and the associated temperature dependence.

There are large numbers of variables in a biological system. The fundamental variables at the life processes at the molecular level seem unclear. Since the work of Pullman et al. [7] on nucleic acids, it is generally accepted that the mobile π electrons has an important role in the biological activities of macromolecules. However, the traditional quantum biochemistry cannot treat a large class problems relating to the conformational variation of biological macromolecules such as protein folding, signal transduction and gene expression regulation. In fact, for a macromolecule consisting of n atoms there are $3n$ coordinates if each atom is looked as a point. Apart from 6 translational and rotational degrees of freedom there are $3n-6$ coordinates describing molecular shape. The molecular shape is the main variables responsible for conformational change. It has been shown that the bond lengths, bond angles and torsion (dihedral) angles form a complete set to describe the molecular shape.

For a complex system consisting of many dynamical variables the separation of slow/fast variables is the first key step in investigation. In a synergetic study Haken [8] proposed that the long-living systems slave the short-living ones, or briefly, the slow variables slave the fast ones. He indicated that the fast variables can be adiabatically eliminated in classical statistical mechanics. To determine what is the slow variable for a molecular biological system we consider different forms of energy in a macromolecule. The typical chemical bond energy is several electron volts (for example, 3.80 eV for C—H bond, 3.03 eV for C—N bond, 6.30 eV for C=O dissociation). The CG hydrogen bond energy is 0.2 eV and the TA hydrogen bond energy is 0.05 eV in nucleic acids. The energy related to the variation of bond length and bond angle is in the range of 0.4–0.03 eV. While the torsion vibration energy is 0.03–0.003 eV, the lowest in all forms of biological energies. In terms of frequency, the stretching and bending frequency is 10^{14}–10^{13} Hz while that for torsion is 7.5×10^{12}–7.5×10^{11} Hz. Significantly, the torsion energy is even lower than the average thermal energy per atom at room temperature (0.04 eV in 25°C); the torsion angles are easily changed even at physiological temperature. Therefore, the torsion motion can be looked as the slow variable and others including mobile π electron, chemical binding, stretching and bending are rapid variables.

The torsion motion has two important peculiarities. The torsion energy 0.03–0.003 eV (0.7–0.07 kcal/mol) corre-

sponds to vibration frequency in the range of far-infrared spectrum. From the vibrational partition function of a molecule in harmonic conformational potential:

$$Z = (e^{(1/2)\beta\hbar\omega} - e^{-(1/2)\beta\hbar\omega})^{-1}, \quad (1)$$

one deduces the average energy $\bar{E}$ and entropy S readily:

$$\bar{E} = \frac{\hbar\omega}{2} + \hbar\omega(e^{\beta\hbar\omega} - 1)^{-1}, \quad (2)$$

$$S = k_B\{\beta\hbar\omega(e^{\beta\hbar\omega} - 1)^{-1} - \ln(e^{\beta\hbar\omega} - 1) + \beta\hbar\omega\}. \quad (3)$$

For a molecule with many torsion angles the potential can be expanded into harmonic modes and each mode contributes to internal energy and entropy described by eqs. (2) and (3). As is well known, the Boltzmann entropy is related to Shannon information quantity by

$$S = (k_B \ln 2)I. \quad (4)$$

Thus, by means of eq. (3) it can be determined that there is a strong dependence of information quantity on frequency. For example, as $T = 300$ K the information quantity is $I \sim 10^{-6}$ for frequency $\nu = 10^{14}$ Hz, but $I = 0.63$ for $\nu = 10^{13}$, $I = 2.83$ for $\nu = 10^{12}$, $I = 4.14$ for $\nu = 10^{11}$ and $I = 8.74$ for $\nu = 10^9$. As the frequency lower than 10^{13} Hz, the information quantity I increases rapidly. This is the reputed Boson condensation. Since the typical value of torsion frequency is 10^{12}–10^{13} Hz, the torsion vibration may have an important role in the transmission of information in the biological macromolecular system.

The second peculiarity is, different from stretching and bending the torsion potential generally has several minima with respect to angle coordinate that correspond to several stable conformations. It has been shown that the small asymmetry in potential (which does exist for a real macromolecule) would cause the strong localization of wave functions and the localized quantum conformational state can well be defined for a biological macromolecule [9,10].

2   Conformational change as a quantum transition calculated by non-adiabatic operator method

We propose that the conformation variation of a macromolecule is a process of quantum transition between different torsion states. Apart from torsion coordinates, the transition is also related to some fast variables of the system, for example, the frontier electrons of the molecule, the stretching-bending of the molecule and the atomic group connected to the molecule. Thus, the dynamical variables of the system are (θ, x) where x describes the coordinates of fast variables and θ the torsion angles of the molecule. The wave function $M(\theta, x)$ satisfies

$$\left(H_1\left(\theta, \frac{\partial}{\partial\theta}\right) + H_2\left(x, \frac{\partial}{\partial x}; \theta\right)\right)M(\theta, x) = EM(\theta, x), \quad (5)$$

$$H_1 = \sum -\frac{\hbar^2}{2I_j}\frac{\partial^2}{\partial\theta_j^2}+U(\theta), \tag{6}$$

where I_j denotes the inertial moment of the j-th torsion and the torsion potential U is a function of a set of torsion angles $\theta = \{\theta_j\}$. Because the fast variables change more quickly than the variation of torsion angles, the adiabatic approximation can be used. In adiabatic approximation the wave function is expressed as:

$$M(\theta, x) = \psi(\theta)\varphi(x, \theta) \tag{7}$$

and these two factors satisfy

$$H_2\left(x, \frac{\partial}{\partial x};\theta\right)\varphi_\alpha(x,\theta)=\varepsilon_\alpha(\theta)\varphi_\alpha(x,\theta), \tag{8}$$

$$\left\{H_1\left(\theta,\frac{\partial}{\partial\theta}\right)+\varepsilon_\alpha(\theta)\right\}\psi_{kn\alpha}(\theta)=E_{kn\alpha}\psi_{kn\alpha}(\theta), \tag{9}$$

where α denotes the quantum number of fast-variable wave function φ, and (k, n) refer to the conformational (indicating which minimum the wave function is localized around) and the vibrational state of torsion wave function ψ, respectively.

Because $M(\theta, x)$ is not a rigorous eigenstate of Hamiltonian $H_1 + H_2$, there exists a transition between adiabatic states that results from the off-diagonal elements:

$$\int M_{k'n'\alpha'}^+(H_1+H_2)M_{kn\alpha}\mathrm{d}\theta\mathrm{d}x$$
$$= E_{kn\alpha}\delta_{kk'}\delta_{nn'}\delta_{\alpha\alpha'}+\langle k'n'\alpha' \mid H' \mid kn\alpha\rangle, \tag{10}$$

$$\langle k'n'\alpha' \mid H' \mid kn\alpha\rangle =$$
$$\int \psi_{k'n'\alpha'}^+(\theta)\sum_j -\frac{\hbar^2}{2I_j}\left\{\int \varphi_{\alpha'}^+\left(\frac{\partial^2\varphi_\alpha}{\partial\theta_j^2}+2\frac{\partial\varphi_\alpha}{\partial\theta_j}\ \frac{\partial}{\partial\theta_j}\right)\mathrm{d}x\right\}\psi_{kn\alpha}(\theta)\mathrm{d}\theta, \tag{11}$$

where H' is a Hamiltonian describing conformational transition. The conformational transition can be noted to be related to the fast-variable wave function $\varphi_a(x,\theta)$ and is determined by its θ dependence. Eq. (11) is the generalization of the nonadiabaticity operator of Huang and Rhys in solid state physics [11]. The nonadiabatic matrix element eq. (11) has been calculated elsewhere [10] for a simpler system in which the system consists of only molecular torsions and electrons. Based on the assumption that only electrons serve as the fast variables and the electronic state remains unchanged in the folding ($\alpha' = \alpha$), an analytical formulas for the protein folding rate was deduced. However, in the general case of fast variables not limited to the electronic coordinates (for example, the stretching and bending of single bond always occurs as the fast variables in the torsion

transition) and the electronic state not remaining unchanged in the folding ($\alpha' \neq \alpha$) the calculation is more complex. However, if the perturbation approximation can be used then the θ dependence of fast-variable wave function $\varphi_\alpha(x,\theta)$ can be deduced by the perturbation method as follows:

$$H_2\left(x, \frac{\partial}{\partial x};\theta\right)$$
$$= H_2\left(x, \frac{\partial}{\partial x};\theta_0\right)+\sum_j\left(\frac{\partial H_2\left(x, \frac{\partial}{\partial x};\theta\right)}{\partial\theta_j}\right)_0(\theta_j-\theta_{j0})$$
$$\equiv H_2\left(x, \frac{\partial}{\partial x};\theta_0\right)+\sum_j h^{(j)}\left(x, \frac{\partial}{\partial x}\right)(\theta_j-\theta_{j0}), \tag{12}$$

$$h^{(j)}\left(x, \frac{\partial}{\partial x}\right)=\left(\frac{\partial H_2\left(x, \frac{\partial}{\partial x};\theta\right)}{\partial\theta_j}\right)_0, \tag{13}$$

$$\varphi_\alpha(x,\theta)=\varphi_\alpha(x,\theta_0)$$
$$+\sum_j(\theta_j-\theta_{j0})\sum_{\beta\neq\alpha}\frac{h_{\beta\alpha}^{(j)}}{\varepsilon_\alpha^{(0)}-\varepsilon_\beta^{(0)}}\varphi_\beta(x,\theta_0). \tag{14}$$

Inserting eq. (14) into eq. (11), only the second term is retained and one has

$$\langle k'n'\alpha' \mid H' \mid kn\alpha\rangle$$
$$= \sum_j\frac{\mathrm{i}\hbar}{\sqrt{I_j}}a_{\alpha'\alpha}^{(j)}\int \psi_{k'n'\alpha'}^+(\theta)\frac{\partial}{\partial\theta_j}\psi_{kn\alpha}(\theta)\mathrm{d}\theta, \tag{15}$$

$$a_{\alpha'\alpha}^{(j)}=\frac{\mathrm{i}\hbar}{I_j^{1/2}}\int \varphi_{\alpha'}^+(x,\theta_0)\sum_\beta{}'\frac{h_{\beta\alpha}^{(j)}}{\varepsilon_\alpha^{(0)}-\varepsilon_\beta^{(0)}}\varphi_\beta(x,\theta_0)\mathrm{d}x. \tag{16}$$

Starting with eqs. (15) and (16) we will be able to complete the calculation of transitional rate and obtain a formulas for the protein folding rate. The further calculation will be given in next section. Here we shall make a further discussion on the meaning of the nonadiabaticity operator.

Without adiabatic approximation the total wave function $M(\theta, x)$ should be expanded as:

$$M(\theta, x)=\sum_\alpha \psi_\alpha(\theta)\varphi_\alpha(x,\theta), \tag{17}$$

where $\varphi_a(x, \theta)$ is the fast-variable wave function satisfying eq. (8). Inserting eq. (17) into eq. (5) we obtain coupled equations for $\psi_\alpha(\theta)$:

$$\sum_{\alpha'}\left\{\left(\sum_j -\frac{\hbar^2}{2I_j}\frac{\partial^2}{\partial\theta_j^2}+U(\theta)+\varepsilon_{\alpha'}(\theta)\right)\delta_{\alpha'\alpha}+f_{\alpha\alpha'}(\theta)\right\}\psi_{\alpha'}(\theta)$$
$$= E\psi_\alpha(\theta), \tag{18}$$

$$f_{\alpha\alpha'}(\theta) = \sum_j \left\{ -\frac{\hbar^2}{2I_j} \int \varphi_\alpha^*(x,\theta) \frac{\partial^2}{\partial\theta_j^2} \varphi_{\alpha'}(x,\theta)\mathrm{d}x \right.$$
$$\left. -\frac{\hbar^2}{2I_j} \int 2\varphi_\alpha^*(x,\theta) \frac{\partial}{\partial\theta_j} \varphi_{\alpha'}(x,\theta)\,\mathrm{d}x \frac{\partial}{\partial\theta_j} \right\}. \quad (19)$$

Note that eq. (19) is exactly the expression for nonadiabaticity operator whose matrix element has been given by eq. (11). Neglecting the non-diagonal term in eq. (18) in first-order approximation we obtain

$$\sum_j \left\{ -\frac{\hbar^2}{2I_j} \frac{\partial^2}{\partial\theta_j^2} - \frac{\hbar^2}{2I_j} \int \varphi_\alpha^*(x,\theta) \frac{\partial^2}{\partial\theta_j^2} \varphi_\alpha(x,\theta)\mathrm{d}x \right.$$
$$\left. -\frac{\hbar^2}{2I_j} \int 2\varphi_\alpha^*(x,\theta) \frac{\partial}{\partial\theta_j} \varphi_\alpha(x,\theta)\,\mathrm{d}x \frac{\partial}{\partial\theta_j} \right\} \psi_\alpha(\theta)$$
$$= (E - U(\theta) - \varepsilon_\alpha(\theta))\psi_\alpha(\theta). \quad (20)$$

Eq. (20) can be put in the form of Berry's phase [12]. Set Berry's connection:

$$A_{\alpha j} = \mathrm{i} \int \varphi_\alpha^*(x,\theta) \frac{\partial}{\partial\theta_j} \varphi_\alpha(x,\theta)\mathrm{d}x, \quad (21)$$

eq. (20) can be rewritten as:

$$\sum_j \left\{ \frac{\hbar^2}{2I_j} \left(\mathrm{i}\frac{\partial}{\partial\theta_j} + A_{\alpha j} \right)^2 \right\} \psi_\alpha(\theta)$$
$$= (E - U(\theta) - \varepsilon_\alpha'(\theta))\psi_\alpha(\theta), \quad (22)$$

$$\varepsilon_\alpha'(\theta) = \varepsilon_\alpha(\theta) + \sum_j \frac{\hbar^2}{2I_j} \left(A_{\alpha j}^2 - \int \frac{\partial\varphi_\alpha^*(x,\theta)}{\partial\theta_j} \frac{\partial\varphi_\alpha(x,\theta)}{\partial\theta_j} \mathrm{d}x \right)$$
$$\cong \varepsilon_\alpha(\theta). \quad (23)$$

The second equality in eq. (23) is due to the additional term being a minor correction to $\varepsilon_\alpha(\theta)$, in the same order as the already neglected non-diagonal term $f_{\alpha\alpha'}(\alpha' \neq \alpha)$. Thus set

$$F_\alpha(\theta) = \exp\left\{ \mathrm{i}\sum_j \int^{\theta_j} A_{\alpha j}(\theta)\mathrm{d}\theta_j \right\}. \quad (24)$$

One has

$$\left(\frac{\partial}{\partial\theta_j} - \mathrm{i}A_{\alpha j}(\theta) \right) F_\alpha(\theta)\psi_\alpha(\theta) = F_\alpha(\theta)\frac{\partial}{\partial\theta_j}\psi_\alpha(\theta),$$

$$\left(\frac{\partial}{\partial\theta_j} - \mathrm{i}A_{\alpha j}(\theta) \right)^2 F_\alpha(\theta)\psi_\alpha(\theta) = F_\alpha(\theta)\frac{\partial^2}{\partial\theta_j^2}\psi_\alpha(\theta)$$

or

$$F_\alpha(\theta)^{-1} \left(\frac{\partial}{\partial\theta_j} - \mathrm{i}A_{\alpha j}(\theta) \right) F_\alpha(\theta) = \frac{\partial}{\partial\theta_j}$$

$$F_\alpha(\theta)^{-1} \left(\frac{\partial}{\partial\theta_j} - \mathrm{i}A_{\alpha j}(\theta) \right)^2 F_\alpha(\theta) = \frac{\partial^2}{\partial\theta_j^2}. \quad (25)$$

By replacement

$$\psi_\alpha(\theta) = F_\alpha(\theta)\psi_\alpha'(\theta) = \exp\left\{ \mathrm{i}\sum_j \int^{\theta_j} A_{\alpha j}(\theta)\mathrm{d}\theta_j \right\}\psi_\alpha'(\theta) \quad (26)$$

in eq. (22) and by multiplication of $F_\alpha(\theta)^{-1}$ on the left finally we have

$$\sum_j \frac{-\hbar^2}{2I_j} \frac{\partial^2}{\partial\theta_j^2} \psi_\alpha'(\theta) = (E - U(\theta) - \varepsilon_\alpha(\theta))\psi_\alpha'(\theta). \quad (27)$$

The fast variables have been removed in the equation of torsion wave function $\psi_\alpha'(\theta)$. Moreover, the resulting eq. (27) takes the same form as eq. (9), the basic equation for torsion wave function in the adiabatic approximation. $\psi_\alpha'(\theta)$ differs from $\psi_\alpha(\theta)$ only by a phase factor as accorded to eq. (26). So, the influence of fast variables on the system has been fully taken into account through a unitary transformation. The above discussion gives deeper understanding on the meaning of slow variables slaving fast variables and on the reasonability of adiabatic approximation. Simultaneously, we find that the difference between various models of fast variables can be expressed by a unitary transformation of the torsion wave function. As the fast-variable wave function is real, the normalization of $\varphi_\alpha(x,\theta)$ leads to $A_{\alpha j}$ vanishing for all j. This indicates the existence of fast variable of this type does not change the torsion wave function at all.

3   Protein folding rate deduced from quantum conformational transition

Start from eqs. (15) and (16) and insert them into the transition rate:

$$W = \frac{2\pi}{\hbar} \sum_{\{n\}} \left| \langle k'n'\alpha \mid H' \mid kn\alpha \rangle \right|^2 B(\{n\},T)\rho_E, \quad (28)$$

where

$$B(\{n\},T) = \prod_j B(n_j,T) = \prod_j \mathrm{e}^{-n_j\beta\hbar\omega_j}(1 - \mathrm{e}^{-\beta\hbar\omega_j}),$$

$$\beta = \frac{1}{k_\mathrm{B}T}$$

is the Boltzmann factor and

$$\rho_E = \frac{1}{\partial E_f / \partial N_f} = \frac{1}{\hbar \overline{\omega}'},$$

($\overline{\omega}'$ is the average of ω_j' over j) means state density. The transition rate is divided into two part, W = W_{dia} + W_{ndi} (W_{dia} —the diagonal part and W_{ndi}—the non-diagonal part)

$$W_{\text{dia}} =$$

$$2\pi\hbar \sum_{\{n\}} \sum_j^M \frac{1}{I_j} \left| a_{\alpha'\alpha}^{(j)} \right|^2 \left| \int \psi_{k'n'\alpha'}^+(\theta) \frac{\partial}{\partial \theta_j} \psi_{kna}(\theta) \mathrm{d}\theta \right|^2 B(\{n\},T)\rho_E,$$

(29)

$$W_{\text{ndi}} = 2\pi\hbar \sum_{\{n\}} \sum_{j \neq l}^M \frac{(a_{\alpha'\alpha}^{(j)})^* a_{\alpha'\alpha}^{(l)}}{\sqrt{I_j I_l}}$$

$$\times \left(\int \psi_{k'n'\alpha'}^+(\theta) \frac{\partial}{\partial \theta_j} \psi_{kna}(\theta) \mathrm{d}\theta \right)^* \int \psi_{k'n'\alpha'}^+(\theta) \frac{\partial}{\partial \theta_l} \psi_{kna}(\theta) \mathrm{d}\theta$$

$$\times B(\{n\},T)\rho_E,$$

(30)

where $\theta = \{\theta_1, \ldots \theta_N\}$, $\{n\} = \{n_1, \ldots, n_N\}$ and M means the number of torsion angles correlated to fast variables. The calculation of overlap integral of vibrational wave function with derivative $\frac{\partial}{\partial \theta_j}$ can be performed by using the phonon annihilation/production operator:

$$\xi_j = \left(\frac{I_j \omega_j}{2\hbar} \right)^{1/2} \left(\theta_j + \frac{\hbar}{I_j \omega_j} \frac{\partial}{\partial \theta_j} \right),$$

$$\xi_j^+ = \left(\frac{I_j \omega_j}{2\hbar} \right)^{1/2} \left(\theta_j - \frac{\hbar}{I_j \omega_j} \frac{\partial}{\partial \theta_j} \right),$$

(31)

which satisfies $[\xi_j, \xi_k^+] = \delta_{jk}$, and

$$-\frac{\hbar^2}{2I_j} \frac{\partial^2}{\partial \theta_j^2} + \frac{I_j \omega_j^2}{2} \theta_j^2 = \left(\xi_j^+ \xi_j + \frac{1}{2} \right) \hbar \omega_j = \left(n_j + \frac{1}{2} \right) \hbar \omega_j.$$

For single mode case when $\omega = \omega'$ we deduce the transition rate:

$$W = \frac{\pi}{\hbar} |a_{\alpha'\alpha}|^2 \{ (\overline{n}+1) I_V(p-1) + \overline{n} I_V(p+1) \}.$$

(32)

I_V is the overlap integral of harmonic wave function [13]:

$$I_V = \left(\frac{\overline{n}+1}{\overline{n}} \right)^{p/2} J_p(2Q\sqrt{\overline{n}(\overline{n}+1)}) \mathrm{e}^{-Q(2\overline{n}+1)},$$

(33)

in which,

$$\overline{n} = (\mathrm{e}^{\beta\hbar\omega} - 1)^{-1},$$

$$Q = I\omega(\delta\theta)^2 / 2\hbar, \quad p = \frac{\delta E}{\hbar\omega}.$$

(34)

$\delta\theta = \theta_k^{(0)} - \theta_{k'}^{(0)}$ is the angular displacement and $\delta E = E_k - E_{k'}$ the energy gap between two minima of the torsion potential (k and k' refer to the initial and final conformational state respectively). The notation J_P denotes the modified Bessel function and here p is related to the net change in oscillator quantum number. By use of the asymptotic formula for Bessel function [14]:

$$\mathrm{e}^{-z} J_p(z) = (2\pi z)^{-1/2} \exp(-p^2 / 2z), \quad \text{for} \quad z \gg 1. \quad (35)$$

The function I_V can be further simplified. Taking $\overline{n} > 1$ (equivalent to $\hbar\omega < 0.69 k_B T$ which is satisfied for the typical torsion frequency) into account, eq. (33) can be simplified to

$$I_V = (2\pi z)^{-1/2} \exp\left(-\frac{p^2}{2z} \right) \exp \frac{\delta E}{2 k_B T}$$

(36)

with

$$z = (\delta\theta)^2 \frac{k_B T}{\hbar^2} I. \quad (37)$$

Note that for the typical value $(\delta\theta)^2 = 0.01$, $I = 10^{-37}$ g cm^2 one has $z = 40$ and the condition $z \gg 1$ is fulfilled.

For multi-mode case (mode number N) we can deduce

$$W_{\text{dia}} = \frac{\pi}{\hbar} \sum_j^M |a_{\alpha'\alpha}^{(j)}|^2 \left\{ (\overline{n}_j+1) I_{Vj}(p_j-1) \sum_{\{p_l\}} \prod_{l \neq j}^N I_{Vl}(p_l) \right.$$

$$\left. + \overline{n}_j I_{Vj}(p_j+1) \sum_{\{p_l\}} \prod_{l \neq j}^N I_{Vl}(p_l) \right\}. \quad (38)$$

To simplify $I_V = \sum_{\{p_j\}} \prod_j I_{Vj}$ we use a formulas deduced in ref. [10] to write

$$\sum_{p_1 + \ldots + p_n = p} \exp(-z_1) J_{p_1}(z_1) \exp(-z_2) J_{p_2}(z_2) \ldots \exp(-z_n) J_{p_n}(z_n)$$

$$= \frac{1}{\sqrt{2\pi}} \frac{1}{\sqrt{z_1 + \ldots + z_n}} \exp\left\{ -\frac{p^2}{2(z_1 + \ldots + z_n)} \right\}. \quad (39)$$

With aid of eq. (39) the above eq. (38) can be rewritten in a simplified form:

$$W_{\text{dia}} = \frac{\pi}{\hbar} \sum_j^M |a_{\alpha'\alpha}^{(j)}|^2 \{ (\overline{n}_j+1) I_V(p-1) + \overline{n}_j I_V(p+1) \}, \quad (40)$$

where $I_V(p \pm 1)$ is given by

$$I_V(p) \equiv \sum_{\{p_j\}} \prod_j I_{Vj}$$

$$= \frac{1}{\sqrt{2\pi}} \exp\left(\frac{\Delta E}{2 k_B T} \right) \left(\sum_j^N z_j \right)^{-\frac{1}{2}} \exp\left(-\frac{p^2}{2\sum_j^N z_j} \right), \quad (41)$$

$$(z_j = (\delta\theta_j)^2 \frac{k_B T}{\hbar^2} I_j, \quad \sum_j^N p_j = p = \Delta E / \hbar\bar{\omega}, \quad \Delta E = \sum_j^N \delta E_j),$$

$$I_V(p \pm 1) = \frac{1}{\sqrt{2\pi}} \exp\left(\frac{\Delta E}{2k_B T}\right) \left(\sum_j^N Z_j\right)^{-\frac{1}{2}} \exp\left(-\frac{(p \pm 1)^2}{2\sum_j^N Z_j}\right). \tag{42}$$

Sarai and Kakitani [15] studied radiationless transitions of molecules with large nuclear rearrangement. By using generating function method [16] they deduced a similar formula but no clear analytical expression was obtained. Note that in their formula of W_{dia} the additional terms:

$$Q_j\{(6\bar{n}_j^2 + 6\bar{n}_j + 1)H(0) - 2(\bar{n}_j + 1)(2\bar{n}_j + 1)H(\hbar\omega_j)$$

$$-2\bar{n}_j(2\bar{n}_j + 1)H(-\hbar\omega_j) + (\bar{n}_j + 1)^2 H(2\hbar\omega_j)$$

$$+\bar{n}_j^2 H(-2\hbar\omega_j)\}$$

appeared but we have shown that these terms equal zero because of

$$H(\pm\hbar\omega_j) \cong H(\pm 2\hbar\omega_j) \cong H(0)$$

and the result is essentially identical with the proposed result herein.

The non-diagonal term W_{ndi} calculated by generating function method gives [15]:

$$W_{ndi} = \sum_{j\neq l} \frac{\pi}{\hbar}(a_{\alpha'\alpha}^{(j)})^* a_{\alpha'\alpha}^{(l)} \sqrt{Q_j Q_l}$$

$$\{(2\bar{n}_j + 1)(2\bar{n}_l + 1)H(0) + 2(\bar{n}_j + 1)\bar{n}_l H(\hbar\omega_j - \hbar\omega_l)$$

$$-2(2\bar{n}_j + 1)(\bar{n}_l + 1)H(\hbar\omega_l) - 2\bar{n}_j(2\bar{n}_l + 1)H(-\hbar\omega_j)$$

$$+(\bar{n}_j + 1)(\bar{n}_l + 1)H(\hbar\omega_j + \hbar\omega_l) + \bar{n}_j\bar{n}_l H(-\hbar\omega_j - \hbar\omega_l)\}. \tag{43}$$

Here $H(x)$ is the Fourier transformation of phonon-generating function, expressed as:

$$H(x) = \int dt \exp\{-i\hbar^{-1}(\Delta E - x)t)\}G(t).$$

Because of the number N of torsion modes cooperatively participating in the transition are not small, $\Delta E \gg \hbar\omega_j$, all factors $H(x)$ in eq. (43) are essentially the same. Thus we have

$$W_{ndi} = \sum_{j\neq l} \frac{\pi}{\hbar}(a_{\alpha'\alpha}^{(j)})^* a_{\alpha'\alpha}^{(l)} \sqrt{Q_j Q_l}(-3\bar{n}_j + 3\bar{n}_l)H(0) \cong 0 \tag{44}$$

as the difference between $\bar{n}_j$ and $\bar{n}_l$ can be neglected

$\left(\dfrac{\bar{n}_j - \bar{n}_l}{\bar{n}_j} = \dfrac{\omega_l - \omega_j}{\omega_l}\right)$. Thus the total rate W is given by the diagonal part, eq. (40).

Since the net variation p of phonon number in torsion

transition is much larger than 1 on account of the torsion mode number N large enough we have $I_V(p) \cong I_V(p \pm 1)$ and eq. (40) is further rendered to

$$W = W_{dia} = \frac{\pi}{\hbar} \sum_j^M \left|a_{\alpha'\alpha}^{(j)}\right|^2 \{(2\bar{n}_j + 1)I_V(p)\}$$

$$\cong \frac{2\pi}{\hbar^2 \bar{\omega}'} M\bar{a}^2 k_B T I_V, \tag{45}$$

where $\bar{a}^2$ means the average of $\left|a_{\alpha'\alpha}^{(j)}\right|^2$ over j and $\bar{n}_j \approx \dfrac{k_B T}{\hbar\omega_j} \gg 1$ is used in the last equality.

In above deduction the same frequency for initial and final states has been assumed. The result needs be generalized to the case $\omega_j \neq \omega_j'$. Consider a system consisting of N oscillators and study the free energy difference ΔG between the initial and final states. From the statistical mechanical consideration as the final frequencies of the oscillators shifted from $\{\omega_j\}$ to $\{\omega_j'\}$, the free energy difference ΔG will be expressed by

$$\Delta G = \Delta E + \sum_j \frac{1}{\beta} \ln \frac{\omega_j}{\omega_j'} = \Delta E + \lambda k_B T, \tag{46}$$

$\left(\lambda = \sum_{j=1}^N \ln \dfrac{\omega_j}{\omega_j'}\right)$. Therefore, through the replacement of ΔE in eq. (40) or eq. (45) by ΔG, eq. (46), we obtain the transitional rate for the case of non-equal frequencies $\omega_j \neq \omega_j'$ [10,17]. Further, by using the asymptotic formula for Bessel function (eq. (35)), eq. (45) can be rewritten in a form as:

$$W = \frac{2\pi}{\hbar^2 \bar{\omega}'} I_V' I_E',$$

$$I_V' = \frac{\hbar}{\sqrt{2\pi}\delta\theta} \exp\left\{\frac{\Delta G}{2k_B T}\right\} \exp\left\{\frac{-(\Delta G)^2}{2\bar{\omega}^2(\delta\theta)^2 k_B T \sum_j^N I_j}\right\}$$

$$\times (k_B T)^{1/2} \left(\sum_j^N I_j\right)^{-1/2}, \tag{47}$$

$$I_E' = \sum_j^M \left|a_{\alpha'\alpha}^{(j)}\right|^2 \cong M\bar{a}^2.$$

where

$$\delta\theta = \sqrt{\langle(\delta\theta_j)^2\rangle_{av}}.$$

Eq. (47) is our final result. It is interesting to note that eq. (47) takes a similar form as the folding rate formula deduced in ref. [10] for the system consisting of only molecular torsions and electrons, such that

$$W = \frac{2\pi}{\hbar^2 \bar{\omega}'} I_V I_E$$

$$= \frac{\hbar^3 \sqrt{\pi}}{2\sqrt{2}\delta\theta\bar{\omega}'} \exp\left\{\frac{\Delta G}{2k_B T}\right\} \exp\left\{\frac{-(\Delta G)^2}{2\bar{\omega}^2 (\delta\theta)^2 k_B T \sum_j^N I_j}\right\}$$

$$\times (k_B T)^{-1/2} \left(\sum_j^N I_j\right)^{-1/2} \left(\sum_j^M \frac{a_j}{I_j}\right)^2 \qquad (48)$$

with $I_V = \dfrac{1}{k_B T} I_V'$ and $I_E = \dfrac{\hbar^4}{4}\left(\sum_j^M \dfrac{a_j}{I_j}\right)^2$.

Eqs. (47) and (48) can be used for unfolding as well as for folding. The unfolding rate W (unfolding) is easily obtained by the replacement of ΔG by $-\Delta G$ and $\bar{\omega}'$ ($\bar{\omega}$) by $\bar{\omega}$ ($\bar{\omega}'$) in W (folding). Thus we have

$$\ln\left\{\frac{W(\text{folding})}{W(\text{unfolding})}\right\} = \frac{\Delta G}{k_B T} + \frac{(\Delta G)^2}{2k_B T\varepsilon}\left(\frac{\bar{\omega}^2 - \bar{\omega}'^2}{\bar{\omega}'^2}\right)$$
$$+ \ln\frac{\bar{\omega}}{\omega'}, \qquad (49)$$

($\varepsilon = \bar{\omega}^2 (\delta\theta)^2 \sum_j^N I_j$). Eq. (49) indicates the condition of dynamical balance $W(\text{folding}) = W(\text{unfolding})$ for protein folding is slightly different from the usual equilibrium condition for chemical reaction $\Delta G = 0$ because of the different bias samplings in frequency space of $\{\omega_j\}$ and $\{\omega_j'\}$, $\bar{\omega} \neq \bar{\omega}'$.

4 Application and discussion: temperature dependence of protein folding rate

4.1 Temperature dependence of rate

The temperature dependence of the transition rate reflects the essence of the folding dynamics of a protein. The comparison between theoretical calculation and experimental data on the temperature dependence of the rate will be able to give better insight into the folding mechanism. The theoretical formula for the folding rate has been given in eq. (47) (or eq. (48) for a simplified system). To obtain quantitative result one should calculate the number of torsion modes N in advance. The value of N describes the correlation degree of multi-torsion transition in the folding. Based on the idea that the folding is equivalent to a quantum transition between conformational states for any two-state protein we assume that N is obtained by the numeration of all main-chain and side-chain dihedral angles on the polypeptide chain except those on the tail of the chain which does not belong to any contact. A contact is defined by a pair of

residues at least four residues apart in their primary sequence and with their spatial distance no greater than some threshold (say, 0.65 nm in the following study). Suppose the length of the chain (after removing residues on the tail) being n and the number of the i-type residue on it being n_i', Each residue contributes 2 torsions on the main chain and c_i' torsions on the side chain, c_i' equals 0–4 for different residues [18,19]. The total number of torsion modes N for a given polypeptide chain is given as:

$$N = 2n + \sum_i c_i' n_i', \quad (i = 1, 2, \cdots, 20). \qquad (50)$$

As seen from eqs. (47) and (48), to find the temperature dependence of folding rate one should know the relation between ΔG and temperature in advance. By using the relation of ΔG with ΔE (eq. (46)) and by the expansion of ΔE at melting temperature T_c, $\Delta E(T) = \Delta E(T_c) + m(T - T_c)$, we can assume a linear relation between free energy change ΔG and temperature. This linearity has been tested rigorously by experiments ([20], Figure 1). Set $\eta = \dfrac{\Delta E(T_c) - mT_c}{\Delta E(T_c)}$. Assuming that 1) the measured value of folding free energy decrease is denoted by ΔG_f and 2) the measurement is carried out at temperature T_f, then one has

$$\Delta G_f = \Delta E(T_c)\{\eta + (1-\eta)T_f / T_c\} + k_B T_f \lambda. \qquad (51)$$

Inserting above into eq. (47) or eq. (48) we obtain the temperature dependence of logarithm rate [20,21]

$$\ln W(T) = \frac{S}{T} - RT \pm \frac{1}{2}\ln T + \text{const},$$

(symbol + for eq. (47) and − for eq. (48)), $\qquad (52)$

where const means temperature-independent term and

$$S = \frac{\eta\Delta E(T_c)}{2k_B}\left(1 - \frac{\eta\Delta E(T_c)}{\varepsilon}\right), \qquad (53)$$

$$R = \frac{k_B}{2\varepsilon}\left(\lambda + \frac{m}{k_B}\right)^2 = \frac{k_B}{2\varepsilon}\left(\lambda + \frac{(1-\eta)\Delta E(T_c)}{k_B T_c}\right)^2$$

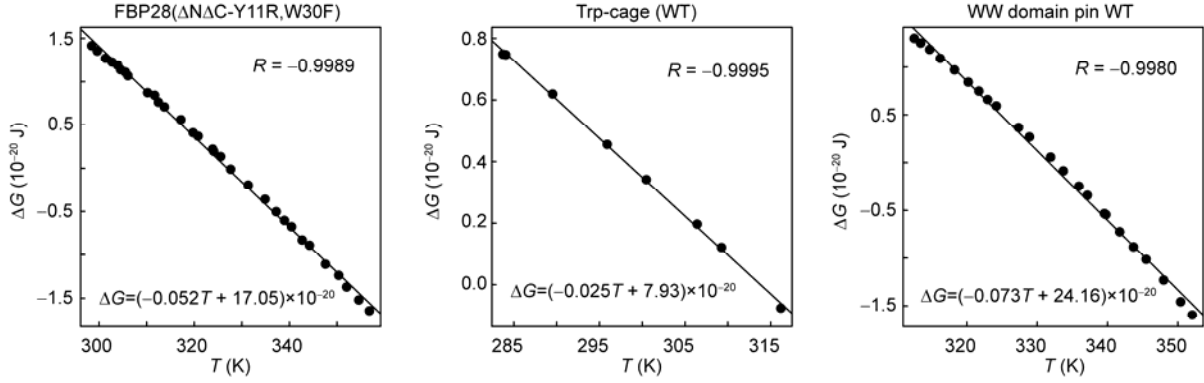$$= \frac{1}{2\varepsilon k_B T_f^2}(\Delta G_f - \eta\Delta E(T_c))^2 \qquad (54)$$

with

$$\varepsilon = \bar{\omega}^2 (\delta\theta)^2 \sum I_j = NI_0 \bar{\omega}^2 (\delta\theta)^2. \qquad (55)$$

Finally we have

$$\frac{d\ln W}{d\left(\frac{1}{T}\right)} = S - \frac{1}{2}T + RT^2, \quad \text{(from eq. (47))} \qquad (56a)$$

Figure 1   Figures on free energy ΔG vs. temperature T for typical proteins. ΔG in unit J, T in unit K. Experimental free energies ΔG changing with temperature are plotted for three typical proteins. The regression analysis shows a good linear relation existing between ΔG and T for each protein. For other proteins it gives similar good linear relations between free energy and temperature. Details can be found in ref. [20] of the text.

$$\frac{d \ln W}{d\left(\frac{1}{T}\right)} = S + \frac{1}{2}T + RT^2. \quad \text{(from eq. (48))} \quad (56b)$$

Note that eq. (52) in two cases differs only by an additive term $\frac{1}{2}\ln T$. This makes the difference of $\ln W(T+\Delta T)$ $-\ln W(T)$ in two cases ($\Delta T \approx 50°$ for the full range of the measured temperature in experiments) being $\ln\left(1+\frac{\Delta T}{T}\right)$ only, which is about 1.5% of the observed $\ln k_f$. Therefore the temperature dependence of folding rate deduced from two models is effectively the same. The reason is the temperature dependences of folding rate caused mainly by torsion motion, but not by fast-variables.

The experiments on rate-temperature relationships in protein folding exhibit the explicit characteristics of non-Arrhenius behavior [6]. All these characteristics can be explained by temperature-dependent terms in eq. (52). The last term RT^2 in eq. (56) is the primary term contributed to the curvature of Arrhenius plot. To make more quantitative comparison between theory and experiments Lu and Luo [20,21] studied 16 proteins for which the experimental data on temperature dependence of the rate and folding free energy are currently available. They found that the theoretical eq. (56) is in good agreement with the experimental rate-temperature relation for each protein (Figure 2). Moreover, by using S, R and the equilibrium free energy at some temperature T_f as input, the torsion potential parameters for each protein can be consistently calculated.

In above studies the number of torsion modes N is calculated from eq. (50) and it takes a value larger than 100 for most polypeptide chains. This indicates the correlation degree is generally large, consistent with the idea that many torsion angles participate in a quantum transition cooperatively in protein folding. We have studied how the experimental temperature dependence of folding rate gives a constraint in the determination of correlation degree N. Since

the torsion parameters $\eta \Delta E(T_c)$ and ε have been calculated from the experimental slope parameters S and R, one easily finds $\overline{\omega}^2$ is inversely proportional to N as seen from the expression of ε, eq. (55). The maximal torsion frequency observed in experiments is about 7.5×10^{12} Hz. This gives the minimal allowable N, $N_{th} = \text{Itg}\dfrac{\varepsilon}{I_0\,(\delta\theta)^2\,\overline{\omega}_{max}^2}$ where Itg$x$ denotes the minimal integer larger than x. The slope parameters S and R, torsion parameter $\overline{\omega}\delta\theta$, correlation degree N and the associated threshold N_{th} for 16 proteins are listed in Table 1. It is found that nearly all of these proteins have $N_{th} > 1$. Therefore, to explain the temperature dependence of folding rate the introduction of coherent multi-torsion transition is necessary.

The multi-torsion coherence model can successfully explain not only the curious non-Arrhenius temperature-dependencies of the folding for a given protein, but also the specific statistical distribution of the folding rates for all measured two-state proteins. It has been shown that in multi-torsion coherence model the analytical formula on folding rate eq. (47) is consistent with all existing experimental data of 65 two-state proteins and the correlation between theoretical prediction with experimental folding rate has attained 73%–78% ([20], Figure 3). Recently, Garbuzynskiy et al. [5] indicated that the measured protein folding rates fall within a narrow triangle. The existence of this triangle can be understood in our quantum folding model.

4.2   Decoherence time of torsion

One of the least-understood areas of physics is the boundary between quantum and classical mechanics. In recent years the role of quantum decoherence was widely recognized by physicists [22,23]. Due to quantum entanglement with the environment the coherence or the ordering of the phase angles is lost between the components of a system in a quantum superposition. It was believed that the decoherence makes the quantum picture ceasing to be effective for a
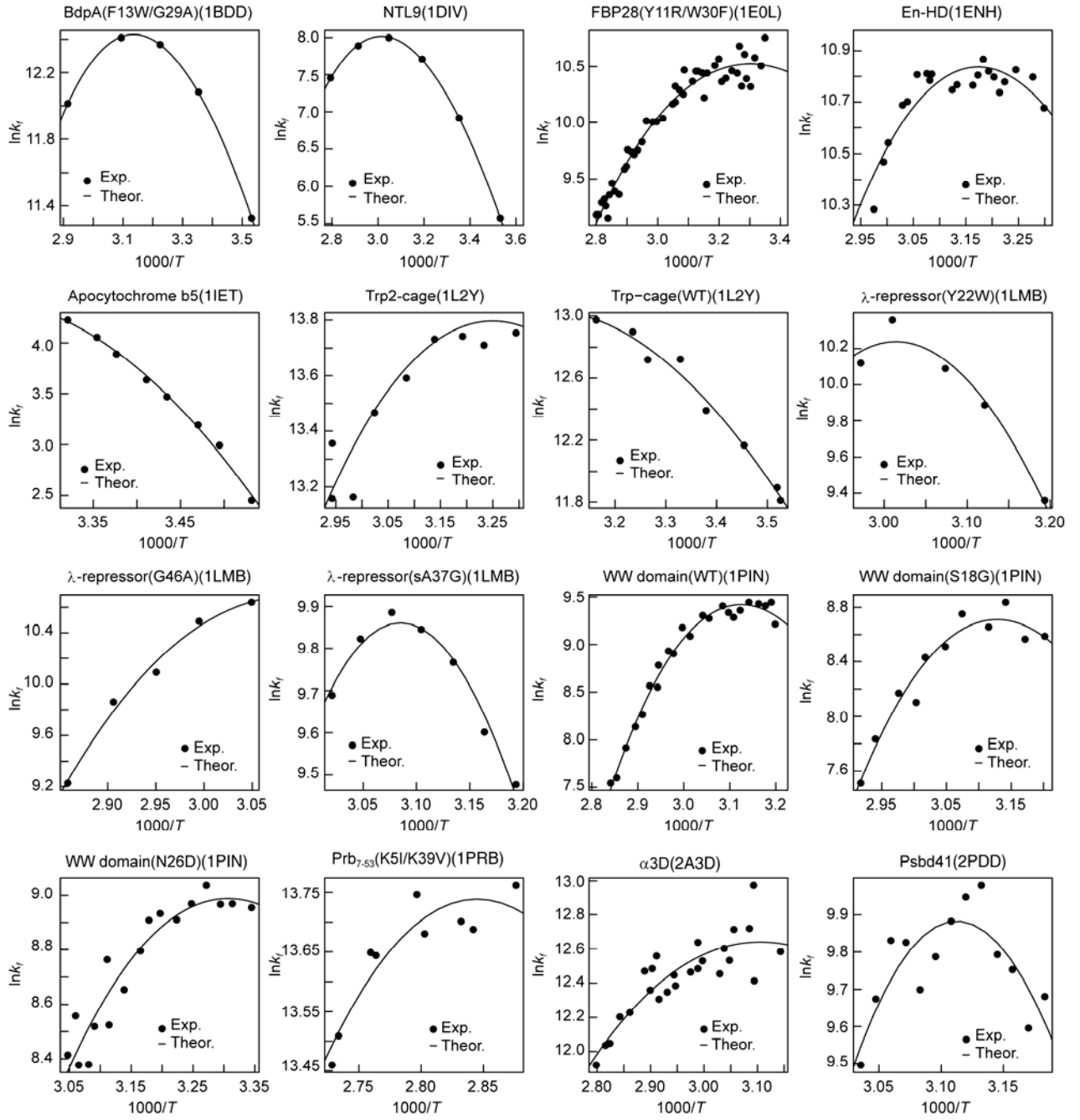
Figure 2 Figures on folding rate vs. temperature for 16 proteins. Model fits to overall folding rate k_f vs. temperature $1000/T$ for 16 proteins. Experimental logarithm folding rates are shown by "●", and solid lines are theoretical model (eq. (47) or eq. (56a)) fits to the folding rate (k_f in unit s^{-1}, T in unit K). Details can be found in ref. [20] of the text.

macromolecular system.

The decoherence effect is estimated by computing the decoherence time of the molecular system under thermal environment. The rigorous solution of decoherence time is difficult but some simple models were proposed. One such model introduced in ref. [23] showed the decoherence time

$$\tau_D = \tau_R \left(\frac{\hbar}{\Delta x \sqrt{2mk_{\mathrm{B}}T}} \right)^2$$

where τ_R is the relaxation time

due to the interaction of the particle with a scalar field and $\dfrac{\hbar}{\sqrt{2mk_{\mathrm{B}}T}}$ the thermal de Broglie wavelength, m the particle mass and Δx the dimension of particle. It leads to $\tau_D = 10^2 \tau_R$ for an electron but about $10^{-2} \tau_R$ for an atom (carbon), much shorter than the electronic decoherence time. To study the decoherence effect on protein folding, we use the same model to the torsional angular motion and deduce

Table 1   Temperature dependence of folding rate and torsion parameters for 16 proteins[a]

PDB code	S	R	$\bar{\omega}$ ($\times 10^{12}$ Hz)	N	N_{th}
1BDD	−24669	0.2441	1.4153	212	8
1DIV	−32076	0.2930	0.9649	229	4
1E0L	−16241	0.1780	1.5995	97	5
1ENH	−33182	0.3345	0.8424	227	3
1IET	−70322	0.7322	0.5463	346	2
1L2Y(P12W)	−14796	0.1602	1.4398	73	3
1L2Y(WT)	−18957	0.1774	0.7023	73	1
1LMB(WT)	−83920	0.7613	0.7684	307	4
1LMB(G46A)	−30292	0.3313	0.6155	307	3
1LMB(SA37G)	−112897	1.0766	1.4154	307	11
1PIN(WT)	−69675	0.6812	1.1677	129	4
1PIN(S18G)	−77113	0.7565	1.0819	128	3
1PIN(N26D)	−27063	0.2990	0.9520	129	3
1PRB	−47886	0.3893	1.3737	179	7
2A3D	−18486	0.1812	1.0186	273	6
2PDD	−159403	1.5560	0.7321	152	2

a) The PDB code for each studied protein is given in column 1. S and R are best-fit slope parameters of the folding temperature dependence [20], $\bar{\omega}$ is the torsion frequency calculated from S, R and N (the average torsion inertial moment of atomic groups in polypeptide $\langle I_j \rangle = I_0 = 10^{-44}\,\mathrm{kg\,m^2}$ and the average angular shift in the torsion potential $\delta\theta = 0.1$ are assumed). N is the number of torsion modes of the polypeptide chain calculated from eq. (50). N_{th} is the threshold of N as the torsion potential satisfies the condition $\omega < \omega_{max} = 7.5 \times 10^{12}\,\mathrm{s^{-1}}$.
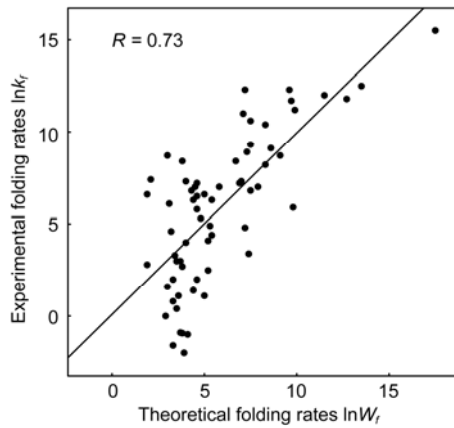
Figure 3   Comparison between theoretical and experimental folding rates for 65 two-state proteins. Theoretical predictions are calculated from a model based on eq. (47). In calculation the free energy per molecule $\Delta G / k_B T$ is assumed as a linear function of $\sqrt{N}$. The details of the calculation can be found in ref. [20]. If the free energy are taken from experiments directly then the correlation R between experimental $\ln k_f$ and theoretical prediction $\ln W_f$ increases to 0.783.

a similar formulas for torsional decoherence time:

$$\tau_D^{(tor)} = \tau_R \left(\frac{\hbar}{\Delta\theta \sqrt{2Ik_BT}} \right)^2 > 10^4 \tau_R \left(\frac{\hbar}{\sqrt{2Ik_BT}} \right)^2 \cong \tau_R, \quad (57)$$

where $\Delta\theta$ is the uncertainty of torsional angle, I the torsional inertia moment of atomic group. and $\sqrt{2Ik_BT} = J_{therm}$ the thermal angular momentum. By using the uncertainty relation and $\Delta\theta\,\Delta J \approx \hbar$ (ΔJ is the uncertainty of

angular momentum) the first equality of eq. (57) can be rewritten as $\tau_D^{(tor)} \approx \tau_R \left(\frac{\Delta J}{J_{therm}} \right)^2$. In the next inequality of eq. (57), $\Delta\theta \leqslant 0.5°$ (about one tenth of the angular shift $\delta\theta$ in torsion potential) and $I = 10^{-37}\,\mathrm{g\,cm^2}$ have been taken. By comparing the torsion decoherence with electronic and atomic decoherence time we find, if the relaxation rates $\left(\frac{1}{\tau_R} \right)$ are same in three cases then the decoherence effect on molecular torsion is in the midst of the electron and the atom. In fact, because of the thermal average over torsional vibration states used in our calculation the thermal excitation effect of the scalar field (representing the environmental perturbation) has been partly taken into account. The surplus interaction of the scalar field interaction with torsion subsystem should be weaker and the torsional relaxation rate decreases. Thus, even if the quantum coherence for the macromolecule as a single particle may have been destroyed the coherence in the torsional degree of freedom still works. This gives an explanation on the reasonability of the quantum calculation of the protein folding adopted in this article. Moreover, the multi-torsion correlation observed in the folding as indicated in the above seems to give direct evidence on the possible existence of the torsional quantum coherence in the macromolecular system. It is expected that the instantaneous dihedral transition observed in the duration of microseconds will be able to give more evidences on the quantum nature of protein folding.

4.3   Prospects in application

Apart from two-state protein folding the preliminary studies on other potential applications of the present theory were worked out, which include the generalization from two-state protein to multi-state protein folding [24], the protein photo-folding (the photon emission or absorption in protein folding and the inelastic scattering of photon on protein) [25] and the histone modification in nucleic acid through atomic group binding [26] have been derived. For various problems, different forms of fast variables are slaved by the same slow variable—the torsional vibration and torsional transition. A recent report [27] indicated that the reprogramming of the stem cell can be realized through a pure physical approach, and demonstrated that the sphere morphology helps maintaining the pluripotency of stem cells. Although the exact mechanisms of these new results remain elusive; however, we speculate that several discrete quantum conformational states and the transition between them may exist and can be discussed in the framework of the present understanding [28].

In principle, the quantum coherence occurs in all degrees of freedom of torsion angles of the macromolecule as long as the related inertial moments of the atomic group are sufficiently small enough to reduce the decoherence effect. In addition to the torsion angles on polypeptide chain of the protein the coherence may extend to torsion angles on the sugar-phosphate backbone of the DNA molecule. The DNA chain contains alternating links of phosphoric and sugar (deoxyribose) and every sugar is attached to a nitrogen base. Each nucleotide has 6 torsion angles, namely, ω and ω' around P—O single bond, ϕ around O-CH_2, ψ around CH_2-ribose , χ around ribose-base and the sixth linked to next nucleotide. Except ψ other five torsion angles have more than one advantageous conformations (potential minima). These torsion degrees may participate in the quantum transition in the nucleic acid or in the interacting system of nucleic acid and protein. The basic formulas deduced above for protein folding can be generalized to these systems.

The existence of a set of coherent quantum oscillators of torsion-vibration type of low frequency and the quantum transition between torsion states—this forms a universal mechanism for a large class problems of the conformational change in molecular biology. We have formulated a theory on the quantum conformation transition and discussed the comparison between theory and experiments on the temperature dependence of protein folding rates. More rigorous experimental tests on the concept of quantum conformational transition and further applications of the theory are waited for.

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