Detecting conformational change by current transport in proteins: the case of bacteriorhodopsin monolayers

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Abstract. Recent experiments on the light receptor bacteriorhodopsin have revealed the protein conductive properties and connected them to its sensing action. In particular it was shown that the super-Ohmic I-V characteristic acquired in dark, changes in the presence of green light, with an enhancement of current at increasing bias values. Here we propose a current transport model for proteins able to reproduce experimental data, mainly the dependence of current on their three dimensional (tertiary) structure. The model is based on a resistance network model and implements a tunneling mechanism of charge transfer between the amino-acids constituting the protein.

1. Introduction

Charge transport in biological materials is a topic receiving much attention both from a theoretical and an experimental point of view [1]. In doing so, new techniques have been developed, both to perform measurements and implement theoretical models [2, 3, 4]. In this respect, particular attention was devoted to proteins, which are quite interesting for their function-topology correlation. Among proteins, recently some experiments have investigated the charge transport characteristics of the light receptor bacteriorhodopsin (bR). This protein is present in the purple membrane of Halobacterium salinarum, which is organized as a 2D crystal lattice with a thickness of about 5 nm (the protein size). Furthermore, monolayers of bR are enough easy to be manipulated for experimental testing [3] being very stable under external stress. In particular, current voltage (I-V) characteristics were explored with two different techniques: first with an electrode-bilayer-electrode structure [5], and second within a conductive AFM device [6]. In the former measurements, the light-dependent conductivity was also explored. In the latter measurements, the transition between a direct and an injection tunneling regime was analyzed. Both experiments provided interesting hints on the protein conductivity. First, the main result of both the experiments is that a charge transport is detectable and that the current voltage characteristic exhibits a significant super-linear behaviour. The common interpretation of this behaviour is that charge transport is controlled by a tunneling mechanism [5]. Furthermore, the light dependence of the I-V characteristics reveals an enhancement of current in the presence of light, with respect to the dark case, for a fixed bias value. These
results make bR a very intriguing material for investigation also from the theoretical point of view. In this paper we present a theoretical model able to reproduce the main features of the experiments with the aim of capturing the essence of the conduction-topology correlation in proteins.

2. Model

We produce a protein backbone by mapping its 3D structure into a graph whose nodes correspond to the protein amino-acids. The position of each amino-acid is taken as that of its Cα atom, as given by the protein data bank \[7\]. Finally, two nodes are connected with a link only if their distance is less than an assigned cut-off radius \( R \). The value of \( R \) has the role of an interaction radius, and the graph is an interaction map, naturally reflecting the protein topology. Finally we fix the kind of interaction by interpreting each link as a privileged channel of charge transfer \[4, 8\], thus attributing to it a finite resistance

\[ r_{i,j} = \frac{\rho_{l_{i,j}}}{A_{i,j}} \]

where \( \rho \) indicates the resistivity, taken the same for all the amino-acids, the pedices \( i, j \) refer to the amino-acids between which the link is stretched, \( l_{i,j} \) is the link length and \( A_{i,j} \) is the cross-sectional area shared by the amino-acids:

\[ A_{i,j} = \pi \left( R^2 - \frac{l_{i,j}^2}{4} \right) \]

Accordingly, the graph becomes a resistance network. By taking appropriate contacts and applying an external bias, the electrical network is solved within a linear circuit analysis.

2.1. Direct tunneling

To account for the super-Ohmic I-V characteristics we implement a tunneling mechanism of charge transfer between amino-acids as follows. The value of the link resistivity is taken to assume two different values, \( \rho_{\text{MAX}} \) which corresponds to a nearly insulating material, and \( \rho_{\text{MIN}} \ll \rho_{\text{MAX}} \). The possibility for the link to switch from the high to the low resistivity is linked to a voltage driven tunneling mechanism through a rectangular potential barrier. For low applied voltages, we adopt the JWKB approximation for quantum tunneling, i.e. the transition probability \( P_{i,j} \)

\[ P_{i,j} = \exp \left[ -\frac{2l_{i,j}}{\hbar} \sqrt{2m(\Phi - \beta eV_{i,j})} \right] , \quad \Phi > eV_{i,j} ; \quad (1) \]

where \( V_{i,j} \) is the potential drop between the couple of \( i, j \) amino-acids, \( \Phi \) is the potential barrier and \( \beta \) a numerical parameter accounting for the geometrical shape of the barrier, here taken as \( \beta = 1 \). For \( \Phi \leq eV_{i,j} \) \( P_{i,j} = 1 \), i.e. all the charges are transmitted through the barrier, and this condition determines the value of \( \Phi \).

In this way, charge transport across the protein is modelled as a sequential direct tunneling mechanism over distances of a few Å, which we believe to be more feasible than a single tunneling across the 5 nm entire protein. Furthermore, the model is able to produce different responses with respect to different conformations, i.e. different illumination conditions.

2.2. Fowler-Nordheim tunneling

In the presence of intense applied voltages, the approximation of rectangular potential barrier is no longer valid, and the barrier is better described by a triangular or round triangular shape. The semi-classical approach to this problem furnishes the Fowler-Nordheim (FN) tunneling probability \[9, 6\]:

\[ P_{FN}^{ij} = \exp \left[ -\left( \frac{2l_{i,j}\sqrt{2m}}{\hbar} \right) \frac{\Phi}{eV_{i,j}} \frac{\Phi}{2} \right] , \quad \Phi \leq eV_{i,j} ; \quad (2) \]

which leads to a \( \ln(I/V^2) \propto 1/V \) behaviour. At low bias, the direct tunneling probability, Eq. (1) can be also used \[9\]. In this case the value of \( \beta \) which provides the two regime matching
is $\beta = 1/2$ (triangular barrier). Notice that this choice leads to an overestimation of $\Phi$ with respect to the rectangular shape. As a matter of fact, the condition $eV_{i,j} = \Phi$ only separates the direct from the FN regime, while the direct probability goes to unity for $eV_{i,j} = 2\Phi$. In this model, the continuous transition from direct to FN tunneling is reproduced by the relation:

$$
\rho(V) = \begin{cases} 
\rho_{\text{MAX}} & \Phi > eV \\
\rho_{\text{MAX}}(\frac{\Phi}{eV}) + \rho_{\text{min}}(1 - \frac{\Phi}{eV}) & \Phi \leq eV 
\end{cases}
$$

(3)

Accordingly, in the presence of a FN tunneling, the resistance link takes the $\rho_{\text{min}}$ value, otherwise, it takes the $\rho(V)$ value.

2.3. Materials
To model bacteriorhodopsin we have taken the protein data base (PDB) entries 2NTU and 2NTW which label the native (in dark) and activated (in green light) states, respectively [7]. These are not the only protein representations given in PDB but, being obtained under the same experimental conditions [8], they are considered as the most reliable. In any case, the model was tested also on protein representations in different activation states, like those labelled 1M0K-1M0M, and the results were found to be compatible with those reported here.

3. Results
Figure (1) reports the comparison between experimental data [5] and theoretical calculations performed with two different barrier heights $\Phi = 59$ meV and 53 meV, respectively. Because of the symmetry of simulated data with respect to the transformation $V \rightarrow -V$, we report the 59 meV data for positive bias and the 53 meV data for negative bias. Despite of the small difference in the barrier values, calculations produce significant different resolutions at $V=1$ V, which the maximal current response given by experiments corresponds to. In particular, Fig. (1) shows a larger resolution for the smaller $\Phi$ value, while the behaviour of the native state is better reproduced by the larger $\Phi$ value. Furthermore, data reported in Ref. [5] suggest large error bars on experimental curves (up to 50 %), so that our estimation of the barrier height has to be considered as indicative [4].

Since charge transport in disordered organic materials can be described as due not to a single but to a Gaussian distribution of potential barriers [1, 10], we have calculated the I-V characteristics by using a Gaussian distributed $\Phi$ values within an average value of 59 meV and two dispersion $\sigma$ values: $\sigma = 19$ meV, 94 meV, respectively. The results are reported in Fig. (2) where we can appreciate an effective improvement of the fit for the large dispersion. Finally, we have also considered the case of a high voltage where the FN tunneling becomes dominant, as reported in Ref. [6]. In doing so, as fitting parameter we have found a potential barrier higher than in the previous case, $\Phi = 194\pm25$ meV. This larger value of $\Phi$ is mainly due to the choice of a triangular barrier and also the difficulty to compare the results of two, so intrinsically different, experiments [5, 6]. Figure 3 reports the fitting data of experiments [6] and also the calculated values for the representation of the activated state 2NTW. In the inset we can appreciate the current enhancement in the range 0-1 V, which is the same of that observed in ref.[5], although the absolute value of the currents is lowered by a factor of three. The origin of this discrepancy is attributed to the different experimental procedures.

4. Conclusions
We have presented a resistor network model to investigate the correlation between a conformational change and the variation in electrical transport of a sensing protein. To this purpose we have investigated the change of the static I-V characteristics. The theory is validated
on recent experiments carried out on layered structures of bR, a light-activated protein, which evidences a substantial increase of the current, at a given voltage, when passing from dark to the presence of a green light. Even if remaining mostly qualitative, the best agreement with experimental data is obtained when considering a maximum interaction radius of 6 Å and an average barrier energy of 59 meV with a Gaussian distribution. Furthermore, taking advantage of its flexibility, the model is implemented by introducing the FN tunnelling and shown able to reproduce satisfactorily the experimental data of [6], but with a barrier energy of about 194 meV, significantly higher than that of direct tunneling through a rectangular barrier. At present this discrepancy remains an open problem which needs further investigation.

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