Vibrational Energy Transfer in Helices

David M. Leitner
Department of Chemistry and Chemical Physics Program, University of Nevada, Reno, Nevada 89557
(Received 7 July 2001; published 16 October 2001)

Rates of vibrational energy transfer in the five largest $\alpha$ helices of myoglobin are calculated. Energy transfer in helices occurs by anharmonic coupling of spatially overlapping localized normal modes in resonance, which is also the mechanism for energy transfer among localized modes of a glass. As a result, rates of energy transfer from higher-frequency modes of the helices typically vary little with temperature. Variation of the energy transfer rate with mode frequency is captured by a model of an anharmonic one-dimensional glass.

DOI: 10.1103/PhysRevLett.87.188102 PACS numbers: 87.15.–v, 63.22.+m, 87.14.Ee

Our picture of the relation between protein structure, dynamics, and function ultimately requires an understanding of the flow of energy through the protein, including energy flow into and away from reaction centers, enzyme-substrate binding sites, and components involved in allosteric transitions [1]. While anharmonicity plays a pivotal role in a protein’s vibrational dynamics and energy transfer [1,2], it has also been suggested that certain structural features of proteins serve as efficient pathways for vibrational energy to flow. In particular, the $\alpha$ helix has been speculated to provide a conduit for vibrational energy transport to and from reaction centers and across cell membranes [3,4]. Recent spectroscopic studies [4–6] of myoglobin provide much information on energy flow in a modest-sized protein whose structure is highly helical (Fig. 1a), but different conclusions about the efficiency of energy transport through helices based on the spectrum of the amide I band of myoglobin [4] and several globular peptides [7] leave unresolved the question as to whether the $\alpha$ helix plays any special role in energy transfer. In this Letter, we calculate the rate of vibrational energy transfer in the five largest $\alpha$ helices of myoglobin, which range from 16 to 24 residues. We find that energy transfer in the $\alpha$ helices is not particularly efficient and is comparable to transfer along other portions of the protein backbone. The $\alpha$ helix is a quasi-1D anharmonic aperiodic object comprised of atoms bound together by a wide range of forces. Variations of energy transfer rates with mode frequency of the helices and with temperature are captured by an appropriately parametrized model of an anharmonic 1D glass.

Analogies between proteins and glasses have been exploited for some time [8], and here we make connections between their mechanisms for energy transfer. Recent theoretical and computational work [9–11] has helped elucidate how vibrational energy flows in a glass. The simplest case is a 1D glass, for which all but of order $N^{1/2}$ of the $N$ normal modes of vibration are localized spatially to regions smaller than the glass, increasingly so as the mode frequency increases [12]. Excitations of localized normal modes in a glass, called locons [10], cannot transport energy from one end of the glass to the other. Locon transport in a glass arises from anharmonic coupling of overlapping localized normal modes in resonance [10,11]. We see below that most normal modes of the five largest $\alpha$ helices of myoglobin are also localized. It was recently pointed out that energy from a localized mode in myoglobin is transferred to a small number of resonant modes that overlap in space [13], which is the principle for locon transport in a glass [10,11]. One consequence of localization in a 1D glass is the nearly temperature-independent energy transfer rate from modes with frequency $\omega \gg k_BT/\hbar$. We show below that the same holds for higher-frequency modes involving backbone vibrations of the helix, including the well-studied amide I band.

We consider first the normal modes of the $\alpha$ helices of myoglobin, which were computed with MOIL [14].

![Fig. 1. (a) Ribbon diagram of sperm whale myoglobin. Normal modes and vibrational energy transfer in the five largest $\alpha$ helices, labeled A, B, E, G, and H, are calculated. (b) Normalized distribution of normal mode frequencies, binned into 50 cm$^{-1}$ intervals, of the helices (solid line) and the model 1D glass described in the text (dashed line) are plotted.](188102-2)
Coordinates for the atoms in the helices were taken from the minimum-energy structure of myoglobin, and the new minimum energy structures for each helix were subsequently computed, followed by the normal modes. The normal mode frequencies for the five helices range from 3 to 1850 cm\(^{-1}\), as well as a range of higher-frequency modes above 3100 cm\(^{-1}\) corresponding to CH and OH stretches that we do not consider here. The density of the normal modes of the helices as a function of mode frequency is plotted in Fig. 1b. In a harmonic periodic chain, the normal modes carry energy without resistance from one end of the chain to the other. However, the vast majority of normal modes of an aperiodic chain are spatially localized and cannot carry heat. The extent to which a mode involves the atoms of the helix is estimated by the participation number for mode \(\alpha\) [15],

\[ P_\alpha = \left( \sum_{n=1}^{N} (e_n^\alpha)^2 \right)^{-1}, \]

where \(e_n^\alpha\) are components of normalized vibrational eigenstates, and \(N\) is 3 times the number of atoms of the helix; \(P_\alpha\) can, in principle, range from 1 to \(N\), the former when there is localization to one component of an atom and the latter when the magnitude of each component is \(N^{-1/2}\). The average \(P_\alpha\) vs \(\omega\) for the five helices is plotted in Fig. 2. The vibrations are generally more localized with increasing frequency. The number of vibrational modes up to 1850 cm\(^{-1}\) is 456, 411, 505, 455, and 550 for helix A, B, E, G, and H, respectively; since on average each helix has 475 modes, we see that even at low frequency only about 10% participate in a vibration. Nevertheless, the low-frequency vibrations extend over several residues of the helix. As a measure of the number of residues contributing to a mode, we calculate the information entropy

\[ S = -\sum_{n=1}^{N_{res}} p_i \ln p_i, \]

where \(N_{res}\) is the total number of residues in the helix and \(p_i\) is the projection of all coordinates of a residue onto a normal mode of the helix. If each residue is represented equally, then

\[ S = \ln N_{res}, \]

where \(S = 0\) if a vibration is localized to a single residue. Then \(e^S\) is roughly the number of residues that a normal mode spans. The average value of \(e^S\) for the five helices vs frequency is also plotted in Fig. 2, where we observe trends that closely match those of the participation number. At frequencies below \(=200\) cm\(^{-1}\), the modes span roughly ten residues, about half the number of residues that make up the helices. At higher frequency, there is a gradual decline to a participation of one to five residues, with the larger number involving modes where atoms vibrate along the backbone. For instance, modes that lie in the amide I band, in the range 1550 to 1700 cm\(^{-1}\), involve larger numbers of atoms and residues than modes at somewhat lower or higher frequencies.

Most normal modes of the helices, like those of an aperiodic chain, cannot carry energy from one end to the other. Anharmonicity generates energy transfer among the localized normal modes. In our calculations of energy transfer we consider only the contribution of cubic anharmonic terms and neglect all terms of higher order, which is reasonable if we restrict ourselves to low temperatures. At low temperatures, the energy transfer rate is dominated by processes that involve the decay of a vibrational excitation into two others, such that \(\omega_\alpha = \omega_\beta + \omega_\gamma\). The energy transfer rate, \(W_\alpha\), of mode \(\alpha\) is then given by

\[ W_\alpha = \frac{\hbar \pi}{8 V_{\alpha \beta \gamma}} \left( 1 + n_\beta + n_\gamma \right) \times \delta(\omega_\alpha - \omega_\beta - \omega_\gamma), \quad (1) \]

where \(n_\alpha\) is the occupation number of mode \(\alpha\), which at temperature \(T\) we take to be \(n_\alpha = (e^{\frac{\omega_\alpha}{k_B T}} - 1)^{-1}\). The matrix elements \(\Phi_\alpha = \frac{\partial^2 V}{\partial Q_\alpha \partial Q_\beta} |_{Q_\alpha = 0, \delta Q_\beta = 0}\) appear as the coefficients of the cubic terms in the expansion of the interatomic potential in normal coordinates, computed numerically as

\[ \Phi_\alpha = \langle \alpha | \frac{\partial^2 V}{\partial Q_\alpha \partial Q_\beta} | \alpha \rangle \approx \frac{\partial^2 V}{\partial Q_\alpha \partial Q_\beta} |_{Q_\alpha = 0, \delta Q_\beta = 0}/2 \delta Q_\gamma, \]

where \(Q_\alpha\) is a mass-weighted normal coordinate, and \(Q_0\) is the equilibrium position of the helix in normal coordinates.

We have computed the vibrational energy transfer rate with Eq. (1) for the five largest \(\alpha\) helices of myoglobin. The average transfer rate in the helices as a function of frequency is plotted in Fig. 3a, where the temperatures were chosen to be \(T = 45\) and \(135\) K. We observe in Fig. 3a an overall gradual decline in the energy transfer rate with increasing mode frequency, with variations in the range 0.2–1.0 ps\(^{-1}\) above 400 cm\(^{-1}\). A decline in the transfer rate with mode frequency is expected for a 1D glassy system whose normal modes are localized or spatially disordered [11]. We observe in Fig. 3a that the vibrational energy transfer rates are not very sensitive to the temperature above about 500 cm\(^{-1}\), and nearly temperature independent above 1250 cm\(^{-1}\), with the notable exception of modes with frequencies in the range 1700–1750 cm\(^{-1}\). Temperature dependence of the energy transfer rate implies that energy is flowing directly into the low-frequency modes of the helices. Since the temperature dependence largely decreases with increasing mode frequency, we can...
conclude that as the mode frequency increases there is less direct energy transfer to low-frequency modes. Such a trend, as we see below, is characteristic of energy transfer in a 1D glass. This trend arises because the frequencies of modes that are localized in space tend to “repel” one another [10,11]; modes with similar frequencies do not overlap in space. As a consequence, energy transfer to modes with similar frequencies and the remainder to low-frequency modes occurs very slowly. There is as mentioned an exception to this trend at 1700 to 1750 cm⁻¹, which lies just above the amide I band. We have found that the modes for which the decay rate is temperature dependent correspond to CO stretches in certain side chains, particularly belonging to the glutamine residue of the A, B, and H helices. A significant character of the same CO stretch is found for modes in this frequency range that lie about 15–20 cm⁻¹ apart, and a mode of the latter frequency that overlaps the side chain is available for energy transfer. Decay rates of the CO stretches of the amide I band, from about 1600 to 1700 cm⁻¹, are not very temperature sensitive, as has also been observed experimentally [6]. Notable variation in the energy transfer rate among the five helices also occurs at low frequency (<50 cm⁻¹). At 45 K, transfer rates of 12 and 33 ps⁻¹ in the G and B helices are higher than the ≈1 ps⁻¹ in the others. At ≈400 and 700 cm⁻¹, transfer rates in the G helix are 6 and 4 ps⁻¹, respectively, higher than the ≈1 ps⁻¹ in the others. We note that the measured decay rate of the amide I band around 100 K is about 0.5 ps⁻¹, somewhat faster than the 0.2 ps⁻¹ that we have calculated. This difference could arise from the fact that neither residues of loops nor water molecules are included in our calculations, which are carried out only to third order in the anharmonicity; each of these factors would tend to reduce the rate.

We turn now to a model of an anharmonic 1D glass, a chain of N equally spaced atoms of unit mass connected by random forces. For the calculations discussed below we take an ensemble of five chains of N = 500 atoms so that the 2500 glass modes are comparable to the total of 2377 modes computed for the five helices with frequencies below 1850 cm⁻¹. The potential energy of the glass is given by $V = V_2 + V_3$, where $V_2$ is the potential energy to second order, $V_2 = \frac{1}{2} \sum_{n=1}^{N} f_n (u_n - u_{n+1})^2$, where $u_n$ is the position of atom n and $f_n$ is the force constant. [Since we express frequencies in cm⁻¹, it will be convenient to express $f_n$ in units of (cm⁻¹)².] Anharmonicity arises from $V_3 = \frac{1}{3!} \sum_{n=1}^{N} g_n (u_n - u_{n+1})^3$. The normal mode frequencies are obtained from the eigenvalues of the Hessian matrix, whose diagonal elements are $f_n - f_{n-1}$.

By contrast, the diagonal elements of the Hessian matrix for the α helices are the sums of numerous terms accounting for a larger number of local interactions. In fact, the distribution of the latter resembles the positive half of a Gaussian centered at 0, whose standard deviation we have found to be $9.5 \times 10^5$ (cm⁻¹)². We take the force constants, $f_n$, to be randomly distributed in the positive half of a Gaussian such that the standard deviation of the distribution of $f_{n-1} + f_n$, the diagonal elements of the Hessian of the model, matches that for the helices. We have also introduced a large-$f_n$ cutoff of $1.2 \times 10^6$ (cm⁻¹)² to prevent mode frequencies much higher than the band edge for the helices. Then $f_n$ is taken from a distribution of positive Gaussian random variables with standard deviation $6.0 \times 10^5$ (cm⁻¹)² and cutoff $1.2 \times 10^6$ (cm⁻¹)². For the diagonal elements of the Hessian matrix of this model we find a standard deviation of $9.3 \times 10^5$ (cm⁻¹)², close to that for the helices. In Fig. 1b we compare the normal mode density of the harmonic 1D glass consisting of five chains of $N = 500$ with the normal mode density of the helices. The secular variation of the mode density of the helices with mode frequency reveals specific features reflecting their constituents and interactions. Nevertheless, these features appear as fluctuations around the mode density of the model.

Vibrational energy transfer in the model glass arises from the anharmonicity, $V_3$. The cubic anharmonic constants should vary as $g_n = cf_n/a$, where $a$ is a lattice spacing, and $c$ is a constant of order 1. The constant $c/a$ is our one fitting parameter, chosen so that the average decay rates of the glass match those of the helices; $a$ is a few Å so that $c/a$ should lie in the range 0.1–1 Å⁻¹. Each $f_n$ is chosen randomly from the distribution specified above.
and we then set the average \( g_n \) in terms of the average \( f_n \) as \( g_n = \frac{1}{n} f_n \). The energy transfer rate, \( W_\alpha \), is given by Eq. (1), where for this model it is straightforward to calculate \( \Phi_{\alpha\beta} = \sum_n c_n^\alpha c_n^\beta e_n^\alpha e_n^\beta Q_n^\alpha Q_n^\beta \), where the sum is over all sites \( n \), \( n' \), and \( n'' \). In Fig. 3b we compare the vibrational energy transfer rate in the glass to the energy transfer rate in the helices at \( T = 45 \) K. For the cubic anharmonic coefficients of the glass we have chosen \( c/a = \frac{1}{3} \AA^{-1} \), which yields energy transfer rates that above 300 cm\(^{-1} \) agree well with the transfer rates of the helices. In Fig. 3c we plot the energy transfer rate of the model at 45 and 135 K. The transfer rate becomes less dependent on temperature with increasing mode frequency, the same trend as in Fig. 3a for the helices. As mentioned earlier, the small temperature dependence of the energy transfer rate of the higher-frequency modes implies that almost no energy decays to the low-frequency modes of the glass, and is a consequence of localization. In a 1D glass energy flows from a mode with frequency \( \omega_\alpha \) to pairs of modes in resonance with mode \( \alpha \) whose frequencies lie largely in the range \( \omega_\alpha/3 \) to \( 2\omega_\alpha/3 \) [11].

These results imply that energy transport in \( \alpha \) helices of proteins is not particularly efficient. If, optimistically, a wave packet could travel coherently over the localization length, \( \xi \), we could estimate the energy diffusion coefficient as \( D(\omega) = \xi^2 W \). For modes involving backbone vibrations we find four residues participating in a vibration, reasonably consistent with the estimate of 8 \( \AA \) by Hamm et al. for \( \xi \) corresponding to modes of the amide I band of the globular peptide scyllatoxin [7]. Then if energy transfer rates are somewhat less than 1 ps\(^{-1} \), we could expect \( D = 50 \frac{\AA^2}{ps} \). In fact, \( D \) is probably smaller. In a 1D glass the mean-free path, \( l \), for sound waves is shorter than \( \xi \), by an order of magnitude for models studied [17]. If \( l = 1 \) \( \AA \) and \( c = 10 \frac{\AA}{ps} \) [4,7], then \( D = l^2 c = 10 \frac{\AA^2}{ps} \). In their time-resolved spectroscopic study and analysis of heat flow through myoglobin, Hochstrasser and co-workers take \( D = 15 \frac{\AA^2}{ps} \) to arrive at the observed time of 20 ps for much of the energy to transfer from the heme through the globin and out to the surrounding water, which is consistent with the smaller estimate for \( D \). Recent molecular dynamics simulations [18] reveal that the faster component of water heating that is observed, about 7 ps [5], arises from direct contact between the isopropionate groups of the heme and water and so does not involve energy flow through the helices. Earlier molecular dynamics simulations [19] on cytochrome c also revealed no particular preference for energy propagation through well-defined secondary structures.

In summary, we have calculated rates of vibrational energy transfer in the five largest \( \alpha \) helices of myoglobin. Variation of the energy transfer rate with mode frequency is mimicked by that of an anharmonic one-dimensional glass. The temperature dependence of the energy transfer rate in the helices and the 1D glass is similar, particularly for helix modes involving backbone vibrations; differences are observed for the transfer rate from modes localized to side chains of the helix. Energy transfer in the helices, as in the 1D glass, occurs predominantly by hopping of localized vibrations (locons) along the chain resulting from anharmonic coupling of spatially overlapping localized modes in resonance. The frequencies of normal modes localized to nearby regions of a 1D glass generally lie far apart. For this reason, little direct energy transfer from high- to low-frequency modes occurs in the helices, as indicated by the typically small temperature dependence of the rate at higher frequency, and consistent with the observed [6] weak temperature dependence of the amide I band.

This work was supported by the Camille and Henry Dreyfus Foundation and by the National Science Foundation (NSF CHE-0112631).

---