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H-Bond vibrations of the α-helix

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The collective low frequency longitudinal vibrational modes of the α-helix are isolated using Dean's method, (P. Dean, *Proc. Phys. Soc., London*, 1959, **73**, 413; P. Dean, *Proc. R. Soc. London, Ser. A*, 1960, **254**, 507), which considers the different masses of the amino acids involved. The spectrum range extends up to $f = 100\ \mathrm{cm}^{-1}$ for the α-portion of several proteins within the range of experimental results (S. Cusack, J. Smith, J. Finney, B. Tidor and M. Karplus, *J. Mol. Biol.*, 1988, **202**, 903).

I. Introduction

Native protein macromolecules and their synthetic analogs have the general formula $(–CO–CHR–NH–)_n$ where R are the amino acid residues. One of the secondary structure of these polypeptides, is the well-known α-helix of Pauling and Corey.[1] The higher-order structure of these biomolecules is stabilized by weak bonds *e.g.* salt bridges, hydrogen bonds, van der Waals forces, *etc.*, this is reflected in the existence of low frequency phonons which impart to the molecule *flexibility* (small force constant) and *complexity* (large reduced mass);[2] as a consequence there emerge internal movements as the interbase hydrogen-bond breathing modes in B-DNA.[3] Also these low frequency phonons can be excited by thermal energy kT ($200\ \mathrm{cm}^{-1}$), giving to the molecule a great adaptability to the environment.

It has not been possible to decompose the measured spectrum of a protein molecule into the individual atomic dynamic contributions. Also, the uncertainty of the experimental data by neutron scattering studies is approximately 15%.[4] Nevertheless, several theoretical techniques have contributed to increase the understanding of the internal dynamics of proteins: normal mode analysis[5–17] and molecular dynamics simulations.[4,18–21] In these techniques the classical equations of motion for the atoms are solved simultaneously, all atoms and degrees of freedom of the molecule are treated explicitly and some collective modes remain hidden. The observed spectrum is very sensitive to the distribution of low-frequency modes.[22]

In the α-helix structure the series of hydrogen bonds, each operating between the C=O group of a given monomer unit and the N–H group of the fourth proceding unit, holds together the different turns of the helix forming an angle of approximately 26° with the helix longitudinal axis. There are 3.6 residues per turn in an α-helix, which corresponds to 5.4 Å (1.5 Å per residue). The amino acids are linked by peptide bonds. With regard to the vibrational longitudinal spectrum the α-helix as a whole can be approximated as a linear masses system of coupled oscillators.[6–8] The observations by laser Raman spectroscopy,[9] show the pronounced low-frequency peaks at ≈ 29 and $32\ \mathrm{cm}^{-1}$ for α-chymotrypsin and pepsin, respectively. To explain the above experimental results, Suezaki and Gō,[10,11] likened the native globular proteins to continuous elastic spheres and spheroidal bodies in low-frequency breathing motions. Also Chou,[12] considered the α-helix as a mass-distributed spring and applied this continuity model to studying the hydrogen-bond modes of the α-structures studied by Suezaki and Gō.[10]

In determining the hydrogen-bond modes of several α-structures we consider each amino acid of mass m_i (see Table 1) as having spherical shape linked together by hydrogen-bond with the corresponding amino acid (see Fig. 1). We believe that this is a more realistic approximation in the determination of hydrogen-bond vibrations.

II. Dean's method

When the oscillators have different masses there is no analytical expression for the allowed frequencies and it is necessary

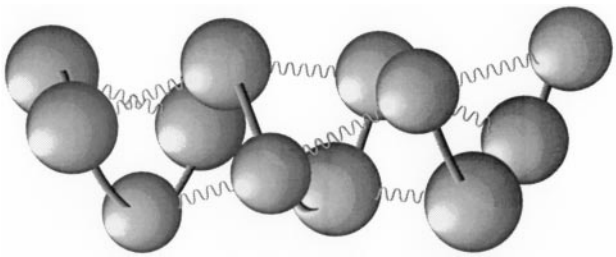

Fig. 1 Schematic drawing of the α-helix, the spheres represent the amino acids and the coils the hydrogen bonds.

Table 1 Amino acid masses[a]

Ala	Arg	Asn	Asp	Cys	Gln	Glu	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val
A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V
71	156	114	115	103	128	129	57	137	113	113	128	131	147	97	87	101	186	163	99

[a] Molecular weight of amino acid minus that of water.[36] 1 dalton $= 1.6734 \times 10^{-24}$ g.

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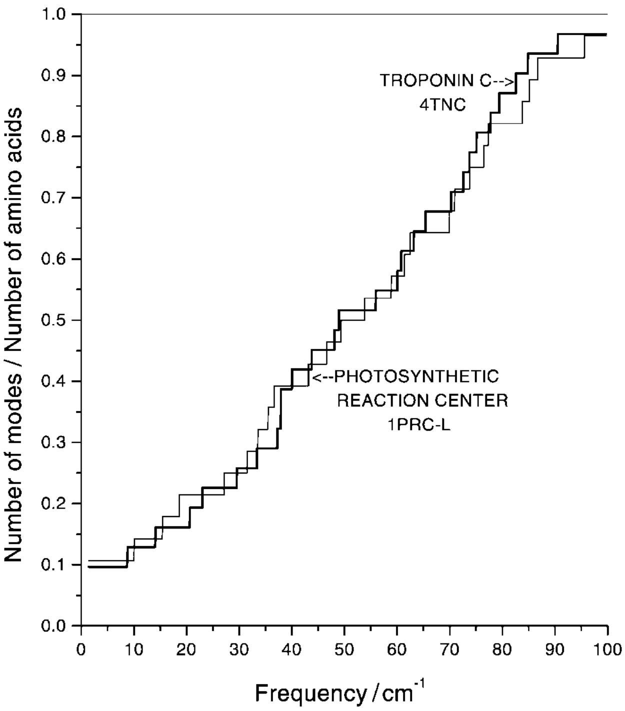

Fig. 2 α-Helix hydrogen bonds vibrations, $k = 0.11$ mdyn Å^{-1}.

to employ a computational method. In Dean's method the spectral distribution $M(\omega)$ is generated, which represents the number of modes less than any given argument ω. Dean's method is useful when the oscillators are different since it yields quantitatively accurate results for the vibrational spectra of disordered linear systems.

We define $v_i = \omega_i^2$, ($\omega_i = 2\pi f_i$, f_i being the eigenfrequency in Hz corresponding to the eigenmode i) for a chain of N masses m_i each of which is coupled harmonically to its nearest neighbours, the v_i are given as the eigenvalues of an $N \times N$ matrix $\boldsymbol{A}_N$, defined by

$$A_{ii} = \alpha_i,$$
$$A_{i,\,i+1} = A_{i+1,\,i} = \beta_{i+1},$$
$$\text{all other} \quad A_{i,\,j} = 0,\ (i, j = 1, 2, \ldots). \tag{1}$$

the α_i and β_i depend on the chain structure:

$$\alpha_i = \frac{(k_i + k_{i-1})}{m_i},$$
$$\beta_i^2 = \frac{k_{i-1}^2}{m_i m_{i-1}}, \tag{2}$$

where k_i is the force constant between the masses i and $i + 1$. Ref. 23 and 24 describe how one could compute the number $M(v)$ of eigenvalues of the matrix $\boldsymbol{A}_N$ less than any given argument v. It was shown that Sturm's theorem leads to the equation

$$M(v) = n(v) \tag{3}$$

where $n(v)$ is the number of variations in sign between adjacent members of the sequence of functions

$$g_0 \equiv 1,$$
$$g_j(v) = \det|\boldsymbol{A}_j - v\boldsymbol{I}_j|$$
$$= (\alpha_j - v)g_{j-1}(v) - \beta_j^2 g_{j-2}(v), \tag{4}$$
$$\text{where} \quad \beta_1 \equiv 0, \text{ for } j = 1, 2, \ldots, N,$$

$\boldsymbol{I}_j$ being the unit matrix of order j. Results for the vibrational spectra of disordered chains may therefore be derived simply by the repetition of an elementary cycle of operations, *i.e.*, performing the calculations and noting of the signs of successive $g_i(v)$.

III. Results

The force constant for the hydrogen bonds that we used was $k = 0.11$ mdyn Å^{-1} = 11.0 N m^{-1} in accordance with ref. 25. Then eqn. (2) becomes:

$$\alpha_i = \frac{2k}{m_i},$$
$$\beta_i^2 = \frac{k^2}{m_i m_{i-1}}, \tag{5}$$

We have studied the α-portion of several proteins (1BP2, 1ECD, 1HOS, 1LH1, 1MBC, 1MBN, 1MLT, 1PRC-L, 1PRC-M, 1UTG, 1WRP, 2CRO, 2CYP, 2HHB, 3CPV, 3CYT, 3L2M, 4TNC).[26] The sequences of the amino acids in the α-helix segments of the proteins were obtained by processing the Kabsch and Sander program,[27] which uses the Brookhaven protein data files.

As an example of a common behaviour we consider the sequences of the amino acids in the α-helix segments of the photosynthetic reaction center (1PRC-L) and the troponin C (4TNC):

GFWQAITVCALGAFISWMLREVEISRKL (1PRC-L)

FEEFLVMMVRQMKEDAKGKSEEELADCFRIF (4TNC)

The calculated spectra are shown in Fig. 2. We observe that the α-helix band extends up to 100 cm^{-1} ($f = 3 \times 10^{12}$ s^{-1}). The α-segments studied of the mentioned proteins are within this range.

IV. Conclusion

This method has shown to be a simple and powerful tool for predicting the low frequency modes of macromolecules which involve coherent motion of rigidly bound subgroups connected by weak bonds or non-bonded interactions. These low-frequency vibrations are shown to play an important role in mediating interbase H-bond disruption or melting.[28,29] The advantage of this method is that it considers the different masses of the involved units.

The frequencies predicted by this method for the breathing modes of proteins are consistent with the experimental[4,9] and theoretical ones[10–12] estimated by more elementary models on some similar systems.

This method could be also applied to B-DNA polymers in order to study the interbase hydrogen-bond breathing modes[3] and compare with the low-frequency experiments.[30–35]

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