Control of catalytic activity of proteins in vivo by nanotube ropes excited with infrared light

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We discuss the possibility of controlling biological systems, by exciting in the near infrared region hybrid metallic nanotube ropes, dressed with proteins and embedded in the biosystems. If one nanotube, in a double-tube rope, is filled with metallofullerenes and the other is empty, the two tubes change their opposite equilibrium charging during the irradiation. The resulting change of the local electric field can deform proteins attached to the tubes, and change their catalytic properties.

I. INTRODUCTION

Over billions of years, a fascinating internal and external complexity evolved in myriads of competing biological species [1]. For example, many bacteria and multi-cellular organisms use structure-sensitive proteins to biominerlize nanocrystals [2], that form unique nanodevices. These cold-growth techniques [3] could greatly complement growth methods developed by humans. In general, biosystems and artificial nanosystems can coexist and supplement each other in a number of other directions, in particular, during the release of drugs [4]. Their coevolution can lead to the formation of new hybrid bio-nano (BIONA) systems, with unprecedented organizational and functional level.

In this Letter, we discuss possible forms of communication between BIONA components. The (direct) “talk” from the nanosystem to the biosystem could be realized by controlling catalytic activity of its proteins. The (backward) “talk” could be done by the cells, if they change their local micro-environment or emit (electromagnetic) signals. The direct talk, that we explore here in more details, could be based on electrochemical methods, used in bioelectronics [8]. Unfortunately, these techniques require the presence of electrodes [9], that cannot be easily applied inside cells. More promising is thus their combination with contactless methods. Optical techniques [10] are convenient for their selectivity, but the sensitive interior of cells prohibits the use of large optical frequencies that can easily manipulate chemical bonds. We could thus use the fact that cells are transparent (up to 5 mm thick samples) for the near-infrared (NIR) radiation (0.74-1.2 µm).

The activity of biosystems could be manipulated via artificial nanosystems, embedded in them, that absorb in the NIR region. This approach is followed in photodynamic therapies, where tumor cells are destructed chemically, via NIR excitation of porphyrin-based molecules with many extended electronic states [11]. Similar results can be obtained by heating the system locally with ultrasound or microwave radiation or via NIR-radiation heated metallic nanoparticles [12]. Silver and gold nanoparticles [13], that can be produced biologically [14], are naturally excellent candidates for use in bio-control. In order to control tinny cellular sections, one could also think of using nanotubes. Metallic C nanotubes form sensitive detectors in liquid environments [15], and when dressed with bio-molecules, via structure-selective [16, 17] or less specific hydrophobic coupling [18], they can work as sensitive biosensors [19].

II. NIR-RADIATION CONTROL OF PROTEIN ACTIVITY

The bio-control could be elegantly realized by a hybrid nanotube rope, heated by NIR-radiation, that is formed of two adjacent metallic C nanotubes, where one is (peapod) filled with metallofullerenes [17] and the other is empty. In peapods, electrons can be transferred to/from the C$_{60}$ fullerenes under electric bias [18]. In isolated metallofullerenes like Dy@C$_{82}$, several electrons are passed from Dy to C$_{82}$. When these are used in a peapod, the transferred electrons can be passed further to the nanotube [19]. In a double-rope formed by this peapod and a “twin” (empty) nanotube, the last would absorb the excessive charge too, so the two would become oppositely charged. This process can be partly inverted at elevated temperatures [19], since the metallofullerenes have levels close to the Fermi level [20, 21].
In Fig. 1 we schematically show the NIR-control of protein (enzyme) activity, based on this process. The NIR excitation heats the two nanotubes, so that electrons, released in equilibrium from the fullerenes to the peapod and the twin tube, become transferred back. This transfer is accompanied by recharging of the tubes, and the resulting change of the local electric field causes deformation of proteins, that are selectively attached to the nanotubes. Their new conformation can be realized by moving a charged tip of one of its domains (see Fig. 2). We model this process, by evaluating first the potential energy of a charge \( q \) at the position \( \mathbf{r} = (x, y) \). The two cylinders with charge densities \( \sigma \) and \(-\sigma\) have their centers at \( \mathbf{r}_1 \) and \( \mathbf{r}_2 \), respectively. The potential energy of the charge \( q \) is formed by the direct Coulombic component

\[
V_C(\mathbf{r}) = \frac{\sigma q}{2\pi \varepsilon} \ln \left( \frac{|\mathbf{r} - \mathbf{r}_1|}{|\mathbf{r} - \mathbf{r}_2|} \right)
\]

that can be either positive or negative, depending on which of the oppositely charged tubes is closer. It also has a negative screening component, originating in the reflection of the external charge in the metallic tube, that close to the surface of both tubes has the form

\[
V_S(\mathbf{r}) \approx -\frac{q^2}{16\pi \varepsilon} \left( \frac{1}{|\mathbf{r} - \mathbf{r}_1| - r_T} + \frac{1}{|\mathbf{r} - \mathbf{r}_2| - r_T} \right)
\]

Here, we simply add the screening potentials of the two tubes, neglecting thus multiple reflections.

Typically, structural domains in proteins perform hinge or shear motion. These domains are often formed by (rigid) \( \alpha \)-helices, connected by (flexible) \( \beta \)-sheets. The structures (conformations) of deformed proteins in nature are usually close in energies, so that they can be flipped over by room temperature energies \( k_B T \). The conformations of the externally controlled proteins should have different catalytic properties and be more energetically distant, so that they are not changed at room temperatures.

In the present system, where the control of protein’s motion is realized via dynamical charging of nanotubes, we can also consider these two generic (hinge and shear) configurations, shown schematically in Fig. 2. Since, the tubes are different and become charged in equilibrium,
the proteins should be able to distinguish them and deposit on them asymmetrically (see Figs. 1-2). In the bend configuration (left), the trajectory of the controlled protein domain is practically vertical, toward one of the tube’s centers. In the shear configuration (right), the trajectory of the domain goes approximately in parallel with the vector connecting the tube’s centers of masses.

We assume that the balance of internal forces in the protein, in the presence of equilibrium charging of the tubes, adjusts the charged tip to a position \( r_0 = (x_0, y_0) \). The dependence of the protein energy around (close to) this position can be considered to be parabolic

\[
V_T(r) = V_C(r) + V_S(r) + V_R(r),
\]

where the constants \( C_x, C_y \) describe rigidity of the deformed protein \(^{23}\). Their values should be such that the difference in energies \( \Delta E \) between the used conformations is \( kT_B < \Delta E < 100 \ \text{kJ/mol} \ (1 \ \text{eV}) \), where the last value is the lower energy limit required to deform individual protein domains \(^{23}\).

**IV. DISCUSSION OF THE PROTEIN MOTION**

In order to estimate which of the configurations, in Fig. 2, can be more easily controlled, we calculate the distance over which the protein domains move during the NIR-radiation induced charge transfer. The tip moves from the equilibrium position \( r_0 \) to a new position \( r_0' \), given by the local minimum of the total potential

\[
V_T(r) = V_C(r) + V_S(r) + V_R(r),
\]

In Fig. 3 (up), we search this minimum for the “hinge” configuration, shown in Fig. 2 (left). The tube centers are located at \( r_{1,2} = (x_{1,2}, y_{1,2}) \), \( x_{1,2} = \mp 1.1 r_T \), \( y_{1,2} = 0 \). We present the dependence of the potentials \( V_C, V_S, V_R \) and \( V_T \) on the \( y \)-distance from the center of the nanotube, and assume that a unit charge \( q = e \) is at the tip of the domain \(^{23}\). The results are calculated for the (effective) charge density \( \sigma = 0.1 \ \text{e/nm} \) (equilibrium) and \( \sigma = 0 \) (irradiation). We position the domain tip at \( x_0 = x_2, y_0 = 2.5 r_T \) and use the rigidity constant \( C_y = 2 \ \text{eV/nm}^2 \). We can see that the change of the \( V_C \) potential energy, due to the induced charge transfer, is small, while \( V_S \) is rather large. With the above parameters, the \( V_T \) potential can locally compensate the steep \( V_S \), so that close to the tubes their sum is almost flat. Then, the weak \( V_C \) potential can control the position of the local minimum in \( V_T \), but the overall motion is quite small (thin and thick solid line correspond to irradiation and equilibrium, respectively). The magnitude of motion could be enlarged, if we let the \( V_T \) potential to loose the local minimum in the absence of irradiation. Then the domain position would fluctuate from being adjacent to the tube to being almost at \( r_0 \).

Such a large motion can be obtained directly in the “shear” configuration, shown in Fig. 2 (right). Here, the in-plane (of the tubes) components of the screening forces largely cancel each other, and the out-of-plane components are not effective. Thus the system responds more sensitively to the charging given by \( V_C \), as we show in Fig. 3 (down). We use parameters, \( x_0 = 0, y_0 = 1.5 r_T \) and \( C_x = 0.5 \ \text{eV/nm}^2 \), so that \( V_R \) can flatten the two-well minima of \( V_S \). In equilibrium, the tube charging causes that \( V_T \) develops a minimum, close to one of the \( V_S \) minima. During the irradiation, the charging decreases and the minimum shifts to \( x = 0 \). Since the two conformations are shifted in energy by \( \Delta E \approx 50 \ \text{meV} \), they would not flip one to another at room temperatures \( kT_B < 30 \ \text{meV} \). This domain motion is large enough to control the protein (enzyme) activity. It could open or block pockets on the “back side” of the protein, that is not exposed to the nanotube, and change the catalytic strength of the proteins.

We have demonstrated that NIR-radiation excited hybrid nanotube ropes could control the activity of proteins *in vivo*. Nanotube systems might also directly activate...
chemical reactions used in phototherapy, in particular, if special “porphyrin-like” defects are formed in the nanotube walls. In vitro, one could also bias nanotubes externally in order to control biochemical reactions or use them in other applications on the nanoscale.

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