Bio-Electronics and Bio-sensors

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Introduction

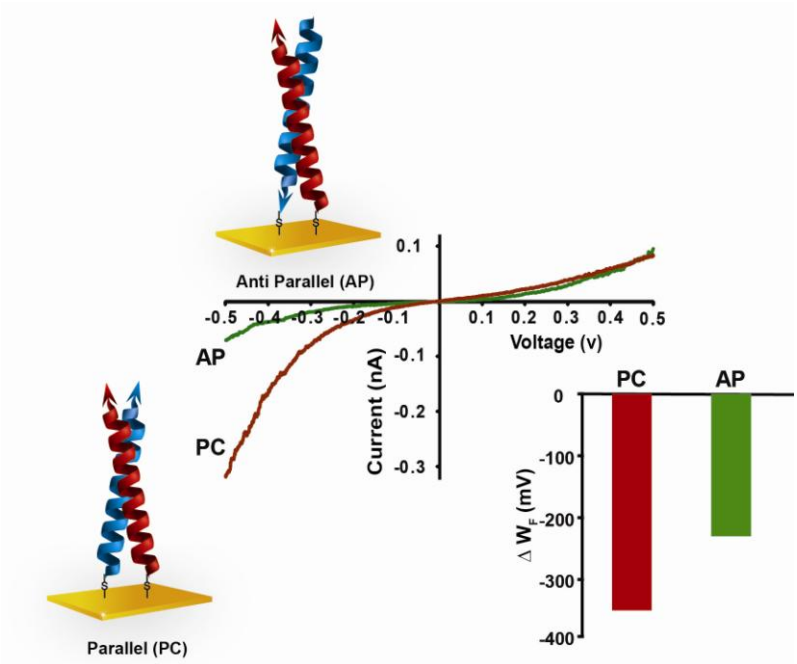
The machinery of the natural system is comprised of a large variety of functional nanometric objects mostly based on proteins. **The need to detect proteins (in applications related to healthcare, water pollution, and bio-war) on one hand, and the desire to exploit the unique properties of proteins for the preparation of novel functional materials, are the main motivations for the research in our lab.** We believe that our studies, which highlight the synergic influence of biology on nanotechnology research and *vice versa*, opens the way to the preparation of novel advanced devices, which will be either based on protein like materials or targeted at the characterization of natural proteins at the single molecule level. If you want to read more about our research refer to the links below, or read our published results.

Bio-Electronics

Proteins perform diverse functions in nature, which are commonly based on their dynamic conformation. Many of these processes involve charge transfer. We hypothesized that by utilizing *De-Novo* design approach, the unique properties of proteins can be exploited in the fabrication of novel electronic materials. Thus far we have tested this hypothesis using two common protein motifs, α - helix (link to coiled coil section) and β - sheet (link to Nanotubes and fibers section), as building blocks for the designs of synthetic proteins. In such designs the synthesized peptides self-assembled and fold into a desired functional material structure. We have further developed a bio-inspired approach for the formation of organic –inorganic hybrids (link to Inorganic peptide binders) for electronic applications.

Coiled coil based molecular switches. We have demonstrated that the unique propensity of proteins to undergo conformational changes, which is widely used in nature for controlling cellular functions, can be used as a mechanism to control the behavior of electronic devices. We have designed and prepared new dimeric coiled coil proteins that adopt different conformations due to parallel or anti-parallel relative orientations of their α-helix peptide monomers. In a recent publication in *JACS* we have shown for the first time that by controlling the conformation of these proteins, attached as monolayers to gold, a quantitative modulation of the gold electrode work (W_F) function is achieved. Furthermore, charge transport through the proteins as molecular bridges was found to be controlled by the different protein conformations, producing either rectifying or ohmic-like behavior.

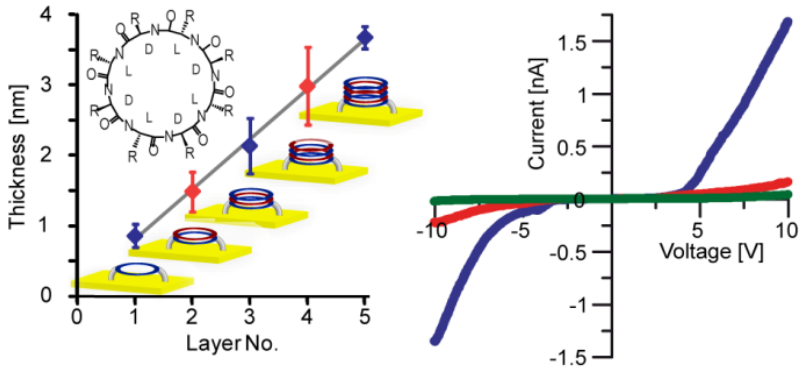
The implementation of such proteins in device applications, in particular for solar energy conversion applications, will be obtained by the targeted engineering of proteins that will be functionalized specifically in order to perform the desired function and will be equipped with other units that will ensure their stable assembly in the desired device configuration.



The I-V curve of the parallel and anti-parallel coiled coil proteins show switching between rectifying and "ohmic like" behavior. The work function (in the inset) shows an increase in the work function due to the elimination of the polar PC groups from the surface.

Nanotubes. The self-assembly propensity of peptides has been extensively utilized in recent years for the formation of supramolecular nanostructures. In particular, the self-assembly of peptide into fibrils and nanotubes makes them promising building blocks for electronic and electro-optic

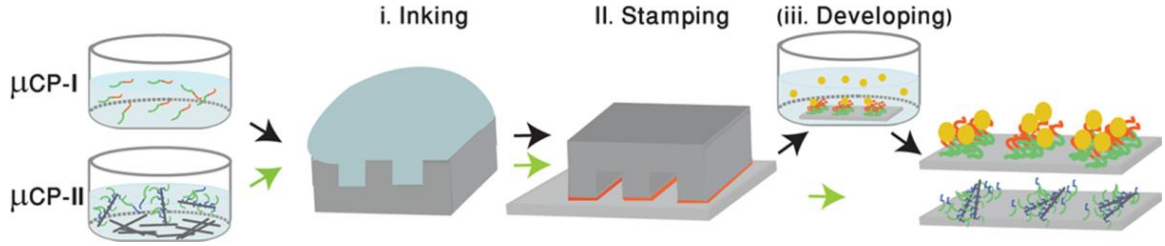
applications. However, the mechanisms of charge transfer in these wire like structures, especially in ambient conditions, are not yet fully understood. By combining principles of layer - by - layer deposition with the propensity of D,L α-cyclic peptides to self-assemble into nanotubes, based on β-sheet like interactions, we have developed a novel approach for assembling peptide nanotubes vertically oriented on gold surfaces. Using this novel fabrication methodology, we have fabricated molecular junctions, with conductive atomic force microscopy tip as a second electrode. Studies of the junctions' current-voltage characteristics as function of the nanotube length revealed an efficient charge transfer in these supramolecular structures with a low current attenuation constant of 0.1 $Å^{-1}$, which indicated that electron transfer is dominated by hopping. Moreover, the threshold voltage to field-emission dominated transport was found to increase with peptide length in a manner that depends on the nature of the contact with the electrodes. For more information refer to our publication in *Nanoscale*.

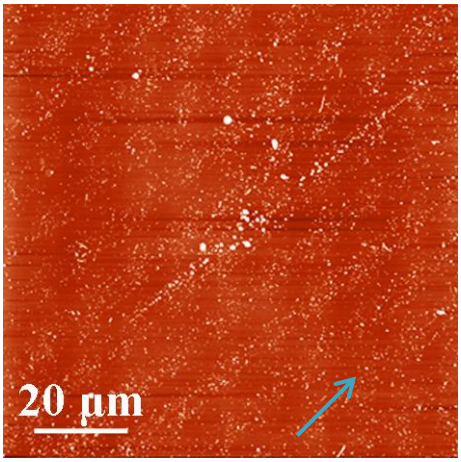


The thickness of peptide nanotubes layer as function of number of LbL deposition cycles is shown on the left (measured by ellipsometry). The resulting I-V curves for the first (blue, second (red) and third layers (green) are shown on the right (measured by CP-AFM).

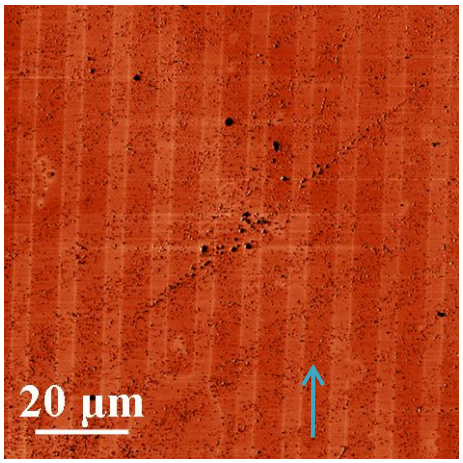
Peptide templates for the formation of inorganic electronic devices. Single crystals, patterned at the micro- and nano-meter scale, are important components in various electronic, sensory, and optical devices. Inspired by biomineralization processes, we study the possibility to use peptides for the alignment of inorganic materials in functional device configurations, and, at the same time, for modulating their electronic properties. To this aim we use peptide sequences that were recently identified using biological libraries to specifically interact with corresponding inorganic compounds. Thus, we have designed peptides with affinities to two different inorganic materials and utilized them as single-layer linkers for deposition and patterning of corresponding nanoparticles. Attachment and spatial organization of the nano-crystals on solid support was accomplished by patterning the peptides using soft lithography techniques. The great feasibility of the developed patterning processes for use in microelectronic and nanoelectronic applications was demonstrated by the choice of two technologically important nanoparticle systems: carbon nanotubes (CNTs) and gold colloids, which were deposited on silica surfaces. The flexibility of this methodology has allowed the formation of novel multi-nanoparticles patterns of both the CNTs and gold colloids on the same substrate. Details of this techniques are presented in a paper in *Nanotechnology*.

Printing process





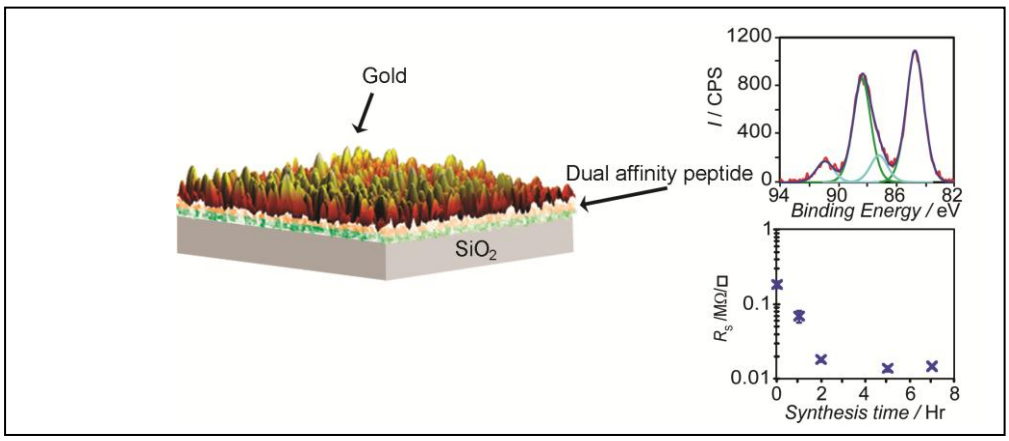
AFM Topography image.
Arrow represents direction of stripes pattern of CNTs



AFM phase image.
Arrow represents direction of stripes of pattern of gold colloids.

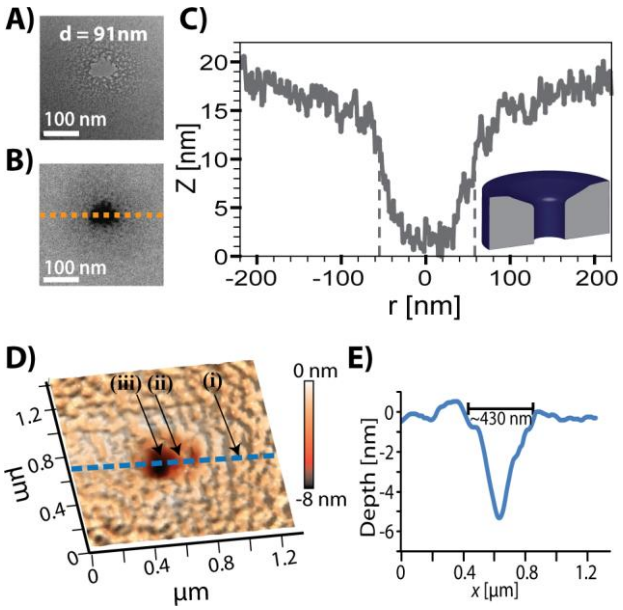
We have further utilized these dual affinity peptide binders for the growth of continuous gold films on a silicon-oxide substrate. In a publication in *J. Mat. Chem.* we have shown that the resulting films are comprised of disk shaped crystalline gold nanoparticles (NPs), and analyzed the gold - peptide interactions, demonstrating the role of charge transfer processes. Moreover, the ability to define patterns of the peptide on the surface has been utilized for defining gold film patterns on the surface.

We are currently involved in a very innovative project aiming at studying the effect of peptide binding on the electronic properties of semiconductor surfaces.



Biosensors

Controlled fabrication of nanopores by focused electron beam induced etching. While extensive research in our lab focuses on the utilization of biological molecules for nanotechnology applications, we are also interested in using advanced nanotechnology tools in order to fabricate devices that will aid in understanding biological processes. In the fabrication of these devices we still look at nature for inspiration. An exciting example is the utilization of nanopores as biosensors. In the cellular system, protein based nanopores and nano-channels are being used for controlled transfer of ions and bio-molecules through the cell membrane. Our aim is to mimic this system in an artificial surrounding in which we can study the interactions between the molecules and the nanopores rims during the transit and exploit them in Biosensing applications. Toward this aim we have recently developed a novel focused electron beam induced etching (FEBIE) process, in which the chemical etch of silicon nitride by XeF_2 gas is enhanced by an electron beam, facilitating localized reactions. This process eliminate the need high energy electrons of transmission electron microscope (TEM) or focused electron beam (FIB), making it more accessible. We have explored the effects of several process variables, such as time, pressure and electron energy, on the etching process, and have gained understanding of the NP formation mechanism and the resulting 3 dimensional structure. We are now able to controllably manufacture apertures with size ranging from 15 to 200 nm diameter in silicon and silicon nitride membranes. This work has been published in two manuscripts in the journal *Nanotechnology*. Future work will focus on the application of the nanopores for biosensing and related applications.



Top view TEM bright field image of nanopores prepared by FEBIE is shown in A together with thickness map extracted from the EELS signal. A cross section of the membrane thickness obtained from the EELS (C) signal and AFM image (D) and its cross section € have allowed us to determine the shape of the nanopores as illustrated in the inset of panel C

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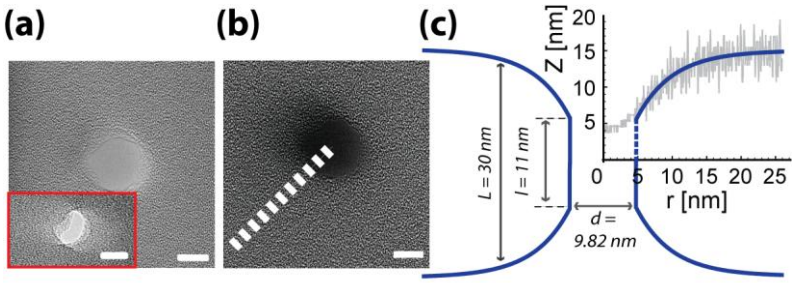
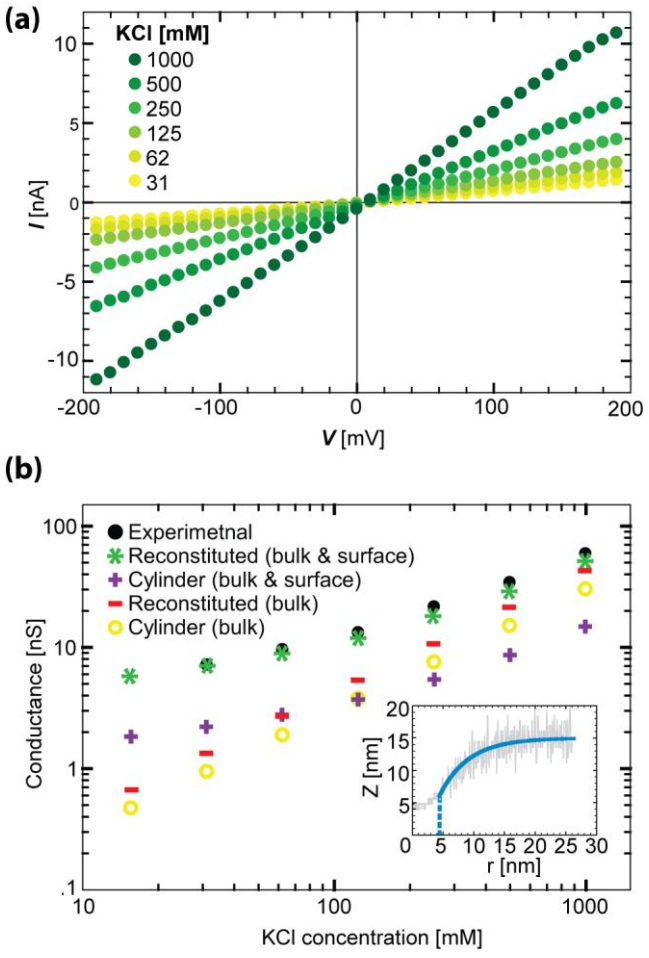
Evaluating nanopores structure function relations. In nanopore biosensors, detection is obtained through the change in the ionic current when a molecule translocates through the nanopore, yielding both quantitative and qualitative analytical information. The dependence of the conductance signal on the nanopore three dimensional shape, makes it important to decipher the later with high precision. In collaboration with the work of Prof. Kaplan form the Materials Science and Engineering department at the Technion, we performed a detailed study, based on electron microscopy (EM) analysis to accurately extract the NP shape and correlate it with the observed ion conductance. Furthermore, in order to avoid the elaborated EM work required in order to extract the

NPs' shape, we have developed a computational model that enables constructing the NP shape from the dependence of its conductance on the solution ionic strength. This further enables monitoring dynamic changes in the NP shape during sensing experiments. For further details see our publication in *APL*.



On the top (right) we show the cross section of a nanopore drilled by focused electron beam drilling. This cross section was extracted from the top view (left), tilted images (inset) and thickness map (center), all extracted by electron microscopy.

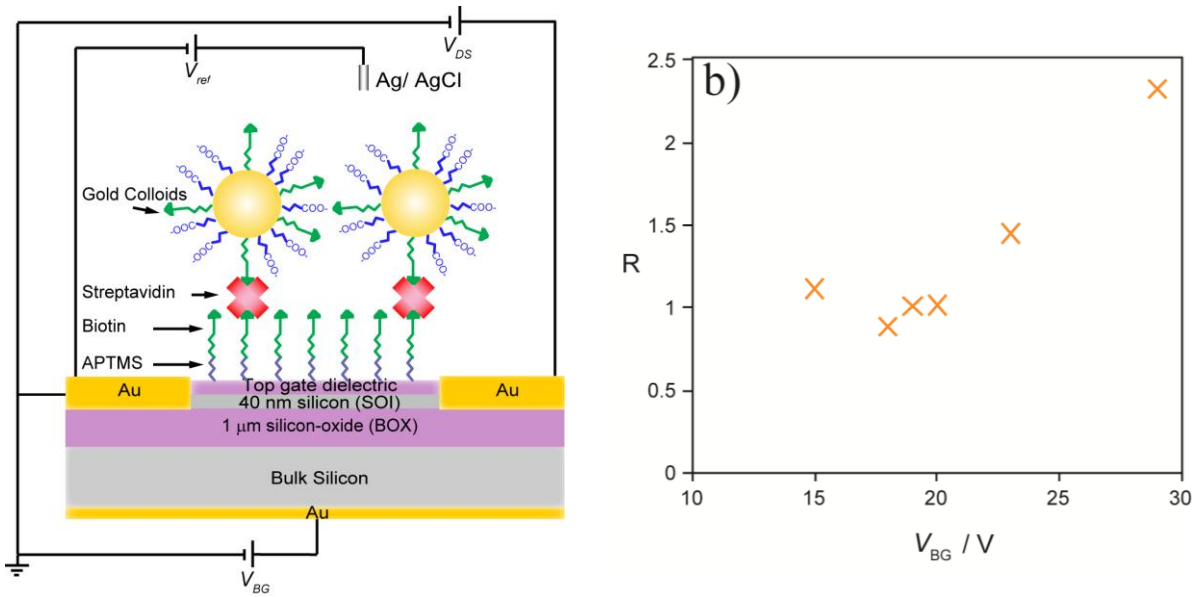


Current voltage of the same pore as function of ionic strength are shown in above. Conductance values were extracted for fitting (B). The resulting shape, and its comparison to the shape extracted from the TEM analysis are shown in the inset.

Field effect transistor biosensors. The utilization of field-effect transistor (FET) devices in biosensing applications have been extensively studied in recent years. Qualitative and quantitative

understanding of the contribution of the organic layers constructed on the device gate, and the electrolyte media, on the behavior of the device is thus crucial. In a publication in *ACS Nano* we present an analysis of the contribution of different organic layers on the pH sensitivity, threshold voltage, and gain of a silicon-on-insulator based FET device. We have further monitored how these properties change as function of the electrolyte ionic strength. Our results clearly show that in addition to electrostatic effects, changes in the amphoteric nature of the surface also affect the device threshold voltage. We have thus shown for the first time that apart from the distance of an analyte from the surface, the relative contribution of charge and dipole dictates the detection sensitivity. Furthermore, we have analyzed for the first time the influence of the dielectric properties of the layers on the device gain. A reduction in the gain was found with the successive construction of each layer. These results demonstrate the multilevel influence of organic layers on the behavior of the FET devices.

The detailed understanding of device performance has led us to develop a novel method for affecting the Bio-FET recognition signal post analyte binding; providing a tool for signal amplification. To achieve this goal we introduced an excess amount of charge and dipole, using functionalized gold colloids, by a sandwich type secondary antibody binding protocol. This enabled us to manipulate the signal in a selective manner. (See our publication in *Electroanalysis*).



On the left the amplification process is presented. The amplification factor as function of the back gate voltage is shown on the right.