APPLICATIONS OF THE ORGANIC THIN FILM TRANSISTOR: BIOLOGICAL SENSING AND FRAGILE X SYNDROME

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ABSTRACT

This project aims to evaluate the suitability of the organic film transistor as a sensor, and more specifically, to help determine if the pentacene thin-film transistor may be used as a biological sensor for future research relevant to Fragile X Syndrome, a genetic disorder associated with congenital mental retardation. In Fragile X Syndrome, individuals do not produce Fragile X Mental Retardation Protein (FMRP), and although the overall effect of this absent production is known, the exact function of the FMRP is not. The transistor was exposed to biological and control environments representative of the environments that it will be exposed to in its potential application as a biological sensor; its potential future application will involve helping determine the function of the FMRP. These environments consisted of several components: water, bovine serum albumin (BSA), transfer RNA, a salt solution known as Moine buffer, RNase inhibitor, Fragile X Mental Retardation Protein (FMRP), and FMR1 RNA. The experiments performed involved exposing the transistor to each component individually, with the exception of the RNAse inhibitor, the FMR1 RNA, and the FMRP, as well as exposing the transistor to a combined solution of all the components (an RNA binding assay) and observing the transistor's response through its current-voltage characteristics before and after the exposure. The experiments performed helped identify changes in fabrication that could be made for more optimal sensing as well as changes that could be made in the environment to ensure the transistor's response was not largely due to a less important component of the solution. With these changes in mind, the organic thin film transistor may be able to contribute to research on the FMRP and to help us to understand more about the mechanism important in giving rise to Fragile X Syndrome.

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1. INTRODUCTION

The thin-film transistor has been of invaluable use to today's technology. Invented in 1935, substantial research in thin-film transistors did not begin until 1970s when their use in liquid crystal displays was considered and explored.[1] Thin-film transistors offer several advantages over the original metal oxide semiconductor field effect transistor (MOSFET), which include, among many, lower costs of production and an easier production process. These advantages make the thin-film transistor's widespread use for many applications more attractive.

Of particular interest in today's research is the organic thin-film transistor. The organic thin film transistor is a thin-film transistor which uses an organic compound (a carbon containing compound) in the semiconducting channel. Organic materials are of particular interest because they can often be tailored, for example by varying functional groups in the material, for specific uses, are low cost for large-scale applications, and are generally, but not always, environmentally stable.

Although organic thin film transistors have seen widespread use in displays, very little research has been done on their use in sensor technology. Some recent work has focused on their use in vapor sensing, liquid sensing, and some biological sensing, providing some information on its suitability as a sensor.[2]

The main objective of this project is to evaluate whether or not the organic thin film transistor has the ability to be useful as a biological sensor, more specifically in the case of Fragile X Syndrome, a genetic disorder associated with mental retardation. The transistor will be exposed to a biological environment to determine whether or not it has potential as a sensor, and additionally, to determine if the biological environment can be optimized so that the transistor is able to specifically sense the agents about which information is desired or if changes can be made in the fabrication of the transistor that would optimize its sensing abilities.

The transistor will be exposed to a solution which is relevant to future experiments. This solution will contain several components: water, bovine serum albumin (BSA), transfer RNA, a salt solution known as Moine buffer, RNase inhibitor, Fragile X Mental Retardation Protein (FMRP), and FMR1 RNA. Each of these will be tested individually in order to observe the response the transistor has to each individual component. All of the components were tested individually with the exception of the RNase inhibitor, the FMRP, and the FMR1 RNA. Following these individual testings, the combined solution was tested, both with and without BSA. Since BSA is known to coat the surface of those surfaces that it comes in contact with, it could dominate the response of the transistor. As a result, the combined solutions with and without BSA were tested to check for this possibility.

2. BACKGROUND

2.1. THIN FILM TRANSISTORS

The thin-film transistor differs structurally in several ways from the MOSFET used in silicon technology. A MOSFET typically has a gate on top of the structure, while the source and drain are doped regions which lie beneath the metal source and drain contacts. The channel, through which charge carriers pass, is typically beneath the gate electrode and dielectric stack. In the thin-film transistors, the semiconducting material (and thus the channel) may be on top of the drain and source electrodes, and the gate is typically on the bottom of the structure, although structures with the gate on the top of the structure and top contacts are also used. The electrodes in the thin film transistor are composed of a metal. Typically, the electrodes are composed of gold for reasons that have to do with the energy barrier, or rather the contact potential of the metal-semiconductor interface.

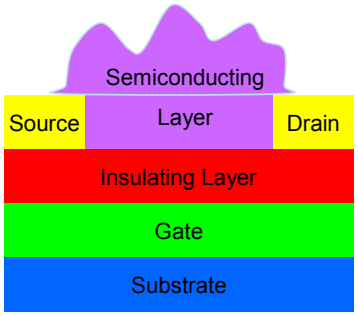

Figure 2.1.1: A TFT

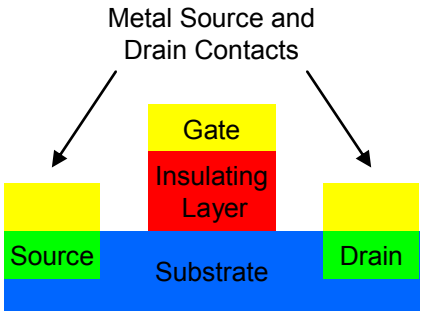

Figure 2.1.2: A MOSFET

The energy barrier at this interface is determined in part by the energy difference between the Fermi level, defined as the valence band at absolute zero, of the metal and the lowest unoccupied molecular orbital for n-type materials, and the highest occupied molecular orbital for p-type materials. [3] Ideally, this energy barrier must be small in order for carriers to be injected across this interface and for the device to conduct and turn on without a large applied voltage. For a material such as pentacene, which is p-type, this barrier is dependent upon the difference between the Fermi level in the metal and the highest occupied molecular orbital in the semiconductor material and thus depends on work function of the metal involved.

The work function Φ_M is a measure of how much energy is needed to remove an electron from a solid metal to a point infinitely far from the solid and is generally measured in electron volts (eV). In this case, the work function of the metal is given by the difference between the metal vacuum level, the energy of an electron at a location where the potential of the metal solid has no influence[4], and the Fermi level[5]:

$$\Phi_M = E_F - E_{VAC}(M).^{6} \tag{2.1.1}$$

To produce desirable characteristics, the work function of the metal should line up with the highest occupied molecular orbital in p-type materials and the lowest unoccupied molecular orbital in n-type materials. However, if chemical interactions, such as dipoles, exist at the metal-semiconductor interface, then the above mentioned design principle is inadequate, since this can shift the location of the molecular orbital levels relative to the Fermi level. Gold is often chosen

for p-type materials since it is has a large work function and thus lines up well with the highest occupied molecular orbital of many p-type semiconductor materials. Figures 2(a) and 2(b) from C. R. Kagan's *Thin Film Transistors* illustrate this design principle.[7]

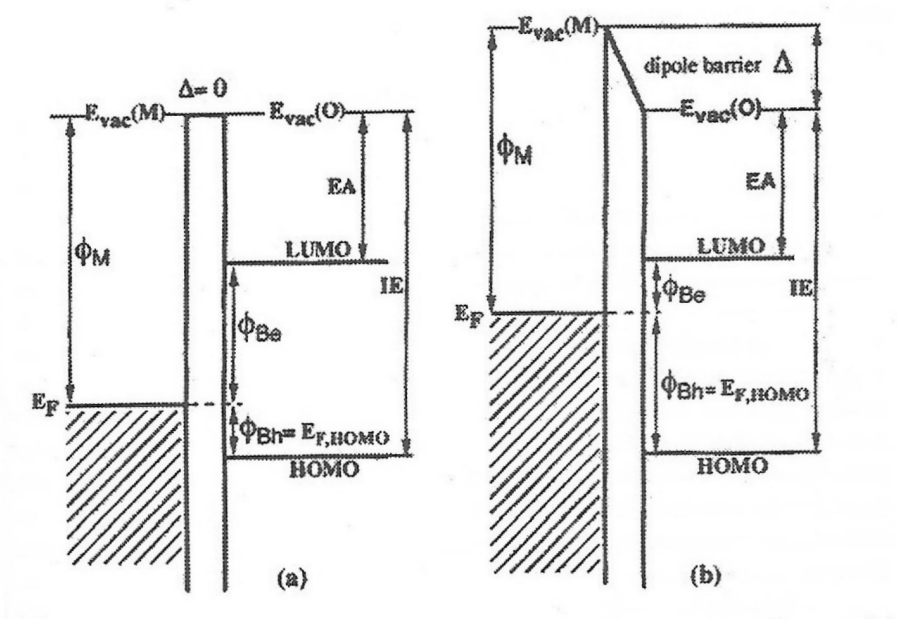

Figure 2.1.3(a): Energy Diagram without interfacial effects

Figure 2.1.3(b): Energy Diagram with an interfacial dipole

Although the organic thin film transistor is composed of different materials and often more must be taken into consideration in its design, it is still governed by the equations that governed by the metal oxide field effect transistor.[8]

In the linear regime, where $V_{DS} < V_{GS} - V_T$, the magnitude of the drain to source current is given by:

$$I_D = W/L * C * \mu * [(V_G - V_T) * V_{DS} - V_{DS}^2/2]. \quad (2.1.2)$$

In the saturation regime, where $V_{DS} > V_{GS} - V_T$, the magnitude of the drain to source current is given by:

$$I_D = W/2L * C * \mu * (V_{GS} - V_T)^2, \quad (2.1.3)$$

where C is the capacitance between the gate and the semiconducting material, μ is the mobility, W is the width and L is the length of the transistor. V_{GS}, V_{DS}, and V_T, are the gate-to-source voltage, drain-to-source voltage, and threshold voltage, respectively.[9]

One application of the organic thin film transistor currently being researched is in the area of sensor technology, where their ability to be used as biological and chemical sensors is being explored. Some, but not a lot, of research has been done on their use as sensors, as thin-film transistors have been found to have some potential as glucose sensors[10], and have shown some ability to sense liquids such as lactic acid[11] as well as certain chemical vapors, such as that

of primary alcohols like α-sexithiophene.[12] In addition, some research has been done on the thin film transistor's ability to differentiate between molecules such as double-stranded and single-stranded DNA.[13]

The ability of these transistors to sense the presence of a particular agent upon exposure is largely dependent on the interaction between the transistor and the agent. Often when the transistor is exposed to the agent, a change in mobility or threshold voltage can occur.

The threshold voltage and mobility can be determined via re-expressing the data. A linear relationship between the drain to source current and voltage can be found by taking the square root of both sides while the transistor operates in the saturation regime:

$$\sqrt{(I_D)} = \sqrt{[(W/2L) * C * \mu]} * (V_{GS} - V_T). \quad (2.1.4)$$

This takes the slope-intercept form of a straight line, since V_T is known to stay fixed:

$$\sqrt{(I_D)} = \sqrt{[(W/2L) * C * \mu]}V_{GS} - \sqrt{[(W/2L) * C * \mu]}V_T. \quad (2.1.5)$$

From the linear relation described above, both V_T and μ can be determined.

A change in threshold voltage can result from the agent doping the transistor with negative charges, while a change in mobility can result from a chemical reaction between surface molecules and the agent, as well as from doping from the agent, which changes the conductivity. A change in such properties of the transistor can be detected by analyzing data from the characteristic current-voltage curves of the transistor discussed above, more specifically the I_D versus V_{DS} as well as the I_D versus V_{GS} curves.

2.2. FRAGILE X SYNDROME

Fragile X Syndrome is a condition that has been shown to be linked to congenital mental retardation. In those who exhibit Fragile X Syndrome, the FMR1 gene on the X chromosome has too many repeats of a particular sequence of base pairs, CGG. This causes that segment of the gene to be deactivated via methylation of that segment, thus inhibiting the copying of the FMR1 gene, which in turn prohibits the production of the Fragile X Mental Retardation Protein (FMRP). Relatively recent research has led to a debatable conclusion that the FMRP decides which RNA targets are translated into proteins near synapses, where nerve cells communicate with each other. Although not much is known about how the FMRP directly affects the development of someone who exhibits Fragile X Syndrome, the lack of this protein is known to cause mild to severe mental retardation, depending on the level of methylation.[14]

Also known is that the FMRP is an RNA-binding protein, and that it binds its RNA specifically. The affinity with which a protein binds a target RNA is often directly related to its function – the greater the affinity of the protein for its RNA, the more important its function. RNA-binding proteins with high affinities are often associated with a specific function, such as monitoring translation; whereas, RNA-binding proteins with low affinities have less specific functions such as helping with RNA transport.[15] This project involves preliminary testing to determine if the use of organic thin film transistors will be applicable to this case and will be of use in helping discover more about the FMRP and how its absence directly affects development of those who exhibit Fragile X Syndrome.

3. MATERIALS AND METHODS

3.1. FABRICATION OF TRANSISTORS

Preparation and fabrication of the transistors is detailed under Section 4, **Preliminary Results**.

3.2. EXPOSING THE TRANSISTOR

In order to expose the transistor to various media, the individual agents were dropped into the channel by hand using a syringe, generally a plastic Norm-Ject 30 gauge 1mL syringe. Neither the area of the drop nor the position of the drop was taken into account in any of the analysis.

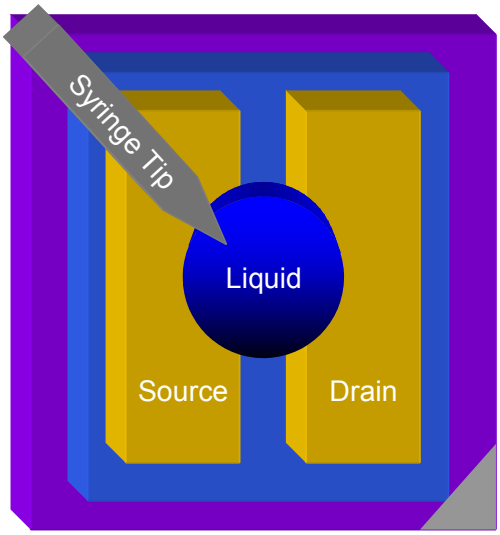

Figure 3.2: Application of liquid into the channel of the transistor.

3.3. SOLUTION PREPARATION

Solution preparation was necessary before exposing the transistor to the RNA binding assay with and without BSA. The results of these exposures can be found in Section 5.5, **Exposure to RNA Binding Assay without BSA (All Agents Combined without BSA) and** Section 5.6, **RNA Binding Assay with BSA (All Agents Combined)**.

The procedure followed for this solution preparation was based upon a document whose main reference can be found in C. Schaeffer, et al., "The fragile X mental retardation protein binds specifically to its mRNA via a purine quartet motif," in *The Embo Journal*.[16] The solution preparation is largely based on a protocol established by Hervé Moine at the Institut de Génétique et de Biologie Moleculairé et Cellulaire in Strasbourg. This process was greatly aided by Kevin Miyashiro of Dr. Jim Eberwine's laboratory at the University of Pennsylvania's pharmacology department.

4. PRELIMINARY RESULTS

4.1. PENTACENE TRANSISTORS (I)

In order to perform these experiments, thin film transistors had to be obtained and tested. On 6 June 2007, organic thin film transistors using pentacene as the semiconducting material were fabricated at IBM's T. J. Watson Research Center in Yorktown Heights, New York and tested. These transistors were made using a pentacene precursor, which aids in allowing insoluble pentacene to be deposited on the surface of the wafer. Since pentacene is not soluble at room temperature, it is treated with a precursor, N-sulfinylacetamide 2[15] in refluxing chloroform with methyltrioxorhenium catalyst, which converts it to a compound soluble in chlorinated hydrocarbons, THF, and dioxane. The pentacene precursor was deposited onto the surface of the wafer to form the thin-film semiconducting material, followed by an annealing step: the product is then heated at a temperature of anywhere from 120˚C to 200˚C and then returns to the original compound, pentacene (see Figure 4.1.1).[17] Following this, the edges of the transistor were cleaned with acetone using cotton-tipped applicators, to remove leakage to the gate. The corner of the wafer was chipped and coated with eutectic Indium-Gallium to make contact to the gate.

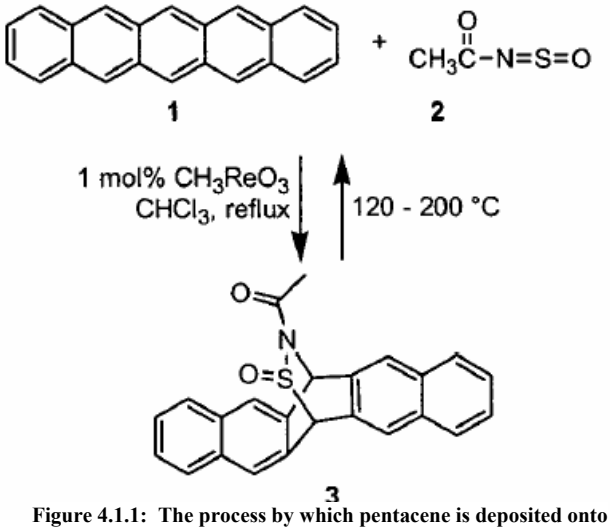

Figure 4.1.1: The process by which pentacene is deposited onto a wafer

The devices were then tested on a probe station using a semiconductor parameter analyzer.

Upon testing, the current-voltage characteristics showed that the transistor was not acting characteristically. The most plausible reason for this occurrence was that we believe a mistake was made in the deposition of the metal electrodes and that copper rather than gold was deposited. Since the work function of gold is 5.1 whereas for copper it is 4.7.[18] For transistors fabricated using copper for the metal electrodes and pentacene as the semiconducting material, the energy barrier at the metal-semiconductor interface is too high for charge carriers to pass the barrier and for the device to conduct properly. The work function no longer lines up with the highest molecular orbital and the energy barrier is too large for charge carriers to surmount, resulting in undesirable behavior.

Figures 4.1.2 and 4.1.3 display the characteristics of a transistor fabricated at IBM when tested in the labs located at the University of Pennsylvania.

Looking at Figures 4.1.2 and 4.1.3, the drain-to-source current is comparable to the current going into the gate. Ideally the current going into the gate should be very small, and the

current going through the channel should be several orders of magnitude higher; this is not the case here.

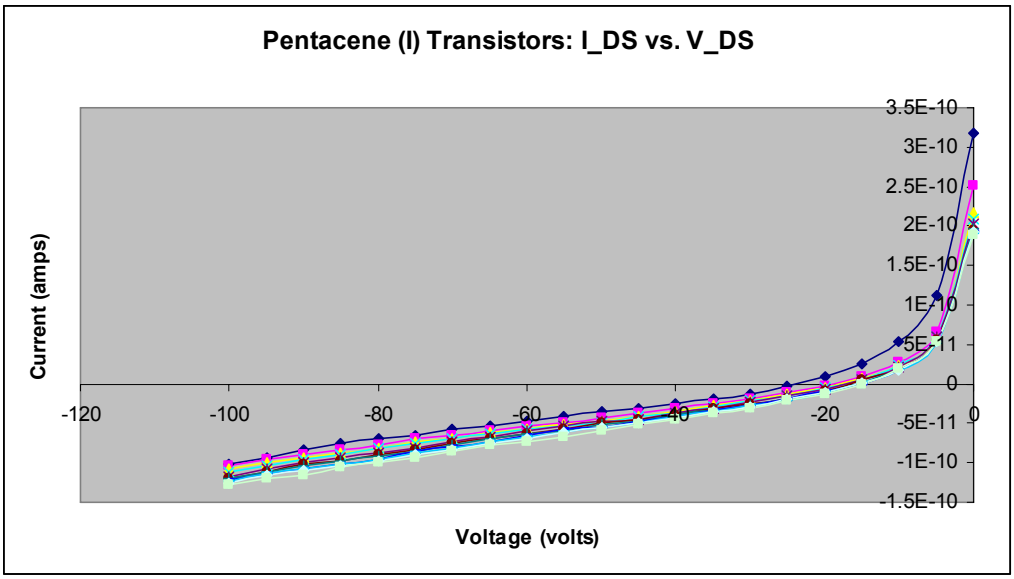

Figure 4.1.2: I_{DS} vs. V_{DS} for Pentacene Transistor

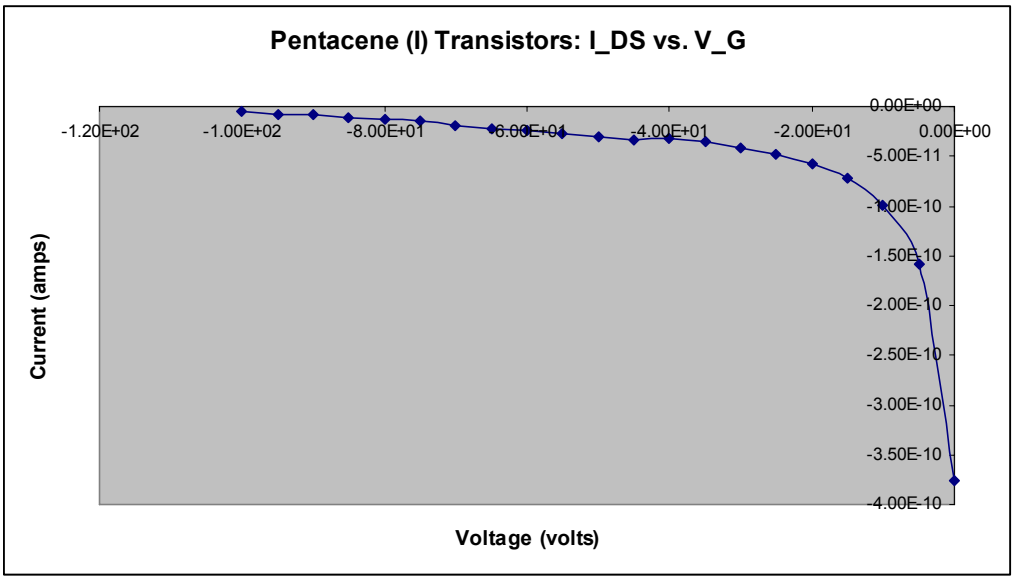

Figure 4.1.3: I_{DS} vs. V_G for Pentacene Transistor

4.2. P3HT TRANSISTORS

Following the attempt to fabricate pentacene thin film transistors, an attempt to make transistors from P3HT, or poly(3-hexylthiophene-2,5-diyl), molecular formula $(C_{10}H_{18}S)_n$[19], was made. The P3HT was obtained from Dr. Russ Composto's lab at the University of Pennsylvania. Regioregular P3HT was obtained from Sigma-Aldrich. 5.8 milligrams of P3HT was mixed with 0.5 milliliter choloroform ($CHCl_3$), forming a dark purple solution. It was then put into an ultrasonic water bath to promote proper mixing of the compounds, and then filtered with an Acrodisc 13CR syringe filter, with a 13 millimeter diameter, 0.2 micrometer pore size PTFE membrane, and Luer fitting. It was then spun onto the wafer for 45 seconds at 1500 rpm.[20] The edges were cleaned with acetone as mentioned earlier in Section 4.1, **Pentacene Transistors (I),** and the corners of the transistor wafers were then scratched with a scribe and chipped prior to application of Indium Gallium to the corner.

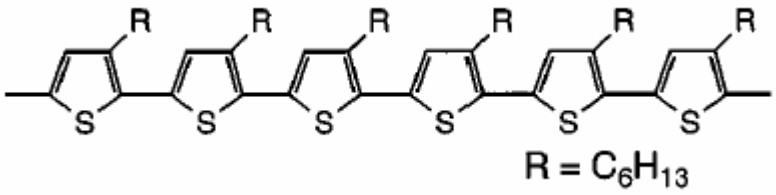

Figure 4.2.1: Regioregular poly(3-hexylthiophene)

The wafer onto which the P3HT was spin cast onto was first plasma cleaned and then treated with HMDS. Another round of wafers was also plasma cleaned, but was not treated with HMDS before the P3HT was spin cast onto it. Although HMDS is normally used to promote adhesion of photoresist, it has been shown to improve mobility when applied to a wafer before applying P3HT. HMDS lowers the surface energy of the wafer, which is desirable because it increases the mobility of the charge carriers through these molecules.[21]

However, the transistors fabricated with P3HT also did not produce desirable characteristics. The main problem was that the gate current was only one order of magnitude lower than the drain to source current in the I_{DS} versus V_G data, which means that there was a large leakage path from the gate.

There are a few possibilities of why these transistors did not function properly. One of the more plausible reasons is the material on the edge of the wafer was not removed properly when the edges were cleaned with acetone, resulting in a lot of leakage. A much less probable reason is that the P3HT was not purified enough. Though the P3HT was filtered using the above described filter, the most likely problem was that the type of P3HT obtained from Sigma-Aldrich inherently contained bits of metal contamination which may have caused undesirable impurities. Iron (III) chloride ($FeCl_3$) is often used as a catalyst to convert 3-hexylthiophene to form P3HT polymer.[22] There may have been residual iron (III) chloride in the P3HT if the P3HT was not extremely pure. Both the before mentioned reasons result in undesirable behavior.

Figures 4.2.2 and 4.2.3 display the characteristics obtained when the P3HT Transistors were tested.

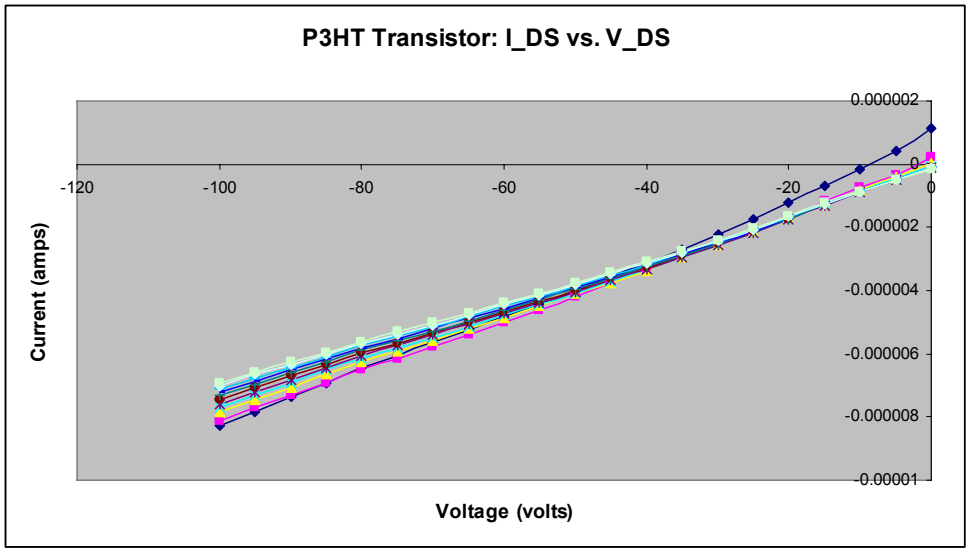

Figure 4.2.2: I_{DS} vs. V_{DS} for P3HT Transistor

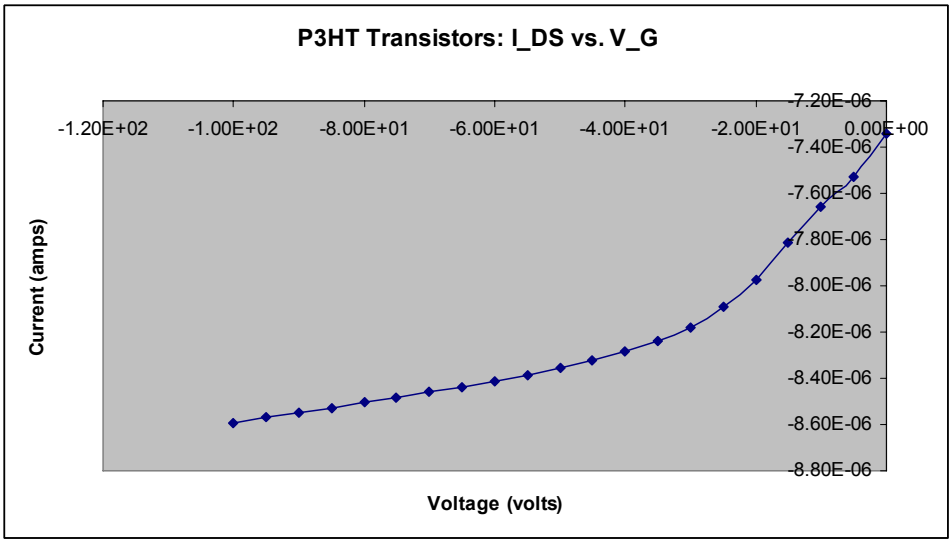

Figure 4.2.3: I_{DS} vs. V_G for P3HT Transistor

4.3. HBC TRANSISTORS

After the attempt to fabricate wafers from P3HT, an attempt was made to fabricate transistors from HBC, or hexabenzocoronene. The transistors as well as the HBC were obtained from Colin Nuckoll's group at Columbia University. The synthesis process for HBC can be found in Angewandte Chemie Supporting Information 69451.

HBC is an aromatic compound, one in which the compound forms a ring with alternating single and double bonds. This compound has some desirable properties because it self-organizes itself into molecular stacks which lie parallel to the surface.[23]

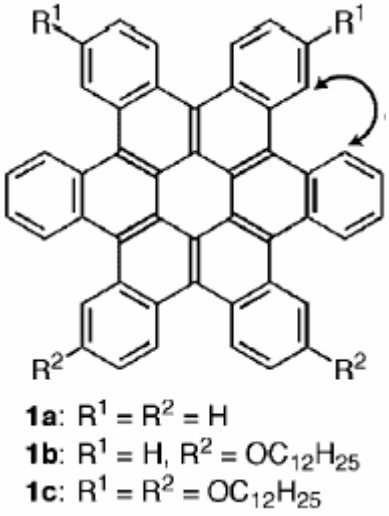

Figure 4.3.1: Hexobenzocoronenes

A solution of hexabenzocoronene was made with from 2 milligrams +/- 0.1 milligram with approximately 2 milliliters toluene; a transparent yellow solution was formed. It was then put into a sonicator (ultrasonic water bath) to mix thoroughly. The solution was placed in a glass bottle, since toluene is known to dissolve some plastic containers.[24]

The wafers onto which the solution was deposited onto were first plasma cleaned. The solution was spin cast at a rate of revolution of 3000 rpm for 45 seconds onto the wafer. The samples were then brought to the microfabrication lab, put on a hot plate for 30 minutes at 119-120˚C, and then brought back to 29˚C (though more desirably it should have been brought back to room temperature); the cooling process took around one hour.[25]

Unfortunately, these samples did not show proper characteristics either. This could have been for a number of reasons, one being that when creating the gate via scratching the surface with a scribe, the scratch was too deep, or perhaps to difficult to clean. Also, given that the dielectric of the thermally oxidized silicon wafer were thin (around 3000 angstroms), when probes were put on the drain and source pads or too high a voltage was applied, the dielectric could have been broken.

Figures 4.3.2 and 4.3.3 show the characteristics taken from an HBC transistor.

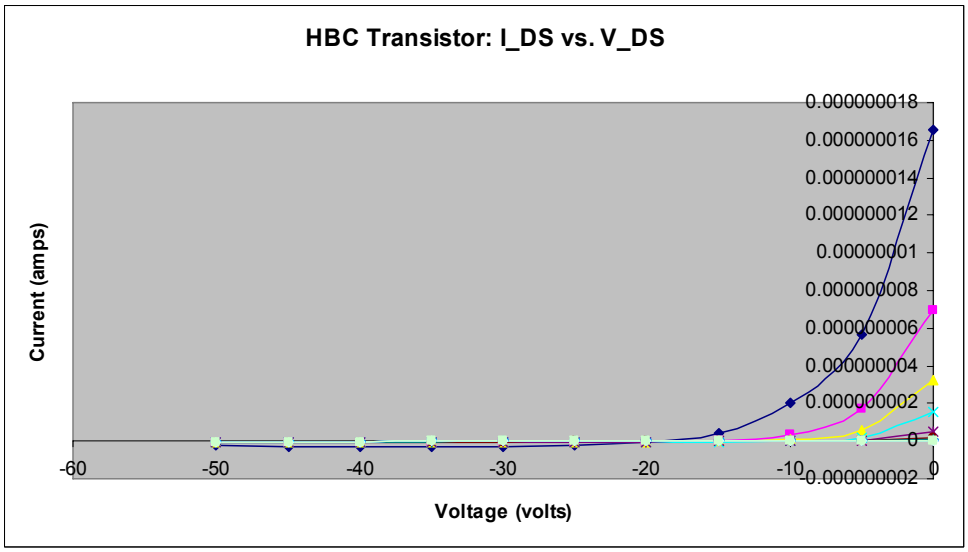

Figure 4.3.2: I_{DS} vs. V_{DS} for HBC Transistor

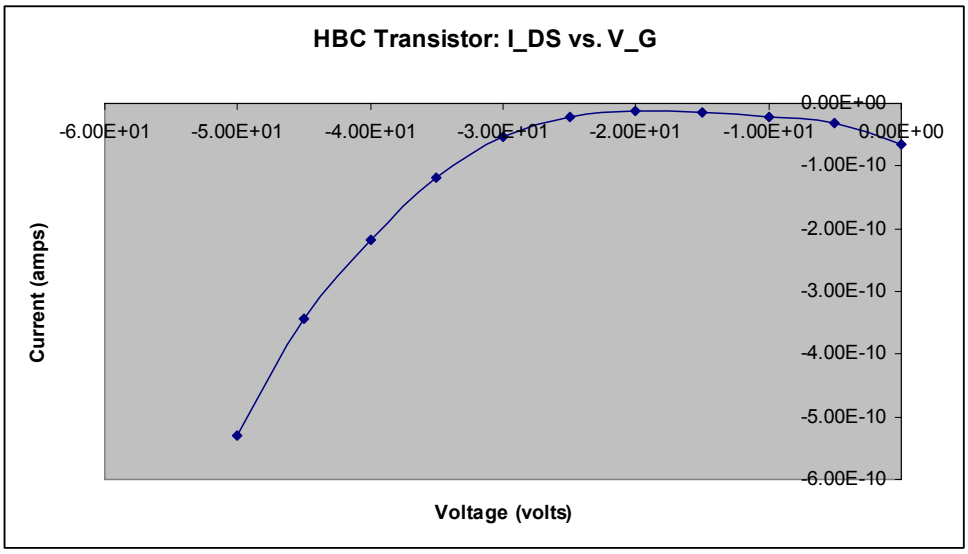

Figure 4.3.3: I_{DS} vs. V_G for HBC Transistor

4.4. PENTACENE TRANSISTORS (II)

Working pentacene transistors were obtained from the IBM Labs at Yorktown Heights on 27 July 2007. These transistors were prepared in the same manner as described in Section 4.1, **Pentacene Transistors (I).**

Figures 4.4.1 and 4.4.2 display the characteristics taken with these transistors.

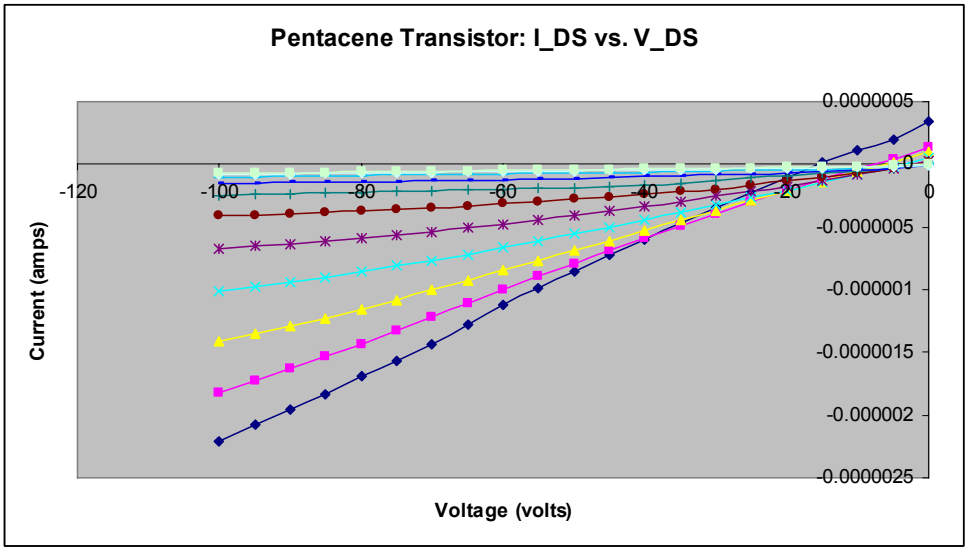

Figure 4.4.1: I_{DS} vs. V_{DS} for Pentacene Transistor from 31 July

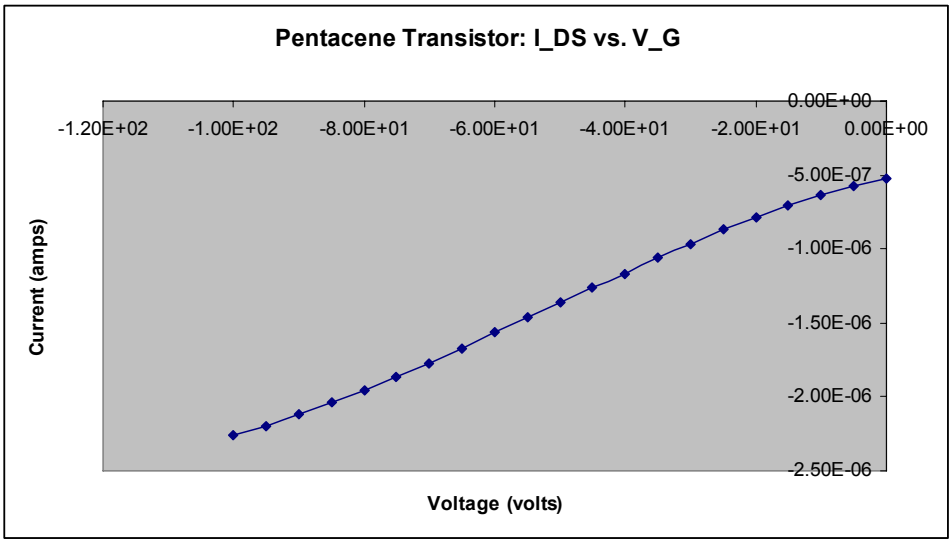

Figure 4.4.2: I_{DS} vs. V_G for Pentacene Transistor from 31 July

5. RESULTS FROM CONTROL EXPERIMENTS

5.1. WATER EXPOSURE

In order to run the full experiment on the transistor, many of the agents in the solution had to be tested separately. First, the transistor's response to distilled, deionized water was tested. In particular distilled, deionized water was preferred because it does not contain undesirable ions and it has not draw carbon dioxide from the air, which could possibly contaminate reactions in the combined solution. In general, having the medium be as inert as possible was desirable.

A small drop of water was delivered to the transistor channel using a 21 gauge needles with Hamilton microliter syringe. By taking current-voltage characteristics (both I_{DS} versus V_{DS} and I_{DS} versus V_G) before and after exposure, the transistor was checked for its response to the water; additionally, its degradation over time during exposure to the water was also tested but will not be shown here.

Some problems were experienced with the application of the water droplet to the channel of the transistor. When an electric field was applied, the drop would often move over to the electrode at which a negative voltage was being applied. As a result, the transistor was measured under the application of both high (-100 volts to 100 volts) voltages and low (-10 volts to 10 volts) voltages. This response of the water droplet was found to be voltage dependent, as the drop did not disperse when lower voltages were applied.

First, the transistor characteristics upon its first exposure to water are shown for higher voltages (range -100 volts to 100 volts). When run at these voltages, the water droplet moved to the drain electrode, and it is possible that one of the probe tips may have gotten wet. The transistor exposed has a channel length of 95 micrometers, and the channel width was around 1500 micrometers.

The transistor prior to application of the water had a threshold voltage of -20 volts, and the original mobility was found from μ = (slope of the linear fit)^2 * (L/W) * 2*L*W/C, where C was found by ε*(L*W)/d, where d is the dielectric thickness, and is 5000 angstroms, or 5E-5 cm, and $\varepsilon = 3.9\varepsilon_0 = 3.45$E-13 F/cm. From this formulation, the mobility was found to be around 0.0165 cm^2/V-s.

Figures 5.1.2. and 5.1.3 show the characteristics taken after the transistor was exposed to the distilled, deionized water.

After exposure to water, the threshold voltage was found to be -7.1 volts, and the mobility became 9E-4 cm^2/V-s. The water appeared to have decreased the mobility as well as the magnitude of the threshold voltage. The amount by which the threshold voltage was decreased seems unusually high, and it is possible that when the water droplet dispersed, that it resulted in a connection between the two probes which caused a parallel ionic current.

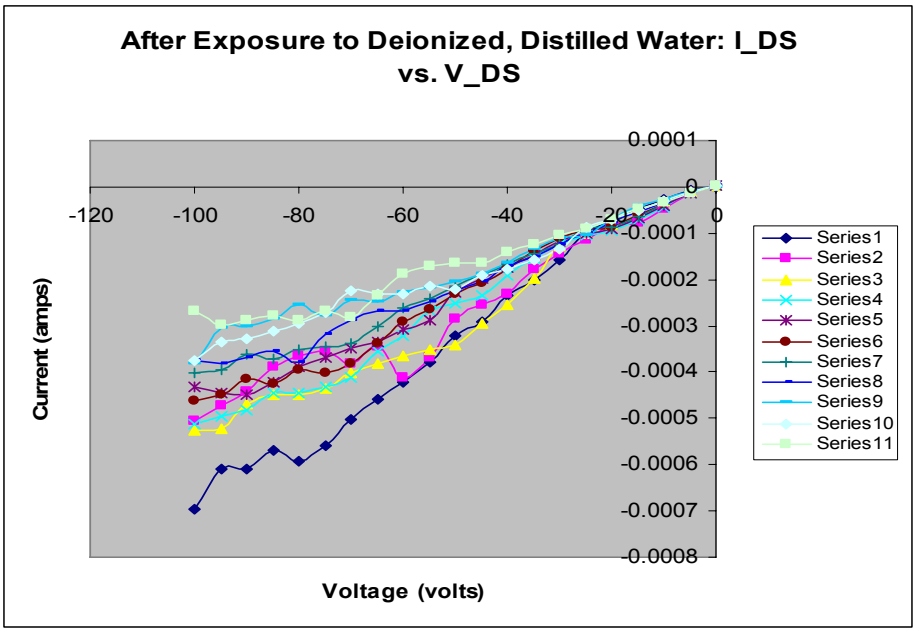

Figure 5.1.1: I_{DS} versus V_{DS} after exposure to deionized, distilled water

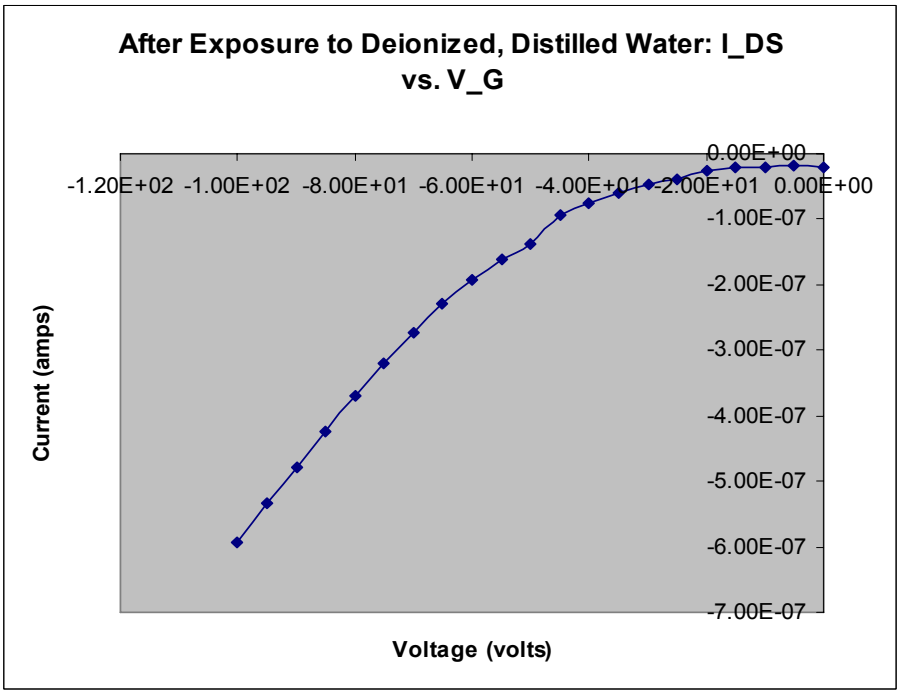

Figure 5.1.2: I_{DS} versus V_G after exposure to deionized, distilled water.

5.2. MOINE BUFFER EXPOSURE

Next, transistors were exposed to Moine buffer in two concentrations, 1X and 2X. The Moine Buffer is a salt solution and was used because it has been successfully used in RNA binding assays, especially in those involved with FMRP. Moine buffer contains (in 1X concentration) 50 mM Tris(hydroxymethyl)aminomethane buffer (pH 7.4), 1 mm $HgCl_2$ and 1mM ethylene diamine tetracetic acid (also known as EDTA; pH 8), 150 mM KCl, and 1mM dithiothreitol (DTT).[26] The Moine buffer showed very little tolerance for any applied voltage in the 2X concentration, as the drop dispersed no matter the applied voltage. This could be a result of the Moine Buffer being a salt solution and thus containing ions, making it more susceptible to applied electric fields. Only data at the higher applied voltages will be shown since the characteristics at lower voltages were inconclusive and did not provide much insight.

Figures 5.2.1-4 show the characteristic curves of the transistor before and after being exposed to Moine buffer at higher voltages. The transistor had a length of 25 μm and a width of 1000 μm.

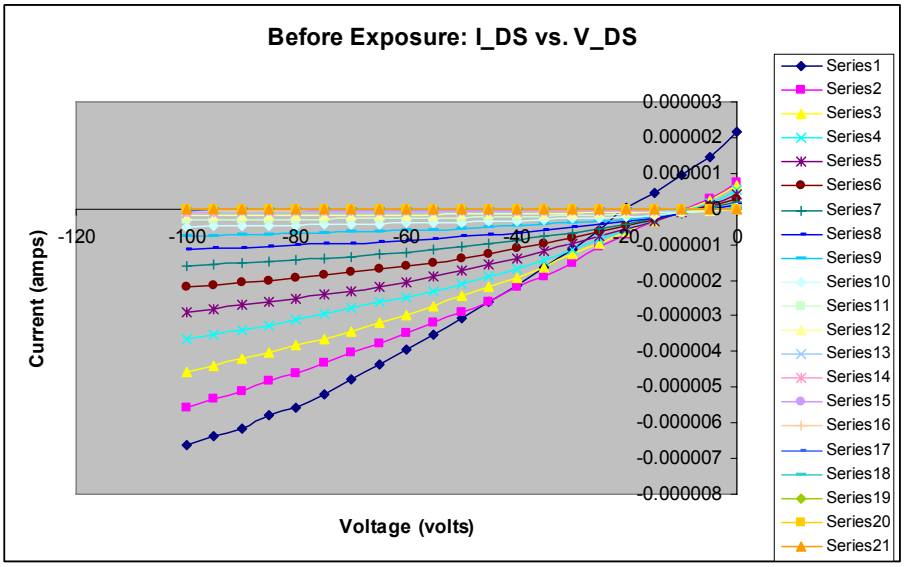

Figure 5.2.1: I_{DS} versus V_{DS} before exposure to Moine buffer (2X)

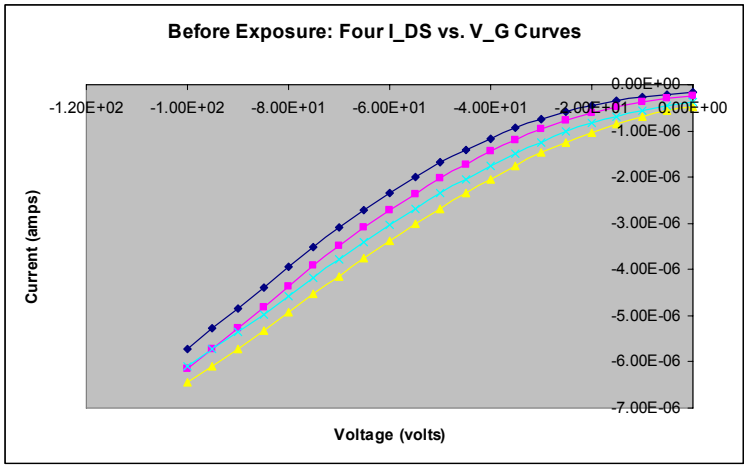

Figure 5.2.2: I_{DS} versus V_G before exposure to Moine buffer (2X)

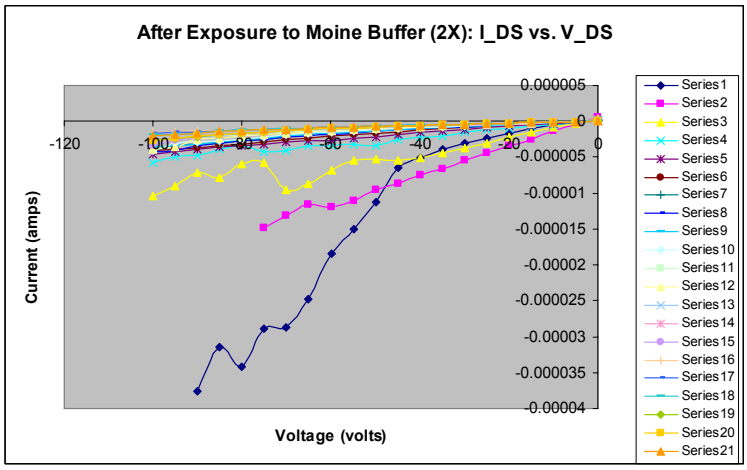

Figure 5.2.3: I_{DS} versus V_G after exposure to Moine buffer (2X)

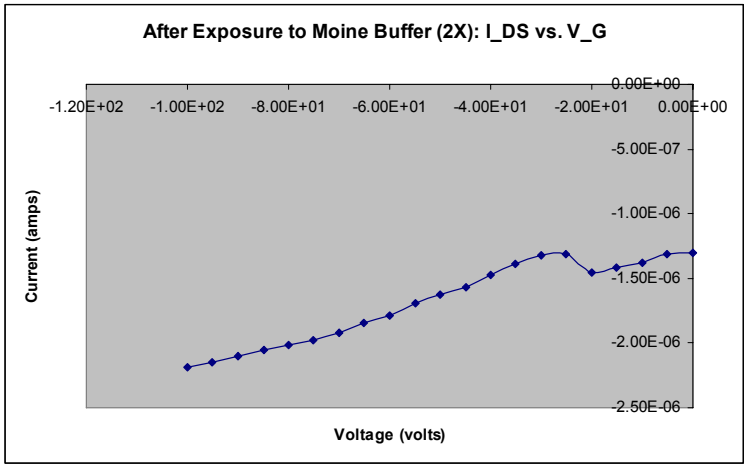

Figure 5.2.4: I_{DS} versus V_G after exposure to Moine buffer (2X)

Based on Figure 5.2.3, the new threshold voltage and mobility after exposure were unable to be extracted using the methods discussed in the introduction since a linear fit of $I_D^{1/2}$ vs. V_G yielded impractical values for both metrics. For this reason, a comparison of mobility and threshold voltage before and after the exposure was unable to be made for the high voltage range. However, the characteristics of the transistor before and after exposure are being shown above for visual comparison. After exposure to the Moine buffer, the current levels in general were higher; however, this was seen to a greater extent in the I_{DS} versus V_{DS} curves. The difference between the saturation and linear region was seen to a lesser extent in these curves as well. Although it is possible that the Moine buffer actually increased mobility, since the drop did disperse, it is also possible is that a short resulted between the two probes, which caused these

higher current levels. Another possibility is that the Moine buffer, a salt solution which contains ions, could have doped the material providing more charge carriers.

The Moine buffer was diluted to half of its original concentration and was tested at a concentration of 1X as well at both high and low voltages. At both voltage ranges, the drop of Moine buffer dispersed. Only the higher voltages will be shown here since the lower voltage ranges do not provide more insight. The transistor to which the Moine buffer (1X) was applied had a length of 25 μm and a width of 1500 μm.

Figures 5.2.5-8 show the current-voltage characteristics before and after the exposure.

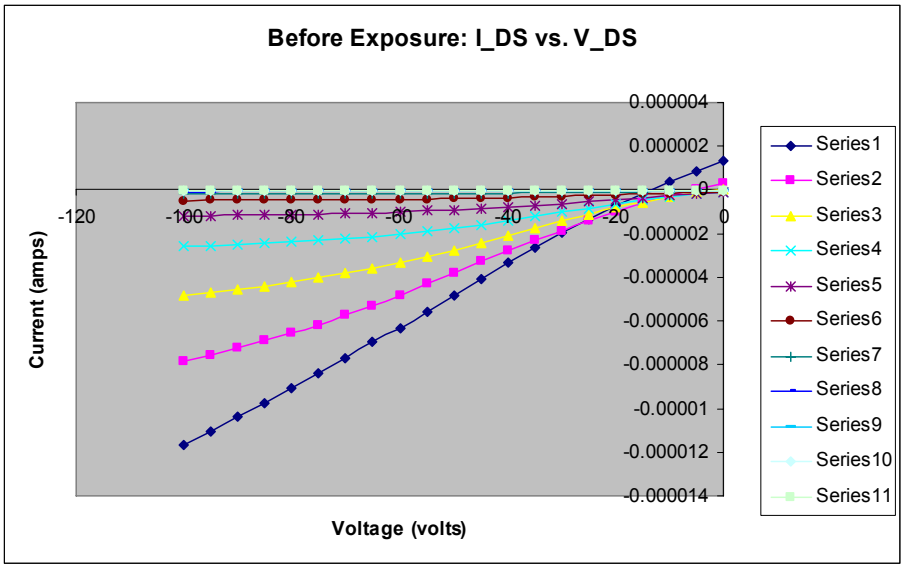

Figure 5.2.5: I_{DS} versus V_{DS} before exposure to Moine buffer (1X)

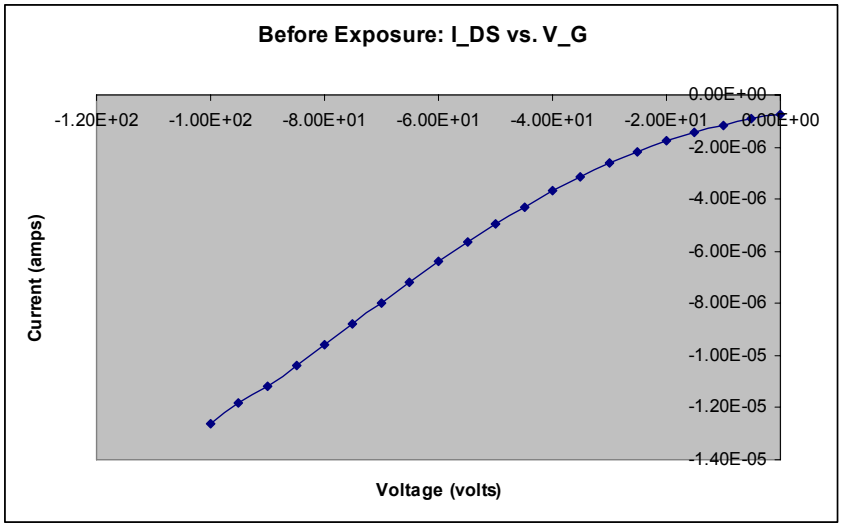

Figure 5.2.6: I_{DS} versus V_G before exposure to Moine buffer (1X)

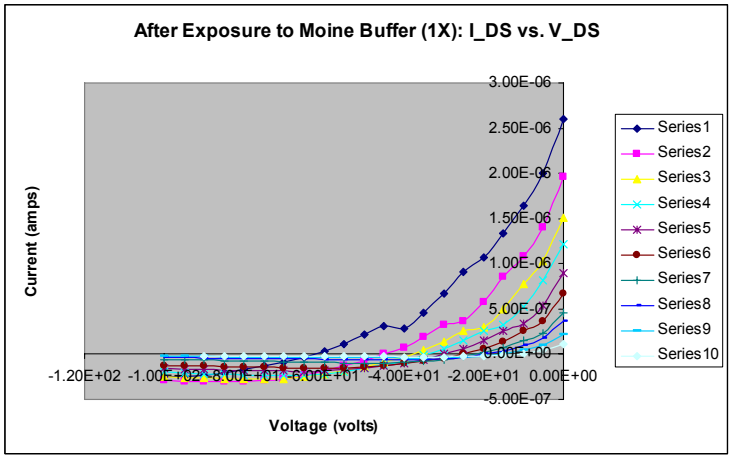

Figure 5.2.7: I_{DS} versus V_{DS} after exposure to Moine buffer (1X)

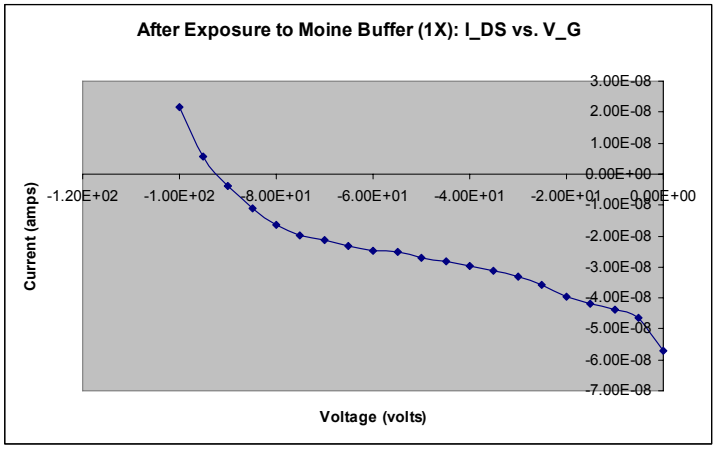

Figure 5.2.8: I_{DS} versus V_G after exposure to Moine buffer (1X)

The Moine buffer (1X) demonstrates a relatively high amount of leakage, as can be observed from the I_{DS} versus V_G curve. This leakage could be the result of another path for the current to follow: a short could have formed between the probe ends so that the current could travel through the Moine buffer. Moreover, the Moine buffer, because it is a salt solution, could provide ions and therefore provide charge carriers, as stated before.

5.3. BSA EXPOSURE

Next, a transistor was exposed to BSA. The BSA is important to the combined solution because it prevents nonspecific binding between the protein and the RNA, and it also facilitates the specific binding and promotes proper folding of the protein and RNA.[27] Whether the drop of

BSA dispersed was dependent on the magnitude of the voltage. When run at the higher ranges, the drop did disperse; whereas, when run at lower voltage ranges, the drop stayed intact.

As a result of the obtained I_{DS} vs. V_G curves, no proper linear fit could be obtained from the data in order to determine the values of the threshold voltage and the mobility after exposure. However, Figures 5.3.1-4 are given for visual comparison of the transistor's characteristics before and after exposure.

Figures 5.3.1-4 display the characteristic curves of the transistor before and after being exposed to BSA with lower applied voltages. The transistor that was exposed had dimensions of 95 µm for the channel length and 1500 µm for the channel width.

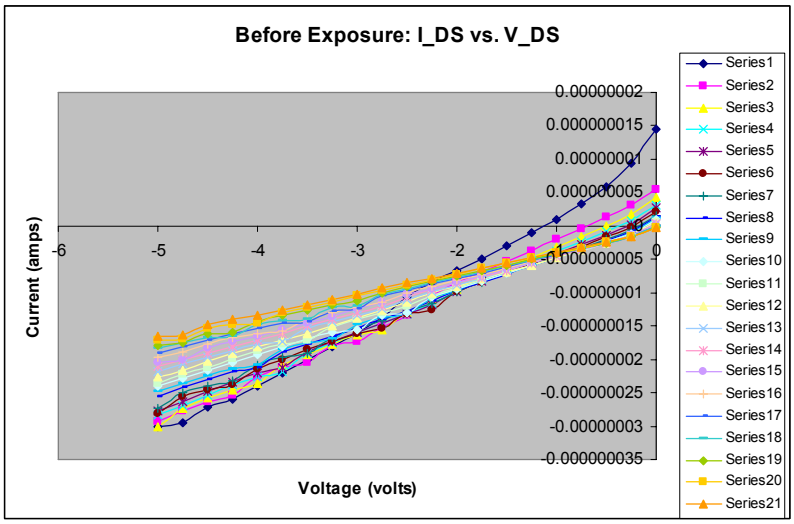

Figure 5.3.1: I_{DS} versus V_{DS} before exposure to BSA

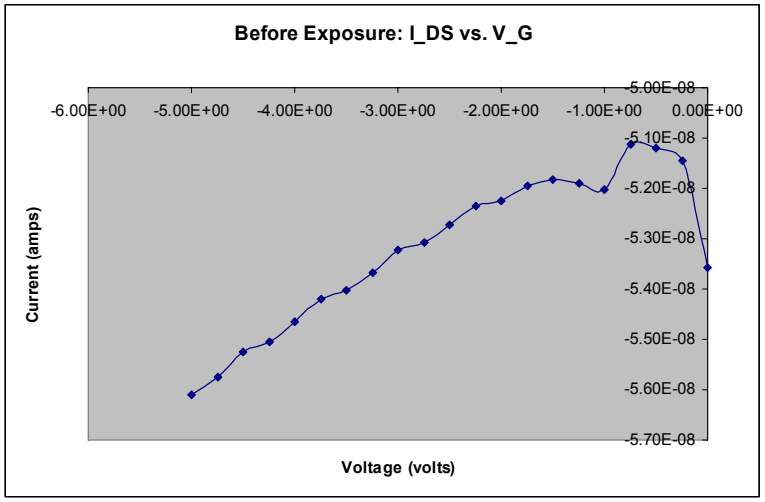

Figure 5.3.2: I_{DS} versus V_{DS} before exposure to BSA

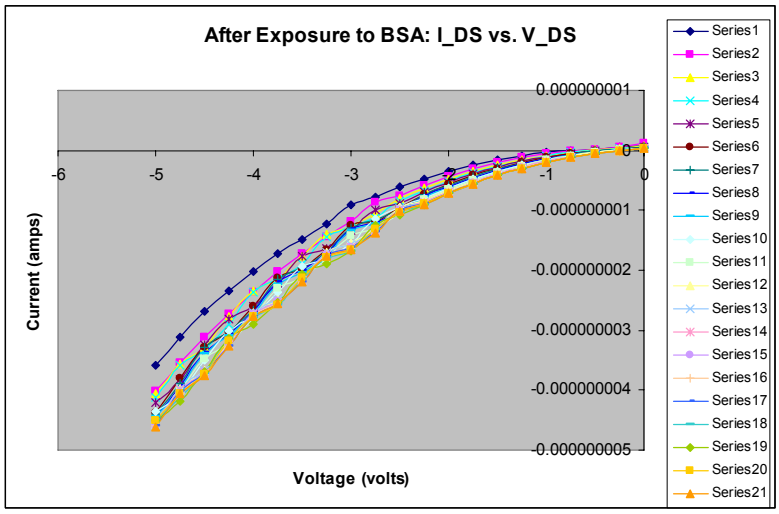

Figure 5.3.3: I_{DS} versus V_{DS} after exposure to BSA

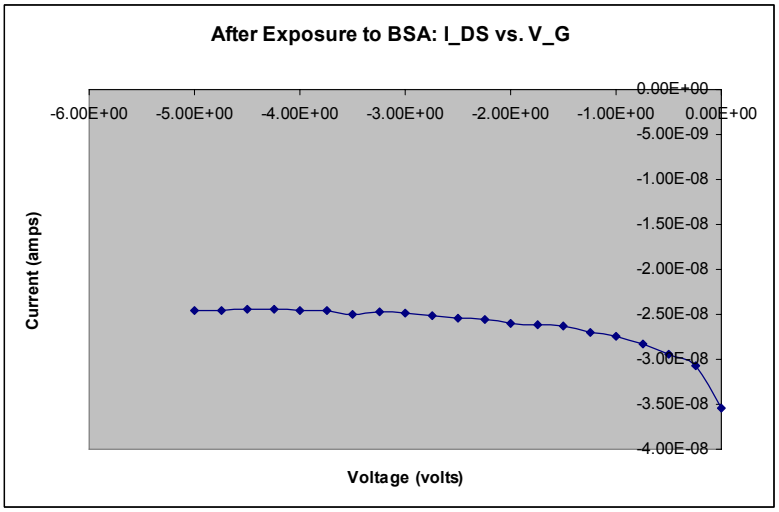

Figure 5.3.4: I_{DS} versus V_G after exposure to BSA

From these graphs, one can see very little difference in the current levels – they tended to have stayed around the same order of magnitude. The BSA seemed to have changed the order of the curves for each applied gate voltage in I_{DS} versus V_G. Before exposure, the higher the gate voltage, the greater the magnitude of the drain to source current. However, after exposure, the higher the gate voltage, the smaller the magnitude of the drain to source current.

The characteristic curves when the transistor was exposed to higher voltage levels are shown in Figures 5.3.5-8.

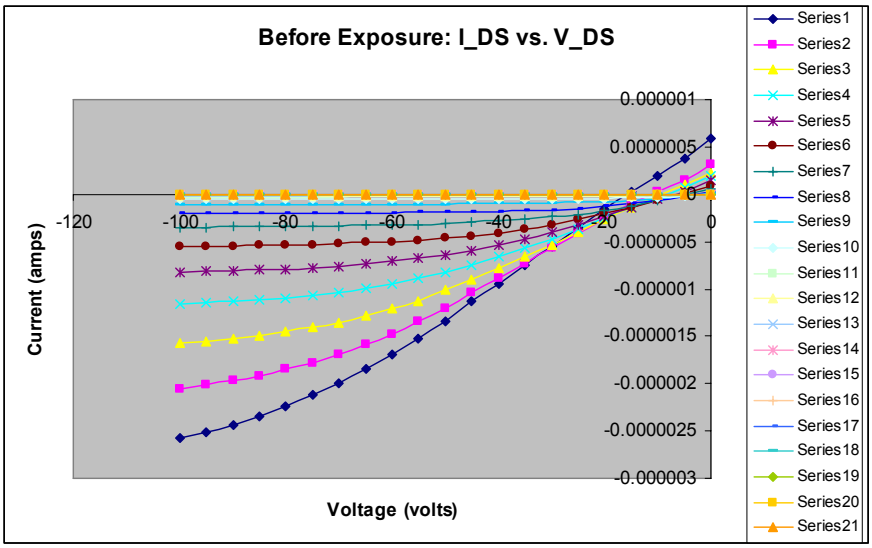

Figure 5.3.5: I_{DS} versus V_{DS} before exposure to BSA

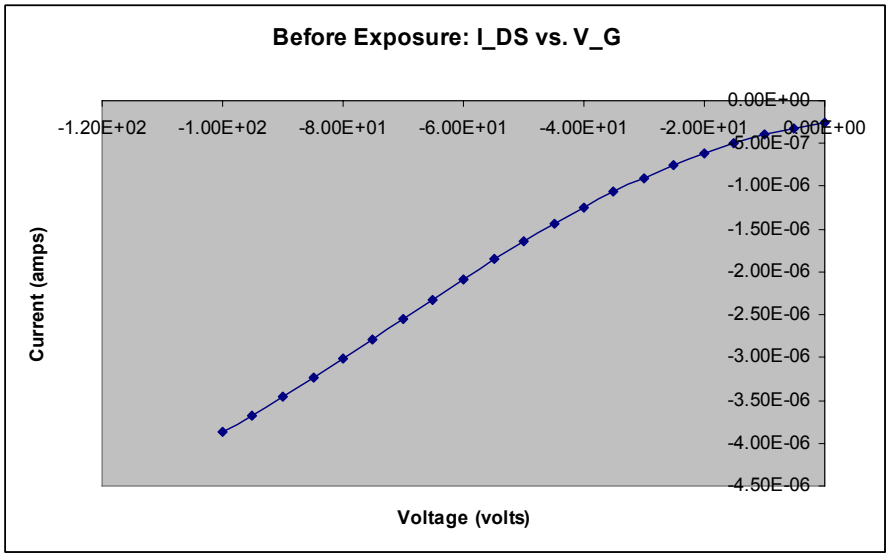

Figure 5.3.6: I_{DS} versus V_G before exposure to BSA

At higher voltages, the transistor seemed to exhibit a lack of dependence on the gate voltage for the I_{DS} versus V_G curves. Additionally, the current was found to be at very high levels.

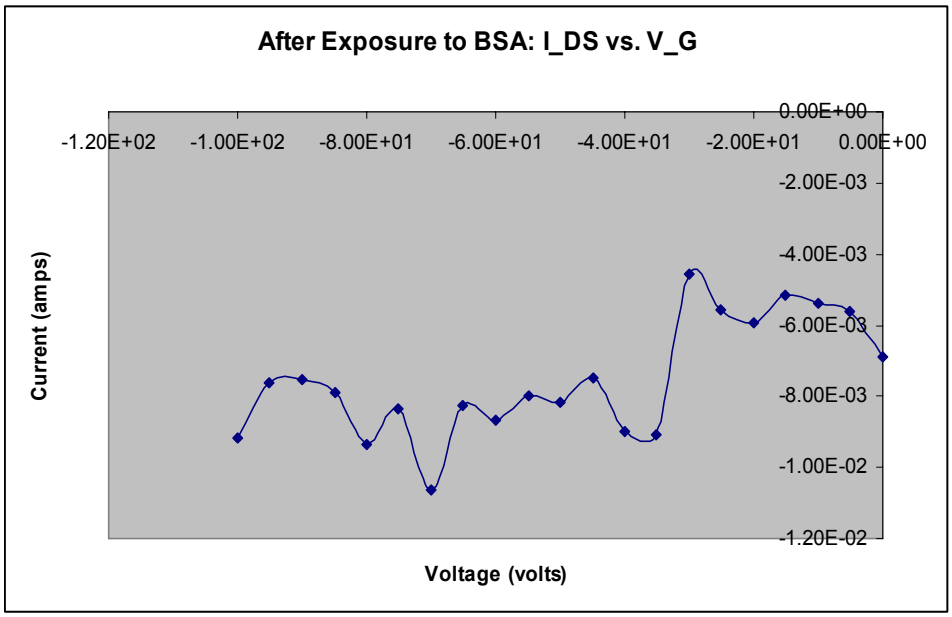

Figure 5.3.7: I_{DS} versus V_{DS} after exposure to BSA

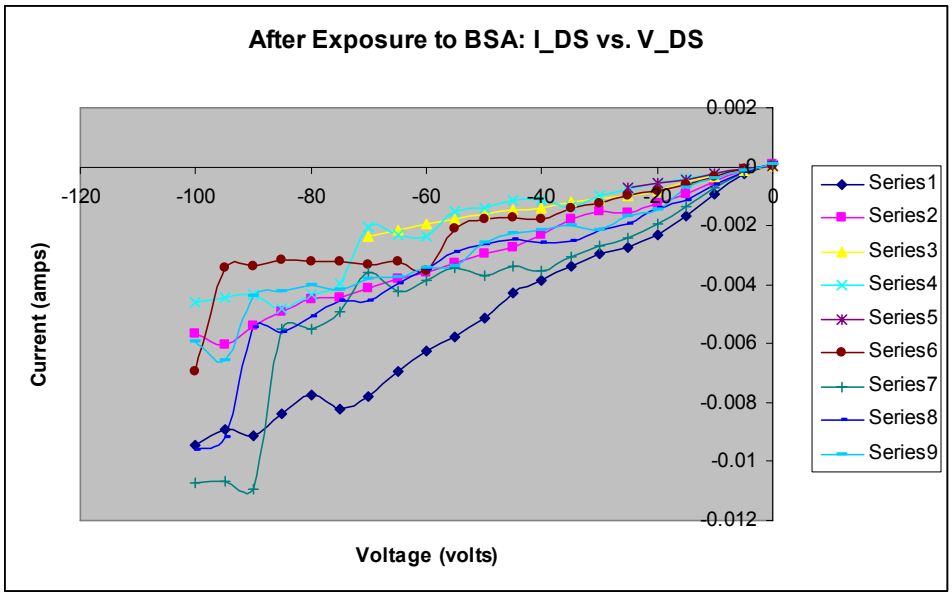

Figure 5.3.8: I_{DS} versus V_G after exposure to BSA

5.4. tRNA EXPOSURE

The transistors were also exposed to tRNA, which is important to the solution because it also helps block nonspecific binding, which is undesirable for this particular solution.

Figures 5.4.1-8 display characteristics obtained when the tRNA was applied and tested at both high and low voltages. When the tRNA was applied, the drop dried very quickly, and before the tests were able to be run. However, the assumption was made that it dried on the surface of the transistor rather than evaporated, so no new amount of tRNA was applied. The transistor on which the tRNA was applied had a length of 25 µm and a length of 1500 µm.

Figures 5.4.1-4 are the characteristics before and after tRNA was applied at the higher voltage range. Once again, the I_{DS} versus V_G curve that was extracted after the tRNA was applied to the transistor would not allow a good linear fit when $I_{DS}^{1/2}$ versus V_G was taken and therefore the threshold voltage and mobility that could be extracted are not stated here.

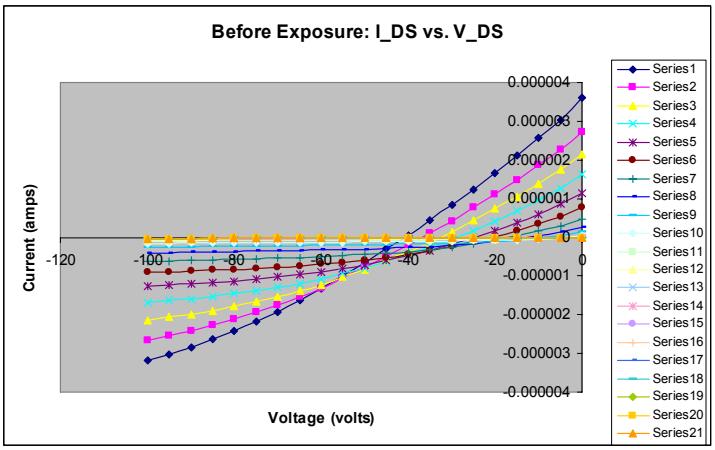

Figure 5.4.1: I_{DS} versus V_{DS} before exposure to tRNA

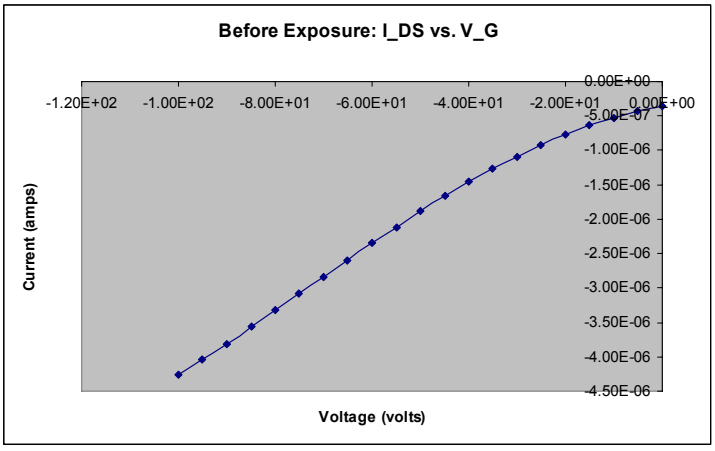

Figure 5.4.2: I_{DS} versus V_G before exposure to tRNA

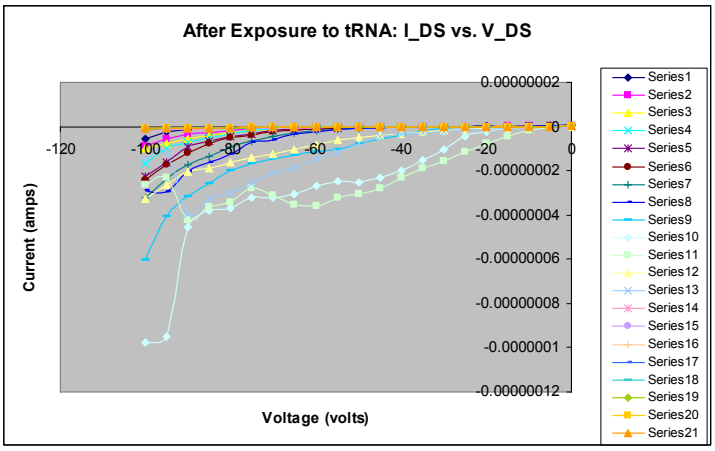

Figure 5.4.3: I_{DS} versus V_{DS} after exposure to tRNA

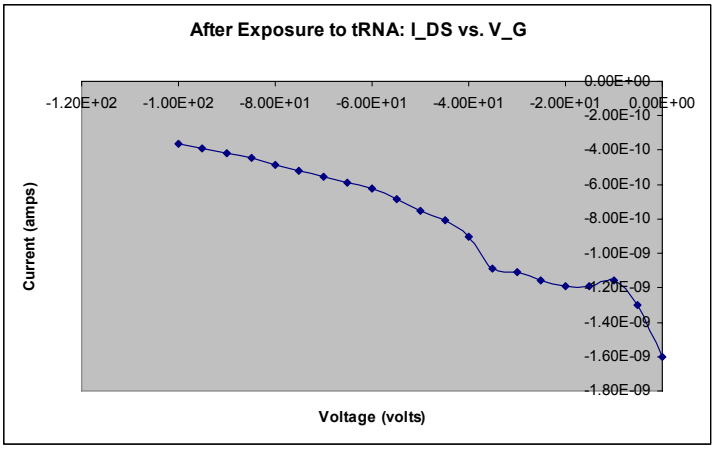

Figure 5.4.4: I_{DS} versus V_G after exposure to tRNA

Figures 5.4.5-8 display the characteristics at the lower applied voltages.

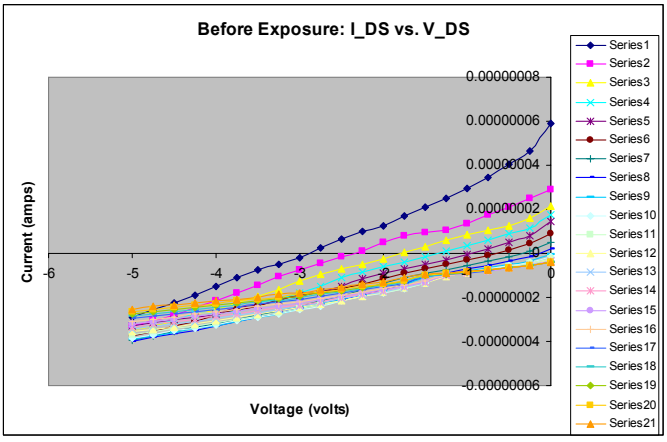

Figure 5.4.5: I_{DS} versus V_{DS} before exposure to tRNA

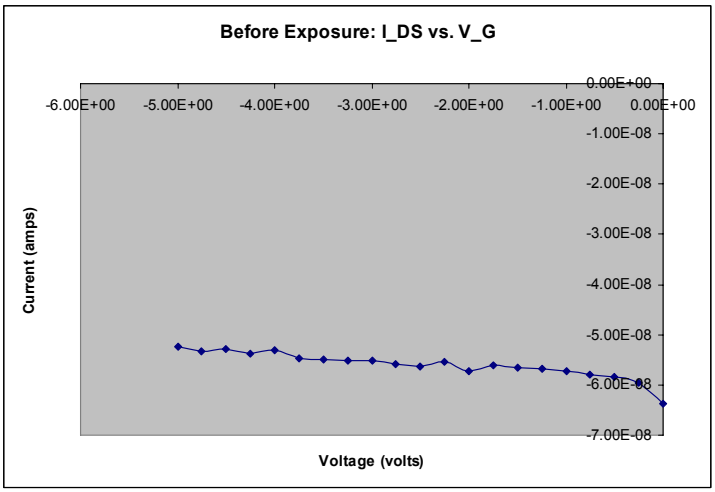

Figure 5.4.6: I_{DS} versus V_G before exposure to tRNA

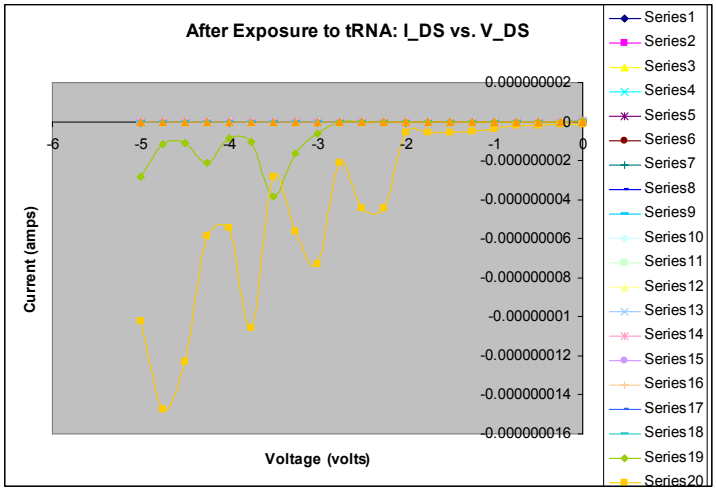

Figure 5.4.7: I_{DS} versus V_{DS} after exposure to tRNA

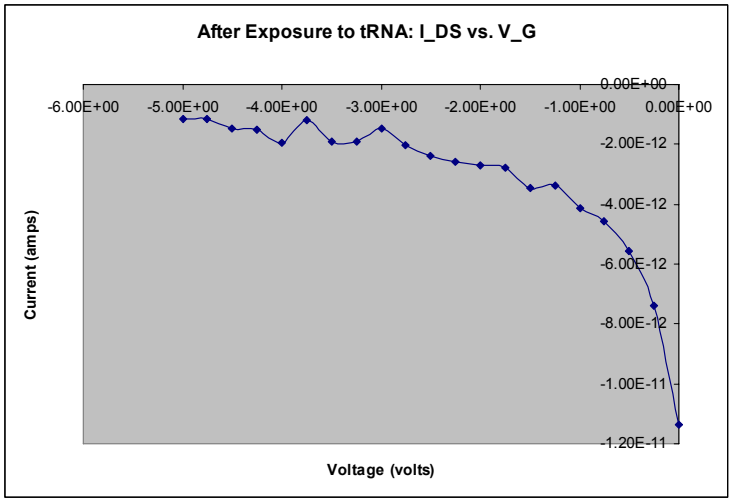

Figure 5.4.8: I_{DS} versus V_G after exposure to tRNA

Exposing the transistor to tRNA seemed to depress the current to very low levels, and when low voltages were applied, only the noise of the machine was apparent in the I_{DS} versus V_{DS} curves. The transistor which was exposed to tRNA had a width of 1500 µm and a length of 25 µm.

5.5. EXPOSURE TO RNA BINDING ASSAY (ALL AGENTS COMBINED)

Figures 5.5.1-4 display the characteristics taken when the transistor was exposed and run at the higher voltage range, before and after exposure. All of the factors combined seemed to depress the current to relatively low levels and at high voltages, the I_{DS} versus V_G curves no longer exhibit the linear and saturation regions that the transistor exhibited before. The I_{DS} versus V_G curve seems to also exhibit some lack of dependence on the gate voltage. The transistor which was exposed had a length of 95 µm and a width of 1000 µm.

When the electric field was applied, the combined mixture seemed to split apart into its components. The liquid mixture separated – part of the solution moved toward the source and drain, and part of the solution spread around the transistor and was green in color. The electrodes became slightly delaminated. This occurred both times a trial was run; however, in the second trial, the drop stayed intact although parts of the solution still split as described above.

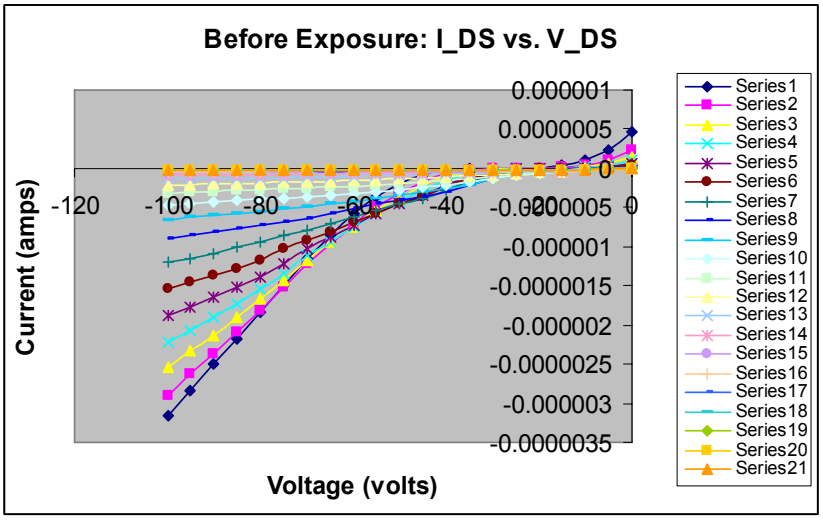

Figure 5.5.1: I_{DS} versus V_{DS} before exposure to RNA binding assay

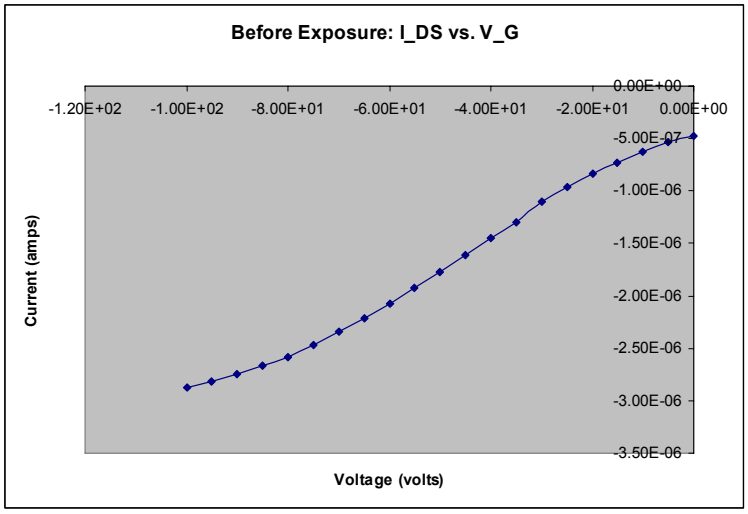

Figure 5.5.2: I_{DS} versus V_G before exposure to RNA binding assay

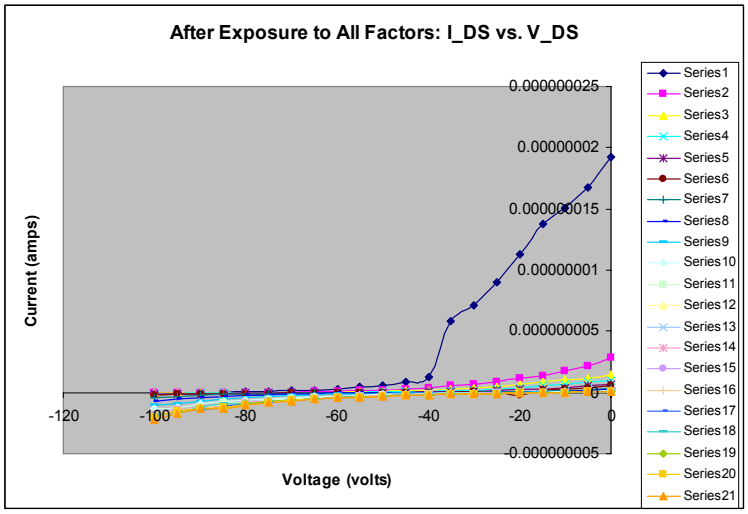

Figure 5.5.3: I_{DS} versus V_{DS} after exposure to RNA binding assay

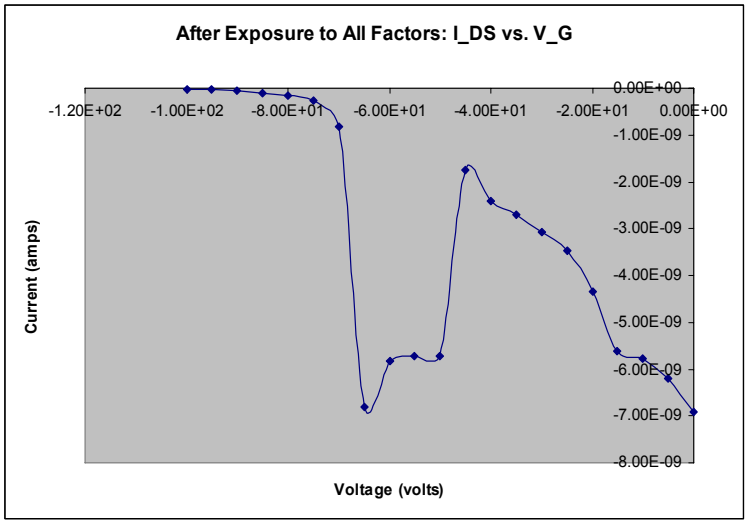

Figure 5.5.4: I_{DS} versus V_G after exposure to RNA binding assay

5.6 EXPOSURE TO RNA BINDING ASSAY WITHOUT BSA (ALL AGENTS COMBINED WITHOUT BSA)

The transistor was also exposed to all factors except BSA, since BSA is known to have some properties that could dominate the response. The response showed in Figures 5.6.1-4 seemed to be somewhat similar to that of the response with BSA – more details on this will be discussed Section 6, **Discussion and Conclusion**. The current levels were around the same order of magnitude before and after the exposure. Once again, the threshold voltage and mobility could not be extracted from the curves taken after exposure. The transistor that was exposed had a length of 95 µm and 1000 µm.

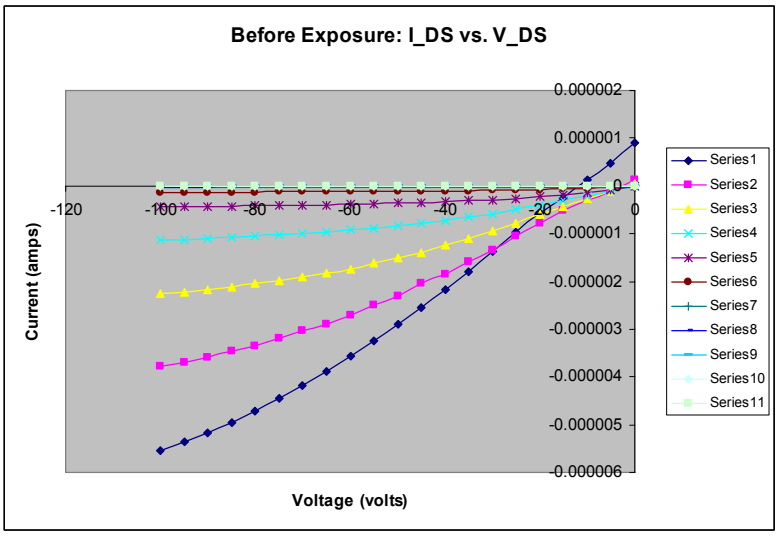

Figure 5.6.1: I_{DS} versus V_{DS} before exposure to RNA binding assay without BSA

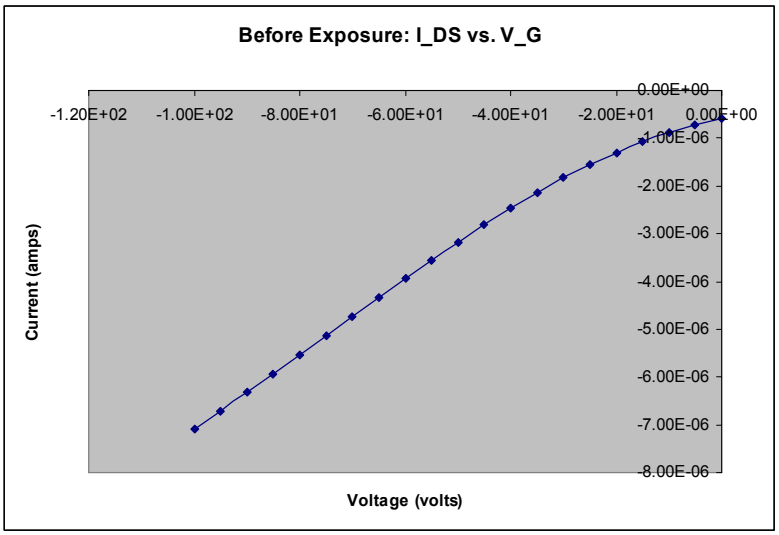

Figure 5.6.2: I_{DS} versus V_G before exposure to RNA binding assay without BSA

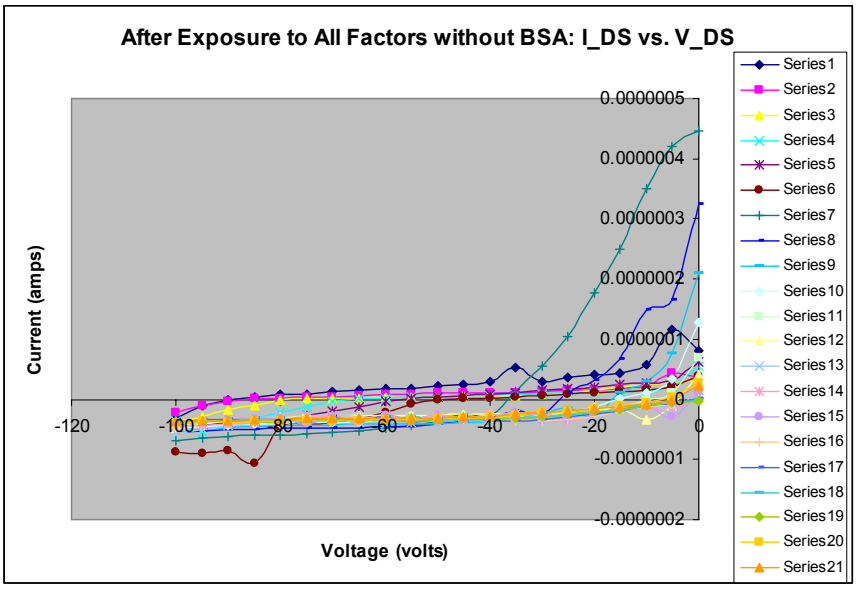

Figure 5.6.3: I_{DS} versus V_{DS} after exposure to RNA binding assay without BSA

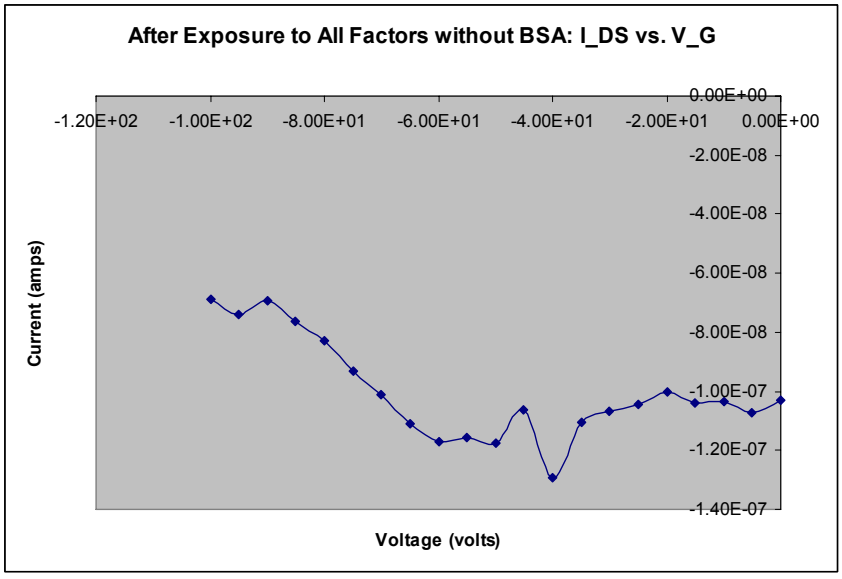

Figure 5.6.4: I_{DS} versus V_G after exposure to RNA binding assay without BSA

6. DISCUSSION AND CONCLUSIONS

The general aim of this project was to determine if the organic thin film transistor was suitable for biological sensing in the case of Fragile X Syndrome, and whether the biological environment or the construction of the transistor could be optimized in order to make the transistor be more sensitive to the RNA and protein rather than the other agents in the solution. Based on these experiments, the results point towards both better construction of the transistor, and a slight optimization of the solution.

In general, most of the agents caused a decrease in current levels and often caused the device to act uncharacteristically, with the exception of BSA which caused an obvious increase in current. Many of these changes could have been due to the transistor's design being unsuitable for this particular application, since often some form of degradation or undesirable behavior on the part of the agent (the agent migrating towards an electrode, or not staying in the transistor channel). In order for the transistor to be more suitable for sensing applications, the transistor must be fabricated with more attention to details that would allow the transistor to withstand this biological environment. First, since the drop of liquid being applied to the channel of the transistor often dispersed and spread to other parts of the transistor, a microfluidic channel to contain the liquid evenly spread throughout the channel (so no variance due to the area and location of the drop was caused) within the transistor would be desirable. Additionally, coating the source and drain with fluorinated polymer[28] would better protect the source and drain from any damage should the liquid escape the microfluidic channel. Also, since the individual effects of the protein and the RNA were not tested, it would be wise in the future to test these individually to observe their isolated effects on the transistor. Also, the drop size and area should be taken into account, although if a microfluidic channel allowed for even spreading of the liquid, then this would not necessarily have to be a large concern.

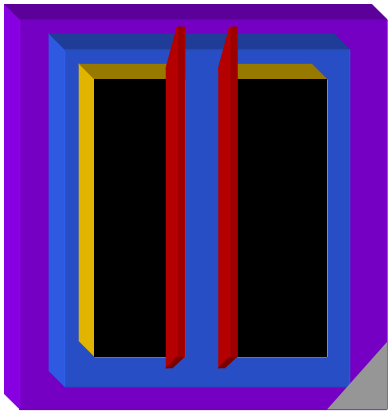

Figure 6: An optimally designed transistor; in red is the microfluidic channel, in black is the fluorinated polymer

In addition to changing the design of the transistor, there is some potential for the solution to be optimized. As discussed before, BSA is known to coat the surface of whatever it is applied to and possibly may have coated the channel of the transistor and positioned itself below any of the other agents; thus the transistor's response could be mostly due to the BSA rather than other agents. Looking at the graphs of all the agents combined (Figures 5.5.1-4) and comparing with the graphs of the BSA (Figures 5.3.1-5.3.8), this seems plausible. Additionally, the shapes of the I_{DS} versus V_G curve at the higher voltage range for both the RNA binding assay with BSA and the BSA alone are similar, and both seem to exhibit some independence of the gate voltage. Future work using optimally designed transistors could determine whether BSA truly does play a strong role in dominating the transistor's response – if so, then perhaps it can be excluded from the RNA binding assay, as it is not necessary.

With these suggestions, the pentacene thin film transistor's sensing abilities may contribute to gaining information about Fragile X Syndrome and the FMRP.

7. CONTINUING RESEARCH

Using the knowledge of the ability of the thin-film transistor to sense chemical and biological particles, as well as the information about the FMRP and the FMR1 RNA discussed earlier, a continuing project will seek to utilize the organic thin film transistor to help provide more information about the FMRP as well as the FMR1 RNA, both of which play important roles in the cause of Fragile X Syndrome.

Certain domains in the FMRP will be isolated to determine more about the affinity of the protein for particular RNA targets, or strands. In order to isolate certain units in the protein, one domain (a protein unit) will be removed from each sample. Within the FMRP, there are three particular domains that are of particular interest: the KH1 domain, the KH2 domain, and the RGG box. There are around 80 RNA targets that will eventually be tested. The testing will begin with a strand of FMR1 RNA.

The RNA targets will be combined with various FMRP samples along with Moine buffer, BSA, tRNA, and RNse inhibitor, and will then be applied to the transistor. The solution will be placed into the channel of the transistor. Once combined, some level of binding between the protein and the RNA should occur depending on the strength of the affinity between them. The transistor will be exposed to each of these combined samples, and the response of the transistor will be analyzed and will hopefully yield information about the affinity between the two agents. Additionally, these combined samples will be compared with the transistor's response when exposed to the FMRP and the FMR1 RNA combined in their unaltered form. Samples in which the protein has a higher affinity for the protein should cause a different response than those which have a lower affinity.[29]

The aim of exposing the transistor to these various combinations of RNA and FMRP is to contribute to the research concerning Fragile X Syndrome. As stated before, not much is known with regard to exactly how the absence of the FMRP affects development. If the transistor reacts similarly to some samples, then a conclusion can be drawn as to why these samples are similar. These similarities will hopefully be able to be related to the affinity between the protein and the RNA, and thus contribute to determining the function of the FMRP and towards research on Fragile X Syndrome.

8. ACKNOWLEDGEMENTS

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9. REFERENCES

[1] C.R. Kagan and P. Andry, eds. *Thin-Film Transistors*. New York, Marcel Dekker, Inc., 2003, pp. 1-34.

[2] See references 9 through 12.

[3] S.M. Sze. *Semiconductor Devices: Physics and Technology*. Canada, Bell Telephone Laboratories, Inc., 1985, p. 248.

[4] Matter Glossary: Glossary of Materials Science. Available: http://www.matter.org.uk/glossary/index.asp

[5] Kagan *Thin Film Transistors* 363.

[6] Sze *Semiconductor Physics* 160-162

[7] Kagan *Thin Film Transistors* 362. Figure 2(a) and 2(b) are from 363.

[8] However, for the thin film transistor, these equations are approximate.

[9] James C. Sturm, "Lecture Notes," unpublished. Chapter VI.6, pp.277-279.

[10] D.J. Macaya, et al. (2007, October). Simple glucose sensors with micromolar sensitivity based on organic electrochemical sensors. *Sensors and Actuators B* [Online]. 123(1), pp.374-378. Available: http://www.sciencedirect.com/science?_ob=ArticleListURL&_method=list&_ArticleListID=611602463&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=aa6cb3d62e9de85634c194492ec60a2b

[11] T. Someya, et al. (2002, April). Integration and Response of Organic Electronics with Aqueous Microfluidics. *Langmuir* [Online]. 18, pp.5299-5302. Available: http://proxy.library.upenn.edu:6931/cgi-bin/abstract.cgi/langd5/2002/18/i13/abs/la020026z.html

[12] B. Crone, et al. (2001, April). Electronic sensing of vapors with organic transistors. *Applied Physics Letters* [Online]. 78 (15). Available: http://proxy.library.upenn.edu:2088/getabs/servlet/GetabsServlet?prog=normal&id=APPLAB000078000015002229000001&idtype=cvips&gifs=yes

[13] Q. Zhang et al. (2007, March). DNA Hybridization Detection with Organic Thin Film Transistors: Toward Fast and Disposable DNA Microarray Chips. *Biosensors & Bioelectronics*. 22(12), pp. 3182-3187. Available: http://www.sciencedirect.com/science/journal/09565663

[14] The National Fragile X Foundation. "What is the Cause of Fragile X Syndrome?" Available: http://www.fragilex.org/html/cause.htm

[15] K. Miyashiro, private communication, June-August, 2007.

[16] C. Schaeffer, et al. (1995). The fragile X mental retardation protein binds specifically to its mRNA via a purine quartet motif. *The EMBO Journal* [Online]. 20(17), pp.4803-4813. Available: http://embojournal.npgjournals.com/emboj/journal/v20/n17/index.html

[17] A. Afzali, et al. (2002, April). High Performance, Solution-Processed Organic Thin Film Transistors from a Novel Pentacene Precursor. *Journal of American Chemical Society* [Online]. 124(30), p.1. Available: http://proxy.library.upenn.edu:6931/cgi-bin/abstract.cgi/jacsat/2002/124/i30/abs/ja0266621.html

[18] C. R. Kagan, private communication, June-August 2007.

H. Craig Casey, Jr. *Devices for Integrated Circuits: Silicon and III-V Compound Semiconductors*. New York: John Wiley & Sons, Inc., 1999, p. 231.

"Work Functions for Photoelectric Effect." Available: http://hyperphysics.phy-astr.gsu.edu/hbase/tables/photoelec.html

[19] Figure 4.2.1 was taken from the below resource.
Z. Bao, et al. (1996, August). Soluble and processable regioregular poly(3-hexlthiophene) for thin film field-effect transistor applications with high mobility. *Applied Physics Letters* [Online]. 69(26), 4108-4110. Available: http://scitation.aip.org/vsearch/servlet/VerityServlet?KEY=APPLAB&smode=strresults&CURRENT=&ONLINE=YES&SMODE=&ver=&sti=&arttype=&possible1=thin+film+field-effect+transistor+applications+with+high+mobility&possible1zone=title&bool1=and&possible2=&possible2zone=multi&bool4=and&possible4=&possible4zone=author&sort=chron&maxdisp=25&threshold=0&frommonth=&fromday=&fromyear=&tomonth=&today=&toyear=&fromvolume=69&fromissue=26&tovolume=69&toissue=30&page=1&origquery=&vdk_query=&chapter=0&docdisp=0&%5Bsearch%5D.x=31&%5Bsearch%5D.y=17

[20] The process by which the P3HT was prepared was primarily taken from the below reference.
H. Sirringhaus, et al. (1999, October). Two dimensional charge transport in self-organized, high mobility conjugated polymers. *Letters to Nature* [Online]. 401, pp.685-688. Available: http://www.nature.com/search/executeSearch?sp-q=Two+dimensional+charge+transport+in+self-organized%2C+high+mobility+conjugated+polymers&sp-c=10&sp-x-9=cat&sp-s=date&sp-q-9=NATURE&submit=go&sp-a=sp1001702d&sp-sfvl-field=subject%7Cujournal&sp-x-1=ujournal&sp-p-1=phrase&sp-p=all

[21] C. D. Dimitrakopoulos, et al. (2002, January). Organic Thin Film Transistors for Large Area Electronics. *Advanced Materials* [Online]. 14(2), pp.99-117. Available: http://www3.interscience.wiley.com/search/allsearch?mode=quicksearch&WISindexid1=WISall&WISsearch1=organic+thin+film+transistors+for+large+area+electronics

S. Saudari, private communication, July 2007.

[22] T. Chen, et al. (1995, January). Regiocontrolled Synthesis of Poly(3-alkylthiphenes) Mediated by Rieke Zinc: Their Characterization and Solid-State Properties. Journal of Americal Chemical Society [Online]. 117(1), pp.233-244. Available: http://pubs3.acs.org/acs/journals/toc.page?incoden=jacsat&indecade=1&involume=117&inissue=1

[23] S. Xiao, et al. (2005, November). Molecular Wires from Contorted Aromatic Compounds. Angewandte Chemie International Edition. 44(45), pp. 7390-7394. Available: http://www3.interscience.wiley.com/search/allsearch?WISsearch2=Molecular+Wires+from+Contorted+Aromatic+Compounds&WISindexid2=WISall&mode=quicksearch&products=journal&contextLink=%3Ca+href%3D%22%2Findex.html%22+target%3D%22_top%22%3EHome%3C%2Fa%3E+%2F+%3Ca+href%3D%22%2Fbrowse%2F%3Fsubject%3DCHEM%22+target%3D%22_top%22%3EChemistry%3C%2Fa%3E+%2F+%3Ca+href%3D%22%2Fbrowse%2F%3Fsubject%3DCH00%26titles%3Dtrue%22+target%3D%22_top%22%3EChemistry++%28general%29%3C%2Fa%3E&contentOID=26737&contentTitle=Angewandte+Chemie+International+Edition&WISindexid1=issn&WISsearch1=1521-3773

Figure 4.3.1 was taken from the above source.

[24] C. Yang, private communication, July 2007.

[25] S. Xiao, et al. (2005, November). Supporting Information: Molecular Wires from Contorted Aromatics. Angewandte Chemie.

[26] This process was based on a protocol given to me by Kevin Miyashiro. The document cited the following source as its main reference.

C. Schaeffer, et al. (1995). The fragile X mental retardation protein binds specifically to its mRNA via a purine quartet motif. *The EMBO Journal* [Online]. 20(17), 4803-4813. Available: http://embojournal.npgjournals.com/emboj/journal/v20/n17/index.html

[27] K. Miyashiro, private communication, June-August, 2007.

[28] T. Someya, et al. (2002, April). Integration and Response of Organic Electronics with Aqueous Microfluidics. *Langmuir* [Online]. 18, pp.5299-5302. Available: http://proxy.library.upenn.edu:6931/cgi-bin/abstract.cgi/langd5/2002/18/i13/abs/la020026z.html

[29] K. Miyashiro, private communication, June-August, 2007. The biological information in this paragraph and the preceding paragraph was explained by Kevin Miyashiro.