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The influence of dipole–dipole interaction on the low-frequency vibrations in alpha-helix proteins

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Abstract

The quasi-continuity model proposed by Chou (Biophysical Chemistry, 30 (1988) 3) for calculating the dominant low-frequency vibration modes of α-helix protein molecules is modified by taking into consideration the effects of secondary interactions, in particular the dipole–dipole interaction. Chou's results are modified through adaptation of the force constant of the helical spring.

Keywords: Dipole–dipole interaction; Quasi-continuity model; α-Helix proteins; Low frequency vibration modes

1. Introduction

Many experiments have confirmed the existence of low-frequency vibrations with wave numbers of 10–40 cm^{-1} in protein molecules. Consequently, various models have been proposed in an attempt to reveal the mechanisms of such internal motions (See Chou's review article [1]). The quasi-continuity model proposed by Chou [1–4] might be one of the most successful models to calculate the dominant low-frequency vibration modes of protein molecules. Chou's model first considered the α-helix, the most fundamental structural element in protein molecules, and compared it with a mass distributed spring. The force constant k of the spring can be subdivided in two components expressed by k_H^S and k_H^B which are the stretching and bending force constants of the hydrogen bond, respectively. Considering different terminal conditions, Chou derived the formulas for calculating the fundamental frequency of different α-helix proteins. Calculations on internal vibrations of α-chymotrypsin, pepsin, lysozyme and insulin molecules were performed. The results are in good agreement with the experimentally observed values. The vibrations of some other biomacromolecules and their biological functions were also summarized in [1].

Chou only considered the H-bond interaction between the peptide units, which is the most important factor related to the low-frequency vibrations of α-helix proteins. However, there also exist some second-order interactions between the peptide units which are jointed by H-bonds, such as dipole–dipole, dipole-induced dipole, charge–charge, charge–dipole interactions, etc. The dipole–dipole interaction, abbreviated as DDI hereafter, seems to be the strongest one among

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these secondary interactions. Considering the DDI, we will modify Chou's results through adapting the force constant of the helical spring. According to Ref. [5,6], The permanent dipole moment of each peptide unit is 3.5 D in the direction of the N–H and O–C bond. We take the following example to show how the DDI influences the vibration frequency of the spring.

2. Model

In Fig. 1. m_1 and m_2 represent two atomic groups in a large biological system. u_1 and u_2 are the dipole moments of m_1 and m_2 respectively. We consider the simple case that u_1 and u_2 are in the same direction and on the same line which joins the centroids of m_1 and m_2. The zigzag line denotes the H-bond. When m_1 and m_2 vibrate in the small vicinity of their equilibrium positions along the x-axis, the H-bond can be considered as an elastic spring with a stretching force constant k_H^S. We use x_1 and x_2 to represent the displacements of m_1 and m_2 from their respective equilibrium positions. The distance between m_1 and m_2 can be expressed as $d+(x_2-x_1)$, where d is the distance between the centroids of m_1 and m_2 when the spring is in its natural state.

The DDI potential and force between u_1 and u_2 are $E_d=-(2u_1u_2)/\varepsilon(d+x_2-x_1)^3$ and $F_d=-(6u_1u_2)/\varepsilon(d+x_2-x_1)^4$, respectively, where ε is the dielectric constant of the medium in which m_1 and m_2 exist.

The total force between m_1 and m_2 can be written as:

$$F_{12}=F_{\text{H-bond}}+F_d = -k_H^S(x_2-x_1)-\frac{6u_1u_2}{\varepsilon(d+x_2-x_1)^4}. \quad (1)$$

For small vibrations, we have $|x_2-x_1| \ll d$, and we may expand F_d into Taylor series up to the first order, then we obtain

$$F_{12}\approx -k_H^S(x_2-x_1)+\frac{24u_1u_2}{\varepsilon d^5}(x_2-x_1) - \frac{6u_1u_2}{\varepsilon d^4}. \quad (2)$$

Let

$$k'=k_H^S-\frac{24u_1u_2}{\varepsilon d^5}, \quad (3)$$

then we have

$$F_{12}=-k'(x_2-x_1)-\frac{6u_1u_2}{\varepsilon d^4}, \quad (4)$$

where k' is the modified stretching force constant of the elastic spring (H-bond) between m_1 and m_2. It is seen that due to the DDI, the force constant becomes smaller, accordingly, the vibration frequency of m_1 and m_2 lower. The constant term in eq. (4) does not affect the vibration

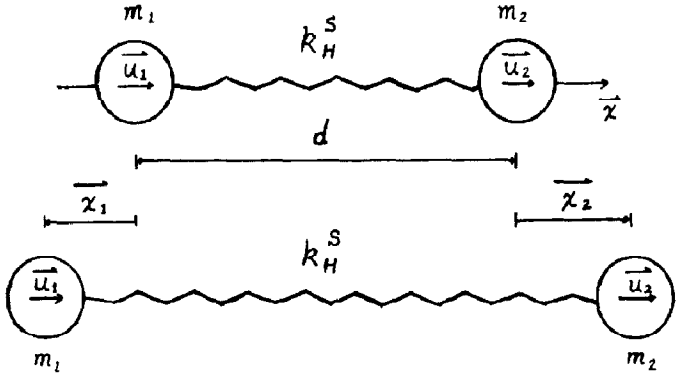

Fig. 1. The schematic presentation for describing the motion of m_1 and m_2 in an α-helix protein.

frequency at all. It only causes a small change (nearly 1%) of the equilibrium distance between m_1 and m_2, and hence we will neglect it further.

3. Results and discussion

We can explain qualitatively why the DDI softens the spring. The force produced by the DDI is always attractive between m_1 and m_2. When $d + x_2 - x_1 < d$, the attractive force increases and its direction is contrary to that of the repulsive force produced by the spring. When $d + x_2 - x_1 > d$, the attractive force decreases, and this is equivalent to adding a repulsive force with the same magnitude as that of the attractive force decreasing between m_1 and m_2. On the other hand, in this case, the force produced by the spring is attractive. It is seen that the effect of the DDI on the motion of m_1 and m_2 is always contrary to that of the spring (H-bond). Consequently, the modified force constant k' is smaller than k_H^S.

Under different terminal conditions of the α-helix, Chou derived three formulas for calculating the fundamental frequency [1]. Here we take only one example to explain how the DDI modifies Chou's formula. When the two ends of the α-helix are linked to two fragments of masses M_1 and M_2 respectively, Chou's formula is (see eq. 27 in Ref. [1])

$$\tilde{\nu} = \frac{\nu}{c} = \frac{1}{2\pi c}\sqrt{\frac{k}{M^* + (\beta_1^3 + \beta_2^3)M_H/3}} \qquad (5)$$

where k is the stretching force constant of the helix, M_H the mass of the α-helix, and $\beta_1 = M_2/(M_1 + M_2)$, $\beta_2 = M_1/(M_1 + M_2)$ and $M^* = M_1M_2/(M_1 + M_2)$. When the α-helix has 11 amino-acid residues, the expression of k can be written as [1]

$$k = \tfrac{12}{7}k_H^\alpha = \tfrac{12}{7}\left[\left(k_H^S\cos\theta\right)^2 + \left(k_H^B\sin\theta\right)^2\right]^{1/2}$$
$$= 0.20\ 10^{-8}\text{N/Å}, \qquad (6)$$

where $\theta \approx 26°$ is the angle between the helix axis and the constituent H-bonds [1], and $k_H^S = 0.13\ 10^{-8}$N/Å and $k_H^B = 0.03\ 10^{-8}$N/Å [1].

In α-helix proteins, each unit has a dipole moment of $u = 3.5$ D (1D $= 10^{-18}$ g$^{1/2}$ cm$^{5/2}$ s^{-1}) whose direction is basically the same as that of H-bond stretching. Using the DDI in the expression of k, we obtain

$$k = \tfrac{12}{7}\left[\left(k_H^S - \frac{24u^2}{\varepsilon d^5}\right)^2\cos^2\theta + \left(k_H^B\sin\theta\right)^2\right]^{1/2}. \qquad (7)$$

We take $d = 4.5$ Å, which is the average pitch of the α-helix. Therefore, $24u^2/\varepsilon d^5 = (0.016/\varepsilon)\ 10^{-8}$N/Å. It is difficult to determine the exact value of ε. According to Ref. [5], the effective dielectric constant for non-polar atoms in the protein interior is about $\varepsilon = 2$. Here, we will take ε values of 1, 2 and 3 to calculate the modified force constant k, and compare the effects of the modification of DDI to the low vibrational fre-

Table 1

A comparison of low-frequency wave numbers from this study's and Chou's results, and the modified results of three cases for four kinds of protein molecules

Protein macromolecule	Main α-helix element (residues)	Wave number $\tilde{\nu}$ (cm^{-1})				
		Chou's [Ref.]	Modified			Observed
			$\varepsilon = 1$	$\varepsilon = 2$	$\varepsilon = 3$	
Insulin	B9–B19	22.7 [1,3]	21.6	22.2	22.3	22
Lysozyme	5– 15	27.0 [3]	25.6	26.3	26.5	25
	25– 35	26.2 [3]	24.9	25.5	25.7	25
α-Chymotrypsin	235–245	30.7 [4]	29.1	29.9	30.1	29
Pepsin	225–235	33.0 [4]	31.4	32.2	32.5	32

quencies of biomacromolecules. In these three cases, substituting the values mentioned above into eq. (7), we have for k in 10^{-8}N/Å

$$k = 0.18, \quad (\varepsilon = 1) \tag{8a}$$

$$k = 0.19, \quad (\varepsilon = 2) \tag{8b}$$

$$k = 0.193, \quad (\varepsilon = 3) \tag{8c}$$

By eq. (5), Chou calculated a fundamental frequency $\tilde{\nu} = 22.7$ cm^{-1} for an insulin molecule (See eq. 37 of Ref. [1]). Replacing $k = 0.20$ 10^{-8}N/Å by the three values in (8a, b, c), we obtain the modified frequencies of insulin $\tilde{\nu} =$ 21.6 cm^{-1} ($\varepsilon = 1$), $\tilde{\nu} = 22.2$ cm^{-1} ($\varepsilon = 2$) and $\tilde{\nu} =$ 22.3 cm^{-1} ($\varepsilon = 3$), which are all closer to the observed value of $\tilde{\nu} = 22$ cm^{-1} [3] than Chou's result of $\tilde{\nu} = 22.7$ cm^{-1}.

In Table 1, we list the experimental results, Chou's results and the modified results of the three cases for four kinds of protein molecules, respectively. It is seen that, after the DDI modification, this theory may be more perfect to explain the internal vibration of the biomacromolecules.

The DDI is a secondary interaction and its effect on the vibration frequency is only about 10% of that of the H-bond, but this effect is very important. With a dipole moment for each peptide unit of 3.5 D, a helix consisting of, for example, 10 residues has an overall dipole moment of 34 D, as 97% of the individual peptide dipoles point in the direction of the helix axis [6]. So a complete α-helix structure can be considered as one giant dipole. Two such structures may exert very strong long-range forces (Fröhlich forces) [7] upon each other when their dipole vibrational frequencies are equal (i.e. frequency resonance occurs). We think this kind of long-range interaction plays an important role in biomacromolecules recognizing each other, which is needed in completing their physiological functions. Further investigations to this end are forthcoming.

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