Proteotronics: application to bacteriorhodopsin receptors

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1. Introduction

Recent advances in science and technology, such as the development of techniques and devices for health care and green and renewable energy, are the successful products of the synergy among different disciplines. Therefore, a more comprehensive methodological approach is required, integrating and making more powerful chemical, computational, biological, engineering and physical strategies [1–4]

In particular, we focus on proteotronics, a new emerging discipline aiming to propose and develop innovative electronic devices, based on the selective action of specific proteins.

The paper presents the application of proteotronics in the case of the light receptor bacteriorhodopsin (bR). Bacteriorhodopsin is a protein found in a primeval organism, the Halobacterium salinarum, specifically in a part of its cell membrane called the purple membrane (PM). This membrane is a very thin lipidic film of 5 nm, about the protein height, and shows a quite stable structure. Bacteriorhodopsin is able to convert the sun light into an electrical potential across the host cell membrane. In doing so, the conjugated dye, the retinal, changes its structure, also inducing the complete protein conformational change. Several experiment have analyzed bR, in vitro, both in dark and light.It has been observed that the light protein activation may produce an enhancement of the current as large as the 100% [5]. In the perspective of a future use of this protein in solar cell and green energy production, this outcome is of extraordinary relevance.

The aim is to test the possibility of recovering the activity of this protein outside its natural environment and finally to convert the activation due to light into an electrical signal useful for technological applications and green energy production.

2. Theory

The protein structure-function correlation is here interpreted at the amino acid level, building a graph whose nodes correspond to the amino acid. Each node contains several data, like the amino acid position, taken by the public data banks [6], and its electrical polarization in terms of a specific dielectric constant [7]. These data are used to assign the links between nodes that are associated with an elemental impedance responsible of charge transfer. The procedure to construct the analogous network of the protein requires two steps. In the former, an interaction radius (RC) is assigned. It determines the degree of the graph, because two nodes are connected only if the physical distance between the corresponding amino acids is less than RC. In such a way, the resulting graph has a small-world structure [8], as shown in Figure 1. Furthermore, this kind of network preserves the memory of the protein structure, i.e. it changes if the protein 3D structure changes. In the latter step, the protein function is then introduced, by attributing to the links the role of a specific physical interaction. In present case, it is an electromagnetic interaction, that describes the response of the protein to different electrical solicitations, thus the links correspond to elementary impedances.

In particular, since we are interested in monitoring the impedance *variation* due to the protein activation, we use the impedance of a simple RC parallel circuit, like the couple CPE-Rp in the Randles cell.

Finally, the elemental impedance between the i,j-th nodes is :

$$Z_{i,j} = \frac{I_{i,j}}{A_{i,j}} \frac{1}{\rho^{-1} + i\epsilon_{i,j}\epsilon_0\omega} \qquad (1)$$

where $A_{i,j} = \pi(R_C^2 - I_{ij}^2/4.0)$ is the cross sectional area between two spheres of radius R_C centered on the i-th and j-th node, respectively; $l_{i,j}$ is the distance between these centers, ρ is the resistivity, taken to be the same for each amino-acid ;

$i = \sqrt{-1}$ is the imaginary unit, ϵ_0 is the vacuum permittivity, ω is the circular frequency of the applied voltage. The relative dielectric constant of the couple of i-th and j-th amino-acids, $\epsilon_{i,j}$ is expressed in terms of the intrinsic polarisability of each amino acid. The network is connected to an external bias by using ideal contacts on the first and last amino acid and solved by using standard techniques.In particular, analogously to the well known Hodgkin-Huxley model, the problem statement consists in a set of linear equations whose solution is performed by a computational procedure, based on the Kirchhoff's laws. The network global impedance spectrum is represented by a Nyquist plot for each configuration of the protein 3D structure. The role of the interaction radius, RC, is still an open problem. Recent investigations strongly suggest that it is related to the level of protein activation [9,10] and in the following this conjecture is used to interpret experiments.

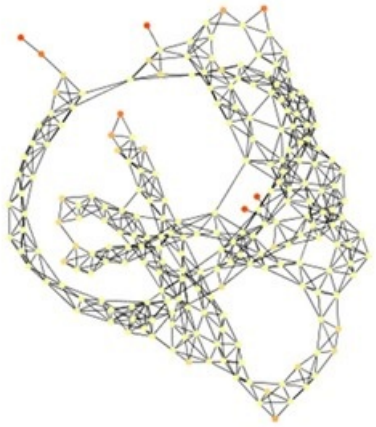

Figure 1. Graphical represantation of bacteriorhdospin in its native stata. Network is obtained by using $R_v = 6$ Å.

3. Results

The discussion of the results takes into account the findings of investigations focused on the measurement of the current-voltage (I-V) characteristic in static conditions, particularly stable for bacteriorhodopsin toward thermal, mechanical and electrical stress [5,11,12]. The protein shows a medium-gap conductivity in dark which can be significantly enhanced by light. The observed I-V characteristics are super-linear, and this feature becomes more evident by increasing the applied bias. Therefore, the charge transport across the protein is mainly attributed to a tunneling mechanism. Tunneling can be described like the crossing of rectangular barriers at low bias (direct tunneling), or the crossing of triangular barriers (injection tunneling), at high bias. In the latter regime, a growth of the protein current of about 5 orders of magnitude has been observed [11]. All these impressive features require a deep investigation about the microscopic origin of the responsible mechanisms. Furthermore, they have arisen great expectations in technology, so inspiring, for example, the realization of a Grätzel cell [13] based on it [14].

In Figure 1, the plot of the protein graph, drawn by using $R_C = 6$ Å, is reported.

The I-V characteristics of bR in dark and light have been calculated by using the aforementioned theoretical approach. In particular, the model parameters have been tuned on the data given by [11], which cover the largest bias range. In such a way, the experiments have been reproduced with good accuracy [7]. Data in light were given by [5] in the range 0-1 V. A fine agreement with these data has been found by taking into account the multiple effects that light produces on a sample of light receptors. In particular, light irradiation transfers energy to the single protein by means of two basic processes: (i) the protein activation, specifically the change of its 3D structure consequent the ligand capture; and (ii) the protein excitation, specifically the increasing of its free-energy without conformational change [10]. In the framework of proteotronics, we introduce process (i) by changing the 3D protein structure input, while process (ii) is described by changing the value of RC . Finally a sample of proteins irradiated with light of appropriate wavelength experiences both the processes, with some proteins activated and some proteins excited. The percentage of activated/excited proteins has been fitted by using a Hill-like equation, and it is associated with a specific value of RC [10]. Therefore, following this scheme, the current response of bR samples has been reproduced by using a binary mixture of native and active states: (i) the sample in light corresponds to $R_C = 6.3$ Åwith 96% of activated proteins,(ii) the sample in dark corresponds to $R_C = 5.8$ Å and 100% of proteins in the native state. By using these guidelines, we reproduce the photocurrent measured in experiments.

Furthermore, the theoretical approach is able to foresee photocurrent over a larger (a priori, arbitrary large) bias range. At present only the bias range described in the inset has been explored by experiments [5].

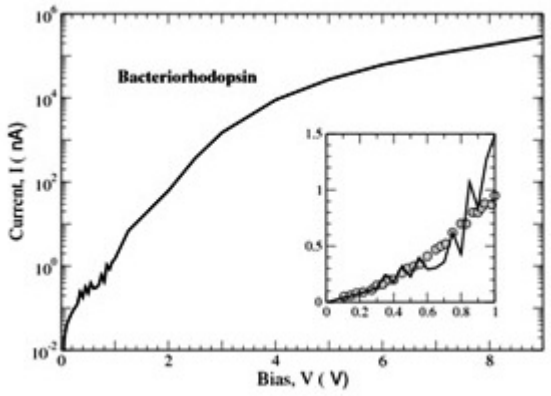

Figure 2. Photocurrent for the bacteriorhodospin, calculated as described in the text. In the inset, the same data in the bias range 0-1 V and the experimental outcome (circles) [5].

3. CONCLUSIONS Proteotronics is an emergent branch of electronics, able to describe the electrical properties of proteins. The model is physically plausible and sufficiently flexible to be tailored for describing different experimental conditions. Here bacteriorhodopsin protein receptor is investigated, with promising chances of being used in developing a new generation of electronic devices for technological applications and green energy production. The results are also of basic interest in advancing the present knowledge on the microscopic mechanisms responsible of protein functioning inside living cells.

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