Electrochimica Acta 140 (2014) 83–95

Contents lists available at ScienceDirect

Electrochimica Acta

journal homepage: www.elsevier.com/locate/electacta

Nanoscale charge transfer in redox proteins and DNA: Towards biomolecular electronics

Juan Manuel Artés[a,b,*], Montserrat López-Martínez[a,b], Ismael Díez-Pérez[b,a], Fausto Sanz[a,b,c], Pau Gorostiza[a,c,d,*]

[a] Institute for Bioengineering of Catalonia (IBEC). 15-21 Baldiri Reixac 08028 Barcelona, Spain
[b] Physical Chemistry Department, University of Barcelona (UB), 1-11 Martí i Franquès, 08028, Barcelona, Spain
[c] Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)
[d] Institució Catalana de Recerca i Estudis Avançats (ICREA)

ARTICLE INFO

Article history:
Received 15 December 2013
Received in revised form 16 May 2014
Accepted 16 May 2014
Available online 27 May 2014

Keywords:
Bioelectrochemistry
Charge transfer
Biomolecular electronics
Single-molecule junction
Nanobiodevice

ABSTRACT

Understanding how charges move through and between biomolecules is a fundamental question that constitutes the basis for many biological processes. On the other hand, it has potential applications in the design of sensors based on biomolecules and single molecule devices. In this review we introduce the study of the electron transfer (ET) process in biomolecules, providing an overview of the fundamental theory behind it and the different experimental approaches. The ET in proteins is introduced by reviewing a complete electronic characterization of a redox protein (azurin) using electrochemical scanning tunnelling microscopy (ECSTM). The ET process in DNA is overviewed and results from different experimental approaches are discussed. Finally, future directions in the study of the ET process in biomolecules are introduced as well as examples of possible technological applications.

1. Introduction

The question of how charges move through molecules has fascinated scientists for decades. The electron transfer (ET) process is the basis of most chemical reactions and biological processes. [1] Examples of these biological processes include cellular respiration, photosynthesis, DNA oxidative damage and most of the enzyme-catalyzed reactions. Thus, understanding the fundamental laws governing ET is important to understand chemical and biological processes. In addition, this knowledge could lead to interesting technological applications.

Most of the diagnostic tools in human health as well as biosensors involve the detection of biomolecules. This detection is usually carried out using different molecular biology techniques combined with optical detection. However, many of them are laborious, time-consuming, expensive and require labile natural products. An electronic readout would be very advantageous, i.e. through the measurement of the "signature" conductivity of individual biomolecules. The systematic measurement of the electrical conductivity of different biomolecules could pave the way for the design of electronic diagnostic tools; improving the sensitivity and reducing the costs of these tools.

On the other hand, the electronic properties of biomolecules combined with their self-assembling capabilities make these molecules promising candidates as building blocks in the emerging field of molecular electronics, a discipline focused on building electronic circuits and devices at the nanoscale using single molecules. [2]

In this review we introduce the study of ET in biomolecules, provide some introductory theoretical background, review the different experimental approaches used to study ET in biomolecules and present an exhaustive study on the ET process involving azurin using electrochemical scanning tunneling microscopy (ECSTM) and related techniques.

2. Charge transfer mechanisms

In order to understand the ET process in biomolecules we will first introduce some fundamentals about charge transfer theory. The subtleties of the ET are governed by the coupling between the charge donor and the acceptor and the decoherence involved in the process. [1,3,4] We can define two mechanisms that are widely accepted to rationalize many of the ET reactions in biomolecules:

* Corresponding authors. Electrical and Computer Engineering department. University of California Davis. One shields avenue. Davis 95616 CA.
E-mail addresses: jmartesvivancos@ucdavis.edu (J.M. Artés), pau@icrea.cat (P. Gorostiza).

http://dx.doi.org/10.1016/j.electacta.2014.05.089
0013-4686/

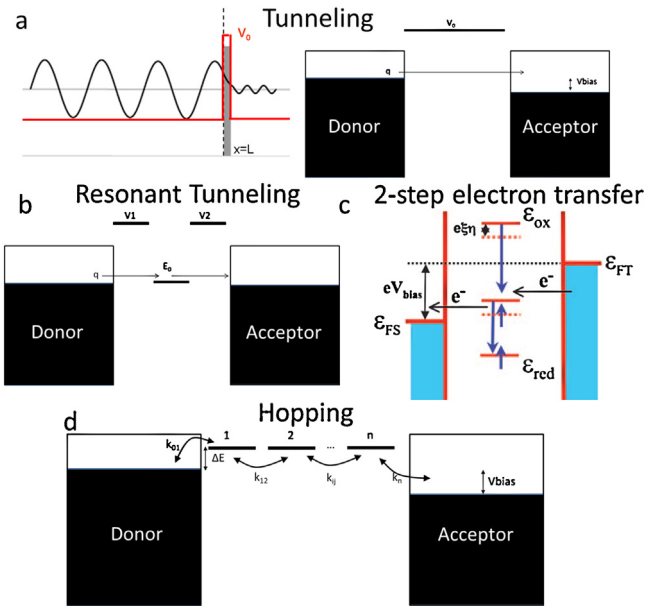

Fig. 1. Charge transfer mechanisms. a) Superexchange tunneling: (left) representation of the wavefunction in a tunneling junction, and (right) energy diagram for a donor acceptor system where a charge q crosses an energy barrier V_0.
b) Resonant tunneling. Energy scheme for a donor acceptor system where the charge crosses a double barrier system (V1 and V2) with a localized state E_0 in the tunneling gap.
c) Two step ET. Schematic energy diagram of the ECSTM showing the relative energy levels of the substrate, the tip, and the redox molecule. ε_{FS} and ε_{FT} denote the Fermi levels of the substrate and the tip, respectively; the energy levels of the redox molecule at the oxidized and reduced forms are represented by εox and εred, respectively. Reproduced with permission from 14, copyright National Academy of Sciences 2005.
d) Hopping. A charge undergoes a thermally activated ET transfer through different states (1,2,...n) in the donor acceptor gap.

tunneling and hopping. In many cases, a combination of both or intermediate situations are found in the ET process involving certain biomolecules. [4,5] In the following sections we overview these two mechanisms and others derived from them that are commonly used in the study of ET in biomolecules. For a more exhaustive description of these concepts we refer the interested reader to books [6] and recent reviews. [3,4,7]

2.1. Tunneling

Most of the biomolecules are assumed to be insulators and, according to classical mechanics, they should constitute an impenetrable energy barrier for a colliding charge. The quantum mechanical effect known as tunneling explains how charges can be transferred efficiently between and through small biomolecules. When a charge hits an impenetrable barrier of nanometric size (see Figure 1a, left), the situation can be described using the time-independent Schrödinger equation. [8] At the left of the potential barrier in fig. 1a, the wavefunction has a sinusoidal behavior. At x = 0, the potential jumps abruptly to a value higher than the energy of the particle and, according to classical mechanics, the particle should not cross. The Schrödinger equation imposes that the wavefunction cannot go to zero abruptly (the wavefunction and its derivative must be continuous and defined at all points). Thus, it can be shown that the wavefunction decays exponentially in the barrier (0 < x < L in fig. 1a). This is the basic expression for electron tunneling and it was confirmed experimentally. [9] The current through the tunneling junction can be described with a function where the rate of ET (k_{ET}) depends on the distance between donor and acceptor (x):

$$k_{ET} \propto e^{-\beta X} \tag{1}$$

The key parameter in this relationship is the distance decay factor β, and it is characteristic of the medium between donor and acceptor. [3,10] An analogous expression can be used to obtain the conductance of a molecule (G) bound between electrodes (fig. 1a, right) in a moderate voltage range:

$$G = \frac{1}{V_{Bias}} = G_0 e^{-\beta d} \tag{2}$$

Where I is the current through the molecule as a consequence of the bias voltage applied between electrodes (V_{Bias}), G_0 is the conductance quantum ($2e^2/h \approx 77.5\ \mu S$), and d is the distance between the electrodes (the length of the molecule).

These expressions are extremely useful for the study of ET in several biomolecules using different techniques.

2.2. Multiple barriers: Resonant tunneling

In systems where intermediate energy states are present, the resonant tunneling model can be applied under the appropriate circumstances. Fig. 1b shows an example of a system with an intermediate energy state E_0 between two barriers. When the incident electron has the same energy as the localized state in the tunneling gap ($E = E_0$), the conductance in the junction at zero bias and ignoring electron spin can be expressed as:

$$G = \frac{4e^2}{h}\frac{k_L k_R}{(k_L + k_R)^2} \tag{3}$$

Where k_L and k_R are the tunneling rates for the first and second tunneling steps, respectively. And in the case where $k_L = k_R$ (a localized state placed symmetrically in the tunneling junction), the conductance becomes $G = e^2/h$, half the conductance of a quantum contact (G_0). Some assumptions are made to arrive to this expression and it represents an ideal case (i.e. a metallic contact between the localized level and the electrodes in the tunneling junction); normally the conductance in the junction is less than $G_0/2$ even in this resonance condition because of different factors (i.e. the resistance at the contacts).

This expression for the resonant tunneling is extremely useful for the qualitative study of molecules with localized states [11,12] and other theories and models were derived later in order to account for other effects [7] (see below).

2.3. Two step tunneling

The two-step tunneling formalism [7] accounts for two sequential tunneling steps with partial vibrational relaxation through a molecule with a localized state (see fig. 1c). The model has been extensively applied in the study of redox molecules in an electrochemical environment, [13–17] and it relates the observable tunneling current to different experimental parameters:

$$I_T = ek\rho(eV_{Bias})\frac{\omega}{2\pi}\left\{\exp\left[\frac{e}{4\lambda kT}(\lambda + \xi\eta + \gamma V_{Bias})^2\right] + \exp\left[\frac{e}{4\lambda kT}(\lambda + V_{Bias} - \xi\eta - \gamma V_{Bias})^2\right]\right\}^{-1} \tag{4}$$

Where I_T is the tunneling current, V_{bias} is the difference of potential applied between electrodes, κ is the electronic transmission, ρ is the density of states, ω is the nuclear vibration frequency, λ is the reorganization energy, k is the Boltzmann constant, T is the temperature, η is the overpotential (sample potential minus the molecule redox potential) and γ and ξ are two model parameters