Deanship of Graduate Studies

AL-Quds University

Single Molecule Based Nanoelectronics

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Introduction

1.1. Introduction

Nanoscience is the study of phenomena and manipulating of materials at atomic, molecular and macromolecular scales, where nano-sciences are lead to a better understanding of properties of materials at the atomic level, or resulting from the reduction of dimensions down to the nanometer range. And many technologies are concerned with producing new industrial materials on nano-meter scale – one of these technologies is nanotechnology- but one of the problems facing nanotechnology actually physics, so physics is different on the nanometer scale, the properties of materials can behave differently and have new characteristics.

Nanotechnologies are anew expression of a fundamental concept concerned with the development of tools for molecular electronics, that can be used first for measuring properties, then for assembling atoms and molecules to create new materials having superior properties useful in the fabrication of nano-electronic devices. So, nanotechnology includes both molecular electronics and nanoscale devices, where it is research's are aimed at building very small machines and electronics and constructing materials

molecule-by-molecule and aggregates that can perform the basic functions of larger electronic components and assemble them into atomically precise molecular electronic devices (Joachim, Gimzewski, Aviram, 2000).

Raw materials of nanotechnology include inorganic matter like metals and semiconductors, molecules like polymers and carbon nanotubes, and biological molecules like DNA and proteins.

Devices that have dimension on a nanometer scale are called nanoelectronic devices; the use of nanoelectronic devices is interested for several reasons. First of all: the basic devices can be small, extremely small. Second: it has the ability to operate with very low supply power. Third: a few numbers of electrons can be enough to represent information (Jaap Hoekstra and Arthur van Roermund, 2000).

Scaling-down devices are one of technological interest, while keeping their capacity constant is one challenge of nanotechnology. Especially at a certain size the material properties become size dependent, and the nanocrystals lose properties suitable for their use in device development, so how small can we go?

1.2. Miniaturization of electronic devices (toward nano-scale devices and the limitation of silicon technology)

When we go down and down, to get the very small world we have a lot of new things that would happen that represent completely new opportunities for design. Atoms on a small scale behave like nothing on a large scale, for they satisfy the laws of quantum mechanics. So, as we go down and become around with the atoms down there, we are working with different laws, and we can expect to do different things. We can manufacture in different ways. We can use, not just circuits, but some system involving the quantized energy levels, or the interactions of quantized spins, etc.

Another thing we will notice is that, if we go down far enough, all of our devices can be mass produced so that they are absolutely perfect copies of one another. We cannot build two large machines so that the dimensions are exactly the same.

At the atomic level, we have new kinds of forces and new kinds of possibilities, new kinds of effects. The problems of manufacture and reproduction of materials will be quite different, and the biological phenomena in which chemical forces are used will produce all kinds of wonderful effects.

Since the mid twentieth century there has been a great deal of interest in the miniaturization of electronic devices by several scientists, so the size of the electronic devices has been decreased year by year for more than twenty years.

By miniaturization, the electronic devices become smaller; electronics are positioned in greater density, and the reduction of size result in both better device performances and higher integration densities (Kawaura, Sakamato, and Baba, 2000). In addition the devices become ultra fast and low power.

For the past several years, techniques for miniaturization electronic devices have been studied, from these techniques electron beam lithography which is one of the most powerful methods for the formation of nanostructures that used in semiconductor device fabrication to transfer a pattern from a photomask (also called reticle) to the surface of a wafer or substrate. This technology can fabricate devices in the 100 nm size range, but there are limitations in the extent to which devices can be fabricated using electron beam lithography (Brian Reiss, Jeremiah Mbindyo, Benjamin Mallouk, Michael Natan, and Christine Keating, 2001). For this reason, there has been a great deal of interest in the development of novel technologies for fabricating smaller devices than can be prepared using electron beam lithography.

One such alternative is the "bottom up" approach where devices are assembled from very small building blocks (Ito and Okazaki, 2000), these building blocks are called molecules which can be assembled by two methods, one is the self-assembly, where intermolecular forces are responsible for the assembly of smaller components into the desired structure, the other method is microscopy, where devices such as the scanning tunneling microscope **(STM)** and atomic force microscope **(AFM)** can be used to manipulate individual components into the desired structure.

This approach is important because it offers two advantages, first the materials of fabrication, since devices can be fabricated from nanoparticles or even individual molecules, so it is feasible to fabricate much smaller devices than can be prepared using electron beam lithography. The second advantage is the cost, modern fabrication facilities for electron beam lithography cost over a billion dollars to build, but one can start self assembling devices for a fraction of that cost (Storhoff, Mucic and Mirkin, Clust, 1997).

1.3. Exploring the possibility of using biological molecule in electronic devices

Biology and electronics have long existed in separate universes. But because biological molecules, like DNA and proteins, are roughly a few nanometers in size, and because physicists and chemists are now learning how to make electronic devices on exactly that size scale, these universes are colliding. The result is a new class of devices that combine the ability of biological molecules to selectively bind with other molecules with the ability of nanoelectronics to instantly detect the slight electrical changes caused by such binding. What's really interesting about this technology is that it allows one to take the inorganic components that normally would be nestled inside an electrical chip and combine them with biological molecules.

The use of biological materials offers many advantages over traditional processing methods to construct the next generation of miniaturized electronics devices, particularly including spatial control on the nanometer scale, parallel self-assembly of multiple electronic components on a single device, and correctability. The critical factors in developing a bio-directed self-assembly approach are identifying the appropriate compatibilities and combinations of biological-inorganic materials, synthesis of the appropriate building blocks, and understanding and controlling building block self-assembly processes (Falini, Albeck, Weiner, & Addadi, 1996).

Biological systems assemble nanoscale building blocks into complex and functionally sophisticated structures with high perfection, controlled size,

and compositional uniformity. These materials are typically soft and consist of a surprisingly simple collection of molecular building blocks arranged in complex architectures. Unlike the semiconductor industry, this relies on serial lithographic processing to construct the smallest features on an integrated circuit (Belcher, Christensen, Hansma, Stucky, & Morse, 1996).

The exquisite selectivity of complementary biological molecules offers a possible avenue to control the formation of complex structures based on inorganic building blocks such as metal or semiconductor nanoparticles. DNA oligomer-nanocrystal complexes, for example, have been examined as building blocks for more complex two- and three-dimensional structures (Mirkin, Letsinger, Mucic, & Stofoff, 1996), and after the discovery that DNA can conduct an electrical current it has an interesting to be useful in nanotechnology for the design of electric circuits, which could help to overcome the limitation that classical silicon-based electronics is facing in the coming years.

Nanocrystal-labeled proteins have also been used to label biomolecular substrates with increased sensitivity (Chan, & Nie, 1998), biological molecules can be used to control the assembly of inorganic nanostructures and hybrid inorganic/organic structures while directing them to self-assemble in the desired manner. Thus, the biological molecules and an unlimited number of different types of nanocrystal building blocks can be mixed in the "pot" and then triggered to self-assemble into their superstructures.

The biological molecules will be basic building blocks in molecular devices such as nanowires for several main advantages (Fabio Pichierri, 2004):

1. Recognition – to be able to attach (or self-assemble) a component to other components or external electrodes.

2. Structuring – to enable construction of variable structures with different lengths and specific details.

3. Conductivity - the ability to transport efficiently charge carriers from one point to another (usually the nanowire ends). Next in importance is stability, heat dissipation etc.

The biological molecule such as DNA and protein will be suitable building blocks because they are provide fantastic structuring and recognition but falls behind with regard to conductivity. There is a clear necessity to develop basic components that will provide the above properties. Moreover, it is desired that the internal structure of the proposed component will allow engineering, when a few components are assembled, of a nanostructure with non-linear electric response that will enable to realize nanoelectronic devices, able to perform different logic functions and suitable for inter-combination, using the composed structure itself and possibly a gate channel.

1.4. Materials and instruments

Atomic force microscope (AFM):

Atomic force microscope (AFM) is a technique used for measuring interactions between nanometer scale objects. Since the invention of the Atomic Force Microscopy (AFM) (Binnig, Quate, and Gerber, 1986) -also called Scanning Force Microscopy- (Binnig and Rohrer, 1985) in 1986, the technique has experienced an enormous growth and its use is, nowadays, routinely in many different fields such as physics, chemistry, biology, biochemistry and molecular biology.

AFM allows imaging the surface of biological macromolecules (Van Noort *et al.*, 1998) and their structures in native conditions, in three dimensions, without staining or shadowing, in air or under liquid conditions (Shao, Mou, Czajkowsky, Yang, and Yuan, 1996). AFM has shown spectacular results not only imaging but also as a nanolithographic tool, for measuring antigen-antibody binding and unbinding forces, and folding and unfolding protein forces (Rief, Gautel, Oesterhelt, Fernandez, and Gaub, 1997). The technique has enough resolution to resolve molecules in air and under physiological conditions. It has been also proved that small proteins are also visible with AFM and that interactions can be imaged (Hansma, Pietrasanta, Auerbach, Golan, and Holden, 2000).

The principle of operation of this instrument is measuring the attractive or repulsive forces between a tip and the sample. The tip, is positioned at the end of a cantilever, is brought into contact with the sample surface and then precedes to raster the sample underneath it. The laser beam deflects off the cantilever and into a photodetector. As shown in (Fig. 1.1).
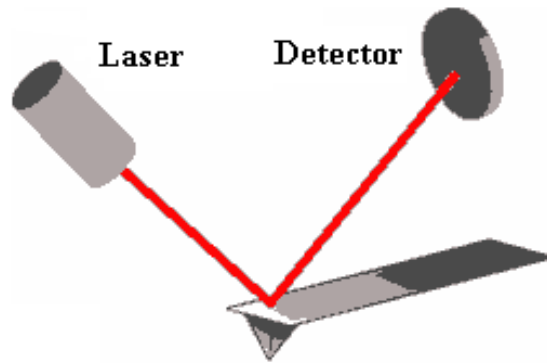
Fig.1.1- Beam deflection system

The optical signal measured by the photodetector is then translated into the sample surface topography (Binnig, Quate, and Gerber, 1986). The tip is attached to a piezoelectric scanner tube as shown in Fig 1.2, which scans the probe across a selected area. And make it possible to create three – dimensional positioning devices of arbitrarily high precision (Gallego-Juárez, 1989).
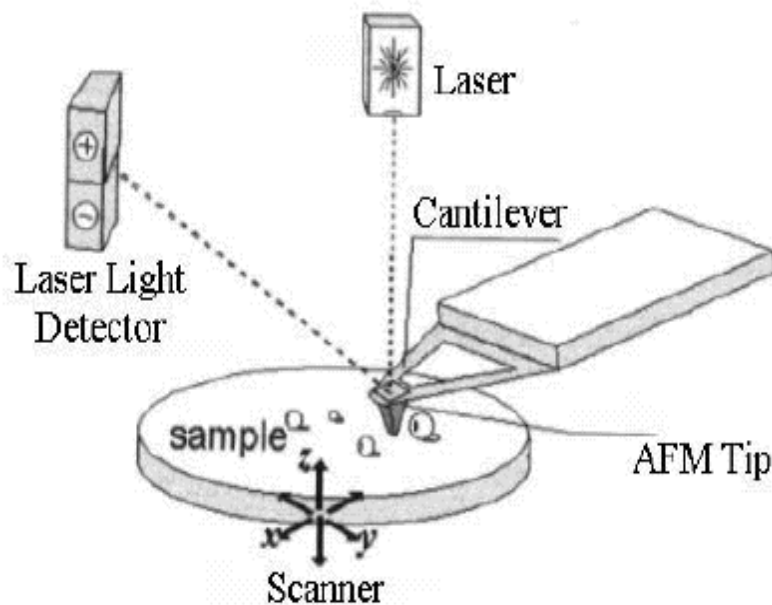
Fig.1.2- AFM schematic

(www.keele.ac.uk/depts/ch/groups/csg/pat/pathome.htm)

 The atomic force microscope (AFM) has been widely used to characterize biomolecules and nano-scale devices. Because biomolecules and cells are usually highly compliant, extremely soft cantilevers with a sharp tip must be used to apply ultra-low level of forces.

So force microscopists generally use one of three types of tip which are generally made of silicon or silicon nitride. These tips are:

The standard tip is a 3 µm tall pyramid with approximately 30 nm end radius (Fig. 1.3.a., Albrecht, Akamine, Carver, and Quate, 1990).The super tip which offers a higher aspect ratio and some time a better end radius than the normal tip (Fig. 1.3.b. Keller, and Chih-Chung, 1992). The ultralever (Fig. 1.3.c), which offers a moderately high aspect ratio and 10 nm end radius.
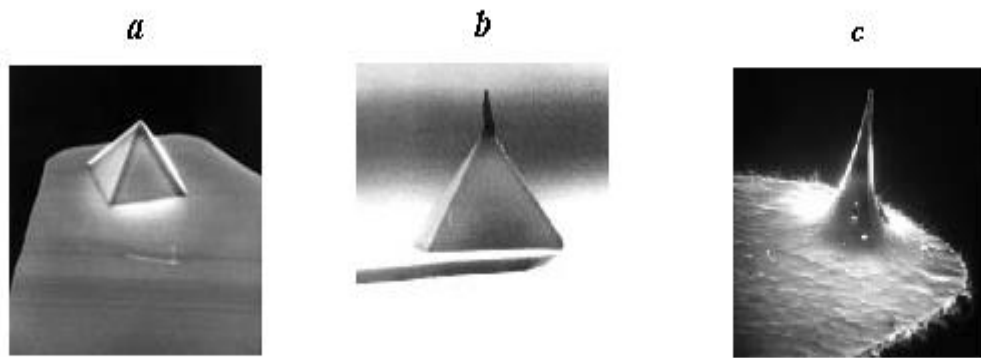
Fig. 1.3- types of tip: a) standard tip, b) super tip, c) ultralever tip.

The atomic force microscope (AFM) can operate in different scanning modes including constant force, contact, non-contact, and tapping mode. (Binnig, Quate, and Gerber, 1986), contact mode is the most common method of operation of the atomic force microscope AFM. As the name suggests, the tip and sample remain in close contact as the scanning proceeds. One of the drawbacks of remaining in contact with the sample is that there exist large lateral forces on the sample as the tip is "dragged" over the specimen. (Albrecht, Grütter, Horne, and Rugar, 1991), non-contact operation is another method which may be employed when imaging by AFM. The cantilever must be oscillated above the surface of the sample. This is a very difficult mode to operate in ambient conditions with the AFM. So a thin layer of water must be exists on the surface of the sample, this thin layer will invariably form a small capillary bridge between the tip and the sample and cause the tip to "jump-to-contact". Tapping mode is the next most common mode used in AFM when operated in air or other gases, the cantilever is oscillated at its resonant frequency (often hundreds of kilohertz) and positioned above the surface so that it only taps the surface for a very small fraction of its oscillation period (Martin *et al.*, 1998).

The atomic force microscopy (AFM) uses the feedback loop to regulates the forces and to acquisition, the feedback loop contains a feed back circuit that attempts to keep the cantilever deflection constant by adjusting the voltage applied to the scanner, so it keep the motion of the object in a fixed relationship to another object (David Baselt, 1993).

Mica:

At present time available AFM substrates for SP1 imaging are limited in types. The conventional support for the biological objects is mica (Hansma, Sinscheimer, Hansma., 1992). Because it has several important disadvantages as AFM support, namely the negative surface charge in solution (Muller, Amrein, Engel, 1997) and a large adhesion.

Mica is hydrous silicates of aluminum and potassium, often containing magnesium, ferrous iron, ferric iron, sodium, and lithium and more rarely are containing barium, chromium, and fluorine. All crystallize in the monoclinic system, but mica is most commonly found in the form of sheets and can splitting into very thin, elastic laminae (James Hedrick, 1999). The entire micas surface can be easily updated by a simple cleaving, by first pressing some adhesive tape against the top mica surface, then peeling off the tape. Some varieties are transparent; resistance to heat is high. Commercially, the most important micas are muscovite (potassium mica) and phlogopite

(magnesium mica). Muscovite, the commoner variety, is usually colorless, but it may be red, yellow, green, brown, or gray.

Gold nanoparticles:

They are fabricated from Gold and have typical dimensions between 2 to 100 nanometers. The size and shape of these structures and therefore the number of electrons they contain, can be precisely controlled; a quantum dot can have anything from a single electron to a collection of several thousands (Zrenner, 2000).

Gold nanoparticles are used for their extensive application in the development of new technologies such as the biotechnology at the nanoscale (Tanaka, 1999).

Gold nanoparticles can be produced using two techniques wet and dray explained elsewhere. (Koel *et al*., 2001) (Tapan Sau, Anjali Pal, Jana, Wang and Tarasankar Pal., 2001) (Gardea-Torresdey , Tiemann , Gamez , Dokken , Tehuacamanero , and Jose-Yacaman , 1999).

SP1-protein:

SP1 protein was isolated from poplar trees; it is exceptionally stable under extreme conditions (elevated temperatures, detergents, organic solvents) and is resistant to proteases (Wang, Pelah, Allargando, Shoseyov and Altman, 2002).

The SP1 gene was cloned and the recombinant protein was purified from bacteria (Wang, Pelah, Alergand, Shoseyov and Altman, 2002).

The complex consists of 12 identical protein subunits (12.4 kDa each), which spontaneously assemble into a uniform ring-like shape (10 nm diameter and 4 nm width) with a central cavity (2.5 nm diameter) as shown in Fig. 1.4 (Wang, Dgany, Dym, Altman, Shoseyov and Almog, 2003), which can be modified and adjusted by using genetic engineering to mutate the N-termini which are exposed to the central cavity. Site directed mutagenesis has already been used to insert metal nanoparticle binding site in the central cavity.
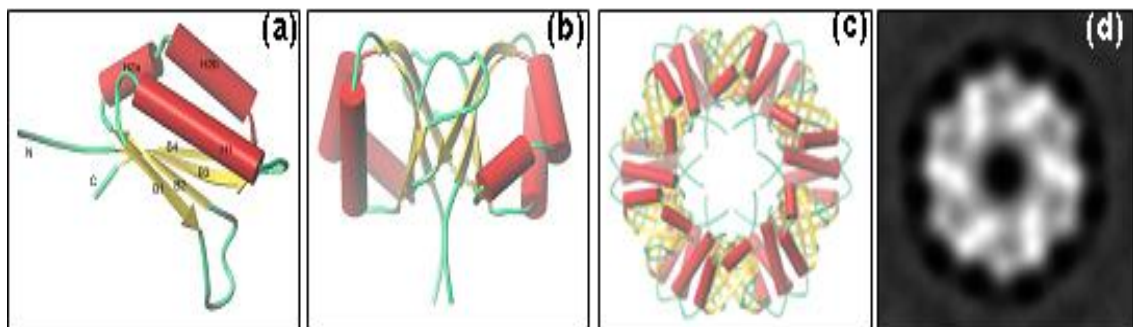
Fig. 1.4-The SP1-protein structure: (a) monomer, (b) dimer, (c) full dodecamer structure (extracted from X-ray) and (d) a transmission electron microscope (TEM) image (averaged 313 times) of a single SP1 ring.

WSxM:

Windows Scanning x (Force, Tunneling, Near Optical ...) Microscope is a powerful Windows application for Data Acquisition and Processing in Scanning Probe Microscopy (SPM). The WSxM program allows the user to easily interact with the SxM microscopes taking advantage of all their features (http://www.nanotec.es/genprog.htm).

The WSxM Scanning Probe Microscopy Software is divided into two well defined parts:

1. Image rendering and data processing, and it used to perform very general processes such as 3D rendering, pseudocolor image representation, Fourier and roughness analysis, data smoothing, cross section profiles...
2. WSxM used as Digital Signal Processor to control the microscope providing flexible and powerful operation in Real Time.

The final scientific objective, The final scientific objective in this study, we propose to construct a building blocks can be used in nanoelectronic devices. To do this we will employ a certain class of stress-responsive, homo-oligomeric proteins (SP1), that will self assemble into a mica surface and will

be used as a scaffold for lodging gold nanoparticles. That will serve as a QDs entrapped in the central cavity of SP1**.**

1.5. Thesis map

Chapter one is a general introduction about nanoelectronics and the miniaturization theory to go from microelectronic to nanoelctronics and the use of biomolecules such DNA and proteins to overcome the limitation of silicon technology.

Chapter two a theoretical review toward nanoelectronics and a brief description for the research problems, while the experimental works, the materials and devices will be discussed in chapter three. The discussions of the results are presented in chapter four. Finally conclusions, suggested future work given in chapter five and references are listed at the end of thesis.

Chapter Two

Chapter two

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Theoretical Review

2.1. Introduction

Since about eight years the scientist and researcher show an exponential interest in the study nanoscience and nanotechnology which involve the working with matter on an ultra-small scale.

Billions of dollars are invested in Nanotechnology each year, nanotechnology laboratories and centers were established all over the world, and also hear at Al-Quds University we established the first Nanotechnology laboratory in Palestine. This lab will enable the researchers at the university to advance in

the field of nanotechnology and take part in the revolution of endless possibilities "Nano".

2.2. Toward nanoelectronics

In this section we show a brief description how nanotechnology developed from an idea to a significant area for research and development, and how it goes to building minuscule machines and electronics.

Nanotechnology are the current expression of a fundamental concept, already presented by Richard Feynman in 1959, during his famous idea that "manipulating and controlling things on a small scale would have enormous number of applications", and he expected that it should be possible making" a thing very small which does what we want "(Bayot, 2001). While in 1974 the first molecular electronic device patented by Nario Taniguchi who used the word nanotechnology to refer to production technology to get the extra high accuracy and ultra fine dimensions on the order of one nanometer (Aviram, & Ratner, 1974).

In 1981, Scanning tunneling microscope (STM) invented by Heinrich Rohrer and Gerd Karl Binnig, the device uses quantum tunneling currents between the microscope tip which positioned within two nanometer of the surface, and the material being observed to produce atomic- scale three dimension images of surfaces with atomic resolution (Rief, Gautel, Oesterhelt, Fernandez, and Gaub, 1997).

Richard Smalley, Robert Curl, and Harold Kroto, in 1985 discovered C60 (Kroto, Heath, O'Brien, Curl, & Smalley, 1985), new form of carbon which known as a buckyball where the carbon atoms are arranged on a spherical shape (Fig.2.1). These new carbons play an important role in the nanotechnology world, especially on carbon nanotubes (Fig.2.2) which discovered in 1991 by Sumio Iijima (Iijima, 1991).
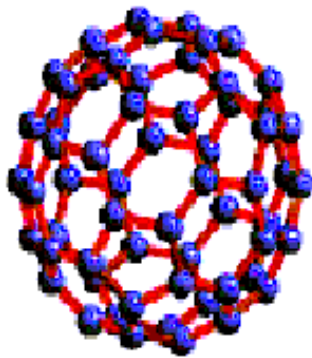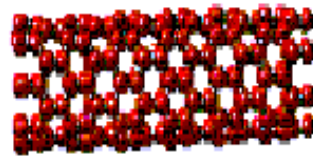

Fig.2.1- Buckay ball   Fig.2.2- Carbon nanotube

The beginning of the real revolution for nanotechnology and the first idea of molecular nanotechnology are presented by Dr. Eric Drexler, when the atomic force microscope (AFM) has invented in 1986 by Binnig, Quate and Gerber, this microscope offering similar resolution to the scanning tunneling microscope, and works like an old-fashioned phonograph, by moving a tip across a surface and detecting the vertical movements resulting from hills and valleys it encounters. Also it has shown spectacular results for imaging and measuring different forces (Rief, Gautel, Oesterhelt, Fernandez, and Gaub, 1997).

In 1987, the researcher recorded their first observation of quantization of electrical conductance, so they are observed step-like variations in conductance through tiny conducting strips, i.e. the conductance is quantized, demonstrating that nanoelectronics is not just smaller, but different. In the same year the first single-electron transistor was created by Theodore Fulton and Gerlad Dolan of Bell Laboratories where the current being switched consists of the movement of a single electron (Fulton and Dolan, 1987).

In 1988 William deGrado, designed a new protein, called alpha 4 from scratch, and manufactured it in laboratory. This protein, which never existed in nature, was more stable than natural proteins. Researchers around the world are now looking at proteins as molecular structures that can be designed and build, just as an IC designer lays out a chip (DeGrado, 1997).

In 1990, Donald Eigler and Erhard Schweizer, working at the IBM Almaden lab showed that individual atoms can be moved and positioned precisely using a tungsten tip of a scanning tunneling microscope, which can pass over individual atoms, feel their shape, and then present that on a computer screen in the form of an image. Individual atoms can be picked up and placed at new locations. In the (Fig.2.3) they show 35 xenon atoms arranged to form the letters "IBM" on the surface of a nickel crystal. The atoms of nickel are not visible (they are smaller than those of xenon, and blur into a smooth background) (Eigler, and Schweizer, 1990).
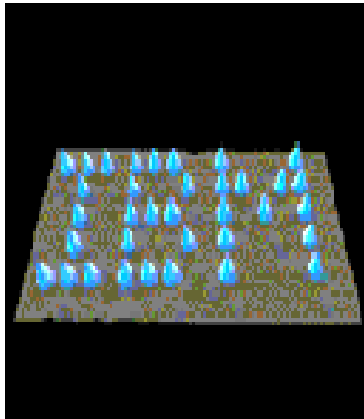
Fig.2.3- IBM written by 35 xenon atoms

In 1991, Sumio Iijima discovered tubes of graphite, called nanotubes, which turn out to have extraordinary strength and interesting electrical properties. By discovering a process to make graphitic carbon needles ranging from 4nm to 30nm in diameter and 1 micron in length, this needle consisted of multiple sheets of graphite rolled into hollow tubes, which have now become known as carbon nanotubes which are long, narrow nanoscale tubes made of multiple layers of carbon atoms arranged in graphite-like sheets (Iijima, 1991).

The first laboratory dedicated to nanotechnology in the US was created at Rice University in 1993. Murray, Norris and Bawendi synthesise the first high quality quantum dots, which are semiconductor crystals typically between 1 and 10 nanometers in diameter and have unique properties between that of single molecules and bulk materials. Quantum dots are very small particles with interesting optical properties: they absorb normal white light and,

depending on their size, emit a range of bright colors. This property arises directly from the very small size of the particle (Chan, & Nie, 1998).

1997 has seen some significant anniversaries in the area of electronics, where Murray Hill, fabricated the 'nanotransistor', a complete metal oxide semiconductor transistor. It was only 60nm wide, consisted of sources, drain, gate and gate oxide and improved the key measures of performance. The key advance was being able to fabricate a 1.2 nm thick gate oxide layer.

Also, in 1997, Nadrian Seeman demonstrated that DNA can be used as a building block for nanoscale mechanical devices. So, Seeman's group at New York University has studied the design and construction of 2-dimensional DNA arrays, which might serve as templates for nanomechanical assembly, In addition to these arrays, Seeman's group, has created a number of DNA-based nanomechanical devices (Yan, Zhang, Shen, Seeman, 2002).

In the same year in 1997 Dekker's group at the Delft University of Technology used scanning tunnelling microscopy to determine the atomic structure of a single-nano tube and their electronic properties and confirmed the relationship between the structure of a nanotube and its electronic properties. And they showed that conductivity through nanotubes is controlled by low dimensional effects such as resonant tunneling and single-electron charging effects (LeRoy, Kong, Pahilwani, Dekker and Lemay, 2005).

In 1999, James Tour at Rice University in Houston reported that they have demonstrated single molecules that switch between ON and OFF states. The function of their molecular switches is based in part on conformational changes - which happen when molecules alter their arrangement by rotation of their atoms around a single bond, effectively changing shape by moving or turning - that determine how and when that conductance switching occurs in those molecules (Chen, Reed, Rawlett, and Tour, 1999).

A self-assembling DNA motor was created by researchers from Bell labs, murray Hill, and Oxford University in 2000. These devices which resemble motorized tweezers are 100,000 times smaller than the head of a pin, and the techniques used to make them may lead to computers that are 1,000 times more powerful than today's machines. The hope is that DNA motors can be attached to electrically conducting molecules to assemble elementary circuits by acting as switches. In general, molecular motors work on the principle of conversion of chemical energy, provided by the hydrolysis of ATP molecules (adenosine triphosphate) into ADP (adenosine diphosphate), into mechanical energy. Many proteins can change their shape using this energy, which results in some kind of motion, depending on the type of protein (Vale, 2003).

In 2001, Cees Dekker and co-workers at the University of Delft in the Netherlands reported they have demonstrated logic circuits with field-effect transistors based on single carbon nanotubes. The transistors show favorable device characteristics such as high gain, a large on-off ratio, and room-

temperature operation nanotube logic (Martel, Derycke, Appenzeller, Wind, and Avouris, 2002).

In 2002 researchers at the University of North Carolina at Chapel Hill and co-workers made frayed wires from single strands of DNA bundled into clusters about 2 nm wide and between 5 and 200 nm long. The wires can be linked together into networks through complementary strands of DNA (Yanze, Lee, Poon, Piquette-Miller, and Macgregor, 2003).

Researchers have recently begun to use DNA to assemble carbon nanotubes into transistors, the building blocks of computer circuits. Such self-assembled, molecular-scale circuitry could be used to make cheaper, higher-performance computers than that using silicon-based chip making technologies. The researchers are looking to design computer circuits that could be assembled automatically by DNA self-assembly process and carbon nanotubes (Eric Smalley, 2004).

2.3.   Biomolecular electronics

Biomolecular electronics is concerned with the use of biomolecules in nanoelectronics, biomolecules such as proteins, DNA, carbohydrates, etc., are stable and work in an aqueous environment and have the ability to self-assemble this makes it possible to produce nanostructure with a precision that is not achievable with classical silicon-based technologies. However, the advantage in using biomolecules rather than synthetic molecules is that important functional properties such as electron transfer. It was found by

many experiments, that the electrical charges can transport through DNA due to the variety of surrounding condition used. This together with the possibility of using genetic engineering as a mean to modify natural proteins to yield mutants with enhanced characteristics makes biomolecules very attractive a technology (Hipps, 2001).

The first idea of using organic molecules for building electronic component refer back to 1974, where Professor Norio Taniguchi describe the precision manufacture of material with nanoscale and in 1980 this idea was developed to what known today, as molecular nanotechnology (Aviram, & Ratner, 1974).

After the development of the atomic force microscope in 1986, the biomolecules become an interested material for manufacturing nanostructure component and there are several groups exploring the possibility of using DNA and proteins in nanoelectronic devices, and study how DNA and proteins behave at a surface.

2.3.1. DNA electronics

DNA is the best molecular electronic device ever produced on the earth because it is electronic properties, and other properties including its size, structural stability and its ability to replicate combined with the pre-existing tools derived from molecular biology, DNA can store, process and provide information for growth and maintenance of living system, DNA is well characterized and ubiquitous, DNA contains information in the nucleotide

sequence, DNA conducts one dimensionally depending on that sequence (Murphy *etal*., 1993).

DNA is ready to use nanowire of 2 nm and can be synthesized in any sequence of four bases i.e. (adenine, thymine, guanine and cytosine). DNA of every living organism consists of large number of DNA segments where each segment represents a processor to execute a particular biological process for growth and maintaining life. Other important characteristics of DNA which makes it material of choice for future molecular devices are: more information in 1ml of DNA than trillion CDs, four bases "A, T, G, C" instead of 0 and 1, extremely energy efficient 10^{-19} operations per job, synthesis of any imaginable sequence is possible and semiconductor are approaching limit (Lalit Bharadwaj and Bajpai, 2002).

There are many research studying the behavior of DNA at the different surfaces, here I will be reported a review for some of these researches, (Polyakov, Erts, Malinovskis, Muiznieks, Tuite, 2003), by using the Atomic force microscope studied the distributed DNA oligomeric arrays on Au (111) and on mica surfaces, and they found that the DNA have the ability to self-assemble on both surfaces as in Fig.2.4.a and Fig.2.4.b.

Fig.2.4.a- DNA on mica   Fig.2.4.b- DNA on Au (III)
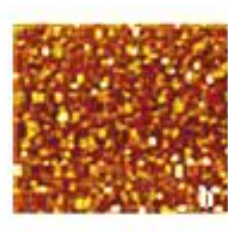
Klinov, Dubrovin, Yaminsky, at the Institute of Bioorganic Chemistry, studied the deposition of DNA molecules on graphite surfaces by the atomic force microscope, so after The samples were incubated for 5 - 10 minutes, and the surface was washed with water, blotted with filter paper and dried with argon, the image was seem to be as shown in (Fig.2.5).
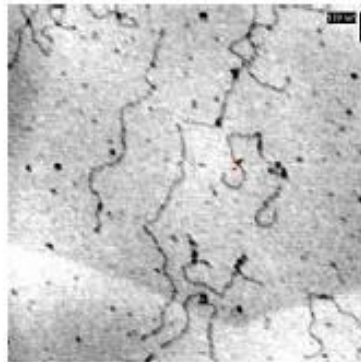

Fig.2.5- the typical image of DNA molecules absorbed graphite

(Calzolari, Di Felice, Molinari and Garbesi, 2002), investigated the principles of quadruple helix nanowires, which is called G- wires consists of a building block called G4, contains four hydrogen-bonded guanines arranged in potassium-rich conditions. This group forming extended stacked wires at the nanoscale length (Fig.2.6) makes them appealing for the development of biomolecular electronics.
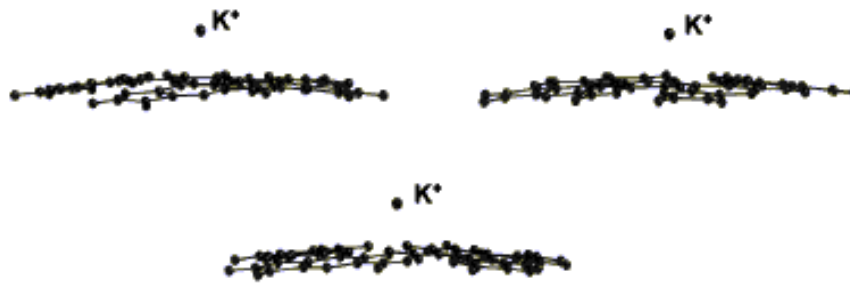
Fig.2.6- G- wire

At 2002, Itamar Willner and Bilha Willner developed a method to generate an Au nanoparticle wire based on DNA. Where Au nanoparticle (1.3 ± 0.2 nm) functionalized with the single psoralen, is intercalated into a polyT/polyA double-stranded DNA. The resulting compound is irradiated to covalently connect the psoralen units to the DNA thymine bases, and then deposited onto mica. Figure 2.7 shows the AFM micrograph of the resulting Au nanoparticle wire formed on the DNA template. The wire has a length of 500–600 nm and a width of 3.5 to 8 nm. Although the AFM image of the Au nanoparticle wire indicates a dense particle-contacted assembly, this picture might be misleading due to the size of the scanning tip (Itamar Willner and Bilha Willner, 2002).
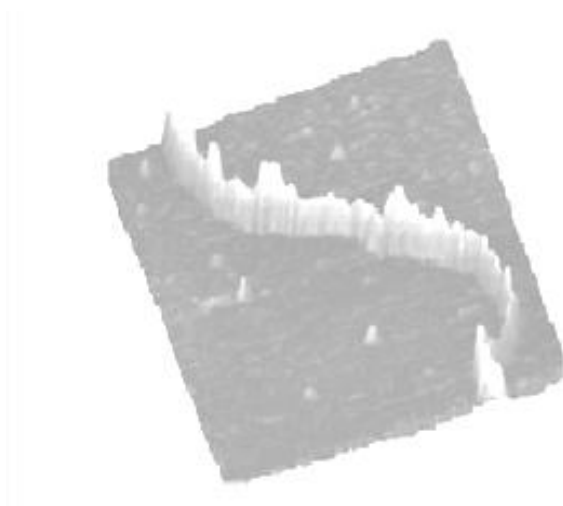
Fig.2.7- AFM image of an Au nanoparticle wire generated on a DNA template

(Hanying, Sung Ha Park, John Reif, Thomas LaBean, and Hao Yan, 2004), studied by using of scanning electron microscopy (SEM), the assembly of streptavidin proteins with 5-nm gold particles , where the gold can be precisely positioned periodically on the self-assembled DNA array (Fig.2.8). And it is found that the distance between the adjacent gold particles in the single-layer arrays is 17 nm, they note that the average length of observed linear arrays incorporating gold nanoparticles is decreased compared to the average length of streptavidin arrays without gold. Possible explanations for this trend include repulsion between neighboring gold nanoparticles carrying electrical charges, decreased biotin-streptavidin binding affinity following gold conjugation.

Fig.2.8 -single-layer streptavidin-gold arrays

2.3.2. protein based nanoelectronics

Proteins are good candidate for biomolecular nanoelectronics, because of their natural functional characteristics, so they have a natural electron transfer activity that can be exploited for the realization of molecular switches and in the implementation of a prototype of protein transistor operating in air and in the solid state, based on this class of proteins (Ross Rinaldi, Giuseppe Maruccio, Adriana Blasco, Paolo Visconti, Valentina Arima and Roberto Cingolani, 2003). although proteins have advantages over other biological molecules that researchers have so far tried to use for nanoelectronics, so it has the ability to creating self-assembling nanostructures and the bonds between the protein fibrils is strong not like the weak bonds between DNA strands that tend to break easily (Erika Jonietz, 2003)

The researchers started with yeast prions-harmless cousins of the proteins that cause mad-cow disease. Under certain conditions, these prions spontaneously form highly stable fibrils. Susan Lindquist and Heinrich Jaeger engineered the fibrils to bind tightly with gold nanoparticles. The result was

producing conducting wires, can be used to build small-scale circuitry for computers, biosensors and other things (Erika Jonietz, 2003).

Although the self-assembly of Mouse immunoglobulin G molecules had been studied when it deposited on mica were imaged with an atomic force microscope at room temperature, and the behavior of these molecules on the surfaces are represented on (Fig.2.9) (Jiye Cai *etal*., 2003).
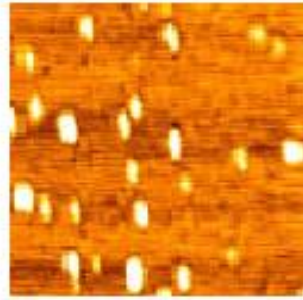

Fig.2.9- Mouse immunoglobulin deposited on mica surface

A group of scientists have studied the tunnelling properties of a number of metalloproteins including the blue copper protein azurin. Azurin is a type I protein of low molecular weight (10-15 kDa); the copper atom is situated approximately 7A from the protein surface, asymmetrically embedded in ahydrophobic core as in (Fig.2.10.) (Lontie, and Editor, 1984).
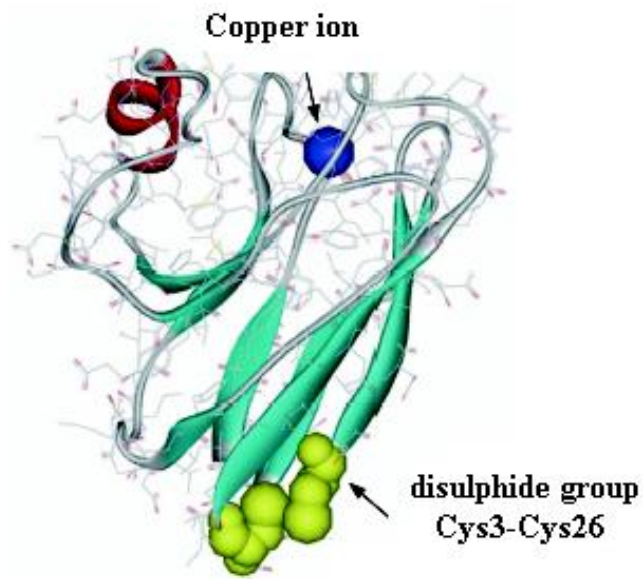
Fig.2.10- Azurin structure

And they are studied the ability of binding azurin molecule to gold substrate by using the tip of atomic force microscope as shown in (Fig.2.11) (Davis, Morgan, Wrathmell and Zhao, 2004). Also (Fig.2.12) illustrates the surface of mica after incubation in azurin solution, and the selfe-assembley of azurin on mica is clearly visible in this case (Andrea Alessandrini, Mimmo Gerunda, Paolo Facci, Bernhard Schnyder, Rudiger Kotz, 2003).
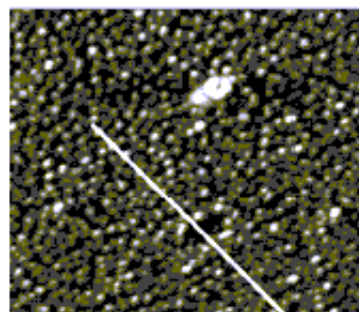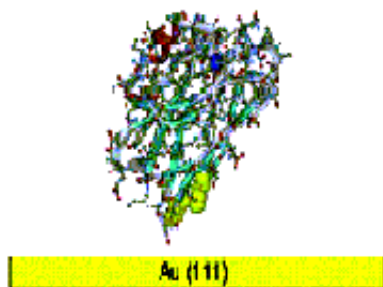
Fig.2.11- azurin bounded.   Fig.2.12- azurin deposited on mica

Nanoscale ordered arrays of metal and semiconductor quantum dots are fabricated by binding preformed nanoparticles onto crystalline protein templates made from genetically engineered hollow double-ring structures called chaperonins, where chaperonins are subcellular structures composed of 14, 16, or 18 subunits called heat shock proteins (HSP60).These (60-kDa) subunits are arranged as two stacked rings 16 to 18 nm tall by 15 to 17 nm wide. Fig.2.13 show how the gold QDs binding to engineered chaperonins, where 5 nm gold QDs bound within the pores of the 3-nm-pore crystalline template. Occupied rings show the QDs (dark areas) are surrounded and held in place by the chaperonins pores. Empty rings have a brighter, less electron-dense appearance (Andrew Mcmillan, Chad Paavola, Jeanie Howard, Suzanne Chan, Nestor Zaluzec and Jonathan Trent, 2002).
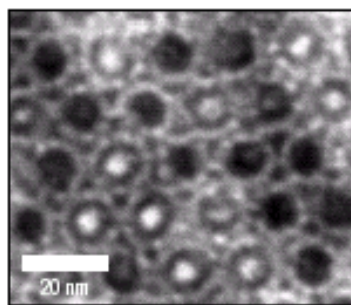
Fig**.2.13- Gold QD binding to engineered chaperonins

Laurel, Anna Plaas, Alan Grodzinsky, Christine Ortiz, at Massachusetts Institute of Technology, Cambridge, MA (USA) and at University of South Florida, Department of Anatomy (USA), they have used Atomic Force Microscopy (AFM) to image the conformation of the aggrecan molecules which are approximately 100 CS-GAGs are covalently bound at extremely high densities to 250 kDa core protein and their aggregating on mica surface the results of this self-assembly are shown in (Fig.2.14).
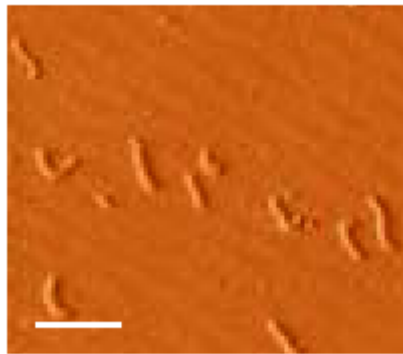

Fig.2.14- AFM contact mode deflection image taken of aggrecan molecules on mica

A group of scientist study the directed assembly of a de novo designed protein on graphite, where a solution of protein was deposited onto freshly cleaved graphite, and the resulting assemblies were imaged with tapping mode atomic force microscopy (AFM). The AFM image shown in (Fig. 2.15) demonstrates that the protein assembles into parallel fibers on the graphite surface (Christina Brown, Ilhan Aksay, Dudley Saville, and Michael Hecht, 2002).
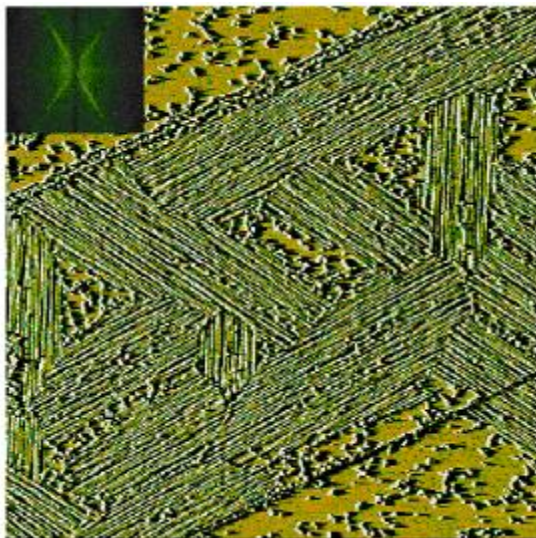
Fig. 2.15- AFM image of protein deposited on highly ordered pyrolytic graphite

As shown above there are many research that done for studying the probability of self- assembly of organic molecules such as DNA and protein on different surfaces, and in this research I studied the self assembly of a special type of protein called SP1 on mica surface and also I studied the self assembly between gold nanoparticles and this protein and my results were shown in chapter four.

Chapter Three

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Objectives

The objectives of the present work are:

1- Morphological characterization of the SP1-protein using AFM.

2- Attachment of gold nanoparticles in the central cavity of SP1 protein.

3- Morphological characterization of the unit cell, SP1-protein with gold nanoparticles at the central cavity, using AFM.

Chapter Four

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The Experimental Work

4.1. The Idea

The main idea in this study is that we want to attach a gold nanoparticle ~1.8 nm to the central cavity of a ring shaped protein, which is called SP1, with 11 nm outer diameter, 5 nm inner diameter and 2.5 nm height to form a building bock; in other word a unit cell as shown in Fig. 4.1, then attach these unit cells together to form more complicated structures like a nanowire. So our work plan will consist of the following steps:

1- Deposition of SP1 on the mica surface to prepare a sample consists of a single Sp1.

2- Growth or attachment of gold nanoparticles in the central cavity of SP1 by preparing a mixture of gold nano-particles and SP1.

3- Deposited of Sp1-Gold nanoparticles hybrids on mica substrate.

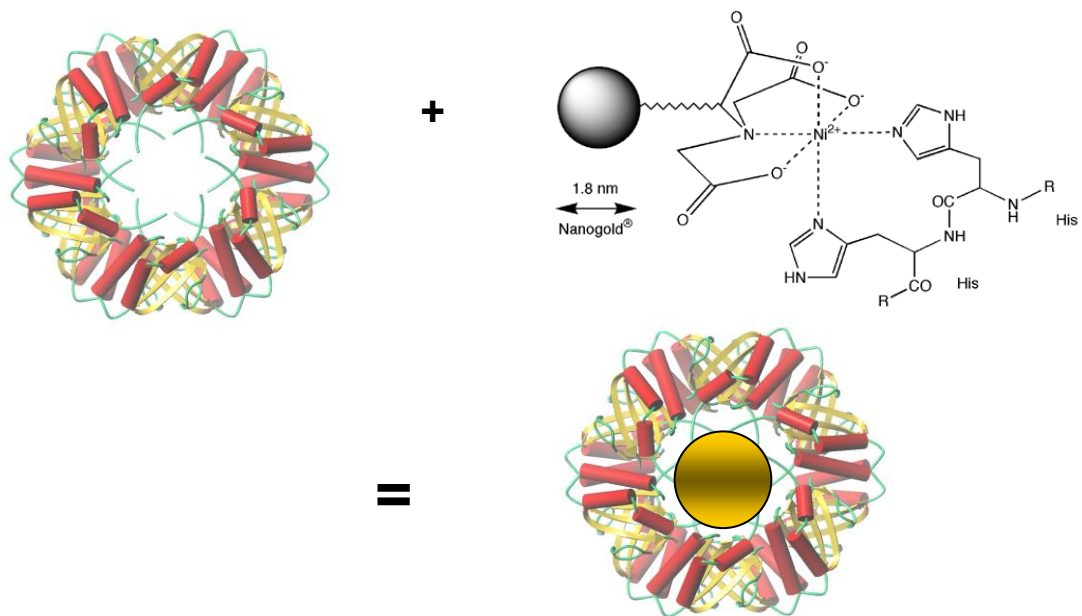4- Morphological characterization of the obtained structures using AFM.

Fig. 4.1- Attachment of gold nanoparticles in the cavity of protein

4.2. Materials and instruments

SP1-protein:

SP1 protein (Stable Protein 1) that used in this study is an initial protein specimen was dissolved in a proper deionized water to obtain a solution with concentration of 0.5 micro g/ml, this solution Fig.4.2 were purchased from fulcrum SP Ltd, at Herzliya, ISRAEL.

Fig. 4.2- SP1 solution

(http://www.fulcrumsp.com/products_SPGuard.htm)

Atomic force microscope (AFM):

The prepared samples were morphologically characterized at the Hebrew university using a" Nanotec AFM" Fig. 4.3 in tapping mode.
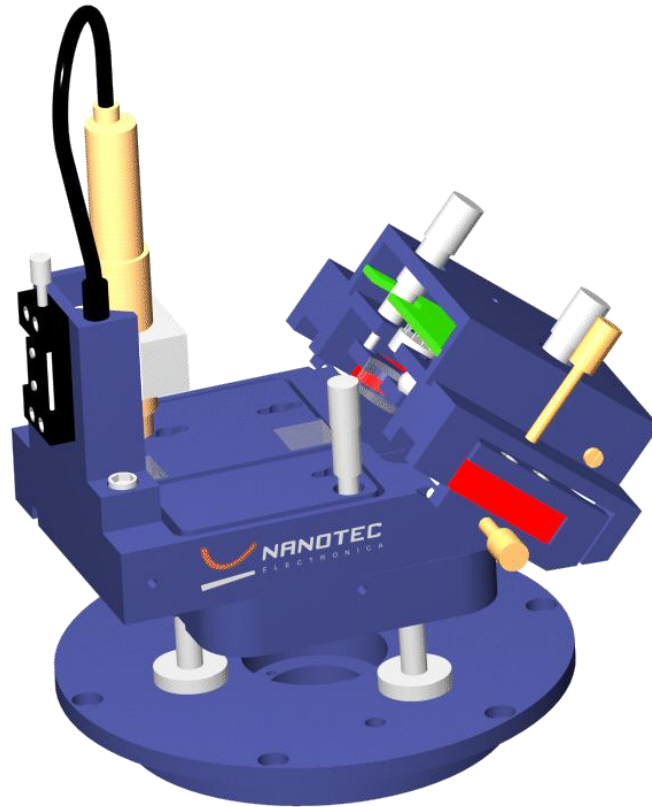

Fig. 4.3-Nanotec AFM

(http://www.nanotec.es/nanotec electronica.htm)

Gold nanoparticles:

The gold nano-particles solution that used in this work is a useful nanoelectronics structure for the self-assembly, with concentration of 2 % (w/v) in toluene

and density of 0.8737 g/mL at 25 °C, this solution was purchased from sigma-Aldrich Ltd, at Rehovot, ISRAEL.

Mica:

Thin mica sheets with dimensions of 1 cm^2 that used in this study were purchased from SPI Ltd, at Talaviv, ISREAL

WSxM:

WSxM 0.4 software was developed by Nanotec company was used for the images analysis, and there are three main types of calculations that were used, the roughness, the density, and the step height.

1. The roughness is used to determine how flat a surface is, this function is located under the analyze menu, to analyze part of an image, highlight the desired part.

2. The density to analyze the density of particles on the surface of the sample, use the particle analysis function under the analyze menu, a histogram was appear on the middle right side of the right screen. And from the 3-D analysis function in the analyze menu we get three dimension image for the sample surface.

3. To determine the step height in an image, we used the step height function under the analyze menu. When the image appears in the step height function, we draw a line along using the cursor along the step, then curve shown the height and the width of the marked site appear.

4.3. sample preparation

4.3.1. Deposition of SP1 on a substrate:

1. The mica surface layer was cleaved with a scotch tape before the depositions of SP1.
2. Ten micro litters of the protein solution of 0.5 micro g/ml concentrations were deposited onto the mica surface using micro pipette.
3. Wait for the required incubation time to take place; through this time the drop of the protein solution is spread all over the 1 cm^2 substrate and the positively charged proteins will bind to the negatively charged mica surface.
4. Upon incubation, the sample was flushed to remove the unbound molecules and salts dissolved in the buffer. For that, the sample was twice rinsed gently with double distilled water.
5. After the sample has been rinsed it was dried on ovens at 30 centigrade for three hours.
6. Thus we have prepared the sample – a piece of mica with deposited molecules on one side.

In my work ten samples were prepared by this method and different incubation time were tested (3, 8, 15 and 20) minutes.

4.3.2. Binding of gold nano-particle to the central cavity of SP1:

A Solution of gold nanoparticles was mixed carefully with a solution of SP1 protein, and lifted for 30 minutes as incubation time for the assembly to take place.

4.3.3.   Deposition of complex on the Mica substrate:

The complex solution that consist from the SP1 protein and the gold nanoparticles were deposit on mica by the method describe above in (3.3.1), different samples with different incubation times (3, 8 and 15) minutes were prepared and tested.

Chapter Five

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Results and discussion

Tens of samples were prepared under two categories

1) SP1 protein without gold nano-particle

   A. SP1 protein on Mica surface with a concentration of 0.5 micro g/ml,
       and 3 minutes incubation time
   B. SP1 protein on Mica surface with a concentration of 0.5 micro g/ml ,
       and 8 minutes incubation time
   C.   SP1 protein on Mica surface with a concentration of 0.5 micro g/ml,
       and 15 minutes incubation time.

D. SP1 protein on Mica surface with a concentration of 0.5 micro g/ml, and 20 minutes incubation time.

2) SP1 protein with gold nano-particle

A. SP1 protein –Gold nanoparticles on Mica surface with a concentration of 0.5 micro g/ml, and 3 minutes incubation time

B. SP1 protein-Gold nanoparticles on Mica surface with a concentration of 0.5 micro g/ml, and 8 minutes incubation time

C. SP1 protein-Gold nanoparticles on Mica surface with a concentration of 0.5 micro g/ml, and 15 minutes incubation time.

All samples were scanned using atomic force microscope in tapping mode at the Hebrew university for topography then, the result was analyzed using the WSxM.

5.1 Topography characterization using AFM

5.1.1 Protein without gold:

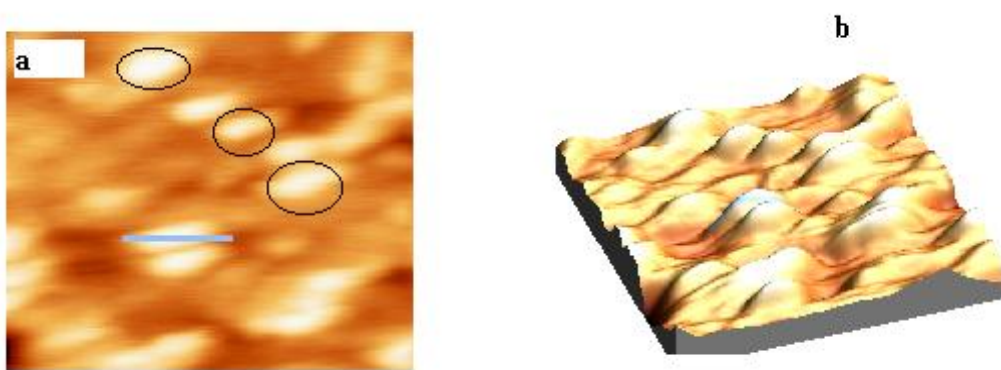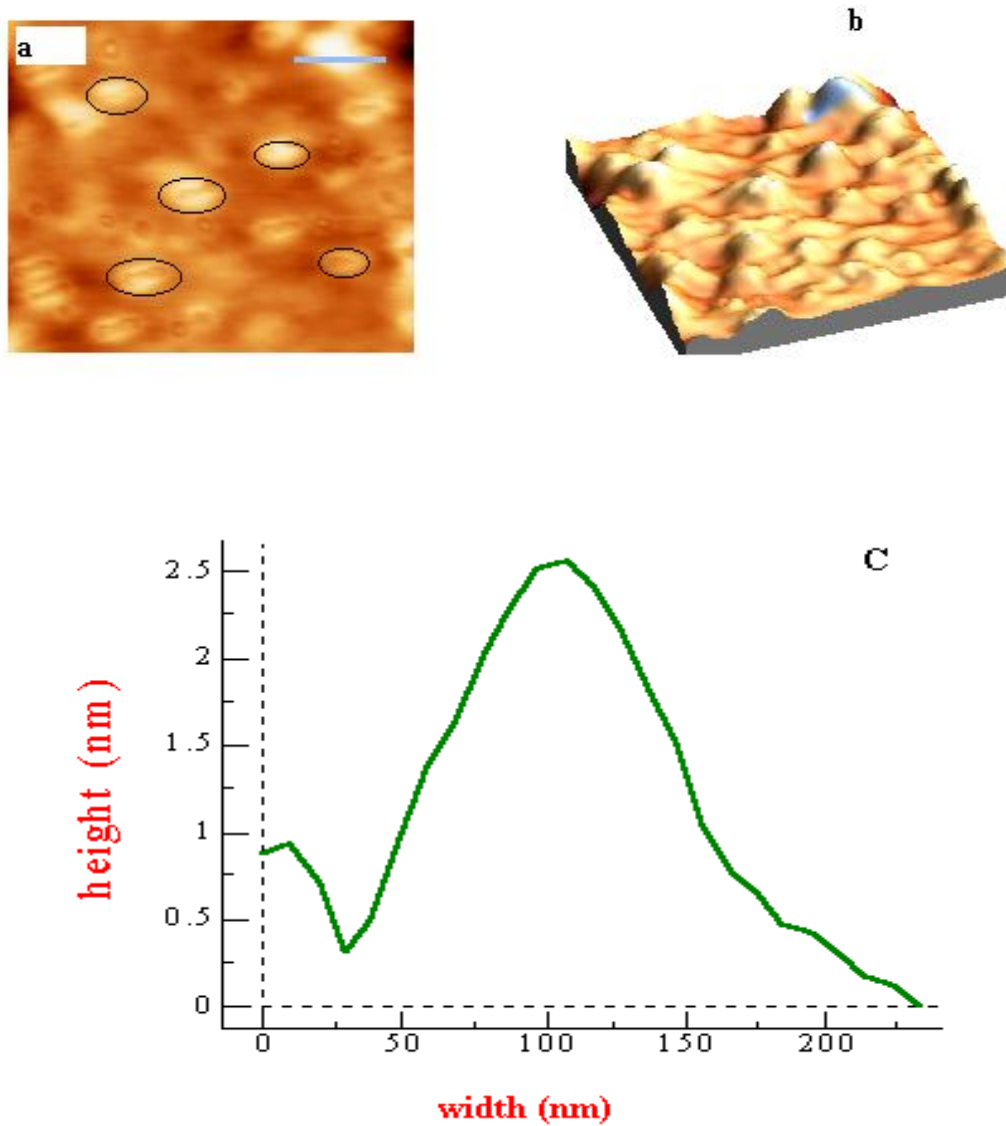**A- SP1 protein on Mica surface with a concentration of 0.5 micro g/ml, and 3 minutes incubation time**
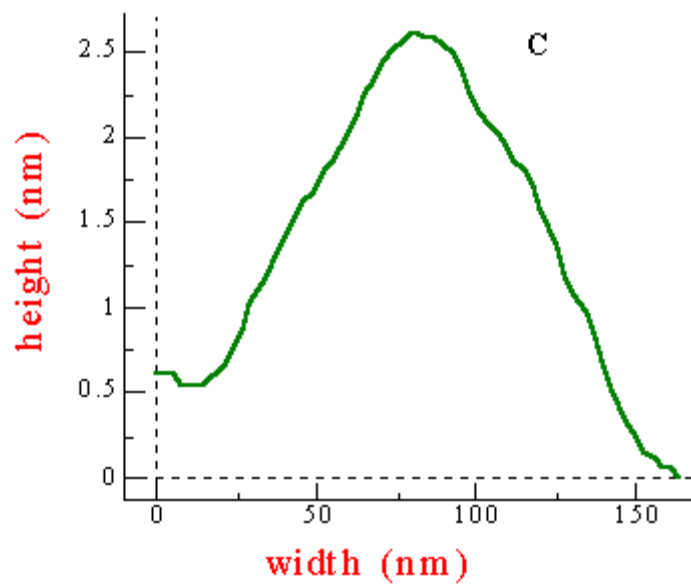
Fig. 5.1- a) AFM topography image of SP1 protein molecules with concentration of 0.5 micro g/ml and incubation time of 3 minutes. b) 3-D structure for the deposited Sp1 on mica substrate. c) Height of SP1 as obtained from the AFM topography image.

B- SP1 protein on Mica surface with a concentration of 0.5 micro g/ml, and 8 minutes incubation time

Fig. 5.2- a) AFM topography image of SP1 protein molecules with a concentration of 0.5 micro g/ml and incubation time of 8 minutes. b) 3-D structure for the deposited Sp1 on mica substrate. c) Height of SP1 as obtained by AFM.

C- SP1 protein on Mica surface with a concentration of 0.5 micro g/ml, and 15 minutes incubation time.
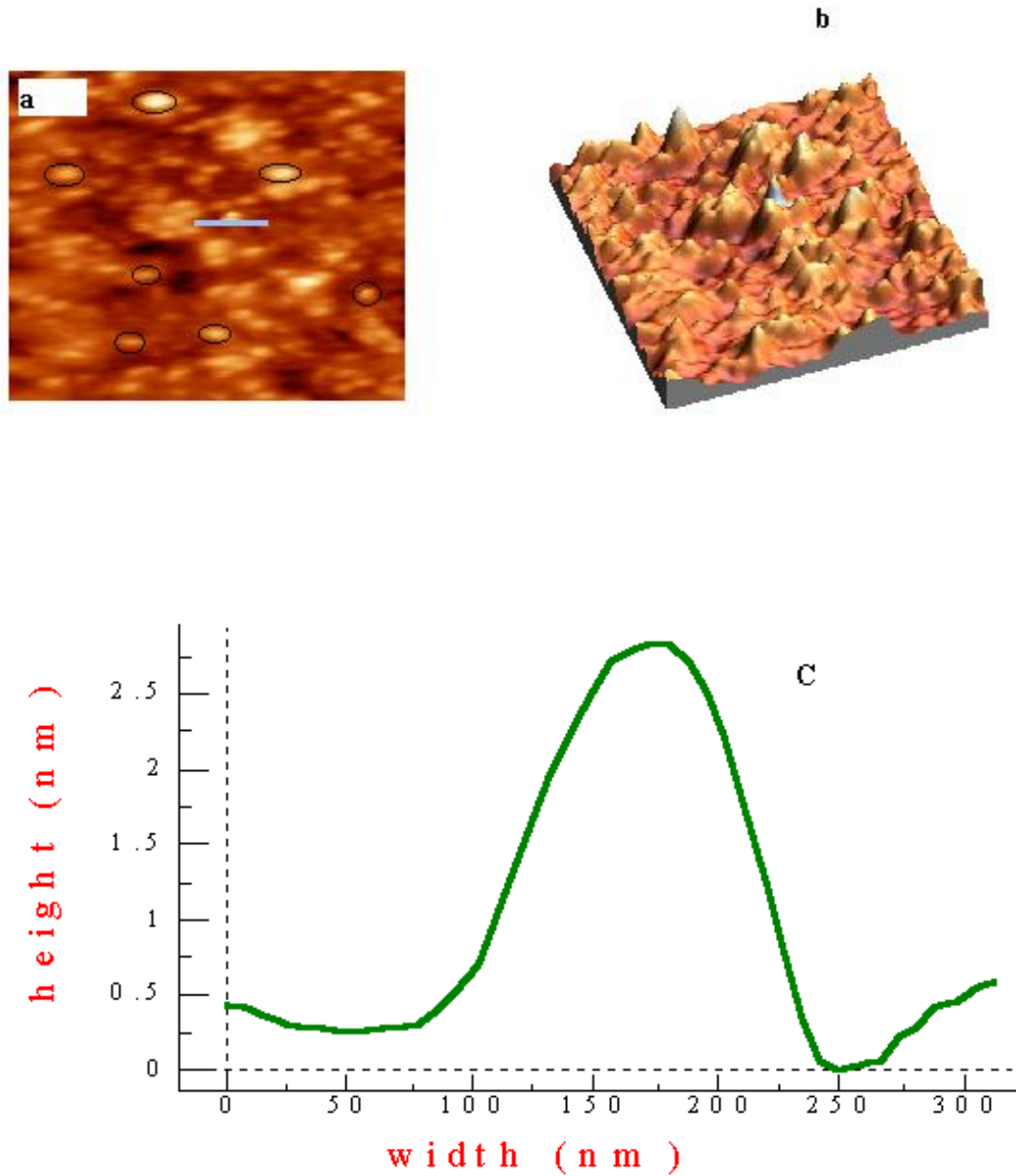

Fig. 5.3 –a) AFM topography image of SP1 protein molecules with a concentration of 0.5 micro g/ml and incubation time of 15 minutes. b) 3-D structure for the deposited Sp1 on mica substrate. c) Height of SP1 as obtained by AFM.

D- SP1 protein on Mica surface with a concentration of 0.5 micro g/ml, and 20 minutes incubation time.
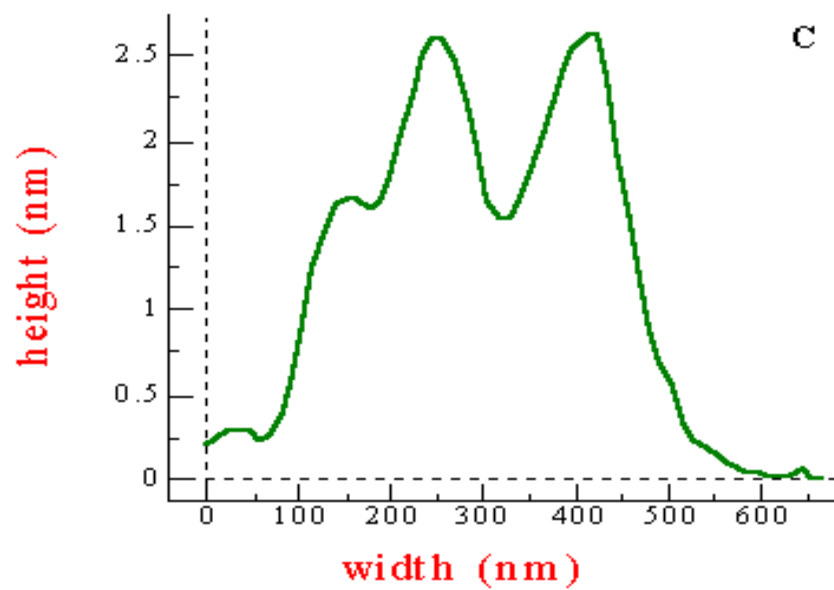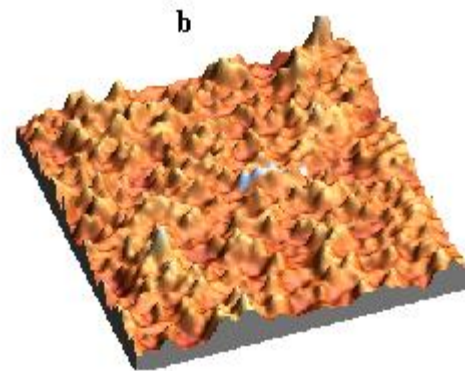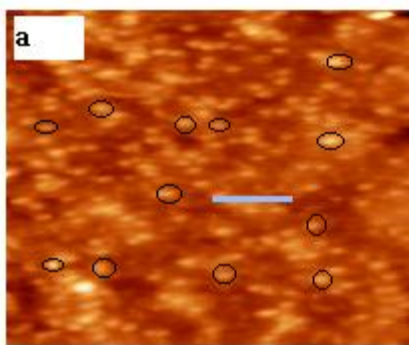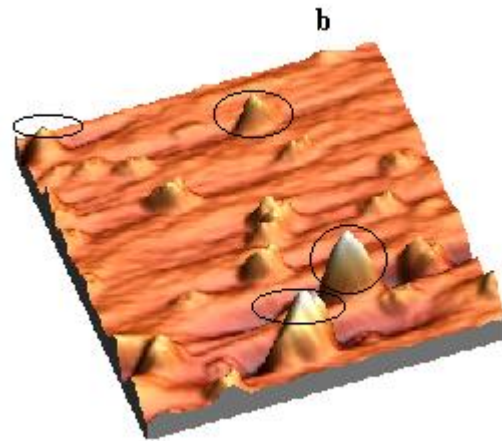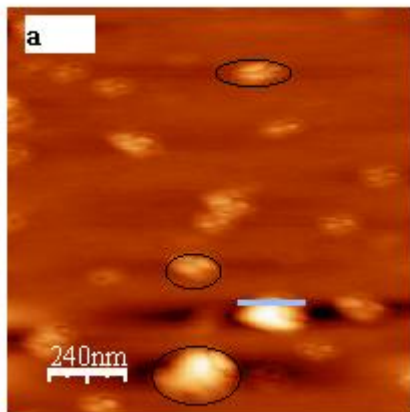
Fig. 5.4 –a) AFM topography image of SP1 protein molecules with a concentration of 5 mg/ml and incubation time of 20 minutes. b) 3-D structure for the deposited Sp1 on mica substrate. c) Height of SP1 as obtained by AFM.

5.1.2 SP1-Gold nanoparticles Cells

A mixture of gold nano-particles and SP1 protein was prepared by the method describe in chapter three, and then a 10 micro litters of the mixture were deposited on the mica for different incubation times as mentioned above.

A- SP1 protein –Gold nanoparticles on Mica surface with a concentration of 0.5 micro g/ml, and 3 minutes incubation time
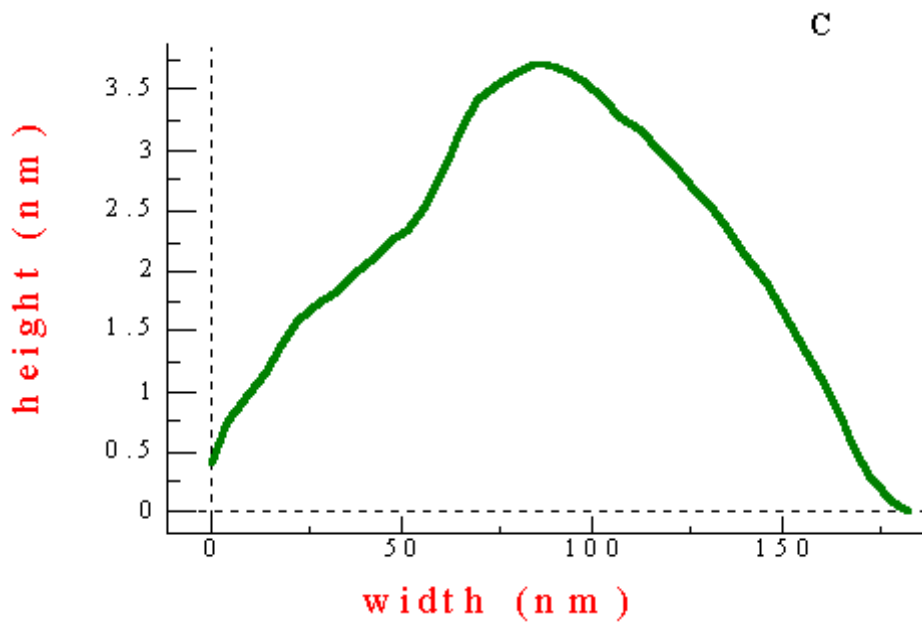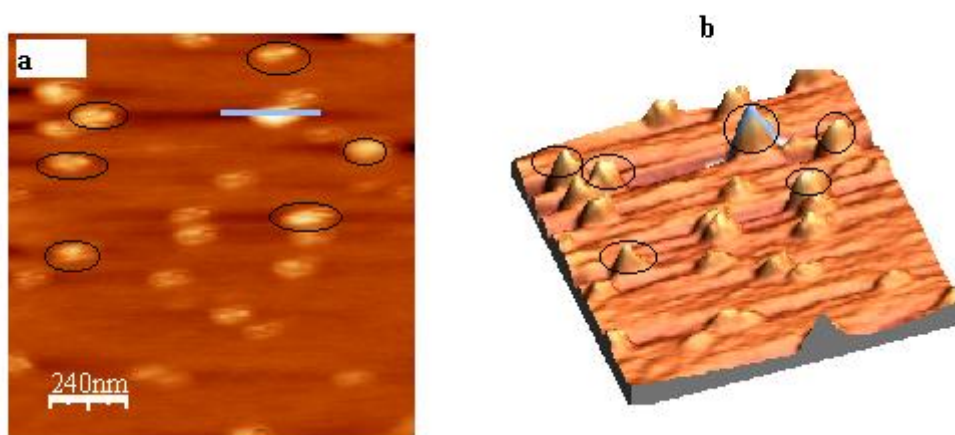
Fig. 5.5- a) AFM topography image of SP1-Gold nanoparticles hybrids with incubation time of three minutes. b) 3-D structure for the deposited Sp1-Gold nanoparticles hybrids on mica substrate. C) Height of SP1-gold nanoparticles hybrids as obtained by AFM.

B- SP1 protein –Gold nanoparticles on Mica surface with a concentration of 0.5 micro g/ml, and 8 minutes incubation time

Fig. 5.6 – a) AFM topography image of SP1-Gold nanoparticles hybrids with incubation time of eight minutes. b) 3-D structure for the deposited Sp1-Gold nanoparticles hybrids on mica substrate. C) Height of SP1-gold nanoparticles hybrids as obtained by AFM.

C- SP1 protein –Gold nanoparticles on Mica surface with a concentration of 0.5 micro g/ml, and 15 minutes incubation time
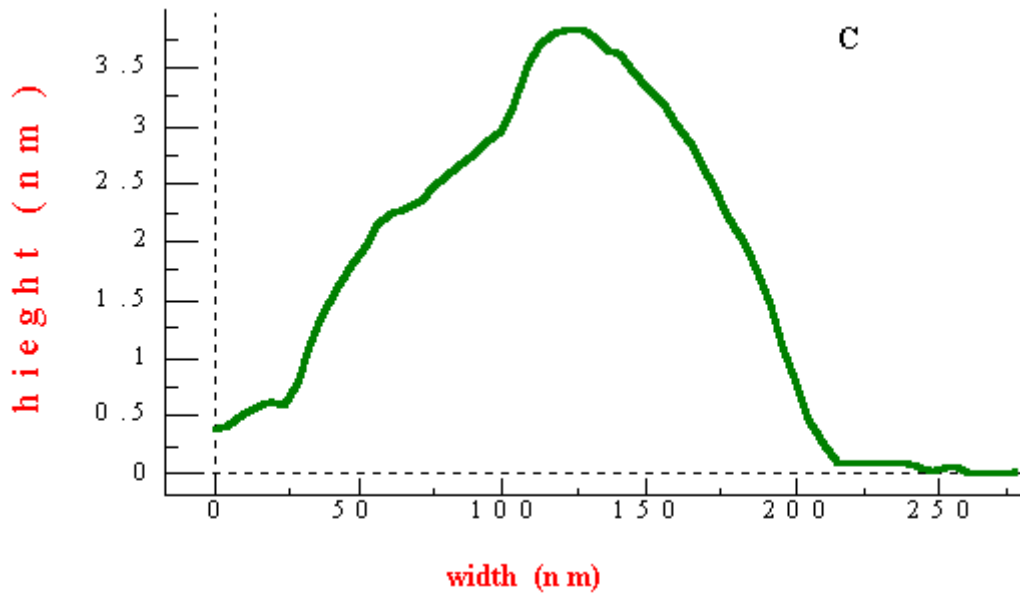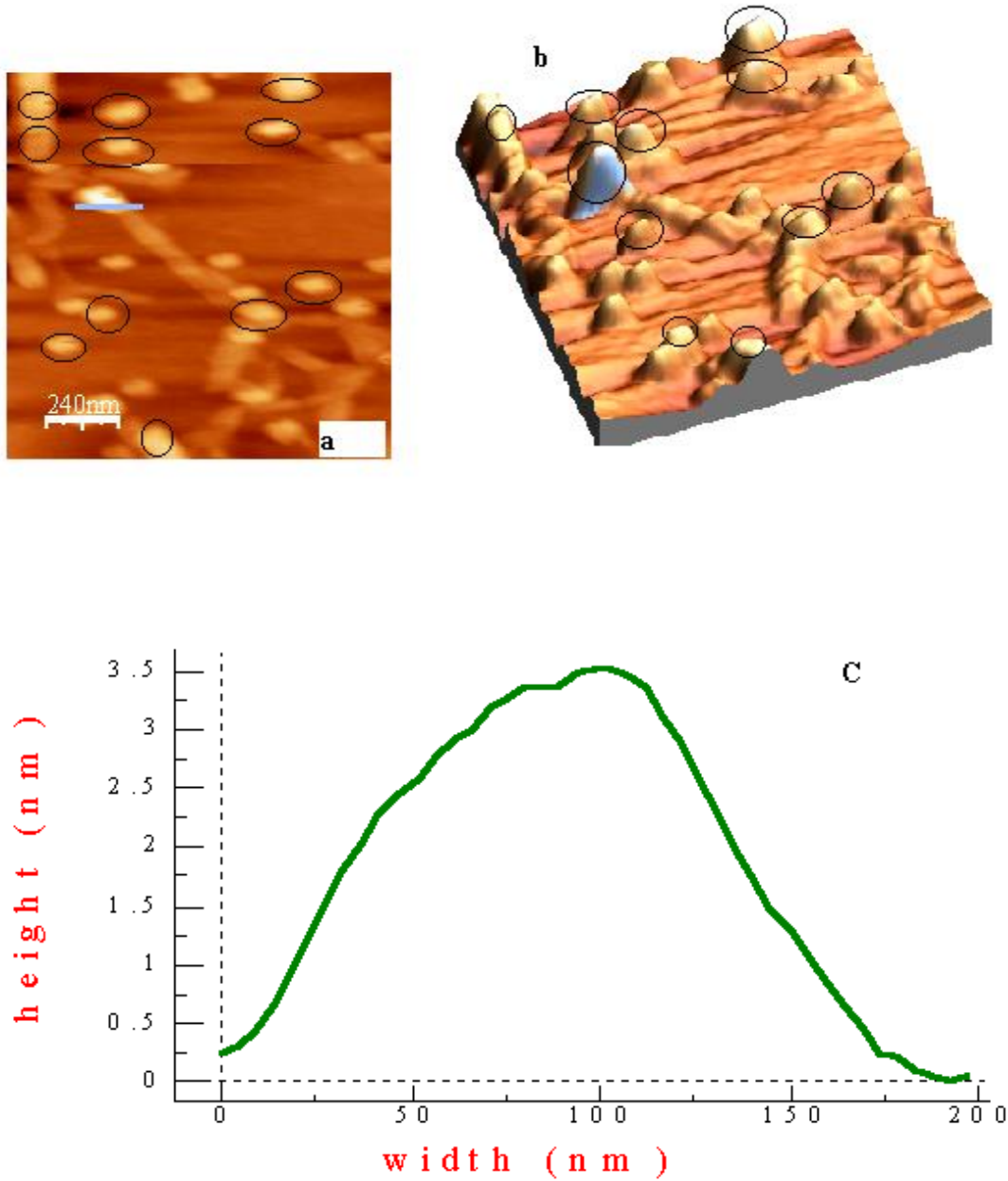

Fig. 5.7 – a) A FM topography image of SP1-Gold nanoparticles hybrids with incubation time of 15 minutes. b) 3-D structure for the deposited Sp1-Gold

nanoparticles hybrids on mica substrate. C) Height of SP1-gold nanoparticles hybrids as obtained by AFM.

5.2 Discussion

The samples were characterized by the AFM on tapping mode and the topography images of single SP1 and SP1-Gold nanoparticles hybrids were analyzed by the WSxM, it was found that the positive SP1 protein was bound with the negative mica surface and the gold nanoparticles were attached to the   cysteine thiol group located in the N-termini of the protein which is expected to behave as an efficient linker and forming covalent bond with the gold.

By scanning the topography images of SP1 and SP1-gold hybrids with the WSxM we found that the height of both structure as we expected and shown table 5.1 and 5.2.

Table 5.1 the height of SP1 assembled on mica surface

Fig. number	Fig. 5.1	Fig. 5.2	Fig. 5.3	Fig. 5.4
SP1 height by (nm $\pm$ 0.2 nm)	2.6	2.5	2.8	2.6

Table 5.2 the height of SP1-gold nanoparticles hybrids as obtained by AFM

Fig. number	Fig 5.5	Fig. 5.6	Fig. 5.7
SP1- gold height by (nm $\pm$ 0.2 nm)	3.7	3.8	3.5

From the data analysis and from the previous curve in 5.1.1 and 5.1.2 it was shown that the width of Sp1 and the width of the unit cell are not (11nm).

This depends on the in plane resolution of the AFM which depends on the geometry of the probe that is used for scanning (Fig.5.8) in general, the sharper the probe the higher the resolution of the AFM image. So the probes near a sample surface are influenced by different forces which can be attractive Van der Waals forces or the elastic repulsion and also adhesion forces will appear.

In the figure below is the theoretical line scan of two spheres that are measured with a sharp probe and a dull probe.
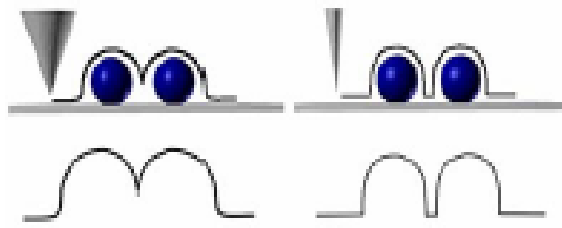
Fig. 5.8- Schematic for AFM resolution

Chapter Six

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Conclusion and future work

6.1 Conclusion

The shape of single SP1 and SP1-Gold nanoparticles hybrids were studied, first the assembled protein (SP1) on the mica surface with different incubation times, second the SP1-Gold nanoparticles hybrids on mica surface for the same concentration and different incubation times.

The AFM image clearly tell us that SP1 molecules were assembled on the mica surface with a satisfactory amounts and this amounts was increased by increasing the incubation time. The measured height of the single SP1 molecules found to be in the range of 2.6 $\pm$0.2 nm.

By studying the topography of the surface it was shown that the molecule of the mixture was assembled to the surface and the measured height of the engineered SP1-gold nanoparticles is about 3.7 $\pm$0.2 nm. This means that the gold nano-particles which are 2 nm in diameter were assembled to the SP1 protein, where a part of the gold nano-particle was immersed in the central cavity of SP1 protein.

6.2 Future works

Our success on the future will pave the way to realize long nanowires and more complex structures that conform to the necessary requirements for nanoelectronics and connect between electrodes Fig. 6.1. In these wires the device functionality is embedded in the structure itself and can be tuned as well, taking into account few key paradigms such as non-linearity and un desired mismatches.
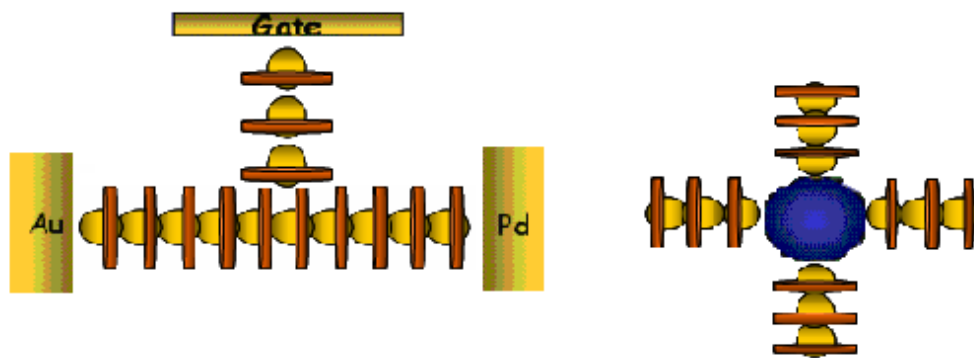
Fig. 6.1- a general scheme of the proposed devices.

After the construction of these building blocks we will do the measurement of the electrical response of these nanowires using electrical transport measurements, between electrodes as well as with conductive atomic force microscope (cAFM) Fig. 6.2.
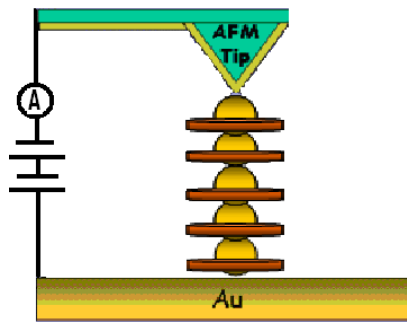
Fig. 6.2- (cAFM) measured the electrical response of nanowires

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