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BIOMOLECULES FOR NANODEVICE APPLICATIONS

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BIOMOLECULES FOR NANODEVICE APPLICATIONS

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ABSTRACT

The density of devices needs to be integrated into various systems increases with the advancement in technology. In order to integrate high density of devices, smaller feature size down to nanometer level has to be achieved. With the current technology, copper may no longer be suitable as interconnect material due to the increase in resistance as the size of the interconnect shrinks and there is an increasing need to explore new materials with novel electron transport properties. Many work has been done on the optical interconnects and the carbon nanotube interconnects as alternatives to the conventional copper interconnects. However, both of these areas have their own limitations.

In this dissertation, peptides are explored as an alternative. The electrical properties of these peptides will be tested, discussed and evaluated with the aim to use the peptides as future interconnects. The main motivation for the use of peptides as an alternative for interconnect arises from the fact that peptides can be readily self assembled in solution onto silicon wafer or any other substrates by controlling the surface chemistry. Self assembly is a fast and cheap process to create interconnects. The peptides will have specific covalent bonding to the substrate unlike carbon nanotube interconnects. In addition, peptide forms atomically precise chain length and the length of the peptide can be varied by changing the number of monomer repeats. The peptides can consist of amino acids which have different functional groups for attachment to specific substrate. For example, cysteine would attach to gold, histidine to nickel and alanine to NH_2 functionalized silicon. In this work on peptides, there are also cysteine and cysteine interaction between the neighbouring peptides, resulting in the formation of disulfide bond. This disulfide bond brings the self assembled peptides closer together forming a highly packed layer. The short distance between the self assembled short peptides resulted in conjugated phenyl rings that give rise to possible charge transportation. In the case of long polypeptide chain, I have shown that the intramolecular bonds resulted in the formation of rigid β sheet secondary structure, which control the distance between the phenyl rings. Again the proximity of the phenyl group at the β turns gives rise to conjugation and hence the possibility of having ballistic electron transport. The versatility

in using the design of peptide to generate interconnect, makes peptide a novel and more possible scheme as compared to carbon nanotubes as future interconnect.

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CHAPTER 1 INTRODUCTION

1.1 Microelectronics and their Interconnects

Electronic devices are basically made up of resistors, transistors, capacitors and inductors. In the twentieth century, the development of three key components- the vacuum tube, the transistor and the integrated circuit mark the history of the electronic devices [1]. In 1883, Thomas Edison discovered the flow of electrons in vacuum from one electrode to another. In 1904, John Fleming making use of the Edison effect to develop a two-element electron tube known as the diode. In 1906, Lee De Forest invented the three-element tube known as the triode. These vacuum tubes made the transmission and the amplification of electrical energy possible. Gulielmo Marconi succeeded in wireless telegraphy in 1896 by using these electron tubes in radio communication. Transistor was invented by a team of engineers from Bell laboratories years after to replace the vacuum tube that was big and bulky. A transistor functions just like the vacuum tube but is much smaller and lighter device that consumes less power.

In 1971, Intel developed the first intergrated circuit microprocessor, Intel 4004 [2]. This processor could perform up to about about 500 additions per joule. In the late 1990s, the microprocessors were capable of performing at 3×10^6 additions per joule because of miniaturization of the circuits. Miniaturization in feature size of the integrated circuits improved the efficiency in many ways [3]. Miniaturization improves the

performance capability by increasing the number of transistors per unit area. This

increases the power efficiency because smaller devices require lesser electrons and the capacitance is also lowered as shorter interconnects give higher speed. There are basically two types of delays in a device; gate delay and interconnect delay (RC delay). As devices shrink, gate delay is decreased and interconnect delay is increased. It will reach a point where the interconnect delay is more dominant in the devices, limiting their capability to be improved any further. Hence, it is very important to reduce the interconnect delay. Interconnect delay can be decreased using lower resistivity materials, lower dielectric constant materials and also decreasing the interconnect length. The advantages of miniaturization are becoming less significant because the improvement in the device performance will be offset by the increase in resistance in the circuit. The device would reach its maximum performance gains at or just below the 50 nm device node, despite the introduction of new generations of metals with higher conductivity and insulators with lower dielectric constant [4]. This is shown in *Figure 1-1* as predicted by

the International Technology Roadmap for Semiconductors (<http://public.itrs.net>) in 2003.

The continual decrease in the feature size of the integrated circuits over the years has generated three major issues [5]; **(1)** Electrical resistivity of sub-50nm conductor lines increases prohibitively with the decrease in dimensions due to the quantum mechanical phenomena and the microstructural limitations (*shown in Figure 1-2*). **(2)** Surface scattering of the electron wave from the boundaries of narrow conductors

Figure 1-2. Effect of line width on electrical resistivity of Cu.

inhibits electronic conduction. This is a serious roadblock to Moore's Law, which states that the number of transistors in a device would double every 18 months, at the most fundamental level. **(3)** As line width approaches the mean free path λ_0 , the surface scattering will inhibit the conductivity in conventional electrical wires.

1.2 Motivation

The miniaturization of devices has reached a point where the interconnect delay is obstructing any improvement in the device performance. A potential strategy would be to exploit quantum mechanical transport mechanisms through molecules or small assemblies of molecules. In such a strategy, ballistic electron phenomena and quantum confinement effects should be used together with nano assembly of individual molecular building blocks to form conducting channel for good conductivity.

In an attempt to overcome problems such as interconnect delay, tunneling of electrons through gate oxide and electromigration issues, there are lots of work done towards the building of molecular devices and logic circuits using self assembled monolayers (SAMs) [6-19]. Not much success has been achieved towards the realization of MOSFET/CMOS based molecular transistor, mainly because of the unknown conduction mechanism, low mobility, difficulty in controlling the length and thickness of these SAMs and the lack of chemical functionalities in them for proper attachment on different substrates in the device structures.

Carbon nanotubes are also explored as an alternative for future interconnect but the main problems with carbon nanotubes is that it is hard to separate the metallic and semiconductor tubes and the functionalization of the nanotubes need to be carried out before the carbon nanotubes can be attached onto specific substrates. These problems of carbon nanotubes can be resolved with the use of peptides.

The main motivation for using peptides as an alternative for molecular interconnect is that peptides can be easily attached onto specific substrates through different amino acid groups. For example, cysteine would attach to gold, histidine to nickel and alanine to NH_2 functionalized silicon. This can resolve the problems faced by carbon nanotubes on selective binding. In addition, peptides can form conjugated phenyl rings for possible ballistic electron transport to occur, making peptides conducting. The non-conducting amino acid groups like alanine and glycine in the backbone can act as a dielectric layer to

prevent the current leakage from the phenyl rings to the silicon wafer. This is a major problem faced by SAMs where the alkyl chain is rather short as compared to peptide. In addition, peptides can readily self assemble via solution phase onto silicon wafer and they can have atomically precise chain length by varying the number of monomer repeats.

Peptides, which are long and have secondary structure, can form rigid β sheet secondary structure. The formation these rigid β sheet controls the distance between the phenyl rings, leading to possible ballistic electron transport. For shorter peptides, cysteine-cysteine interaction which forms disulfide bond, allow better packing of phenyl rings, increasing the possibility of ballistic electron transport.

Based on the above consideration, the peptides were designed and assembled on the substrates using self assembly, Dip-Pen nanolithography, and also electron beam lithography. The peptides are characterized using AFM and the electrical properties of the self assembled interconnects are characterized as well. These peptides can be assembled at the molecular level, molecule by molecule, to form a conducting channel towards realization of molecular device technology.

1.3 Objective

The objectives of this research are:

1. Immobilization of the peptides onto the surface modified silicon substrate and to characterize these peptides using Bioscope II and Digital Instrument Atomic Force Microscopy.
2. To fabricate electrodes/contacts using Soft Electron Beam Lithography (Soft eBL) and Dip-Pen Nanolithography (DPN) for future electrical testing of peptides.
3. To develop two-terminal device fabrication concept using different peptides for transistor application.

4. Test the electrical properties of the immobilized peptides on the two-terminal devices.

1.4 Dissertation outline

Chapter 2 of this dissertation is a review of the literature which discuss the history of interconnects and the challenges faced by interconnect when devices shrink. The details of the work done by other research groups on the charge transfer in peptides will be discussed in this chapter. Literature review on functionalization of silicon wafer with self assembled silane thus allowing peptide with different functional group to be chemically bonded to silicon wafer is presented. Patterning methods such as electron beam lithography and Dip-Pen nanolithography are briefly discussed in this chapter. The fabrication of contacts is very important in order to have an accurate and precise electrical testing. The fabrication methods are discussed in this chapter together with their pros and cons.

Chapter 3 focuses on the materials and the equipment used. The fabrication methods of the devices are also presented.

Chapter 4 focuses on the different patterning methods like electron beam lithography and Dip-Pen lithography. Silicon substrates are functionalized with different silane like aminopropyltriethoxysilane (APTES) and 3-mercaptopropyltrimethoxysilane (MPTMS). Peptides with alanine will contain COOH functional group will bond to NH₂ groups of APTES and cysteine with SH functional group which bond to SH group to MPTMS.

Chapter 5 focuses on the attachment of peptide sequence TyrCysGlyAlaGlyAlaCysAla (free COOH) onto aminopropyltriethoxysilane (APTES) functionalized silicon wafer. After the attachment, electrical testing of the peptide is done for contacts with gap less than 1 μm . field emission scanning electron microscopy (FESEM) and atomic force microscopy (AFM) is used to characterize the contacts.

Chapter 6 focuses on the attachment of long peptide sequence His₆-{(AlaGly)₃GlyLys (AlaGly)₃GlyTyr(AlaGly)₃GlyGlu(AlaGly)₃GlyTyr}₂₅₆ -His₆ onto 3-mercaptopropyl trimethoxysilane (MPTMS) functionalized silicon wafer. After the attachment, the electrical testing of the long peptide is done for contacts with gap of 5 μm. Field emission scanning electron microscopy (FESEM) and atomic force microscopy (AFM) are used to characterize the contacts.

Chapter 7 discusses the conclusion reached based on the results of this study and

Chapter 8 focuses on the future work that can be done in this area.

CHAPTER 2 REVIEW OF LITERATURE

2.1 Interconnects

2.1.1 History of interconnects

In the past generation of the semiconductor industry, aluminium was mainly used as the metal interconnects on devices. Aluminium possesses the following advantages that gave it an edge over the other metals during the selection of interconnect material. Aluminium was selected as the first material for interconnect in the semiconductor industry because aluminium has good conductivity for higher IC speed, low resistance for ohmic contact between aluminium and silicon, good adhesion with insulators such as silicon dioxide, resistance in corrosion, has good deposition and etch properties and good bonding ability and endurance of bonding spot [20]. With the need to scale down the devices to submicron levels, interconnect delay become increasingly more significant compared to gate delay. Interconnect delay is mainly caused by parasitic resistance and capacitance. In early 1990s, metals with lower resistivity such as copper, gold and silver were introduced as an alternative to aluminium because they have lower resistivity compared to aluminium. Gold is a fairly inert metal with low electro migration but it shows little improvement in resistivity and it is rather costly. Silver on the other hand, showed the lowest resistivity but it creates deep levels in silicon gap. This is not favourable and a diffusion barrier needs to be introduced. However, due to the low melting point of silver, building of diffusion barrier is rather difficult due to the high electro migration. Copper appeared to be the best alternative because of the lower resistivity and lower electro migration problem. Copper working as interconnects decreases the resistive part of the interconnect delay making the use of copper as interconnect an attractive alternative [21]. In addition, copper also has higher melting point as compared to aluminium, giving copper an edge over aluminium in term of electro migration and stress migration [22]. However, copper creates deep levels in silicon band gap which is not favourable. With the help of diffusion barrier such as a derivative of tantalum or titanium, copper can be

prevented from diffusing into the transistors. Hence, copper has replaced aluminium since then and has been used as interconnect till this days.

2.1.2 Introduction to interconnects

The role of interconnects in advanced integrated circuits, which contains several millions of transistors, is to link up this transistors within the chip and across the chips. There are basically two level of interconnects in semiconductor devices (*shown in Figure 2-1*). The short interconnects

connecting near the logic gates are known as the local wires and the long interconnects connecting the chips are known as the global wires [23]. The local wires are routed

Figure 2-1. Chip cross-section showing hierarchical interconnects

with the tightest pitch and highest density. The capacitance of the local wire instead of its resistance affect mostly the circuit behaviour as the interconnect resistance is dominated by the driving transistor resistance. Global wires on the other hand are connecting across the chips and hence their length does not scale resulting in larger latency compared to transistor delay. Global wires are made up of thicker copper to minimize the resistance, and are routed with larger pitch to minimize capacitance. Both resistance and capacitance of global wires are important since the delay grows as the square of the length. As the number of transistors within a chip is predicted to increase further over the years, there is a further demand for smaller transistors and narrower interconnects. Scaling degrades the performance of interconnects in terms of delay, signal integrity and reliability. Interconnects are hence viewed as the major limitation in the path for further miniaturization [24]. In order to resolve the issue of rising latency of global interconnects,

optical interconnect can be used for higher speed. Local interconnects can be optimized using a lower dielectric constant material and changing the geometry. Hence, a new innovative material such as carbon nanotubes is introduced since it has a lower dielectric constant.

2.1.3 Imminent challenges for copper interconnects

Copper has dominated over the conventional aluminium in device interconnects in the semiconductor industry. Copper is preferred over aluminium because copper has a lower resistivity than aluminium. However, with the increasing demand from the semiconductor industry, copper interconnect is becoming the limiting factor in the improvements of integrated circuits. In addition, with the introduction of low dielectric materials as insulators, the reliability of interconnects become more challenging since it creates high electro migration problems.

In the past years, as the technology advances, there is an increasing need for higher integration density and higher frequency in order to meet the requirements for higher speed devices. Devices need to be of a smaller feature size in order to fulfill the high packing density. When devices shrink, the feature size for interconnects also need to be shrunk. This continual decrease in the feature size of integrated circuits (ICs) pose issues on the conventional copper interconnects [5]: Electrical resistivity in sub-50nm conductor lines rises prohibitively from its bulk value due to quantum mechanical phenomena and microstructural limitations as the copper interconnect reaches nanoscale. Surface scattering of electron wave from boundaries of ultra-narrow conductors inhibits electronic conduction & stands as serious roadblocks to attaining Moore's Law at the most fundamental level. As line width approaches the mean free path λ_0 , surface scattering inhibits conductivity in conventional copper interconnects. In addition, the presence of a diffusion barrier known as liner, enclosing the copper wire to prevent the diffusion of copper atoms into the dielectric also causes the increase in resistance. The liner has a minimum thickness required to be effective as a diffusion barrier. Therefore,

the overall fraction of the area of liner increases as compared to the copper interconnects, leading to the increase in effective resistivity since the liner is more resistive as compared to copper. The resistivity of the copper interconnects increase tremendously due to the factors mentioned above and these lead to joule heating which stimulates electro migration induced hillocks and voids. The need for increase in current density and use of low dielectric materials further accelerates the shortening of electro migration lifetime of copper interconnect. Decreasing of the size of interconnect leads to the decrease in cross sectional area of copper interconnect. When considering the cross sectional area with liners, the reduction is more severe, increasing the ratio of copper/ cap interface to total copper volume in the interconnect. This would also cause the electro migration lifetime to decrease [25]. Hence, improvement in copper interconnects must be introduced to help limited the cross talk, skin effect, dispersion, signal degradation, power dissipation and electromagnetic interference at higher frequency [26]. In the long run, copper interconnects might no longer be able to fulfill the expectation of the semiconductor industry and the need to explore new materials with novel electron transport properties is much needed.

2.1.4 Demands in future interconnects

Due to the above limitations, traditional copper interconnect would soon be unable to meet the requirements for future interconnects. The future interconnects need to be in the nanoscale range, with high conductivity and high frequency. Potential solutions would be through the discovery of new materials with better material properties, improvements in processing, scaling and novel architectures. In this dissertation, the focus would be on new materials with better properties: **(1)** Optical interconnect which can eliminate the problem of crosstalk and interconnection crossing and also reduce the cost of production and power loss in interconnects. **(2)** Carbon nanotubes which uses quantum mechanical transport mechanisms such as ballistic electron phenomena and quantum confinement effects. **(3)** Peptides which uses quantum mechanical transport mechanisms through molecules or small assemblies of molecule, using ballistic electron phenomena and quantum confinement effects, and nanoassemble individual building blocks at the

molecular level, atom by atom, to form conducting channels towards realization of molecular device technology. With the help of these new research materials, future interconnects can be of higher conductivity, lower interconnect delay, less electro migration, higher frequency and in the range of nanometers.

2.1.5 Optical interconnects as the future global interconnects

Optical interconnects is popular in research areas as the future interconnects. Currently, there are three types of optical interconnects in the market. The three types are the free

space optical interconnects (*shown*

in Figure 2-2), Substrate-mode

optical interconnects (*shown in*

Figure 2-3) and thin film guided-wave

optical interconnect (*shown in*

Figure 2-4) [27]. Due to the

limitations of free space optical

interconnects in terms of its

sensitivity and alignment, other

optical interconnects are proposed

as alternatives. Substrate-mode

optical interconnects guide the

light through a thick substrate by

total internal reflection [28]. This

method is relatively simple to

couple into the system but when

used in long distance transmission,

there would be problem of signal

divergence along the transmission

path. Thin film guided-wave

optical interconnect is hence introduced into the industry. Thin film guided-wave optical

interconnects have difficulty coupling light into the system because discrete set of modes

Figure 2-2. Space optical interconnects

Figure 2-3. Substrate-mode optical interconnects

Figure 2-4. Thin film guided-wave optical interconnect

and coupling angles are required. However, once there is coupling of light into the system, the waves can be controlled without divergence along the transmission path. Every optical interconnects have their respective advantages and disadvantages. The main advantages of optical interconnects over copper interconnects are that there are impedance matching, no cross talk and no aspect ratio limit for optical interconnects. In copper interconnects, termination must be properly designed to have the same impedance to avoid reflections. A lot of power is consumed during this termination process in copper interconnects. However, in optical interconnects, virtually no power is consumed and a beam splitter can be used to tap the optical signal for monitoring with little or no reflections. As feature size shrinks, interconnect gets closer to each other and crosstalk would arise in the case of copper interconnects. Optical interconnects has no problem arising from crosstalk because photons do not interact as easily as electrons [29]. Shrinking feature size of interconnects would also lead to deterioration of bit-rate capacity in copper interconnects. However, in optical interconnects, there is no aspect ratio limit because loss in optical media independent on the modulation bit rate. Hence, optical interconnects provides better properties as compared to copper for future interconnects in devices. However, every material has its disadvantages. The main disadvantages of optical interconnect are that detailed alignment of system must be made to successfully allow proper transmission of waves and that the technology in this area is still immature and costly. More research has to be done to further make optical interconnect fulfill the demands of the future interconnects.

2.1.6 Carbon nanotube as the future local interconnects

Carbon nanotubes has the potential of becoming a good candidate for interconnects because the tremendously high current density of the nanotubes, which can approach 10^9 - 10^{10} A/cm², towards the ballistic transportation of electrons, much higher than copper 400 A/cm² [30]. Carbon nanotubes can be thought of a single atomic layer of graphite rolling to form a seamless cylinder. This resulting structure is called a single walled carbon nanotube. If several single walled carbon nanotubes are layered inside another with varying diameter, a resulting multi walled carbon nanotube is formed (*shown in*

Figure 2-5) [26]. Carbon nanotubes can be classified as metallic or semi conducting depending on the rolling of the carbon nanotube. The semi conducting tubes are commonly used for fabrication of transistors. Metallic tubes are like 1-dimensional metal and can be utilized as an interconnect in devices. Metallic carbon nanotubes are

Figure 2-5. (a) Graphene (b) single walled carbon nanotube (c) Multi walled carbon nanotube

used as stacked interconnects instead of single interconnects because of the benefit of high current density of stacked carbon nanotubes. Carbon nanotubes also have the benefit of no cross talk between the carbon nanotubes due to kinetic inductance, making carbon nanotubes an attractive alternative to future interconnects. However, the setback of carbon nanotube is that we are unable to manipulate them and attach them to different type of substrate. Carbon nanotubes can be grown on or transfer onto silicon wafers [31, 32] and quartz [33, 34] but they do not have functional groups which enable covalent bonding to lots of other substrate. Other setbacks of carbon nanotube are that with current technology, the grown carbon nanotubes cannot be solely metallic but are partially metallic and partially semi-conducting carbon nanotubes and the cost of production of nanotubes is rather high. In addition, contact resistance is also a major problem in carbon nanotubes electrical measurements. In contrast with the resistance between the carbon nanotube and the metallic contacts like gold, the resistance induces by the metallic contact on carbon nanotubes causes the high resistivity. When carbon nanotubes are dispersed onto metallic contacts (bottom contacts), the bending of the carbon nanotubes can lead to the formation of barriers in the tube which will result in undesirable

resistance[35]. When the metallic contacts are placed on top of carbon nanotubes (top contacts), the metallic contacts divide the carbon nanotubes into segments. This leads to barriers forming inside the carbon nanotubes which will result in higher resistance in the carbon nanotubes [36]. Despite the challenges to be overcome, carbon nanotubes remain an alternative that is vigorously studied and improved to become the future interconnects. In this dissertation, peptide biomolecules would be investigated as a possible alternative for future interconnects.

2.2 Peptides

2.2.1 Introduction to peptides

Peptides are biomolecules formed from the 20 naturally occurring amino acids. *Figure 2-6* shows dehydration synthesis reaction (known as condensation reaction) occurs between the COOH group of one amino acid with the NH₂ of the other amino acid, forming a CO-

NH bond which is known as the amide bond or peptide bond. One end of the peptide is called the amino terminal or N-terminal and it has a free amino group. The other end of the peptide with a free carboxyl group is called the carboxyl terminal or C-terminal. Peptides are made of amino-acids linking into a linear chain with overall length up to 100 amino-acids. Scientists nowadays usually describe peptide of 50 amino-acids and more as polypeptides. Peptides have many advantages over conventional polymers since they are able to self assemble hierarchically into stable ordered conformations [37]. Peptides have defined molecular weight, monodispersity, stereoregularity, sequence and composition controlled at monomer level allowing formation of ordered conformations.

2.2.2 Synthesis of Peptides: Genetic Expression

Peptide can be either formed biologically or chemically. Peptides have been formed biologically in animals and plants and are essential to all living things. Scientists have been trying to make improvement in the peptides by genetically engineering the peptides and also chemically synthesizing the peptides. Extraction of useful peptides from animal or plants has been

done with great cost since the peptides are in small quantities. Genetically engineered peptides have hence been studied to increase the supply of useful peptides. Peptides are genetically engineered by substituting the different amino-acids from the naturally occurring sequence. This sequence can be changed by producing a synthetic DNA that encodes this new sequence of the peptide as shown in *Figure 2-7* [38]. The advantage of genetically expressed peptides is that long peptide chains up to 1200 amino-acids can be produced efficiently in large scale by this method; it may be impossible to produce long peptides using chemical synthesis method. Even though the construction of the DNA takes several months, it only has to be done once. After the introducing the DNA into a genetically engineered production organism, the peptide can be produced with great precision and indefinitely. However, the limitation of genetically engineered peptide is that only small changes can be made before the bioactivity of the peptide is completely loss [38].

2.2.3 Synthesis of Peptides: Chemical Synthesis

Chemical synthesis of peptides on the other hand is cost effective and a rapid method when synthesizing short peptides, shown in *Figure 2-8 [39]*. Chemical synthesis of

peptides is classified into two main categories, solution phase synthesis and solid phase synthesis. Synthesis of peptides in solution phase involves the condensation of short peptide sequence via a step growth into a longer peptide sequence. Solution phase synthesis is the most useful way to produce short peptides of 3-6 residues. The advantages are that pure intermediate products are formed after every synthesis steps and it is flexible since the peptides can be deprotected and recombined forming peptides of longer chains. However, the limitation of solution phase synthesis is that it is costly and the difficulty in preparation for cyclization reaction. New strategies in solution phase have been developed by using functional groups for side reaction [40] and using of new coupling reagents [41]. Synthesis of peptides in solid phase involves the stepwise addition of N-protected amino-acids to a peptide chain that is anchored to matrix [42]. Solid phase synthesis has the drawback that the purification of peptides is done only after cleavage from the matrix. However, there are advantages of solid phase synthesis over solution phase. The reaction can now be automated and solubility of peptides is no longer

a problem since it remains on the solid matrix. An additional advantage is that the peptides synthesized by solid phase synthesis is that after cleaving from the matrix can be cyclized to form small peptides of alternating stereoisomer. This alternating stereoisomer allows the rings to form hydrogen bond with adjacent rings like beta sheets, causing self assembly. In this report, both biologically and also chemically synthesized peptides are utilized.

2.2.4 Charge transport in biomolecules/ peptides

It has been commonly known that biomolecules are non-conducting in nature. However, charge conductivity of biomolecules has become an interest recently. There are basically two classes of work on the charge transport through peptide molecules, modeling and experiment work. Sheu et al. investigated on the charge transfer in peptide using bifunctional model and suggested that peptide has near ideal conduction in its isolation state [43]. In contrast to intuitive view that water aids in charge transport, Sheu's modeling studies showed that water molecules in fact inhibited the charge transport process because of thermal fluctuation and protein-water collision. Secondary structure of the peptide changes the charge transport efficiency; a more rigid β -sheet structure of peptide gives a higher conductivity in contrast to more flexible α -helix structure of peptide. Malak et al. discussed the long range electron transfer across the proline oligomer peptide bridges [44]. They believed that electron transfer may occur according to superexchange or hopping mechanism depending on the length of the peptide bridges. Superexchange proved to be more dominating in shorter peptide while hopping mechanism is more dominating for the longer peptide. The rate constant of electron transfer is found by photolysis and radiolysis method. Their data showed that the rate of electron transfer was slower for longer peptide bridge. Electron hole transport through the three electron bond along the peptide chains is another investigation carried out on electron transport through peptides by Chen et al. [45]. Their ab initio molecular dynamics simulation model showed that the oxygen oxygen three electron bonds can be intramolecular or intermolecular, which transport charges along the peptide chains. Oxygen aromatic ring three electron bond is found to be more stable than oxygen sulphur

three electron bond and both are more stable than the oxygen oxygen three electron bond. These three electron bonds formed assist the electron hole migration along the peptide backbone in peptide, serving as intermediate or relay stations. The charge transport along the three electron bonds supported the fact that peptide can be used as conduction wires. DiLabio et al. investigated on the proton-coupled electron transfer (PCET), a type of hydrogen atom transfer (HAT) reaction via computational calculation [46]. They believed that the electron transfer through aromatic peptides is by PCET. PCET differs from HAT because it occurs when a proton and electron are transferred between different sets of molecular orbitals. They showed the hydrogen exchange in tyrosine/phenol couple occurs by PCET and that the electron transfer via π stacking interaction. Benzyl/ toluene couple, a system without H-bonding is also shown to have PCET to some extent. Sek et al. studied on the conductivity through the α -helix peptide molecule using STM probe [47]. The peptide has one $-SH$ bond at each end of the peptide; one $-SH$ bond would be bonded to the gold substrate and the other to the STM tip. Using STM for electrical measurement might cause some distortion in the α -helix peptide secondary structure of the peptide. Sek et al. observed an asymmetrical IV curve which was expected to be due to fact that the peptide has an effective positive charge at N-terminus and negative charged at the C—terminus. Hence, the electron transfer through the α -helix peptide would be greatly determined by the electric field generated by the dipole of the α -helix peptide. This unique property of the α -helix peptide makes it suitable to be used as a rectifier. Giese also investigated on the charge transfer through peptides and DNA [48]. Charge transfer through aromatic side chains are by hopping mechanism from one aromatic side chain to another using solvent as a mediator. Charge transfer is not only through peptide bond but also through space for example water. DNA is more efficient as a mediator but peptide is more flexible than DNA. Other studies on the long range electron transfer through peptide also showed secondary structure and the length of the peptide both influence the rate of electron transfer. Despite many studies are done on charge transfer through peptide, the detailed mechanism of the electron transfer through peptide is still in discussion [49].

2.3 Self Assembly of Silane onto Silicon substrate

Self assembly method has been employed in order to attach the peptide onto silicon wafer. Self assembly monolayer (SAM) has attracted tremendous interest due to their capability to absorb onto specific substrate at molecular level [7, 50]. After absorption, the absorbed molecules reorganize to form a close packed structure through Van der Waals interactions between the aliphatic chains. The first publication in self assembly monolayer was by Nuzzo et al,

Figure 2-9. Condensation reaction of Silane onto Silicon Wafer

publishing on the self assembly of organic molecules on gold to modify the physicochemical properties of gold surfaces because of the bonding between the sulphur group of the organic molecules with gold surface [51]. Silane is silicon-based self assembly monolayer molecule that consists of both organic and inorganic reactive group in the same molecule. The typical structure of silane is $(\text{RO})_3\text{SiCH}_2\text{CH}_2\text{X}$, where RO is a hydrolyzable group such as methoxy, ethoxy, or acetoxy and X is an organofunctional group such as amino, methacryloxy, epoxy or mercapto. Silane is commonly used as a linker to bond an organic material such as polymer to an inorganic substrate such as silicon, glass or metal. It is useful in this report as a linker to bind peptide (organic component) to silicon substrate (inorganic component). *Figure 2-9* shows the condensation reaction of silanes onto silicon substrate [52]. The silanes are reversibly physisorbed onto the hydrated silicon substrate through hydrogen bonding, bringing the silanes near to the water layer on the silicon substrate. Covalent bonding takes place after

the physisorption and water is produced as a side product. During the initial stage, only few molecules are chemisorbed onto the silicon substrate, forming a disordered layer. However, at a longer time, the surface coverage would reach a well ordered and compact layer. The functional group at the other end of the silanes can subsequently react with the functional groups of peptide, forming strong covalent bonds. The thickness of self assembly monolayers can be determined by several methods, including ellipsometry [53] and angle resolved X-ray photoelectron spectroscopy [54]. Atomic force microscopy is also used in measuring the thickness by scratching the self assembly monolayer with the atomic force microscopy tip [55]. In this dissertation, the self assembly monolayer has been patterned in order to use atomic force microscopy to measure the difference in height between the bare substrate and the self assembly monolayer.

2.4 Nanopatterning using lithography techniques

Nanopatterning has been employed in this dissertation in order to characterize the self assembled molecules more easily. In 1980s, when Eric Drexler claimed that nanotechnology will dramatically change the world, many disbelieved him. However, the idea of nanotechnology presently has much appeal to most of the scientist. The driving factors that facilitated advancement in nanotechnology are the need for smaller devices for electronic circuits, the invention of scanning probe microscopy to aid in the observation in molecular level and also the possibility of change in material properties when going down to nanoscale. Conventional lithography techniques such as photolithography [56], microwriting [57] and microcontact printing [57] can produce micro-sized patterns. Over the years due to increasing needs for smaller features down to sub 100 nm since smaller devices now promise higher speed at lower cost. The need for smaller devices leads to the development for nanopatterning. Extreme Ultraviolet lithography (EUV) [58] is used widely in industry to produce nanoscale patterns. In extreme Ultraviolet lithography, the wavelength of the light is smaller leading to the possibility of achieving smaller scale patterns. There are two classes of patterning, the top-down and bottom-up techniques. Top-down technique involves the use of lithography

to decrease the feature sizes of devices and bottom-up technique involves the building of features from molecular level. In this dissertation, both top-down which is soft electron beam lithography and bottom-up which is dip pen lithography have been engaged to pattern the peptides.

2.4.1 Nanopatterning of Peptides with Soft Electron Beam Lithography

Soft electron beam lithography (*e*BL) is a specialized top-down technique for creating the extremely fine patterns required by electronics industry for integrated circuits. This is made possible due to small spot size of the electrons, unlike optical lithography where the resolution is limited by the wavelength of light used for exposure. The electron beam has wavelength so small that diffraction no longer defines the lithographic resolution. *e*BL involved exposing a photoresist to scanning beam of electron in patterned manner, removing either the exposed area or unexposed area depending on the type of resist. Positive resists develop away after exposure, whereas the negative resist remain after exposure after development. A layer of co-

Figure 2-10. Soft *e*BL

polymer is first spun onto the wafer, followed by another layer of PMMA. *Figure 2-10* shows both the co-polymer and PMMA are positive resist that will be broken down by the electron beam after exposure, creating a pattern when it is developed. After the pattern is created, the required molecules can be deposited into the pattern.

2.4.2 Nanopatterning of Peptides with Dip-Pen Lithography

Dip-Pen Lithography (DPN) is first developed in 1999 by Chad A. Mirkin [59]. Dip-Pen Lithography is a bottom-up technique that involves dipping an atomic force microscopy tip into a specially formulated ink and writing this ink onto the substrate. It works just like a pen writing ink onto paper. *Figure 2-11* shows that the water meniscus forms

Figure 2-11. Image of transportation of ink molecules to substrate (From Nanoink)

naturally in air between the tip and substrate and this meniscus aids the transport of ink molecules onto the substrate [60]. There are several variables when considering DPN as a nanolithography method: dwell time, humidity, diffusion coefficient of ink and temperature. The time the tip spends on the substrate is called the dwell time and this is directly related to the size of the pattern created. For example, a 5 second dwell time may create a 10 μm dot while a 10 second dwell time may create a 30 μm dot. Humidity on the other hand would play a part in the size of the water meniscus, allowing more or less ink to flow from the tip to the substrate, hence affecting the amount of ink absorbed onto the substrate. Diffusion coefficient of the ink plays an important role in deciding the rate of writing. Diffusion coefficient is unique for every ink. For example, an ink with high diffusion coefficient may produce a 30 μm line width whereas an ink with a lower diffusion coefficient may produce a 10 μm line width even though they are both written at the same rate. Hence, every ink should be calibrated first before writing in order to produce the line width required. Temperature of the environment will determine how quickly the ink will dry on the tip, thereby limiting the amount of time on hand for patterning the ink onto the substrate. Hence, when writing the peptide molecules using DPN, these conditions have to be taken into consideration.

2.5 Fabrication of contacts

Fabrication of contacts is very important for electrical measurement of the peptides. The contacts can be fabricated vertically or laterally. For vertical contacts, the bottom contact is fabricated first and the self assembled monolayer is deposited followed by the evaporation of top contact. However, this type of contacts is likely to have filamentary pathways of metal atom through the monolayer due to the non continual layer of monolayer. The probability of forming filamentary pathway can be greatly reduced by forming the contacts in an active area smaller than the domain of the self assembled monolayer. If a large area is needed, using cold evaporation technique could also help reduce the chance of forming filamentary pathway. In this dissertation, the focus would be more on the lateral contacts since the peptides would be deposited laterally. Lateral contacts can be formed by normal lithography, and if smaller feature size is needed, mechanically break junction, electrical break junction and *e*BL can be also utilized.

Mechanical break junction was used for molecular device testing by Reed et al [61]. Standard mechanical break junctions are created using electron beam lithography and Ti/Au is evaporated into the patterned formed. Aluminum is evaporated around the gold electrodes, forming a mask to etch through SiO₂ with CF₄/O₂ plasma and aluminum is removed using wet etch. Finally, pyrocatechol-ethylene-diamine is using to etch the

Figure 2-12. SEM image of free standing electrode

Figure 2-13. Image of mechanical breaking setup

exposed Si area. The electrodes are now free standing as shown in *Figure 2-12*. This

device is then placed against two counter support, the piezo element at the back of the device exerts a force, straining the device, causing a fracture in the gold cantilever, forming a mechanical break junction shown in *Figure 2-13*. The disadvantage of mechanical break junction is that it is hard to make a gate electrode because of the gold electrodes are suspended.

Electrical break junction can overcome the disadvantage of mechanical break junction. McEun et al. created electrical break junction using electromigration of thin gold line [62]. Thin Cr/Au wires are created with electron beam lithography with bilayer resist to create an angled trench and angle evaporation is employed to create the contacts as

Figure 2-14. Image of connected gold wire (left) and electrical break junction (right)

shown in *Figure 2-14*. Electrical break junction can be created by passing a controlled current through the Cr/Au wire. One major drawback of electrical break junction is that the non-uniformity of the electrode near the junction.

The best method of forming lateral electrode could be probably by cross beam lithography using focused ion beam (FIB) with electron beam lithography (eBL). This method of fabricating electrodes is employed by Cabrini et al. [63]. Large gold pads were

Figure 2-15. Image of gold pattern using optical and electron beam lithography

created using optical lithography and small 200nm wide gold connecting the two large gold pads is made by electron beam lithography shown in *Figure 2-15*. This electron beam gold wire is thinned using FIB milling to about 50-60nm. Using FIB of 5pA ion current for 3s allows a nano gap of 10nm to be formed shown in *Figure 2-16*.

Figure 2-16. Image of gold pattern using optical and electron beam lithography

2.6 Summary

This chapter introduces the challenges faced by the copper interconnects and the motivation to explore new materials such as peptides. Peptide synthesis, genetic and chemical synthesis, and the charge transport in peptides were covered in this chapter. Self assembly and nanopatterning methods like electron beam lithography and Dip-Pen lithography were elaborated to give better understanding of the peptide attachment. Lastly, this chapter covers the fabrication method of the electrical contacts.

CHAPTER 3 MATERIALS & METHODS

3.1 Materials and Equipments Used

3.1.1 Materials Used

Three types of peptides were used in this work. They are the polypeptide functionalized with silane end group and polypeptide with free SH functional group and single peptide with free COOH functional group. The polypeptides are provided by my collaborator in Northwestern University, Dr Gajendra Shekhawat, and the single peptide designed by my group is synthesized by First Base. Linker molecules such as 3-mercaptopropyl trimethoxysilane (MPTMS) and aminopropyltriethoxysilane (APTES) were bought from Sigma-Aldrich. 95% sulfuric acid (H_2SO_4), 30% hydrogen peroxide (H_2O_2) together with solvents like hexane, dimethylformamide (DMF), anhydrous toluene and isopropyl alcohol (IPA) were from Sigma-Aldrich. Photoresists such as polymethyl methacrylate and ~8.5% methacrylic acid (MMA(8.5)MAA) and polymethyl methacrylate (950 PMMA), and resist developing solution such as 1:1 ratio of methyl isobutyl ketone (MIBK) in isopropyl alcohol (IPA) were bought from MicroChem. AZ9260 positive photoresist and resist developing solution AZ400K were bought from microchemicals. Sodium chloride, potassium chloride, sodium phosphate dibasic dehydrate ($\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$), potassium phosphate monobasic (KH_2PO_4) and sodium Hydroxide were obtained from Sigma-Aldrich. DyLight 488 NHS Ester fluorophore and 10,000 MWCO Dialysis Kit were bought from Pierce Biotechnology. All materials were used without further purification unless otherwise specified.

3.1.2 Equipments Used

Bioscope II and Digital Instrument atomic force microscopy (DiAFM) were used to image the morphology of the linker molecules and peptides on silicon substrates. JOEL 4210 SPM and Keithley probe station were used to measure the electrical properties of the peptides while Quanta 600 Field Emission scanning electron microscopy was used in

the nanopatterning of the wafers. The presence of linker molecules and peptides were determined using fourier transform infrared spectroscopy (FTIR) and fluorescence microscopy of the peptides tagged with 488 NHS Ester Fluorophores.

3.2 Procedures

3.2.1 Nomenclature

Three types of peptides used in this project are listed below:

1. Peptide sequence with free COOH functional group:
TyrCysGlyAlaGlyAlaCysAla(free COOH)
2. Peptide sequence with free SH functional group:
His₆-{(Gly-Ala)₃Gly-Cys(free SH)-(Gly-Ala)₃Gly-Phe}₈-His₆
3. Peptide sequence of silane functionalized peptide(256mer polypeptide):
His₆-{(AlaGly)₃GlyLys(AlaGly)₃GlyTyr(AlaGly)₃GlyGlu(AlaGly)₃GlyTyr}₂₅₆-His₆

3.2.2 Substrate Cleaning

Piranha solution was prepared by mixing 2 parts H₂SO₄ with 1 part 30% H₂O₂. This solution is placed on a hotplate of 65 °C. Silicon wafers are immersed into the piranha solution for 30mins, removed and rinsed thoroughly with DI water and blow dried with N₂ gas.

Piranha solution is a highly oxidative solution which removes any organic or metal contaminants on the surface of the silicon wafer via oxidation and the formation of soluble complexes.

3.2.3 Attachment of Peptide His₆-{(AlaGly)₃GlyLys(AlaGly)₃GlyTyr(AlaGly)₃GlyGlu(AlaGly)₃GlyTyr}₂₅₆-His₆ for concentration studies

The peptides were dissolved in hexane at different concentrations of 0.05 mM, 0.1 mM, 0.25 mM, 0.5 mM and 0.8 mM. Silicon wafers were immersed in the peptide solution overnight. It is then rinsed thoroughly with DI water and blow dried using N₂ gas.

3.2.4 Spin Coating of photo resists onto Silicon Wafer (eBL patterning of wafer)

MMA (8.5) MAA is dispensed onto the silicon wafer such that it covers the whole wafer.

A 3 step program was used for the spin coating process:

1. Spin for 5 seconds at 500rpm
2. Stop for 15 seconds
3. Spin for 45 seconds at 3000rpm

Spin coating involves deposition, spin-up, spin-off and evaporation.

The 3 steps process will generally produce a more uniform layer of MMA (8.5) MAA. The first step allows the liquid to spread across the silicon wafer, during the second step MMA (8.5) MAA attaches onto the silicon wafer and the third step spins off the excess MMA (8.5) MAA from the wafer.

After spin-coating for 65 seconds, the silicon wafer was baked for 1 minute at 175 °C to evaporate off the excess solvent.

An excess PMMA is dispensed onto the MMA (8.5) MAA coated silicon wafer, covering the entire wafer. The same spin coating and post baking process employed for MMA (8.5) MAA was repeated for the PMMA.

Subsequently the PMMA on MMA (8.5) MAA coated wafers were used for soft electron beam lithography (soft eBL).

Figure 3-1. PMMA layer on top of MMA(8.5)MAA

3.2.5 Developing of photo resists to create pattern trenches on silicon wafer (eBL patterning of wafer)

The developing solution was prepared by mixing 1 part of Isopropyl alcohol (IPA) to 1 part of Methyl isobutyl ketone (MIBK) in IPA (1 : 1). This would then give a solution of 1:3 ratio of MIBK to IPA. The electron beam patterned silicon wafers were then developed by immersion into the solution for 80 seconds. After which the wafers were rinsed thoroughly with IPA, DI water and blow dried with N₂ gas.

3.2.6 Deposition of linker molecules on eBL patterned trenches exposing silicon wafers (eBL patterning of wafer)

5 μ l of 3-mercaptopropyl trimethoxysilane (MPTMS) was drop-casted onto the patterned silicon wafer. The solution is then allowed to react with the substrate for 15mins before being removed by rinsing thoroughly with toluene, DI water and subsequently blow dried with N₂ gas.

5 μ l of aminopropyltriethoxysilane (APTES) was placed in a Petri dish. APTES is then allowed to evaporate in an atmospheric chamber under reduced pressure onto the patterned silicon wafer for 1hr. The patterned wafer is then cured at 80⁰C for 2 hours. Finally, it is rinsed thoroughly with toluene, DI water and subsequently blow dried with N₂ gas.

3.2.7 Lift-off/ removal of eBL photo resist (eBL patterning of wafer)

After the deposition of the linker molecules, the PMMA on MMA (8.5) MAA resist that were not exposed to electron beam were being lift-off by immersing the patterned silicon wafer in acetone for 18hrs. After which the silicon wafers with linker molecules were rinsed with toluene, DI water and blow dried with N₂ gas.

3.2.8 Tagging of NHS-ester fluorophores onto peptide molecules with SH and COOH end groups (Fluorescence microscopy studies)

The stock solution of 10x phosphate buffer saline PBS was first prepared by mixing 80.00 g NaCl, 2.00 g KCl, 14.40 g $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ and 2.40 g KH_2PO_4 in 0.8 L of DI water and the solution is further topped to 1L with DI water.

The 1x PBS solution was prepared by taking 0.1 L of the stock solution and topped up to 1 L with DI water. The 1x PBS of pH 9 was prepared by first adding 0.6 L of DI water to 0.1 L of the stock solution. After which, NaOH was added till the pH reached 9.1 and the solution is again subsequently topped up to 1 L with DI water.

1 mg of DyLight 488 NHS-ester fluorophores is dissolved in 100 μL of Dimethylformamide (DMF) and stirred at a low speed to ensure homogenous mixture is obtained. 20 μL of this mixture was pipette into a centrifuge tube containing peptide solution (2 mg/ml peptide in pH 9 PBS). This mixture of fluorophores and peptide is left to react at room temperature overnight.

After 18 hrs of reaction, the solution was then injected into a dialysis kit. The dialysis kit was placed into a beaker containing 700 ml of PBS. The beaker was wrapped fully with aluminum foil to prevent quenching of the fluorophores and left in a cold room under constant stirring for 24 hrs to remove the unreacted fluorophores. The PBS in the beaker was changed 3 times prior to removing the dialysis kit out from the beaker.

Peptide tagged with DyLight 488 NHS-ester fluorophores was removed from the dialysis kit and placed into a tube wrapped with aluminum foil and stored at 4°C . The tagged peptide can be stored for a month. For a longer storage period, the peptide solution can be divided into single-use aliquots and kept at -20°C .

3.2.9 Attachment of Peptide Tagged with NHS-ester Fluorophores on Silicon Wafer (Fluorescence microscopy studies)

10 μL of peptide solution is drop-casted onto the silicon wafers with linker molecules. It was left to react for 2 hrs at room temperature and then rinsed thoroughly with DI water and subsequently blow dried with N_2 gas.

3.2.10 Spin Coating of photo resists onto Silicon Wafer (Fabrication of gold contacts)

Silicon wafer was spin-coated with a positive photresist, AZ9260. A 2 step program was been used for the spin coating process:

1. Spin for 5 seconds at 1500rpm
2. Spin for 30 seconds at 4000rpm

After spin-coating for 35 seconds, the silicon wafer was baked for 6 minute at 110 $^{\circ}\text{C}$. Subsequently the AZ9260 photo resist coated wafers were used for lithography.

3.2.11 Developing of photo resists after lithography (Fabrication of gold contacts)

A developing solution was prepared by mixing 2 part of AZ400K to 5 part of DI water. The exposed area of photo resist on silicon wafers were then developed by immersing in the solution for 90 seconds. After which the wafers were rinsed thoroughly with DI water and blow dried with N_2 gas.

3.2.12 Evaporation of Chromium and Gold to make source and drain (fabrication of gold contacts)

Chromium, gold and the patterned silicon wafers are loaded into the Electron beam evaporator. The system is left to pump down to reduced the number of impurities. A thin layer of chromium is first evaporated onto the exposed area of the wafers to provide better adhesion of gold onto silicon wafer. Gold is subsequently evaporated onto top of Chromium. A thickness of 800 nm of gold is evaporated and the thickness can be gauged from the quartz crystal in the Ebeam evaporator.

3.2.13 Lift-off of photo resists (fabrication of gold contacts)

After the evaporation of chromium and gold, photo resist that were not exposed to light were being lift-off by immersing the silicon wafer in acetone for 8 hrs. After which, the source and drain contacts is rinsed with DI water and blow dried with N₂ gas.

3.2.14 Attachment of Phenylsilane onto Silicon wafer

Phenylsilane (PTS) solution is prepared by dissolving 4ml of phenylsilane in 16 ml of anhydrous toluene. Silicon wafer is immersed into the phenylsilane mixture for 2 hrs. After the silanization of silicon wafer, the wafer is rinsed with anhydrous toluene and then cured in the oven at 80 °C oven for 2 hrs. Phenylsilane formed a more uniform layer during the curing process.

CHAPTER 4 NANOPATTERNING OF PEPTIDES

The ease at which nanopatterning of peptides can be achieved holds the key to the viability of using them as conduction channels. There are many ways at which nanopatterning of peptides can be carried out. They can be done using a top down or bottom up approach. In this chapter, the nanopatterning of peptides using both top down and bottom up approaches will be presented.

4.1 Nanopatterning of Peptides using Soft Electron Beam Lithography (eBL)

One of the techniques used for nanopatterning of peptides is soft *eBL*. This is used because it can be carried out on a variety of different substrates. Soft *eBL* technique was developed at Northwestern University for patterning of sol-gel structures [64]. To show that nanopatterns of peptides can be formed using this method, first the nanopatterns are defined on a silicon substrate. *Figure 4-1* shows the

Figure 4-1. Optical Image of nanopatterns formed by *eBL* technique

optical image of nanopatterns generated using soft *eBL* technique. This optical image confirms the formation of trenches. 3-mercaptopropyl trimethoxysilane (MPTMS) is deposited in these trenches and following that, peptides with free SH functional group is deposited.

Figure 4-2. Topographical image (left) and Cross section view (right) of MPTMS layer

Figure 4-2 shows the topographical image and the cross section view of 3-mercaptopropyl trimethoxysilane (MPTMS) layer. From the cross section view of the domain structure it can be seen that the 3-mercaptopropyl trimethoxysilane (MPTMS) has an average height of 0.82 nm, corresponding to the theoretical height of a 3-mercaptopropyl trimethoxysilane (MPTMS) monolayer of 0.87 nm.

Attenuated Total Reflection - Fourier transform infrared spectroscopy (ATR-FTIR) spectrum of 3-mercaptopropyl trimethoxysilane (MPTMS) layer (shown in Figure 4-3 below) is collected and it shows the stretching of CH₂ group from MPTMS layer, further substantiating that the 3-mercaptopropyl trimethoxysilane (MPTMS) layer is attached onto the silicon wafer.

Figure 4-3. Fourier Transform Infrared Spectroscopy (FTIR) of 3-mercaptopropyl trimethoxysilane (MPTMS) layer on Si wafer

The free functional group for bonding on 3-mercaptopropyl trimethoxysilane (MPTMS) layer is SH group. This SH group would readily bind with SH from the peptide with sequence His₆-{(Gly-Ala)₃Gly-Cys(free SH)-(Gly-Ala)₃Gly-Phe}₈-His₆ to form the disulfide bond (S-S). Once the peptide is deposited, AFM studies of the substrates are carried out. From the cross section view in *Figure 4-4*, the average height of peptide (His₆-{(Gly-Ala)₃Gly-Cys(free SH)-(Gly-Ala)₃Gly-Phe}₈-His₆) (with free SH from cysteine) on MPTMS is 1.92 nm. This shows that there is a height change of about 1.1 nm which is due to the attachment of peptide on 3-mercaptopropyl trimethoxysilane (MPTMS) layer.

Figure 4-4. Topographical image (left) and Cross section view (right) of peptide on MPTMS layer

The deposition of peptide with COOH functional group is also carried out to show the versatility of peptide attachment onto different surfaces. *Figure 4-5* shows the optical image of square nanopatterns generated using soft *e*BL technique. Squares of different sizes are generated to show that soft *e*BL can be used to create different patterns relatively easily. These nanopatterns are

Figure 4-5. Optical Image of square nanopatterns formed by *e*BL technique

deposited with aminopropyltriethoxy silane (APTES) followed by peptide with COOH functional group.

Figure 4-6 shows the topographical image and the cross section view of the domain structure. The height of aminopropyl triethoxysilane (APTES) is about 11.3 nm, which shows that the APTES is a multilayer. This problem of aggregation can be resolved by curing the APTES layer at 80 °C for 2 hours as shown in chapter 5.

The free functional group for bonding on aminopropyl triethoxysilane (APTES) layer is NH_2 . COOH group from the peptide can be attached onto the NH_2 group, forming the amide bond. Figure 4-7 shows the topographical image of peptide with COOH end group (TyrCysGlyAlaGlyAlaCysAla(free COOH)) attached onto the aminopropyl triethoxysilane (APTES) layer. In the cross section view of the domain structure the height measured has an average of 14.2 nm, showing a change of height of about 2.9 nm due to the attachment of peptide on aminopropyl triethoxysilane (APTES) layer. However, because of the roughness in aminopropyl triethoxysilane (APTES) layer, the height change is not a definite confirmation of peptide attachment. Therefore, for this system, in order to prove the attachment of peptides on such surface is successful, this peptide is tagged with NHS-ester fluorophores for further validation.

Figure 4-7. Topographical image (left) and Cross section view (right) of peptide on APTES layer

Fluorescence microscopy is carried out to investigate if the binding of peptides on APTES treated surface is successful. The peptide is tagged with NHS-ester fluorophores. The fluorescence image indicating the presence of NHS-tagged peptide is taken using a fluorescence microscopy. The fluorescence image (shown in Figure 4-8) further validate that peptides are attached onto aminopropyl triethoxysilane (APTES) layer.

Figure 4-8. Fluorescence image of fluorescence tagged peptide

4.2. Nanopatterning of Peptides with Dip-Pen Nanolithography (DPN)

In addition to nanopatterning of peptides using soft *e*BL, DPN is also employed as an alternative method to pattern the peptides in between pre-fabricated electrodes for transistor and interconnect application. Some applications of DPN include the well-documented work with mercaptohexadecanoic acid (MHA) or octadecanethiol (ODT) on gold [65].

Figure 4-9. Phase image of MHA on Gold substrate

Mercaptohexadecanoic acid specifically provides a very good control for writing as it has a controllable diffusion constant. This allows creating of intricate patterns with a mix of lines and dots. *Figure 4-9* shows MHA written in words “MSE – NTU” on gold substrate. The words are clearly defined using the phase image of the scanning after writing using MHA. DPN also has the benefit of writing with different inks and designs which allow peptides to be written onto the functionalized silicon substrate.

Silicon substrates were first deposited with 3-mercaptopropyltrimethoxy silane (MPTMS) or aminopropyl triethoxysilane (APTES). Peptides with free SH functional group (His₆-{(Gly-Ala)₃Gly-Cys(free SH)-(Gly-Ala)₃Gly-Phe}₈-His₆) and free COOH functional group (TyrCysGlyAlaGlyAlaCysAla(free COOH)) are attached onto the

Figure 4-10. Phase image of peptide with SH functional group on MPTMS layer

silanized silicon wafer respectively. *Figure 4-10* shows an AFM phase image of 4

horizontal lines of peptide with SH functional group written on top of a 3-mercaptopropyltrimethoxysilane (MPTMS) coated silicon wafer. This shows that DPN can be employed to pattern the peptide with SH functional group. In addition, peptide with COOH functional group was also written onto aminopropyltriethoxysilane (APTES) coated silicon wafer. *Figure 4-11* above shows phase image of 4 squares of peptide with COOH functional group written on top of aminopropyl triethoxysilane (APTES) covered silicon wafer. This DPN experiment shows that different peptide can be readily written onto different functionalized silicon wafer because of covalent bonding and attachment of the peptide groups to the functionalized substrate.

Figure 4-11. Phase image of peptide with NH₂ functional group on APTES layer

4.3 Conclusion

In this chapter, it is shown that it is possible to use top down approach - *e*BL patterning to create trenches and following that covalently bond linker molecules, such as APTES and MPTMS (silane chemistry), to selective areas of the silicon wafer. Hence, both peptides with COOH and SH functional groups can be specifically bond onto APTES and MPTMS on selective areas respectively. This shows that using *e*BL patterning, peptides with different functional group can be patterned onto specific location of the silicon substrate by selective functionalization. *e*BL is an effective way to pattern peptide on substrate. However, there is a limit to the dimension of trenches formed. When smaller features are required, DPN might be a better choice. Bottom up approach like DPN is effective when small areas of peptide are needed. In this method, the whole silicon wafer

is coated with linker molecules such as APTES or MPTMS. Peptides with different functional groups can then be written on specific location decided by the user to nanoscale dimensions. However, this method can be rather tedious and the writing is inconsistent when the area becomes too large as the ink concentration changes over time due to solvent evaporation. Overall, the patterning of peptides with different functional groups on silicon substrate is rather easy with the linker molecules like APTES and MPTMS. However, depending on the area that need to be patterned, *e*BL or DPN should be carefully weighed for their advantages. For large areas (sub micron and bigger), *e*BL would be a more effective way to pattern the substrate and when sub nanometer dimensions are required, DPN will be more effective.

CHAPTER 5 SYNTHESIS, CHARACTERIZATION AND ELECTRICAL TESTING OF TyrCysGlyAlaGlyAlaCysAla

5.1 Methodology for Synthesis of Short Peptide

Peptides were chemically synthesized to contain specific amino acid sequences. This defined the chain lengths and the conformation to an extremely high degree of monodispersity. It is both cost effective and time efficient to synthesize short oligopeptide using solid phase synthesis. The peptide with repetitive AlaGly sequences was designed and subsequently synthesized via solid phase synthesis by the First Base Company.

5.2 Candidate Peptide Design and Methodology

Peptide has the unique property of being able to be tailored easily to have different functionalities including having conductive channels. This makes them highly suitable for device applications. The chemistry of a peptide can be custom designed using the appropriate amino acid residues. Both the amino acid composition and the length of the peptides will determine the assembly of the peptides. With the correct terminal amino acid groups, peptides can be readily self assembled onto specific substrate. Two typical examples are: with a cysteine terminal group, the peptide could be readily attached to gold, while with a histidine terminal group, the peptide could be attached to nickel.

For this work, a peptide consisting of tyrosine (Tyr), cysteine (Cys), glycine (Gly), and alanine (Ala) with the sequence

Figure 5-1. Chemical structure of TyrCysGlyAlaGlyAlaCysAla(free COOH)

TyrCysGlyAlaGlyAlaCysAla(free COOH) is being used. The structure is shown in *Figure 5-1*. This peptide is designed by my group and the synthesis is carried out by First Base as mentioned earlier. The desired peptide is short and does not give rise to any secondary structure such as β sheet or α helix. Alanine residue is placed at one end of the peptide and the tyrosine residue at the other terminating end of the peptide. Alanine has been selected as the terminal group because of the presence of the free carboxylic group which will bond covalently to NH_2 functionalized silicon (Si) substrate. The backbone of the peptide is made up by glycine and alanine residue to provide a rigid backbone to the peptide and also to provide a separation between the tyrosine residue and the silicon substrate.

It has been shown that for charge conduction to occur in a directed channel, charge transfer between the molecules and the substrate should be avoided [66]. One of the advantages of using peptide as the conduction channel is that the height of this peptide can be synthesized to atomically precise chain length by changing the number of amino acid in the main chain of the peptides. The conjugation of the phenyl rings in the tyrosine residue of the peptide can potentially be used for electron transport if they are packed closed enough to their neighbouring peptide molecules. To facilitate the overlap of the

Figure 5-2. Intermolecular disulfide bonding of Cysteine residues in peptide

aromatic groups of the tyrosine so as to enhance the formation of extended π -electron systems for charge transport to take place, the cysteine residue in the peptide is essential. The π - π overlap due to disulfide bond is shown schematically in *Figure 5-2*. Cysteine has a S-H bond length of 1.34 Å, and disulfide bonds (S-S) has a bond length of 2.06 Å [67]. At close proximity, the peptide is able to form disulfide bond with its neighbours and hence bringing the neighbouring molecules close together. It was reported that the overlapping phenyl rings need to be 3.86 Å or less for π conjugation to occur [66]. Hence the disulfide bond brings the phenyl rings closer together for possible electron transport to happen. If the phenyl rings are arranged close enough, ballistic tunneling can occur and thereby allowing electron conduction to take place. Cysteine residues also provide covalent bonding to gold electrodes at the end of the molecular peptide wire, thus forming a close contact with the gold electrodes.

The advantage of peptide over carbon nanotubes is that peptides are easily synthesized at low cost and the functional groups can be tune with selection of the correct residue to match the required substrate. On the other hand, carbon nanotubes have to be functionalized separately in order for them to have different functional groups that can be bonded covalently to different substrate. In the case of peptide, this functionality can be designed into the molecule and the application is very straightforward since there is the selectivity of the functional group for the substrate.

5.3 Fabrication of gold microelectrodes

Figure 5-3 shows the optical image of microelectrodes formed using photolithography. The optical image shows the source and drains which are not uniform due to limitation in the lithography process. Aminopropyl triethoxysilane (APTES) followed by TyrCysGlyAlaGlyAlaCysAla

Figure 5-3. Optical image of microcontacts

(free COOH) peptide were deposited between these micro-contacts.

5.4 Achieving a More Uniform Layer of aminopropyl triethoxysilane (APTES)

Attachment of aminopropyltri ethoxysilane (APTES) onto silicon wafer was discussed in section 4.1 and Figure 5-4 shows schematically the organization of aminopropyltri

Figure 5-4. Ideal Attachment of Aminopropyltri ethoxysilane (APTES) onto Silicon wafer

ethoxysilane (APTES) on silicon wafer. In the previous chapter, it is shown that it is difficult to deposit a monolayer of APTES on silicon substrate. Hence after APTES is deposited on silicon wafer using gas silanization, curing at 80 °C for 2 hrs is required to

achieve a more uniform and thin layer. The gas phase deposited APTES is not locally uniform as shown in *Figure 5-5*. It can be seen that there are aggregations of APTES giving rise to an average height of 8.34 nm.

Figure 5-5. Topographical image and average height of APTES layer without curing

To achieve a more uniform APTES layer locally, the APTES layer is cured in the oven at 80 °C for 2 hrs, which allow the APTES to arrange into a more uniform layer shown in *Figure 5-6*. Curing increases the uniformity of the layer of APTES over a longer distance giving an average height of 1.41 nm.

Figure 5-6. Topographical image and average height of APTES layer with curing

5.5 Attachment of TyrCysGlyAlaGlyAlaCysAla(free COOH) peptide onto Aminopropyl triethoxysilane (APTES)

The TyrCysGlyAlaGlyAlaCysAla(free COOH) peptide is then attached to the APTES modified Si substrate using solution casting. The solution was left to react for 24 hrs at 4

°C. The free carboxylic acid group from alanine residue can be covalently bonded to the amine group of the APTES. The other end of the APTES molecule is covalently bonded to the silicon wafer via silanization reaction. The ideal attachment process is shown schematically in *Figure 5-7*. The cysteine residue forms disulfide bond between the peptides to provide the rigidity of the layer. The cysteine residues also form covalent bonds with the gold electrodes to form the ohmic contacts. As mentioned earlier, cysteine originally has SH bond length of 1.34 Å and hence the length between the peptide should be 2.68 Å. However, when disulfide bond is formed, the S-S bond length is 2.06 Å which brings the peptide much nearer to each other [67]. The overlapping phenyl rings need to be 3.86 Å or less to form a conducting channel [66]. This disulfide bond brings the phenyl rings closer together for possible electron transport to happen.

5.6 Electrical testing of TyrCysGlyAlaGlyAlaCysAla(free COOH) peptide using Keithley Probe Station with Two-terminal Device Architecture

Electrical measurements of self assembled peptides on silicon substrate were carried out using Keithley 4200 probe station. Peptide of sequence TyrCysGlyAlaGlyAlaCysAla (free COOH) was assembled in between two terminal gold electrodes via solution deposition on top of aminopropyl triethoxysilane (APTES) functionalized silicon wafer as mentioned above.

Figure 5-8 shows current-voltage characteristic of the TyrCysGlyAlaGlyAlaCysAla(free COOH) peptide measured using the probe station. The I-V curve shows that electron tunneling occurs along the phenyl rings of the tyrosine residue of the peptide. This result also shows that the peptides formed ohmic contact with the gold electrodes. Electrical

measurements of both the electrode prior to any APTES or peptide deposition (Blank in Figure 5-8) and the electrode after the deposition of APTES (APTES in Figure 5-8) showed a non-conducting behaviour. Only when the peptide is deposited, the channel became conducting. Refer to the I-V curves in Figure 5-8. FESEM is used to further investigate the effect of channel length of the on the peptide conductivity. A micrograph of the source and drain where the conducting peptide is deposited is shown in Figure 5-9

and Figure 5-10. From the FESEM micrograph, the channel length is found to be about $0.5\ \mu\text{m}$.

AFM images shown in Figure 5-11 give better measurement of the channel length. It can be concluded from the topographical image that the channel length is $0.8\ \mu\text{m}$.

The same peptide was deposited between the electrodes with shorter channel length – 0.1 μm . The dimension of the channel is measured using both FESEM and AFM. FESEM micrograph of the source and drain where the conducting peptide is deposited is shown in *Figure 5-12* and *Figure 5-13*. From the FESEM micrograph, the channel length is about 0.1 μm . In *Figure 5-14*, the AFM image shows that the channel length is indeed 0.1 μm .

Figure 5-12. FESEM micrograph of the source drain 5000X

Figure 5-13. FESEM micrograph of the source drain 20000X

Figure 5-14. Topographical image (left) and Cross section view (right) of peptide between channel length of 0.1 μm .

The electrical measurement of the peptide was conducted using the Keithley probe station. The I-V curves are shown in *Figure 5-15*. The result showed that the peptides

have ohmic contacts with the gold electrodes. From the I-V curve of the channel with peptides, electron tunneling across the phenyl rings of the tyrosine residue of the peptide can be observed. The peptide in the shorter channel length is shown to be more conducting, with a lower resistance – almost an order lower than the longer channel. Hence, the peptide channel is slightly more conducting when the channel length is shorter. A blank electrode and channel after attachment of APTES both were also done to show that the channel is non-conducting before peptides deposition. This gives a conclusive proof that the current is due to the presence of peptides. It is reasonable to expect that the assembly of the peptide to be better when the channel is shorter. Having a more perfect organization of the peptides will allow the phenyl ring in the tyrosine residue to be better packed with respect to their neighbours and hence a more perfect channel for electron conduction.

Figure 5-15. Current-voltage characteristic of peptide on two-terminal devices

The electrical properties of longer channels (exceeding 1 μm) in the presence of peptides have also been tested but they did not give any conducting characteristic in the presence of peptide molecules. Hence there is a limit to the channel length for this peptide to form a conducting channel. This is perhaps relating to the ability of this peptide to self assembly over longer distances. The conductivity of peptide is higher when the electrode channel length is shorter. The conductivity is basically limited by 2 factors, the uniformity of the APTES and peptide layers and also the distance between the contacts.

5.7 Characterization and Electrical Testing of Phenylsilane (PTS)

Since peptides has shown to be able to give rise to conduction channels, it is natural to question the feasibility of using an even simpler molecule - Phenylsilane (PTS). Phenylsilane (PTS) is attached onto a silicon wafer via solution phase attachment. After the attachment in solution phase, the silanized silicon wafer is placed into an 80 °C oven for 2 hrs to allow the formation of a more uniform layer. The schematic of the ideal attachment of phenylsilane can be seen in *Figure 5-16*. Electrical measurement of channel with self assembled phenylsilane is carried out using the Keithley 4200 Probe station.

Figure 5-17 shows the current-voltage characteristic of the phenylsilane (PTS) measured using Keithley probe station. It shows the channel has a semiconducting behaviour instead.

Figure 5-17. Current-voltage characteristic of phenylsilane on two-terminal devices

FESEM micrograph of the source and drain where the phenylsilane is deposited is shown in Figure 5-18 and Figure 5-19. From the FESEM micrograph, the shortest channel length is roughly $0.3\ \mu\text{m}$. It can be seen that although the channel length is shorter than the peptide channel length of $0.8\ \mu\text{m}$, shown in Figure 5-11, but the I-V characteristic of phenylsilane shows that for $0.3\ \mu\text{m}$ channel length, phenylsilane is semiconducting and the current only reached picoamperes whereas peptide can reach tunneling current of nanoamperes. This data proves that peptide is indeed better than phenylsilane in terms of

Figure 5-18. FESEM micrograph of the source drain X5000 **Figure 5-19. FESEM micrograph of the source drain X20000**

application as a molecular wire. This might be due to the fact that peptide has a longer chain and hence the phenyl ring is further away from the silicon substrate than phenylsilane. Hence, there is higher chance for the current to leak from the phenyl ring in the phenylsilane into the silicon substrate due to the overlapping of HOMO LUMO of phenylsilane with that of silicon wafer as compared to the peptides [66].

5.8 Conclusion

In this chapter, short peptide is designed for both attachment to functionalized silicon substrate and also for conduction purpose. The peptides were attached onto silicon substrate via APTES linker by forming the amide bond. It has been demonstrated that the self assembly of peptide with sequence - TyrCysGlyAlaGlyAlaCysAla(free COOH) shows remarkable current-voltage characteristic at dry state without any redox molecules. The charge transfer is through the $\pi - \pi$ overlap of phenyl rings from tyrosine amino residue at the top of the peptide. This peptide is proven to be conducting in a channel narrower than 1 μm and the conductivity of the peptide is proven to be better with decreasing channel length. The conductivity of self assembled peptide shows that they are indeed good candidate for molecular wire where small dimension in submicron range is needed. When compared to phenylsilane, the short peptide that is designed by my group shows conductivity with higher tunneling current whereas phenylsilane shows semi-conductivity with the current reaching only picoamperes. Hence, the short peptide that is designed proved to be better as molecular wire as compared to phenylsilane. This result brings peptide closer to the reality of being used as a molecular wire and in nanoelectronics when the miniaturization of conventional conductors becomes limited by the materials resistivity. It can be seen in this chapter, there is a problem when the channel length gets longer. In the next chapter, this problem can be overcome by designing longer peptides that will form rigid secondary structures prior to deposition on surfaces.

CHAPTER 6 SYNTHESIS, CHARACTERIZATION AND ELECTRICAL TESTING OF 256-MER POLYPEPTIDE

6.1 Methodology for Polypeptides β sheet Engineering

Polypeptides were engineered to contain specific amino acid sequences, defined chain lengths and conformation with an extremely high degree of monodispersity. The polypeptide polymers with repetitive AlaGly sequences was designed and subsequently synthesized via over expression by E.Coli. Molecular biological techniques permit peptide engineering via the replacement of naturally occurring amino acids with synthetic analogues by relaxing the specificity of the aminyl-tRNA synthetase [68-70]. Such a methodology was developed for the synthesis of monodisperse polypeptides for surface-directed assembly.

6.2 Candidate Peptide Design and Methodology

A polypeptide (shown in Figure 6-1) consisting of alanine (Ala), glycine (Gly), tyrosine (Tyr) and histidine (His) with a sequence $\text{His}_6\{(\text{AlaGly})_3\text{GlyLys}(\text{AlaGly})_3\text{GlyTyr}$

$(\text{AlaGly})_3\text{GlyGlu}(\text{AlaGly})_3\text{GlyTyr}\}_{256}\text{His}_6$, was synthesized by my collaborator, Dr.

Shekhawat's group in Northwestern University, US. This polypeptide had the similar conformation as those previously prepared by Parkhe *et al* [71]. The desired polypeptide should adopt an antiparallel β sheet conformation with more sterically demanding amino acids positioned at the β turn so that the system could be stabilized by antiparallel alignment of the dipoles. This molecular design would facilitate overlap of the aromatic groups to enhance the formation of extended π -electron systems potentially contributing to charge transport along the axis of the β sheet. The histidine residues provide a mechanism for covalent attachment to Ni surfaces (e.g. this has been shown for cysteine esters and cysteine containing functional proteins) [72, 73]. In this polypeptide, polyhistidine side group is present so as to enable the polypeptide to form good ohmic attachment to metal electrodes such as nickel.

6.3 Effect of polypeptide solution concentration on the self assembly

As discussed earlier, polypeptide with $n = 256$ were synthesized and the antiparallel β sheet formed by this polypeptide corresponds to a channel length of about 3-5 μm . To evaluate the optimum concentration to use for the deposition on Si substrates, a series of polypeptides functionalized with silane groups at beta turns was dissolved in hexane at different concentrations ranging from 0.01 mM to 0.8 mM. Atomic force microscopy (AFM) surface topography measurements of self assembled polypeptide nanostructures is carried out using BioScope II to evaluate the surface roughness, determine the polypeptide domain structure and evaluate the lamellae assembly. *Figure 6-2* shows the surface morphology and the cross sectional view of polypeptide deposited from a solution with a concentration of 0.05 mM. Topographical image shows the domain structure and shows that the peptides are not properly aligned at this low concentration.

Figure 6-2. Topographical image (left) and Cross sectional view (right) of polypeptide deposited from a 0.05 mM solution

Figure 6-3 shows the surface morphology of polypeptide deposited from a 0.1 mM solution. The topographical image shows the domain structure clearly and indicates that peptides are of short length of about 0.8 μm and vastly dispersed at this low concentration.

Figure 6-3. Topographical image (left) and Cross sectional view (right) of polypeptide deposited from a 0.1 mM solution

In Figure 6-4, this topographical image of the film deposited from a 0.25 mM peptide solution indicates that peptides are long and well dispersed at this concentration. The cross section view shows that the height of the peptide has an average of 1.4 nm,

matching the theoretical value of 1.6 nm. Hence, at 0.25 mM the peptide is at the optimum concentration for formation of a single β sheet of peptide chain.

Figure 6-4. Topographical image (left) and Cross sectional view (left) of polypeptide deposited from a 0.25 mM solution

Figure 6-5 shows the surface morphology of polypeptide when the concentration is further increased to 0.5 mM. The topographical image shows the domain structure and from the figure, it can be seen that the peptides are long and well dispersed at this concentration. However, looking at the cross section view of these domain structures, the average peptide height is found to be of 2.5 nm, indicating that the aggregation of peptide have occurred.

Figure 6-5. Topographical image (left) and Cross sectional view (right) of polypeptide deposited from a 0.5 mM solution

From *Figure 6-6*, the surface morphology of polypeptide deposited from a 0.8 mM solution shows that the peptides are long but dense at this high concentration. *Figure 6-7* also shows the cross section view of the domain structure and the height of the peptide recorded has an average of 2.3 nm which indicates that the peptide is again aggregated. Besides vertical aggregation, horizontal aggregation was also present from the increased width of the peptide seen in the cross section view. From the figures above, it can be concluded that the optimum concentration for the peptide attachment is about 0.25 mM.

Figure 6-6. Topographical image (left) and Cross sectional view (right) of polypeptide deposited from a 0.8 mM solution

6.4 Electrical functionality testing of Polypeptides channel using Two-terminal Device Architecture

Electrical measurements of synthesized polypeptides were carried out using Scanning tunneling microscope (STM). Peptides were assembled in between two terminal electrodes made of Nickel with channel width of 5 μm (shown in Figure 6-7) via solution deposition with 0.25 mM as mentioned above.

Figure 6-7. Optical Image of two-terminal device

A schematic of the polypeptide based molecular wires between a two-terminal device is shown in Figure 6-8 and the direction of the current flow is shown in the same figure.

Figure 6-8. Schematic of polypeptide based molecular quantum crystal wires

One end of the electrode was grounded and STM conducting probe was placed on the other end of the electrode (shown in Figure 6-9). Figure 6-10 shows the current-voltage characteristic of the polypeptide. It can be clearly seen that electron tunneling across the phenyl rings of the polypeptides. In the current-voltage curve, it can be seen that the long peptide is having a semiconducting behavior.

Figure 6-9. Schematic of electrical testing of two-terminal devices using STM

Figure 6-10. Current-voltage characteristic of polypeptide on two-terminal devices

It can be concluded that this long peptide of sequence $\text{His}_6\{(\text{AlaGly})_3\text{GlyLys}(\text{AlaGly})_3\text{GlyTyr}(\text{AlaGly})_3\text{GlyGlu}(\text{AlaGly})_3\text{GlyTyr}\}_{256}\text{His}_6$ has conductivity at longer channel length of 5 μm . The short peptide is no longer conducting when deposited in a channel with length exceeding 1 μm while the long peptide is still semi-conducting for electrode of channel length of 5 μm . The main advantage of the long peptide is that it forms a rigid β sheet that allows phenyl rings to overlap and allow electron transport. The rigid β sheet also allows transportation over longer channel length as shown from the electrical

measurement in this chapter. Hence, it can be concluded that the peptide does have the potential to be used as a molecular interconnect. However, more experiment has to be done to improve the conductivity and also the reliability of the peptide.

6.5 Conclusion

In this chapter, it is found that at 0.25 mM, polypeptide with the sequence $\text{His}_6\{(\text{AlaGly})_3\text{GlyLys}(\text{AlaGly})_3\text{GlyTyr}(\text{AlaGly})_3\text{GlyGlu}(\text{AlaGly})_3\text{GlyTyr}\}_{256}\text{His}_6$ formed long and dispersed peptide chain. This is desirable in order to achieve good electrical conductivity. Using 0.25 mM peptide solution, peptide is deposited between the contacts. In this chapter, a longer channel of 5 μm is used to solve the problem that short peptide do not show any conductivity in channels wider than 1 μm . It has been shown that the self assembly of peptide with the sequence - $\text{His}_6\{(\text{AlaGly})_3\text{GlyLys}(\text{AlaGly})_3\text{GlyTyr}(\text{AlaGly})_3\text{GlyGlu}(\text{AlaGly})_3\text{GlyTyr}\}_{256}\text{His}_6$ shows good current-voltage characteristic at dry state without any redox molecules in channel of length 5 μm . The charge transfer is through the $\pi - \pi$ overlap of phenyl rings from tyrosine amino residue at the β turns of the peptide. This peptide is proven to be semiconducting. With the design of the longer peptide forming rigid secondary β sheet structure, electrons are able to tunnel through the phenyl rings located at the β turns. This rigid β sheet allows better packing as compared to self assembled short peptide in the previous chapter. Thus the long peptide gives rise to semiconducting behaviour even when channel width is 5 μm long.

CHAPTER 7 CONCLUSIONS

In this work, it was demonstrated that nanopatterning of peptides on silicon substrates can be achieved by using both soft electron beam lithography (soft *e*BL) and Dip-Pen lithography (DPN). These two methods basically cover nanopatterning of a range of areas. Atomic force microscopy (AFM) images showed that the silicon is functionalized with 3-mercaptopropyl trimethoxysilane (MPTMS) and the peptide with free SH functional group is attached successfully to MPTMS. Through the measurement of the change of height due to peptide attachment, the peptide is shown to have attached onto the linker molecule. Peptide with free COOH functional group is also shown to be attached to aminopropyltrimethoxysilane (APTES) functionalized silicon substrate by the changes in the height measured using atomic force microscopy images. Further validation of the attachment is provided using fluorescence microscopy. Attachment of peptide with free SH functional group as well as free COOH functional group via DPN has also been proven to be successful. This work demonstrate the ease of writing peptides of different functional end groups onto the different functionalized silicon substrate by making use of surface chemistry. It is generally difficult to synthesize long peptide and hence short peptides with specific free functional groups are designed and synthesized. This work shows that the short chain peptides can be easily attached onto silicon substrate. In this work, peptide with sequence – TyrCysGlyAlaGlyAlaCysAla (free COOH) has been utilized. The self assembled layer is electrically tested and found to be conducting. The self assembled peptide is proven to be more conducting with shorter channel length. This shows that peptide will be a good candidate for molecular wire at submicron region where resistivity of metals becomes a major issue. However, short peptide is no longer conducting when the channel length exceeds 1 μm . This drawback can however be overcome by longer peptide that forms β sheet. In next part of the work, it has been shown that polypeptides with $(\text{His}_6\{(\text{AlaGly})_3\text{GlyLys}(\text{AlaGly})_3\text{GlyTyr}(\text{AlaGly})_3\text{GlyGlu}(\text{AlaGly})_3\text{GlyTyr}\}_{256}\text{His}_6)$ sequence is highly suited for wider channels. The concentration studies of longer silane functionalized polypeptide shows that the optimum concentration for attachment is at 0.25 mM. The electrical properties of

the polypeptide with silane end group at 0.25 mM is tested using scanning tunneling microscopy and the result shows that the polypeptide is semiconducting rather than insulating. This shows that the rigid β sheet of the long polypeptide allows better packing as compared to the self assembled short peptide and shows some conductivity even when channel length is 5 μm long. This promising result shows that peptide is highly probable as a molecular wire and suitable to be used as interconnects in nanoelectronics when conventional miniaturization of conductors becomes limited by the materials resistivity. Peptide molecules provide a good alternative to carbon nanotubes for the application of interconnects in nanoelectronics. They can be easily synthesized and attached onto different surfaces using different amino acid residues. Hence, peptide can be a very versatile material for the next generation of electronics.

CHAPTER 8 FUTURE WORK

The limitation with nanodevices arises from the difficulty in making a defined nanometer gap between the electrodes. Mechanical break junction and electrical break junction has been utilized by several groups for electrical measurement. Scanning tunneling microscopy has also been an alternative. However, a better electrode can be formed using electron beam lithography with focused ion beam. This method create a more defined nanometer gap between the electrodes of better uniformity than electrical break junction and the third electrode can be introduced more easily than mechanical break junction. Using this method, the electrical testing of the peptide can be more accurate and precise.

The limitation of the peptide is that voltage applied cannot exceed 1V since this might lead to heat building up within the peptide channel, hence causing possible breakdown of the peptide. This issue can be further investigated and possibly be improved if the peptide is tested using electrodes that are closer together (nanometer sized channel spacing) since self assembled layers are better packed within a smaller area.

In addition, the mechanism of electron transfer through the peptide has not been covered in this thesis. Electron transfer of peptide has been much studied theoretically using Density functional and Green's functional model. Experimental studies has also been done but most are done in wet state where peptides are dissolved in a solvent phase. In order to use peptide as interconnect, studies of deposited peptide in dry state has to be done. Despite of the fact that peptide has been looked into by scientists, the detail mechanism is still unknown. Electron transfer in peptide molecules should be studied in detail using scanning tunneling microscopy studies.

Detailed studies of different length peptides and the effect of secondary structure in allowing longer range electron transfer would be important to understand. Rather than rigid beta sheet studied in this dissertation, alpha helix may result in good conductivity over long range as well. The effect of varying length and height of the peptide on the conductivity of these peptides can be studied.

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