

Protein charge transport in gas phase

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Abstract

We propose a local heating method via molecular dynamic simulation to investigate the charge transport efficiency along a polypeptide chain in the gas phase. In the protein charge transfer process, the carbonyl groups next to a C_{α} -hinge collide with each other. Within a critical contact distance between O–O atoms, charge starts to transfer otherwise the charge being at rest. This is termed a bifunctional model. In the gas phase and in the low temperature limit, the rotational energy can be transferred with very high efficiency and hence one obtains high charge transport efficiency. (Int J Mass Spectrom 219 (2002) 73–77)
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1. Introduction

Signal transport in proteins is a topic of general interest in biological systems. The transport of charge within the protein structure can be one of the important ingredients of such a process. A second process is the eventual conversion of this signal into a chemical reaction to generate the species of interest [1]. This is a fundamental process in a biological system, which engenders a distal reaction—a reaction at a distance [2]. The charge transport in a real protein, like the α -helix (myoglobin) and the β -sheet (azurine), have been studied, for example, in Gray's experiments [3] which showed that in water the protein β -sheet has somewhat higher efficiency than for the α -helix. The efficiency of charge transport along protein is described in terms of β -value, which is a parameter derived from the super-exchange model [4] that is a

hopping model for electron transfer through sequentially bonded sites. In aqueous system, we find a barrel effect around the protein, which produces lower charge transport efficiency than for the isolated structure.

For a polypeptide chain, each C_{α} -atom contains an N-side and a C-side. The torsional angles around the C_{α} -hinge are confined in a subregion inside the phase space ϕ and ψ defined by the Ramachandran plot, such as that found for the α -helix and β -sheet. When the residue number of a polypeptide chain is larger than four, then the secondary structure of protein is formed and it is now important to define the motion of the torsional angles. To consider the charge transfer process, our model [5] suggests that the charge is locally excited at the C-side of one of the C_{α} -atom, it could propagate between two connected amino acids through O–O atoms collision around the C_{α} -hinge within a certain contact distance or angle [6].

Our previous work [5] for charge transport illustrates that the motion of the torsional angles ϕ and ψ

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can be mapped into a virtual Brownian particle moving inside the Ramachandran plot with a gate. This subregion with a gate part is considered by Baranov and Schlag [6] and is abbreviated as BS box. Hence, the dynamic behavior of charge transport along a polypeptide chain is described by a sequential hopping between several connected BS boxes [7]. In this case, the escape process inside the BS box is a waiting (or rest) process. When the virtual Brownian particle reaches the gate part, the nearby carbonyl groups contact each other, i.e., charge starts to transfer (or fire). This “rest” and “fire” mechanism is called a bifunctional model. In this respect, the corresponding rotational motion of the carbonyl group along the $C_\alpha N$ and $C_\alpha C$ axes of the C_α -hinge dominates the charge transport process. Note that the vibrational mode is not affected at such short time, say on a 150 fs scale.

In this paper, we employ our bifunctional model further to explicitly explain the physical mechanism of the high efficiency observed by Schlag and coworkers for charge transport along a polypeptide chain in the gas phase [8–12]. In their work, laser pulse is applied to excite the C-terminus of the polypeptide chain, after which the charge could migrate to the N-terminus of the polypeptide chain with high efficiency, provided the energetics are satisfied. The experimental temperature is 50–100 K. Under such low temperature condition, the conformational change of the polypeptide chain is quite small and the degrees of freedom involved are few. In this regime, since the vibrational modes are not turned on yet, only the motion of the ϕ and ψ torsional angles are of interest. The motion of the torsional angles in BS box is then ballistic. We apply our bifunctional model and show that a sequential transfer of energy through polypeptide chain has very high efficiency.

2. Molecular dynamic simulation method: local heating

In our previous work [7], we have studied the escape time of the Brownian particle inside a two-dimensional finite box with a static gate. Meanwhile,

we not only adopted molecular dynamic (MD) simulations and demonstrated the concept of the BS box, but also calculated the first passage time (fpt) distribution of $(\text{Gly})_n$ polypeptide chain at temperature 2000 K. This is a global heating procedure and the thermal energy corresponds to the charge energy. In our MD simulation work, we allow the entire small polypeptide chain to be globally heated at 2000 K, and hence many of phonon modes are pumped and make for large-scale fluctuations (Fig. 3 of ref. [5]).

In the present paper, we perform a special local heating method. By using this method, not only can the extra phonon modes created by global heating simulation be removed, but most importantly the concept of Brownian motion inside the BS box can be kept intact. In this section, we briefly summarize our local heating method, and calculate the first passage time distribution without including extra phonon modes.

Firstly, we assume that the angular velocity of the rotational axis along $\vec{C}_\alpha N$ vector is $\vec{\omega} = (\vec{C}_\alpha N / |\vec{C}_\alpha N|) \times \omega$, where a rotational energy $1/2 I \omega^2$ (in unit of thermal energy) is provided to the atoms attached to the ψ -axis, i.e., C, O, and H atoms, and I is the inertial moment. Here the unit of ω is converted into MD velocity. In our MD simulation, we provide a charge energy $E = 1/2 \omega^2$ to the atoms attached to the ψ -axis. Here the charge energy or excitation energy E is expressed in units of thermal energy. The remaining atoms in the polypeptide chain are kept at 300 K the same as the background temperature. We employ more than 3000 configurations to calculate the first passage time distribution. When the distance of O and O atoms between two connecting amino acids is close to a crucial value of about 2.8 Å, we call this a successful collision, in other words, the charge transfer occurs. This critical distance is obtained by an ab initio computation in [6]. Note that we define the efficiency as the ratio of the successful configurations to the number of total configurations before the vibrational modes set in. The simulation time is within 1 ps.

In our simulation, a modified CHARMM 24 program [13] has been employed and implementing the

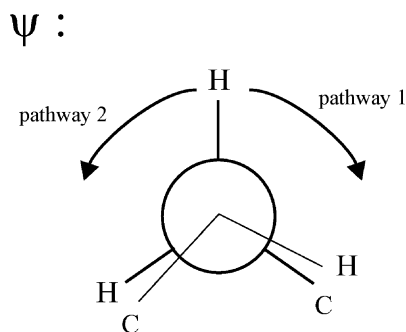


Fig. 1. A scheme for the local heating rotational direction along the ψ -axis of a C_α -hinge.

local heating method already described. The force field is based on CHARMM and includes the all-atom interaction. We employ an instantaneous heating up procedure in about 3 fs or within three molecular dynamic steps. Energy is propagated along the polypeptide chain down to the next nearby C_α -hinge.

Three different kinds of rotational direction (Fig. 1) have been chosen such as positive (pathway 1), negative (pathway 2) and mixed (or random) pathway 1+2 rotation around the ψ -angle. For a random polypeptide chain, the direction of rotation does not show any effect. However, for a native initial configuration, the rotational direction or pathway determines the mean free path or mean free time [14].

The virtual particle motion inside the BS box follows a stochastic process. Our global heating method reveals a large-scale fluctuation of the polypeptide chain and a vast number of vibrational modes are excited. The first passage time distribution of the O–O atoms collision contains the escape process and the vibrational motion at the high temperature. However, the newly developed local heating method depresses the vibrational modes and keeps only the escape process in the Ramachandran plot. For an escape process inside a two-dimensional box with a static gate, the mean first passage time for the escape process, $\tau = \sqrt{2}2\pi/\theta$, is obtained by solving the two-dimensional Smoluchowski equation with radiation boundary conditions where the gate part is situated at the perimeter of the two-dimensional disk and is expressed by the ratio of the gate to the total perimeter length [7]. Here

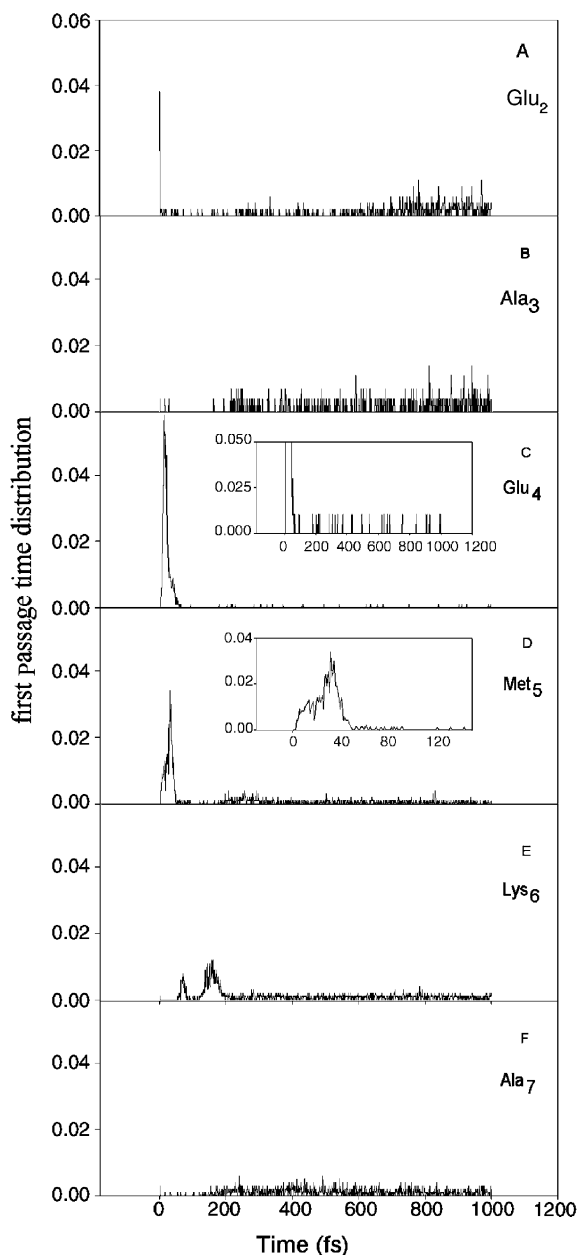


Fig. 2. Plot of first passage time distribution vs. time. In this MD simulation, we provide $E_{1667\text{K}}$ energy to the C-side of Glu₄ (local heating site) and pick up 3000 configurations to obtain the fpt distribution curve. Since the direction of the rotational motion is along the Pep7 chain from its C-side to N-side, the energy propagates forward to Ala₇. At the initial local heating site, there exist a strong sharp peak C. The successive residues show the existence of the peaks in (D–F). The shifting of the peaks in (D–F) confirm the energy transfer.

θ is the maximum gate-opening angle. Moreover, the distance decay factor or β -value can be expressed in terms of the efficiency as $\beta = -\ln(\text{efficiency})/3.7$ assuming an inter-peptide linkage at 3.7 Å.

Our local heating MD simulation result shows that a decreasing efficiency is obtained at intermediate residues away from the excited residue at 300 K. Most importantly, we observe that the charge transfers efficiently before the energy is dissipated.

3. Result and discussion

In order to demonstrate the energy flow along the polypeptide chain, we pick up a small polypeptide chain with seven amino acids (Pep7: Thr₁–Glu₂–Ala₃–Glu₄–Met₅–Lys₆–Ala₇–OH) extracted from a myoglobin (D-helix) crystal structure (protein code

“1mbd” from the protein data bank; National Institute of Standard and Technology). In the MD simulation, the initial configuration of the Pep7 is minimized first (Fig. 3). The local heating excitation energy is about 150 meV ($=E_{1667\text{ K}}$). In order to resolve the energy flow, the polypeptide chain temperature is not renormalized. We study the energy flow along the chain by examining the first passage time distribution. Meanwhile the high efficiency of the successful O–O collision at each residue after local heating is observed.

In Table 1, we list the efficiency at each site. Along the pathway 1 in Fig. 1, the efficiency is high. The detailed physics is clearly shown in the fpt distribution curve in Fig. 2 where we locally excite the C-side of the C_α -hinge at Glu₄. Its efficiency decreases at intermediate residues away from the local heating site. Since we locally heat Glu₄ from its C-side to its N-side along the peptide chain Pep7,

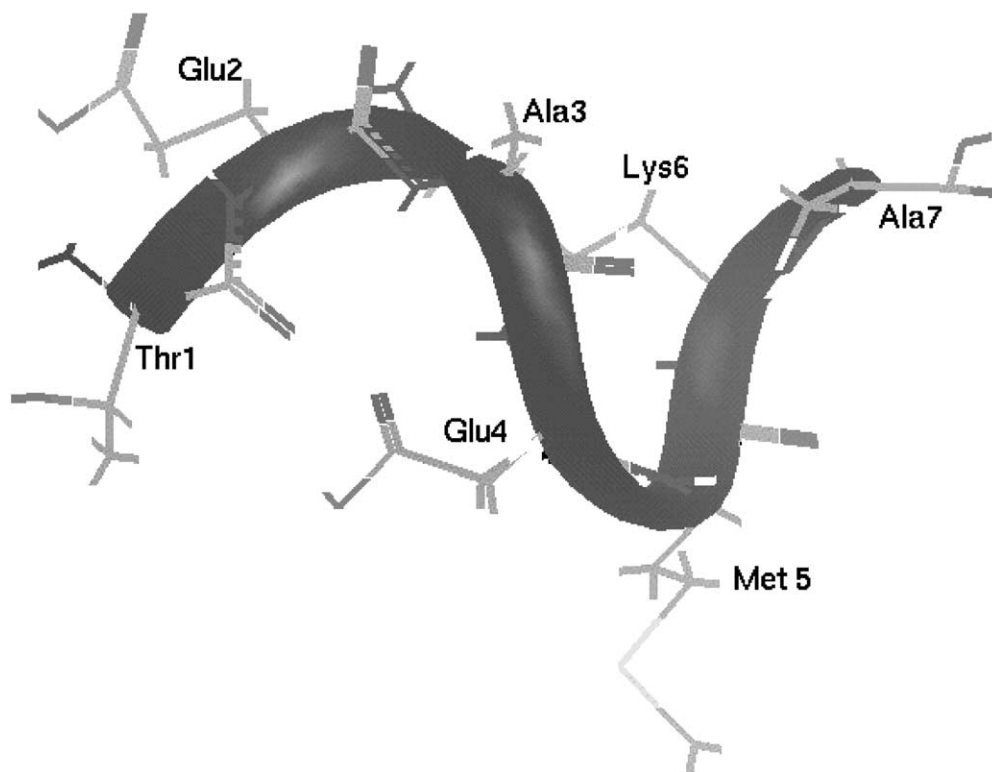


Fig. 3. The initial conformation of the polypeptide chain Pep7 cut from myoglobin α -helix structure.

Table 1
Efficiency at each site away from the local heating site

Residue no.	Efficiency ^a
2	0.13349
3	0.07901
4	0.8668
5	0.3919
6	0.46805
7	0.27867

^a Local heating site: Glu₄. Local heating energy = $E_{1667\text{K}}$. Background temperature = 300 K. Pep7: Thr₁–Glu₂–Ala₃–Glu₄–Met₅–Lys₆–Ala₇–OH.

the fpt distribution curve has very sharp peak at initial time, which corresponds to the driven motion of the carbonyl group. The successive groups such as Met₅, Lys₆ and Ala₇ also show peaks after the propagation of the peak at Glu₄. In other words, the peaks position in Fig. 2D–F are shifted to the right. This strongly supports the notion of energy transfer along the polypeptide chain. Other residues such as Ala₃ and Glu₂ are not along the excitation direction and only receive the bouncing effect after Glu₄ having been excited. Moreover, Ala has a very small side group, its behavior differs from other amino acid and its fpt distribution curve contains no sharp peak.

4. Conclusion

In summary, we have studied the charge transport and energy transfer in polypeptide with a special version of a MD program, which permits local heating. This confirms the distal reaction scheme. This interesting behavior is a direct result of the intrinsic charge transport process within a polypeptide as represented by our bifunctional model. In the gas phase,

the polypeptide chain shows a high efficiency in its charge transport behavior. Our molecular dynamic simulation results again confirm the bifunctional behavior of the charge transport process in gas phase as a ballistic process.

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