Sensing Mechanism of Nanowire Biosensors

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Photo: Philips

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Chapter 1

Introduction to nanowire biosensing

During the last half century, a dramatic downscaling of electronics has taken place [1]. In 1965 Gordon Moore predicted that the number of transistors on a computer chip would double every two years. This is commonly known as Moore's Law. So far Mr. Moore has been right. The downscaling has led to many technological innovations, from supercomputers to pocketsized mobile phones. A new technological opportunity for healthcare can be offered by miniaturized biosensors which use nanowires for sensing, and have potential for on-chip integration [2]. Due to the small dimensions, nanowires have a large surface-to-volume ratio, making them highly sensitive. Due to the high sensitivity, the nanowire biosensor can be used to detect DNA concentrations in biological samples, without having to increase the DNA concentration with time consuming PCR (Polymerase Chain Reactions). Biosensors based on silicon nanowires provide fast, simple, label-free electrical detection of biomolecules. Hundreds of diseases are diagnosable by the molecular analysis of nucleic acids, and the number is daily increasing [3].

Philips saw the opportunity for a direct electrical readout with a fast and inexpensive analysis of samples. The group I worked in at Philips works on nanowire sensing, which has applications ranging from air quality to DNA testing. This thesis is written for this project of Philips Research and focuses on biosensing.

The goal in nanowire biosensing is to use a nanowire field-effect transistor (FET) to measure what the concentration is of a certain biological molecule in the sample. The working principle of a FET is described in chapter [2]. The basic idea of the nanowire sensor is the following (see figure 1.1). The nanowire surface is treated such that the biological molecule of interest can attach to the surface, while other molecules can not. When this is the case the sensor is said to have a high selectivity. Depending on the concentration of biomolecules in the sample, a certain number of molecules will attach
to the sensor surface. The presence of the biomolecules close to the sensor surface changes the electrostatic environment of the sensor. This causes a change in the surface potential, which is what the nanowire FET translates into an electrical signal.

![Figure 1.1: Schematic of nanoscale biosensor. Biomolecules in solution can attach to the sensor surface. The presence of the biomolecules close to the sensor surface is detected by the Field-Effect based biosensor. Source: [2]](image)

The change in electrostatic environment of the sensor can be caused by different properties of the biomolecule. The most commonly accepted influence that the biomolecule has on the electrostatic environment of the sensor is due to its charge. The effect of the charge is strongly influenced by the fact that the solution in which the biomolecules are dissolved usually contains ions.

The ions in the system screen a part of the biomolecule charge, and the detection of biomolecules becomes more difficult. Therefore it is generally suggested that the salt concentration should be kept low. This is however not always possible since biomolecules may deform, or are not able to attach to the sensor surface when the conditions deviate too much from bodily conditions.

Estimations of the sensor signal due to the biomolecule charge which take the effect of ions into account predict less sensitivity than what has been shown experimentally [3]. The source of this experimentally observed signal generation is not well understood [3] [2], and it is suggested [3] that not only the charge of the biomolecules, but also the volume may have an influence on the electrostatic surrounding of the sensor.

The goal of this thesis is to improve the understanding of the detection mechanism of the nanowire biosensor. Therefore not only the effect of the charge of the biomolecules is studied, but also the effect of the volume, while
focusing on the effect of the ions in the biological solution.

The volume of the biomolecule has two effects on the electrostatic environment. First, the dielectric constant will become different in a thin layer on the sensor surface. Second, ions in the vicinity of the sensor surface will be redistributed.

To understand whether the behavior of the nanowire sensor is related to its geometry or that it is a general feature of FETs when used for biosensing, both the effects of charge and of volume have been studied for both the cylindrical nanowire FET and the flat FET. For ease of calculations the nanowire FET is considered to be an infinitely long cylinder, and the flat FET an infinite plane. There was no back gate included in the model, and the FETs are considered to be metallic. The biomolecules were not all included in the model separately, but modelled as a uniform layer. Since the diameter of the nanowires that are fabricated with top-down techniques is in the order of tens of nanometers, no quantum effects need to be included in the models.

In chapter 3 only the influence of the charge of the biomolecules is studied. In chapters 4 and 5 the effect of volume is studied. In chapter 6 results are presented for a dense layer of biomolecules on the sensor surface, while in chapter 5 the surface layer is only partially occupied by biomolecules. Whenever possible analytical expressions are given, in cases where this was not possible the results have been calculated with a finite element computer simulation. In chapter 6 the conclusions are presented, showing the difference between the influence of the charge and the volume of biomolecules, and the difference between the two geometries.
Chapter 2
Basics of biosensing with FETs

The physical mechanism underlying sensing remains controversial, as discussed in the introduction. Previously suggested mechanisms are electrostatic gating, changes in gate coupling, carrier mobility changes, and Schottky barrier effects [4]. Heller et al. [4] have shown that sensing is dominated by electrostatic gating. In this thesis it is studied which properties of the biomolecule and the surrounding electrolyte have the largest effect on this electrostatic gating.

When performing a biosensing experiment one wants to measure an electrical signal and thereby find the concentration of a certain biomolecule in the biological sample. This can be done with the use of a field-effect transistor or FET.

The response of FETs to an applied surface voltage is well known [5]. However, in the case where the FET is used for biosensing, the surface potential is not fixed by a gate, but is both dependent on the environment of the sensor in which the biomolecules and ions are present, and on the characteristics of the FET (section 2.1).

The theoretical description of biosensing, can be divided into two parts. The first part contains the physics of the FET device, and the second part contains the physics in the biological solution. The boundary between these two parts is at the sensor surface. The potential on this boundary is dependent on both parts. In this thesis it was chosen to focus on the second part, the biological solution. For the FET a highly simplified model is taken.

For the description of the physics in the biological solution the properties of the biomolecules, such as the attachment to the sensor surface, the charge, and the volume are necessary. These properties vary greatly from biomolecule to biomolecule, and are also dependent on the physical parameters of the environment such as temperature, local potential and local ion concentration. Here it was chosen to focus on the effect of the electrolyte
on the sensing mechanism. The properties of the biomolecules themselves are not studied. Rough estimations of the value of the charge, the volume, and the number of biomolecules that attach to the sensor surface are made in section 2.2.

As was mentioned in the introduction, the sensing mechanism is studied both for a cylindrical device and for a flat device. The difference in current response of the two different FET geometries to biomolecule attachment is caused by several factors.

First of all different geometries can give different signals because the signal change upon attachment depends on the signal before attachment, and this depends on the area of cross section and the material of the FET device. To eliminate the effects of device size and the specific material used, it is decided to discuss the results of the calculations in terms of the charge induced in the FET per unit length, instead of the current change. This is discussed in section 2.3.

The second factor is that the amount of charge induced on the FET due to a certain surface potential is different, since the two geometries have different capacitances. The induced charge in the FET can be calculated as a function of the surface potential, expressed in terms of its capacitance. The capacitance of semiconductor devices can be very complex. Since the capacitance is not the main topic of interest, simple capacitances have been chosen assuming the FETs are metallic.

Thirdly, the potential on the FET surface is different in the different geometries. It depends not only on the charge of the biomolecules, but also on the capacitance of the FET and the charge in the ionic double layer surrounding the biomolecules and the sensor. Both this capacitance and the charge induced in the double layer are different for the two geometries (section 2.4 and 2.5).

The theory discussed in the remainder of this chapter will be combined to do calculations on different sensing mechanism models in chapters 4 to 5.

2.1 The field-effect transistor

The biosensor discussed in this thesis is based on a field-effect transistor (FET). A simple representation of a FET is given in figure 2.1. The top gate is used to fix the potential on the top of the FET. The conductivity of the semiconductor material underneath the top gate changes as a function of this surface potential.

A semiconductor is characterized by the fact that the fermi level is between the conduction and the valence band. Depending on the circumstances some electrons in the semiconductor material will have enough energy to occupy a state in the conduction band. This number of electrons in the conduction band determines the conductivity of the material. By changing
the top gate potential the energy of the conduction band will change, which increases or decreases the number of electrons in the conduction band (figure 2.2). The conductivity in the path from source to drain is therefore directly dependent on the gate potential. Measuring the electrical signal will tell us what surface potential is applied. The relation between the surface potential and the electrical signal does not have to be a simple function, but can be very complex, and it also depends on the geometry, the material of the device, and the dopant molecules in the material.

Figure 2.2: Band diagram for a FET. In the center an external voltage is applied that causes bending of the bands.

In a chemical field-effect transistor, or ChemFET, the conductivity of the device is also dependent on the surface voltage. Only now the surface potential is not influenced by a top gate, but by molecules on the sensor surface, and the FET can therefore be used as a chemical sensor. When the molecules on the surface participate in a chemical process, the electrostatic surrounding of the sensor surface is changed (for example due to a change
in surface charge), which changes the potential. The same principle can be used for biosensing, where the presence of the biomolecules influences the conductivity of the device (see figure 2.3).

**Figure 2.3:** Schematic cross-section of a ChemFET. The presence of the molecules influences the surface potential. The change in surface potential is translated by the FET into an electrical signal.

The Nanowire FET sensor is similar to the ChemFET, except that the sensitive semiconducting layer of the ChemFET corresponds to a thin nanowire in the nanowire FET (see figure 2.4). It is important that the nanowire surface is functionalized with highly specific receptors, or capture molecules, such that only the specific molecules of interest will be able to attach to the sensor surface and cause a signal. Only then will a measurement of the current provide information on the presence of the biomolecule of interest. It was mentioned before, that the relation between signal and surface potential can be rather complex. Depending on the value of the surface potential, a small change in the potential will result in a large or a small signal. The back gate of the device can be used to tune the FET such that the conductivity of the wire changes fast with a small change in the surface potential.

**Figure 2.4:** (a.) Cross-section of the nanowire sensor along the nanowire axis. (b.) Cross-section of the nanowire sensor perpendicular to the nanowire axis.
In many sensing experiments nanowire FETs are used instead of flat FETs, since the nanowire FET is more sensitive than the flat FET. Some of the benefits of the nanowire FET are the high surface-to-volume ratio, the fast diffusion of biomolecules to the sensor surface, and the fact that only a few attached biomolecules have a large influence on the conductance, also referred to as pinching. These characteristics are a good reason to use nanowires for sensing experiments.

The sensing experiments that are being performed by Philips Research are therefore also done using nanowire FETs. In figure [2.6] a SEM picture is shown of a nanowire device. For a large scale production the use of top down fabrication techniques of the nanowires is required. These fabrication techniques set a lower limit on the diameter of the nanowires of about 30 nm. A lower limit of about 5 nm on the thickness of the isolating oxide is given by the fact that below this thickness the layer is no longer isolating. The length of the wires can be varied, and is usually taken to be in the order of 1 μm. For ease of calculations the nanowire field-effect transistor described above is simplified. The nanowire is considered to be an infinitely long cylinder with a diameter of 2b = 30 nm, covered with an oxide layer with thickness tox = 5 nm, suspended in the biological solution (see figure [2.5]). The influence of the back gate is not taken into account. As mentioned before the device is assumed to be metallic.

![Diagram of a nanowire FET sensor showing the nanowire, the oxide shell, and the receptors, some with a biomolecule attached, surrounded by the electrolyte solution. Source: [2], figure edited.](image)

**Figure 2.5:** Cross-section of the nanowire FET sensor showing the nanowire, the oxide shell, and the receptors, some with a biomolecule attached, surrounded by the electrolyte solution. Source: [2], figure edited.

## 2.2 Biomolecule properties

To understand how the attachment of biomolecules influences the electrostatic environment of the biosensor, some properties of the biomolecules have to be known.

First of all we need to know the relation between the biomolecule concentra-
tration in solution and the surface density of the attached biomolecules on the sensor surface, this will be discussed in section 2.2.1. This is dependent on many factors such as the ion concentration in the electrolyte solution, the local potential, and the temperature.

Second, we need to know what the properties of the biomolecules are that can change the electrostatic environment of the sensor (sections 2.2.2, 2.2.3). In these sections rough estimations of the above parameters will be made.

2.2.1 Biomolecule attachment

The number of biomolecules that attach to the surface depends on a number of factors. One important parameter is the amount of sites on the surface the biomolecule can attach to. This is often referred to as the number of capture molecules on the surface, while the biomolecules of interest are referred to as the target molecules. The density of capture molecules should not be too large, since neighboring capture molecules should not hinder one another to capture a target molecule. This density should be in the range from about $2 \cdot 10^{13}$ to $1.3 \cdot 10^{12}$ molecules cm$^{-2}$ [3]. The number of biomolecules that attach to the sensor surface also depends on the concentration of biomolecules in the sample solution, and the capture and dissociation constants of the binding. In reality these constants and thus the amount of molecules that attach to the surface, are dependent on factors, such as the local potential and the temperature [7]. However, in this thesis a rough estimation of the biomolecule attachment is used and the effect of the above factors is not taken into account. Time dependence is not taken into account, only the steady state situation is considered here.

To estimate the order of magnitude of the biomolecule attachment a DNA molecule is used. A rough estimation of the number of attached
biomolecules in the case of DNA molecules is given by Alam and Nair [2]. For a capture molecule density of $1 \cdot 10^{13} \text{cm}^{-2}$ and an available biomolecule density of $1 \cdot 10^{-9} \text{M}$, the number of attached biomolecules on the surface is $0.23 \cdot 10^{13} \text{cm}^{-2}$.

To visualize the degree of biomolecule attachment the density of capture and target molecules on the sensor surface is shown in figure 2.7. In this figure the capture molecule density is $1.25 \cdot 10^{13} \text{cm}^{-2}$, and the surface density of target molecules, $N$, is $0.31 \cdot 10^{13} \text{cm}^{-2}$. The circles are 2 nm in diameter, which corresponds to the diameter of a DNA helix. Throughout this thesis the number of attached biomolecules is taken to be $0.3 \cdot 10^{13} \text{cm}^{-2}$. It should be considered to be an upper limit of the attached biomolecule density, since in reality we are interested in biomolecule concentrations down to $10^{-15} \text{M}$ (femtomolar).

Figure 2.7: An image showing the density of capture molecules on the sensor surface (white circles, $1.25 \cdot 10^{13} \text{cm}^{-2}$), and the density of biomolecules (red circles, $0.31 \cdot 10^{13} \text{cm}^{-2}$).

The density of biomolecules on the sensor surface is necessary to estimate the effect on the FET, but for this also the properties of the biomolecules, such as the charge and the volume, is necessary. This will be considered in the following sections.

2.2.2 Surface Charge

To know the order of magnitude of the biomolecule charge that influences the conductivity of the FET, again a DNA molecule is taken as an example.

A picture of a DNA helix is shown in figure 2.8. The phosphate backbone of DNA is charged. Each base contains one electron charge. Depending on the length of the DNA fragment under consideration, the biomolecule will have a different charge. However, due to screening of the ions in the elec-
Figure 2.8: A DNA helix oriented perpendicular to the sensor surface. The phosphate backbone is negatively charged. The Debye length for an ion concentration of 0.1 M is shown on the right (picture taken from [3]).

trolyte solution, only the charge that is close enough to the sensor surface will have an influence on the FET. The Debye length gives the length scale over which the fields of the charges in the electrolyte are screened. If a charge is farther away than this Debye length it can be considered to have no influence. The ion concentration of the electrolyte solution must have an ion concentration that is close to physiological solutions. Otherwise the two negatively charged DNA strands will repel each other and the target DNA strand will not be able to attach. Taking an ion concentration of 0.1 M, we find a Debye length of about 1 nm. Within a distance from the surface of 1 nm, 3 DNA bases are present if the DNA helix is oriented perpendicular to the surface, and more if the helix lies flat on the surface. Each base has a charge of one electron charge, e. In an ionic solution with monovalent ions however, counterions compensate for 74 % of this charge [3]. To summarize: every DNA molecule has 3 bases that must be taken into account in the model with a charge of 0.26 e. This leads to the estimation that each biomolecule has a charge of about 1 electron charge, which corresponds to
the value used in literature [2].

Taking the surface density of the attached biomolecules as given in section 2.2.1, we obtain a charge density of attached biomolecules of $0.3 \cdot 10^{13} \text{C}/(\text{cm}^2)$, or $4.806 \cdot 10^{-3} \text{C/m}^2$. Note that DNA is a strongly charged biomolecule, so for other biomolecules, this could be much less.

In addition to the biomolecule charge, the oxide on the FET also contains charge. At the Philips lab oxide charges typically range from $10^{10} \text{e cm}^{-2}$ to $10^{12} \text{e cm}^{-2}$. These values correspond to the typical oxide charges as given in textbooks [9]. Assuming a high quality oxide preparation the oxide charge can be considered to be $10^{10} \text{e cm}^{-2}$. This is more than two orders of magnitude smaller than the surface charge density of the biomolecule charge that was given above, and can be neglected. However, when using an oxide layer of lower quality, or when there is less biomolecule charge in the system, the oxide charge must be included.

In this thesis the biomolecule charge is modelled as a uniform surface charge. The theory described is therefore not applicable to single molecule detection.

### 2.2.3 Volume

To make an estimation of the order of magnitude of the volume of the biomolecule, DNA is taken as an example again. The DNA molecule can be modelled as a rod [10] with diameter of 2 nm. For a sequence of 30 bases the length is about 10 nm [3].

The attachment of the biomolecules changes the properties of the environment of the sensor only in a thin layer. The thickness of this layer is dependent on the orientation of the biomolecules. If they are oriented perpendicular to the sensor surface the thickness of the altered layer is largest, in the case described above this is 10 nm. The total fraction of the volume that is occupied by the biomolecules is small in this layer. If the biomolecules are oriented parallel to the sensor surface the influenced layer is thin, down to 2 nm, but the fraction of the volume in this layer that is occupied by the biomolecules is larger. This volume fraction that is occupied by the biomolecules, from here on called the excluded volume fraction, is calculated below for these two extremes.

In figure 2.9 (a.) the biomolecules are oriented perpendicular to the sensor surface. Taking the density of biomolecules as given in section 2.2.1 we obtain a total excluded volume fraction of $f = N \pi r_{\text{DNA}}^2 = 0.094 \approx 0.1$ in a layer with a thickness of 10 nm, where $N$ is the number of attached biomolecules per cm$^2$, and $r_{\text{DNA}}$ the radius of the DNA helix.

In figure 2.9 (b.) the biomolecules are completely flat on the surface, in a layer with a thickness of 2 nm. The total excluded volume fraction in this case yields $f = N \pi r_{\text{DNA}}^2 l/t_{\text{ido}} = 0.47 \approx 0.5$, with $l$ the length of the DNA segment, above said to be 10 nm, and $t_{\text{ido}}$ the thickness of the layer around
the sensor in which the biomolecules are present, here 2 nm. This equation can also be used when the DNA molecules have an orientation in between perpendicular and flat, such that $t_{\text{bio}}$ has a value between 2 and 10 nm.

DNA has a rather elongated shape. For more round molecules the difference in excluded volume of the two orientations will not be this clear, and the excluded volume fraction and the layer thickness will be in between the two above results.

\[ f(r, d) = N \pi R_{\text{DNA}}^2 t_{\text{bio}} / (r_{\text{bio}}^2), \]

with $b$ the outer radius of the nanowire sensor.

The excluded volume fraction indicates what fraction of the electrolyte solution is pushed away around the sensor surface. This has two effects. The first is that ions are excluded from this region, which changes the charge distribution in the vicinity of the sensor, and thereby decreases the effect of screening. The second effect is that the dielectric constant is different as will be explained in the next section.

### Dielectric Constant

After attachment of biomolecules the dielectric constant in a thin layer on top of the surface of the sensor has a different value than before attachment. This is caused by various factors. First of all, the dielectric constant of the biomolecules differs from that of the surrounding electrolyte solution. So effectively, the dielectric constant around the sensor changes upon biomolecule attachment. In this section a rough estimation will be made of this effect. Other effects, such as reduced intermolecular hydrogen bonding of the water near the macromolecular surface and the high counterion concentrations around the molecules [10], are neglected.
A part of the volume around the sensor has a dielectric constant of the biomolecules, \( \epsilon_{r,\text{bio}} \), in the rest of the volume the dielectric constant is equal to that of the electrolyte solution, \( \epsilon_{r,w} \). The combined material can be described as a uniform layer of an electrostatically equivalent material with a new effective dielectric constant. The problem addressed in this section is what value to take for this effective, new dielectric constant, \( \epsilon_{r,\text{new}} \).

Assuming the biomolecules have a rodlike shape, two different geometries can be considered. One in which the biomolecules are assumed to be oriented perpendicular to the sensor surface, and one in which they are oriented parallel to the sensor surface (see figure 2.9). This gives rise to regions with dielectric constants as shown in figure 2.10.

If one assumes that the biomolecules are oriented perpendicular to the sensor surface the new dielectric constant is given by

\[
\epsilon_{1,r,\text{new}} = f \epsilon_{r,\text{bio}} + (1 - f) \epsilon_{r,w},
\]

If the biomolecules are flat on the surface we obtain

\[
\frac{1}{\epsilon_{2,r,\text{new}}} = \frac{f}{\epsilon_{r,\text{bio}}} + \frac{(1 - f)}{\epsilon_{r,w}}.
\]

with \( f \) the excluded volume fraction as discussed above, and \( \epsilon_{r,\text{bio}} \) the relative dielectric constant of the biomolecule, which is about 2 to 4 for DNA. These results are shown in figure 2.11. It can be seen that the dielectric constant is
changed more upon attachment of biomolecules when the biomolecules are oriented perpendicular to the sensor surface than when they are flat on the surface.

2.3 Sensor sensitivity

A simplified expression for the current through a material due to an applied field is given by

\[ I = \nu_{\text{drift}} q n_c A, \]

where \( \nu_{\text{drift}} = \mu E \) is the velocity of the charge carriers with \( \mu \) the mobility of the carriers, and \( E \) the electric field, \( q \) is the charge of the charge carriers, \( n_c \) is the number of carriers per unit volume, and \( A \) is the area of cross section through the device perpendicular to the direction of current flow.

The current after adsorption of biomolecules is different due to the induced charge per unit length in the FET, \( \Delta \lambda_{\text{FET}} \),

\[ I = \nu_{\text{drift}} q n_c A + \nu_{\text{drift}} \Delta \lambda_{\text{FET}}. \]

In this simple model it is assumed that \( \mu \), and therefore \( \nu_{\text{drift}} \), does not depend on the carrier density. The sensitivity of the sensor is given by

\[ \frac{\Delta I}{I} = \frac{\Delta \lambda_{\text{FET}}}{en_c A}. \]

The above expression shows that the sensitivity of the sensor is strongly dependent on the material chosen via the density of charge carriers, \( n_c \), and on the geometry and size through the size of the cross section, \( A \).

The induced charge in the device, \( \Delta \lambda_{\text{FET}} \), is related to the active surface area of the device, which is, in this case, the total surface of the device.
which is $2\pi r$. The area of cross section $\pi r^2$ of a nanowire FET is small compared to its surface, since the diameter of the nanowire is so small. Often the sensitivity of the nanowire sensor is ascribed to this property, referred to as the high surface-to-volume ratio. A high surface-to-volume ratio, however, can also be achieved in the flat geometry by making thin nanoribbons. Therefore this is not considered to be a characteristic property of a nanowire in this thesis.

For the flat and the cylindrical FET that are compared in this thesis the material is assumed to be the same, and the device geometry is chosen such that the surface areas and the areas of cross section are equal. This relates the radius of the cylindrical device to the width and thickness of the flat device. The width of the flat device, $W$, must be $2\pi(a + t_{ox})$, and its thickness, $d$, must be $d = \pi a^2/(2\pi(a + t_{ox}))$ (see figure 2.12).

To remove the effect of the material used, the results will be discussed in terms of the charge induced in the FETs per unit length, $\lambda_{\text{FET}}$. Assuming the active surface area, the carrier density, and the cross sectional area to be the same in the different situations, the value of the induced charge per unit length, $\lambda_{\text{FET}}$, can be used directly for comparison of the sensitivity of the different model systems. This way the effect of the material and the size is removed, and the effect of presence of the biomolecules and the electrolyte can be studied.

Also the attached biomolecule density on the device surface due to biomolecule absorption is assumed to be the same in both geometries. This gives us two devices with the same amount of biomolecules per unit length on the surface. Under these assumptions the difference between the responses of the two geometries to the same amount of biomolecules can be studied.

### 2.4 Capacitance

The amount of charge that is induced in the FET due to a certain surface potential depends on the capacitance of the device. In this section an expression for the capacitance of a flat and of a cylindrical FET is derived.

The capacitance per unit area of a capacitor is

$$C = \frac{\sigma}{V}, \quad (2.6)$$

with $\sigma$ the charge per unit area on each capacitor plate, and $V$ the potential difference across the two plates.

In the case of the FET the capacitance of the device can be taken as

$$C = \frac{\sigma_{\text{FET}}}{(V_s - V_{\text{FET}})}, \quad (2.7)$$

where $V_s$ is the potential on the surface of the FET and $V_{\text{FET}}$ the potential in the FET. This capacitance is different for different device geometries. The
capacitance of the device gives the charge per unit area induced in the FET for a certain surface potential,

$$\sigma_{\text{FET}} = C(V_{\text{surface}} - V_{\text{FET}}).$$  \hspace{1cm} (2.8)$$

When the FET is grounded and the surface potential is $V_0$ the induced charge per unit area is equal to

$$\sigma_{\text{FET}} = CV_0.$$ \hspace{1cm} (2.9)$$

If the surface potential is positive, a negative charge will be induced in the FET, and vice versa. Since charges of opposite sign will be induced in the FET, the capacitance is a negative quantity. It is seen that for a large capacitance, a small change of the potential will induce a large change in the charge in the FET. Therefore a large capacitance is beneficial for sensitive sensing.

The capacitance of a semiconductor FET can be dynamic and very complex. Since the object of study here is the effect of the electrolyte, a simple
expression is taken for the capacitance, such that all effects can be ascribed to the behavior of the electrolyte.

The device will be considered to be metallic, since this yields a simple expression for the capacitance. This assumption is only valid for the semiconductor FET for a certain range of the surface potential. For non-metallic devices the simple expression of the metallic capacitance that was used throughout this thesis must be replaced by the real, more complex, semiconductor expression. The calculation itself remains the same.

2.4.1 The capacitance of a flat metallic FET

The capacitance of the flat geometry can be calculated by considering a Gaussian pillbox containing a part of the metal-oxide interface. This yields the value of the electric field in the oxide layer. The potential difference between the conducting layer and the oxide surface can then be calculated by integrating the field over the oxide thickness. Fringing of the electric field at the edges is ignored. The capacitance per unit area for the flat geometry is

\[
C_{\text{flat}} = -\frac{\epsilon_0 \varepsilon_{r,\text{ox}}}{t_{\text{ox}}}. \tag{2.10}
\]

2.4.2 The capacitance of a cylindrical metallic FET

The capacitance of the cylindrical capacitor can be calculated by considering a Gaussian surface in the shape of a cylinder in the oxide enclosing the metal core of the cylindrical FET. The result for the capacitance per unit area of the cylindrical geometry is equal to

\[
C_{\text{cyl}} = -\frac{\epsilon_0 \varepsilon_{r,\text{ox}}}{a \ln(1 + \frac{t_{\text{ox}}}{a})}. \tag{2.11}
\]

2.4.3 The capacitances of a flat and a cylindrical metallic FET compared

To be able to compare the capacitances of the two different geometries, the capacitance per unit length is considered for both devices. As discussed before the width of the flat device must be \(2\pi b\), where \(b = a + t_{\text{ox}}\). The capacitance per unit length of the flat FET is equal to

\[
\tilde{C}_{\text{flat}} = \frac{2\pi b \epsilon_0 \varepsilon_{r,\text{ox}}}{t_{\text{ox}}} = -2\pi \epsilon_0 \varepsilon_{r,\text{ox}} \frac{a}{t_{\text{ox}}} \left(1 + \frac{t_{\text{ox}}}{a}\right). \tag{2.12}
\]
The capacitance per unit length of the cylindrical FET is

\[
\tilde{C}_{\text{cyl}} = -\frac{2\pi \epsilon_0 \epsilon_{r,\text{ox}}}{\ln(1 + \frac{t_{\text{ox}}}{a})}.
\]

(2.13)

The capacitance of the flat device is bigger than that of the cylindrical device. This indicates that for the same surface potential more charge is induced in the flat FET than in the cylindrical FET, indicating that the flat FET is more sensitive to small changes in the surface potential. In figure 2.13 the capacitances are plotted as a function of \(\frac{t_{\text{ox}}}{a}\). It can be seen that for a smaller \(\frac{t_{\text{ox}}}{a}\), more charge is induced on the FET devices per unit length. The sensitivity of the FET device to a surface potential therefore increases for smaller oxide thicknesses. In the limit \(\frac{t_{\text{ox}}}{a} \ll 1\) the two capacitances are the same, \(\tilde{C}_{\text{cyl}} \approx C_{\text{flat}}\).

![Figure 2.13: (a.) The capacitances of the flat (green line) and the cylindrical (red, dashed line) metallic FET per unit length of device. In the limit \(t_{\text{ox}}/a \to 0\) the two capacitances are equal as can be seen in (b.) where the ratio \(\tilde{C}_{\text{cyl}}/\tilde{C}_{\text{flat}}\) is plotted. \(\epsilon_{\text{ox}} = 4\).]
2.5 Screening

To ensure proper attachment of the biological target molecules to the capture molecules, biosensing experiments are often performed under physiological conditions. The solution containing the biomolecules therefore has a large ion concentration, which has to be taken into account. The ions in the electrolyte form double layers which screen the electric fields in the system. Depending on the potential in the system, the ions will have a certain distribution, and the other way around, the potential itself is dependent on the distribution of the ions. This means that additional charge of the double layer also has an influence on the potential at the FET surface.

In the following derivations it is assumed that the electric potential in the electrolyte region obeys the Poisson-Boltzmann equation. For a grounded 1-1 electrolyte solution this is (in SI units)

\[ \nabla^2 V(r) = - \frac{eI_0}{\epsilon_0 \epsilon_{r,w}} \left( \exp \left( - \frac{eV}{k_B T} \right) - \exp \left( + \frac{eV}{k_B T} \right) \right) \\
= + \frac{2eI_0}{\epsilon_0 \epsilon_{r,w}} \sinh \left( \frac{eV}{k_B T} \right), \tag{2.14} \]

where \( e \) is the electron charge, \( I_0 \) is the concentration of both the positive and the negative ions in the electrolyte, \( \epsilon_{r,w} \) is the relative dielectric constant of the electrolyte solution, \( k_B \) is the Boltzmann constant, and \( T \) is the absolute temperature. This equation can be used to find the total charge contained in the double layer per unit area of the device.

The Boltzmann statistics in this equation do not take into account the volume of the ions, since the ions in the solution are considered to be point charges. In regions with a high potential the above equation can predict an ion concentration exceeding the concentration maximally possible for hard spheres with a radius of a couple of ångströms, which is the ion radius. For a 1-1 monovalent electrolyte solution of 0.1 M of ions with a size of 2 Å, the ion concentration exceeds the maximum hard sphere concentration at a voltage of 150 mV, which corresponds to a dimensionless potential \( \Psi = eV/(k_B T) \) of about 6. In this thesis, however, most of the time such a potential will not be reached, therefore the Poisson-Boltzmann equation is assumed to be valid here. When higher potentials are reached a modified Poisson-Boltzmann equation has to be used [11].

In the following sections the charge contained in the double layer is calculated as a function of the interface potential \( V_0 \) both for a flat and a cylindrical geometry.
2.5.1 Screening in the flat geometry

In this section the charge in the double layer that is formed on top of a flat potential is calculated. The system is shown in figure 2.14.

![Screening in the flat geometry](image)

**Figure 2.14**: Screening in the flat geometry. The potential is zero in the electrolyte far from the fixed potential surface $V_0$.

The 1 dimensional version of the Poisson-Boltzmann equation for a grounded 1-1 electrolyte is (see equation (2.14)):

$$\frac{d^2 \Psi(x)}{dx^2} = \kappa^2 \sinh(\Psi(x)), \quad (2.15)$$

where $\Psi(x) = eV(x)/(k_B T)$ is the dimensionless potential, $x$ is the distance to the surface where the potential is $\Psi_0 = eV_0/(k_B T)$ (see figure 2.14), and $\kappa$ is the inverse of the Debye length of the solution. The Debye length is the scale over which the ions in the solution screen electric fields. The expression for $\kappa$ is

$$\kappa^2 = \frac{2e^2 I_0}{\epsilon_0 \epsilon_{r,w} k_B T}, \quad (2.16)$$

with $e$ the electron charge, $I_0$ the ion concentration in the bulk of the electrolyte, and $\epsilon_{r,w}$ the relative dielectric constant of the electrolyte.

Rewriting the left hand side of the Poisson-Boltzmann equation, and integrating once over the potential yields

$$\int_{\Psi(x)}^{\Psi(\infty)} \frac{d^2 \Psi(x)}{dx^2} d\Psi = \int_{\Psi(x)}^{\Psi(\infty)} \frac{1}{2} \frac{d}{d\Psi} \left( \frac{d\Psi}{dx} \right)^2 d\Psi$$

$$= -\frac{1}{2} \left( \frac{d\Psi(x)}{dx} \right)^2. \quad (2.17)$$
Integrating the right hand side over the potential yields

$$\int_{\Psi(\infty)}^{\Psi(x)} \kappa^2 \sinh (\Psi(x)) d\Psi = -2\kappa^2 \sinh^2 \left( \frac{\Psi(x)}{2} \right), \quad \text{(2.18)}$$

where for the derivation of the two above equations we used the fact that $d\Psi/dx = 0$ far from the surface due to screening by the ions, and that the solution is grounded so $\Psi(\infty) = 0$.

Combining equations (2.17) and (2.18), we obtain

$$\frac{d\Psi}{dx} = \pm 2\kappa \sinh \left( \frac{\Psi(x)}{2} \right).$$

From Poisson’s equation we know:

$$\int_{x}^{\infty} \frac{d^2 V(x)}{dx^2} dx = -\frac{dV(x)}{dx} = \int_{x}^{\infty} \frac{\rho(x)}{\epsilon_0 \epsilon_{r,w}} dx,$$ \quad \text{(2.20)}

and $\int_{0}^{\infty} \rho(x) dx = \sigma_{DL}$.

This gives the result for the total charge of the ions in the double layer per unit area of the potential interface [12]:

$$\sigma^{\text{flat}}_{DL} = \frac{-2\epsilon_0 \epsilon_{r,w} k_B T \kappa}{e} \sinh \left( \frac{\Psi_0}{2} \right) = -2\sqrt{2\epsilon_0 \epsilon_{r,w} k_B T_0} \sinh \left( \frac{eV_0}{2k_B T} \right). \quad \text{(2.21)}$$

The second line shows the dependence on all physical parameters. From hereon we will keep on working with $\Psi_0$ and $\kappa$, although both contain variables such as $T$ and $\epsilon_{r,w}$. Therefore the dependence on temperature and dielectric constant is no longer manifest. It can be argued however that for biological applications the temperature and the dielectric constant of the solution are constants instead of variables, since the biological system simply imposes a value. The conformation of the biomolecules and possible reactions with other molecules depend strongly on the surrounding medium. In systems that deviate too much from bodily conditions biomolecules can deform, or even disintegrate.

In the above equation the sign was chosen to be negative since for the charges with an opposite sign of the potential it is energetically more favorable to be in the region with that potential, than to be in the bulk of the solution where the potential is zero.

The dependence on $\Psi_0$ is illustrated in figure 2.15. It is seen that for $\Psi \ll 1$ the following approximation is valid

$$\sigma^{\text{flat}}_{DL} = \frac{-\epsilon_0 \epsilon_{r,w} k_B T \kappa \Psi_0}{e},$$ \quad \text{(2.22)}
Figure 2.15: The charge in the double layer per unit area of flat interface potential as a function of the dimensionless interface potential (equation 2.21), and the result of the approximations $\Psi_0 \ll 1$ and $\Psi_0 \gg 1$. The values of the other variables are standard (see table at the end of this chapter).

showing that in this regime the charge of the double layer per unit area is linear in $\Psi_0$. For $\Psi_0 \gg 1$ the correct approximation is

$$\sigma_{DL} = -\frac{e\varepsilon_{r,w}k_BT}{e}\exp\left(\frac{\Psi_0}{2}\right),$$

(2.23)

which has an exponential dependence on the interface potential. As discussed before, the Poisson-Boltzmann theory is not valid for high values of $\Psi_0$. Therefore this large potential approximation is only valid in a small interval of $\Psi_0$, and this approximation should be used with care.

2.5.2 Screening in the cylindrical geometry

In this section the charge in the double layer that is formed around a cylindrical potential is calculated. The system is shown in figure 2.16.

The cylindrical Poisson-Boltzmann equation for a grounded 1-1 electrolyte is:

$$\frac{d^2\Psi}{dr^2} + \frac{1}{r}\frac{d\Psi}{dr} = \kappa^2\sinh(\Psi(r)),$$

(2.24)

with $r$ the distance to the potential surface where $\Psi_0 = eV_0/(k_BT)$ (see figure 2.16).

Rewriting this equation in dimensionless parameters

$$\frac{d^2\Psi}{d(\kappa r)^2} + \frac{1}{\kappa r}\frac{d\Psi}{d(\kappa r)} = \sinh(\Psi(\kappa r)),$$

(2.25)

it is easily seen that for $\kappa R \gg 1$ the second term on the left hand side drops out since $\kappa r \gg \kappa R$ and the flat Poisson-Boltzmann equation is recovered.
The cylindrical Poisson-Boltzmann equation can not be solved analytically. However, this equation has been solved by Ohshima [13] under the assumption that $\kappa R \gg 1$, with $R$ the radius of the cylindrical potential, and $\kappa$ the inverse screening length. The charge of the double layer per unit area of the cylindrical potential is found to be:

$$
\sigma_{DL}^{cy} = -\frac{2k_0 \varepsilon_{\text{r, w}} k_B T}{e} \kappa \sinh\left(\frac{\psi_0}{2}\right) \left[ 1 + \frac{\gamma - 2 - 1}{\cosh^2\left(\frac{\psi_0}{\gamma}\right)} \right]^\frac{1}{2},
$$

(2.26)

where $\gamma = K_0(\kappa R)/K_1(\kappa R)$, with $K_n$ the modified Bessel function of the second kind.

Figure 2.17: The charge in the double layer per unit area of cylindrical interface potential as a function of the dimensionless interface potential (equation 2.26), and the result of the approximations $\psi_0 \ll 1$ and $\psi_0 \gg 1$. The black dots indicate the results of the finite element method. $I_0 = 0.1M, \varepsilon_{\text{r, w}} = 80, R = 15nm$. 
For $\Psi_0 \ll 1$ the above expression can be approximated by

$$
\sigma_{DL}^{cyl} = \frac{-\epsilon_0 \epsilon_r \kappa B T \Psi_0}{e} \left[ 1 + \frac{\gamma^2 - 1}{1} \right]^{\frac{1}{2}}
$$

$$
= \frac{-\epsilon_0 \epsilon_r \kappa B T \Psi_0}{e} \gamma^{-1},
$$

(2.27)

For $\Psi_0 \gg 1$ the following approximation is valid

$$
\sigma_{DL}^{cyl} = \frac{-\epsilon_0 \epsilon_r \kappa B T \Psi_0}{e} \exp(\Psi_0/2),
$$

(2.28)

In figure 2.17 the charge in the double layer is plotted together with the result for the approximations $\Psi_0 \ll 1$ and $\Psi_0 \gg 1$. The black dots indicate the results that were obtained using a finite element computer calculation. It is seen that the analytical results, that were derived using the approximation $\kappa R \gg 1$ [13], agree well with the finite element results. The above derived analytical expression (equation (2.26)) is therefore useful for the situation we are considering here, $\kappa R = 15.5$, and will be used throughout this thesis.

As discussed before, the Poisson-Boltzmann equation is not valid for large values of the potential. Therefore this equation should be used only in a certain interval of $\Psi_0$.

### 2.5.3 Comparing the double layers of the flat and the cylindrical geometries

The charges in the double layers of the two geometries per unit area of the interface potential, $\sigma_{DL}^{flat}$ and $\sigma_{DL}^{cyl}$, are compared most easily by taking their ratio (equation 2.21 and 2.26)

$$
\frac{\sigma_{DL}^{cyl}}{\sigma_{DL}^{flat}} = \frac{1}{\cosh^{2} \left( \frac{\Psi_0}{\kappa} \right)}.
$$

(2.29)

When this expression equals 1 the double layers of the flat and the cylindrical geometry contain an equal amount of charge. This is the case when $\gamma^{-1}$ goes to one, which corresponds to $\kappa R \gg 1$ as can be seen in figure 2.18. When $\kappa R \gg 1$, the radius of the cylindrical potential is large compared to the Debye screening length, $\kappa^{-1}$. It is an intuitive result that the expressions for the flat and the cylindrical geometry are equal when the radius is large compared to the only other length scale in the system, which is the screening length. The above expression also equals 1 when the hyperbolic cosine reaches high values, which is the case for $\Psi_0 \gg 1$.

The flat and cylindrical geometry give identical results for the charge in the double layer, except when $\Psi_0$ and $\kappa R$ are both small.

Figure 2.19 shows the analytical results of the charge in the double layer per unit area, $\sigma_{DL}$, as a function of $\Psi_0$, of the flat geometry (equation 2.21),
Figure 2.18: The function $\gamma^{-1} = K_1(\kappa R)/K_0(\kappa R)$ plotted as a function of $\kappa R$, with $K_n$ the modified Bessel function of the second kind, $\kappa$ the inverse Debye screening length, and $R$ the radius of the cylindrical potential.

and the cylindrical geometry (equation (2.26)), and it shows the results that were obtained for the cylindrical geometry using a finite element method (COMSOL).

Figure 2.19: The dependence of the charge in the double layer per unit area of the device, $\sigma_{DL}$, on the dimensionless potential $\Psi_0$ for two different values of $\kappa R$. The green solid line and the red dashed line are the analytically derived charges in the double layer per unit area of a flat and a cylindrical FET device geometry respectively, $\sigma^\text{flat}_{DL}$ and $\sigma^\text{cyl}_{DL}$. The black dots show the charge in the double layer per unit area of the cylindrical FET calculated with a finite element method, $\sigma_{DL}^{\text{COMSOL}}$.

(a.) To obtain a value of $\kappa R = 0.5$ we chose $I_0 = 0.01\text{M}$ and $R = 1.5\text{nm}$. (b.) The value $\kappa R = 15.5$ is found when using the standard values ($I_0 = 0.1\text{M}$ and $R = 15\text{nm}$). (c.) The ratio of the analytical cylindrical and the flat result for both values of $\kappa R$. In all figures $\epsilon_{r,w} = 80$. 
In figure 2.19 (a.) it can be seen that the three solutions of $\sigma_{DL}$ are clearly different for $\kappa R = 0.5$. The double layer of the cylindrical geometry contains more charge per unit area of device than that of the flat geometry. Figure 2.19 (c.) is a plot of the ratio $\sigma_{DL}^{cyl}/\sigma_{DL}^{flat}$ showing this difference between the analytical expressions in more detail. For small values of $\Psi_0$ the difference is significant, for larger values of $\Psi_0$ the plot tends to 1, indicating that the flat and the cylindrical double layers contain the same amount of charge.

For this value of $\kappa R = 0.5$ the assumption $\kappa R \gg 1$, which was used for derivation of the cylindrical expression [13], does no longer hold. The results of the cylindrical geometry found using a finite element method are also shown. It is seen that even in this regime the analytical calculations still give good results. These results are however not important for biosensing. To reach a value of $\kappa R = 0.5$ a very small radius had to be chosen, $R = 1.5 \text{nm}$, and the ion concentration was not physiological, but $I_0 = 0.01 \text{M}$. Nanowires can be made with such small diameters (e.g. carbon nanotubes), but not with top down methods, which is necessary for large-scale production. Also the physiological ion concentration is necessary for correct binding. Figure 2.19 (b.) therefore shows a more realistic picture where $R = 15 \text{nm}$, and $I_0 = 0.1 \text{M}$. The ratios are again shown in figure 2.19 (c.), where it is seen that the difference between the two geometries is only a few percent for realistic values of $\kappa R = 15.5$.

In figure 2.20 (a.) and (b.) the three solutions are shown as a function of $\kappa R$ for two different values of the potential, $\Psi_0 = 2$ and $\Psi_0 = 6$, respectively. The results of the flat geometry and the results of the analytical and finite element method for the cylindrical geometry look the same, since the difference is only noticeable for very small values of $\kappa R$. Figure 2.20 (c.) is a plot of the ratio of the flat and the cylindrical analytical result for both values of the potential, showing that only for small values of the potential the difference between the two geometries is substantial. The upper limit, and the lower limit are given by the black dashed lines. When $\Psi_0 \ll 1$ equation 2.29 becomes

$$\frac{\sigma_{DL}^{cyl}}{\sigma_{DL}^{flat}} = \gamma^{-1}. \quad (2.30)$$

In figure 2.20 (c.) the black dashed line shows this function as an upper limit for the value of the ratio as a function of $\kappa R$. When $\Psi_0 \gg 1$, the ratio of the charge in the double layer per unit area device in the cylindrical and the flat geometry equals one, which is also shown in the figure.

It was seen that the analytical result of the cylindrical geometry, which was derived using the approximation $\kappa R \gg 1$, gives correct predictions of the double layer charge for biosensing experiments. When comparing the flat and the cylindrical geometry, it was seen that the double layer that forms around a cylindrical potential contains more charge than that surrounding
Figure 2.20: (a.) and (b.) The dependence of the charge in the double layer per unit area of the device, \( \sigma_{DL} \), on \( \kappa R \) for two different values of \( \Psi_0 \). The analytically derived charge in the double layer per unit area of a FET device for the flat geometry, \( \sigma_{DL}^{flat} \) (green solid line) and the cylindrical geometry, \( \sigma_{DL}^{cyl} \) (red dashed line), and the charge in the double layer per unit area of the cylindrical FET calculated with a finite element method, \( \sigma_{DL}^{COMSOL} \) (black dots) are shown. (c.) The ratio of the analytical cylindrical and the flat result for both values of \( \Psi_0 \). In all figures \( \epsilon_{r,w} = 80 \).

a flat potential. Noting however that for realistic nanowire diameters and ion concentrations the value of \( \kappa R \) is 15.5, and that the realistic results are located on the right of the graphs in figure 2.20, it is concluded that for the relevant regime for biosensing, the double layers of the two geometries contain the same amount of charge.
Table 2.1: Overview of the estimations of the physical variables that were made in the previous sections.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ion concentration</td>
<td>0.1 M</td>
</tr>
<tr>
<td>Relative dielectric constant of the ionic solution, $\epsilon_{r,w}$</td>
<td>80</td>
</tr>
<tr>
<td>Relative dielectric constant of the oxide, $\epsilon_{r,ox}$</td>
<td>4</td>
</tr>
<tr>
<td>Relative dielectric constant of biomolecules, $\epsilon_{r,\text{bio}}$</td>
<td>2</td>
</tr>
<tr>
<td>Outer nanowire radius, $b$</td>
<td>15 nm</td>
</tr>
<tr>
<td>Inner nanowire radius, $a$</td>
<td>10 nm</td>
</tr>
<tr>
<td>Oxide thickness, $t_{\text{ox}}$</td>
<td>5 nm</td>
</tr>
<tr>
<td>Density of attached biomolecules, $N$</td>
<td>$0.3 \cdot 10^{13} \text{cm}^{-2}$</td>
</tr>
<tr>
<td>Effective charge of biomolecule</td>
<td>$1 \text{e}$</td>
</tr>
<tr>
<td>Temperature, $T$</td>
<td>293 K</td>
</tr>
</tbody>
</table>
Chapter 3

The Surface Charge Model

In this chapter the charge that is induced in the FET by the presence of the attached biomolecules is discussed. The presence of the attached biomolecules is modelled as a surface charge, $\sigma_S$ (see figure 3.1). This charge is placed directly on the surface of the oxide layer. The value of the biomolecule surface charge is chosen such that the effect of counterions is included (section 2.2.2). A simplified, cylindrical model of the nanowire sensor is considered. The double layer charge is modelled as a surface charge, $\sigma_{DL}$, and will be described with Poisson-Boltzmann theory (section 2.5). The induced charge in the nanowire, $\sigma_{NW}$, which is the quantity of interest, is described as an infinitely thin, uniform layer of charge just below the surface of the nanowire (see figure 3.2). Since the biomolecules are modelled as a surface charge this chapter will be called the Surface Charge Model (SCM). It is based on the work of Alam and Nair [2].

![Figure 3.1: Left: A biomolecule contains multiple charges. Due to screening only the charges close to the sensor surface are sensed by the FET. Right: The biomolecules attached to the sensor surface are modelled as a surface charge with the value of only those charges of the biomolecules that are closer to the sensor surface than a couple of Debye screening lengths.](image)

Using the theory discussed in the previous chapter, all ingredients are available to calculate the amount of charge induced in a FET when the biomolecule surface charge is given. The only relation missing to solve the Surface Charge Model is the fact that all the charges in the system added together, should yield zero charge:
\[ \lambda_{\text{FET}} + \lambda_S + \lambda_{\text{DL}} = 0, \]  

(3.1)

with \( \lambda \) the charge per unit length of FET sensor. This means that all the biomolecule charge on the surface is compensated by the charge in the FET and in the double layer.

Figure 3.2: Figure showing the surface charge densities used to model the system: the charge induced in the nanowire, \( \sigma_{\text{FET}} \), the charge of the adsorbed biomolecules, \( \sigma_S \), and the charge of the double layer of ions, \( \sigma_{\text{DL}} \), are modelled as surface charges. Source [2], figure edited.

The above relation can be derived by enclosing the entire system with a Gaussian surface. The electric fields are screened by the ions in the solution. If one chooses the enclosing Gaussian surface such that one end is in the region where all the fields are screened and the other end in the metal, there are no fields penetrating the surface. Gauss theorem then implies that the total charge inside the surface is zero.

Assuming there are no other charges present in the system except the ions in the electrolyte and the target molecule charge, thereby assuming that the oxide is not charged, and assuming that the metal FET and the electrolyte solution are grounded, \( V(a) = V(\infty) = 0 \), the charge per unit length before biomolecule attachment was \( \lambda_{\text{FET}} = 0 \). After attachment the charge in the FET is \( \lambda_{\text{FET}} \). Therefore the charge induced in the FET upon biomolecule attachment is \( \Delta \lambda_{\text{FET}} = \lambda_{\text{FET}} \). For simplicity the assumption will be made that the FET and the electrolyte solution are indeed grounded. In the final section it will be discussed what the effect is of a potential difference between the FET and the electrolyte.

In the following sections the Surface Charge Model will be solved for the flat, section 3.1, and the cylindrical FET, section 3.2. The cylindrical FET results, which are approximate results, will be compared to the more
accurate results obtained by finite element simulations.

### 3.1 The Surface Charge Model for the flat sensor

In this section an expression will be derived for the charge induced in the flat FET sensor, for a given surface charge. The system is shown in figure 3.3.

![Figure 3.3: The flat FET biosensor. The biomolecule surface charge is indicated with the blue layer, the double layer is formed by the ions, and the green layer represents the induced charge in the FET.](image)

The results of the previous chapter can be directly applied to this system. Recall that the width of the flat device was chosen to be $2\pi b$, to be able to compare the results to the cylindrical FET. With the use of section 2.4, and realizing that the potential across the device is given by $\Psi_b - \Psi_a = \Psi_b$ (see figure 3.3), the expression of the surface charge per unit length of the device induced in the flat FET is found to be

$$\lambda_{\text{FET}} = \frac{2\pi b \xi_{\text{flat}} k_B T}{e} \Psi_b. \quad (3.2)$$

The charge in the double layer was derived in section 2.5. For an interface potential equal to $\Psi_b$, the charge per unit length of sensor in the double layer is

$$\lambda_{\text{DL}}^{\text{flat}} = \frac{-4\pi b\epsilon_0 \epsilon_{\text{r,w}} k_B T}{e} \kappa \sinh \left( \frac{\Psi_b}{2} \right). \quad (3.3)$$

This can be rewritten to obtain

$$\lambda_{\text{FET}} = -\frac{\alpha}{\tau_{\text{ox}}} \lambda_{\text{DL}}^{\text{flat}} \Psi_b, \quad (3.4)$$

and

$$\lambda_{\text{DL}}^{\text{flat}} = -2\alpha k_b^{\text{flat}} \sinh \left( \frac{\Psi_b}{2} \right), \quad (3.5)$$
where the following definitions have been used

\[ \alpha \equiv \frac{2\pi \epsilon_0 k_B T}{e}, \]  

(3.6)

\[ \tau_\text{ox}^{\text{flat}} \equiv \frac{-\epsilon_0}{b C_\text{ox}^{\text{flat}}} \]

\[ = \frac{\ell_\text{ox}}{\kappa_\text{ox}}, \]  

(3.7)

and

\[ \kappa_b^{\text{flat}} \equiv \kappa \epsilon_{r,w}. \]  

(3.8)

Equation (3.7) was obtained by using the explicit expression of the capacitance of the flat metallic FET (equation (2.10)). The above expressions were chosen in such a way that \( \alpha \) can be considered to be a constant, since \( T \) is considered to be constant. As discussed before, the variation of \( T \) is limited due to the sensitivity of biosystems to temperature. The form of \( \tau_\text{ox}^{\text{flat}} \) is chosen such that it gives the relative thickness of the oxide layer. The oxide thickness is made dimensionless by dividing it by \( b \). In electrostatics the relevant length scale is related to the dielectric constant, since the fields in the system are scaled by the dielectric constant. Therefore the expression \( \tau_\text{ox}^{\text{flat}} \) is inversely proportional to the dielectric constant, \( \epsilon_\text{r,ox} \). The same line of reasoning holds for \( \kappa_b^{\text{flat}} \). The inverse of \( \kappa \) is the Debye length. This is scaled with another length scale in the system, \( b \), and the dielectric constant of the medium, \( \epsilon_{r,w} \).

The above expressions can be substituted into equation (3.1), to obtain:

\[ -\frac{\alpha}{\tau_\text{ox}^{\text{flat}}} \Psi_b + \lambda_S - 2\alpha \kappa_b^{\text{flat}} \sinh \left( \frac{\Psi_b}{2} \right) = 0. \]  

(3.9)

This equation can be solved numerically for \( \Psi_b \). This can then be used with the capacitance to find the charge induced in the FET, which is the quantity of interest. The numerical solution is plotted as a function of the biomolecule charge per unit length of the sensor for two different ion concentrations in figure 3.4. This figure shows that for increasing surface charge the potential at the surface of the sensor increases. This is an important result since it describes the sensing mechanism. Increasing the surface potential will increase the charge induced in the FET, which changes the conductivity of the device. Attachment of charged biomolecules will increase this surface charge per unit length on the sensor, and thereby the conductivity of the device. The second interesting aspect shown in this figure is that for a larger ion concentration the potential at the surface of the sensor increases. This indicates that due to screening by the ions in the solution the sensitivity of the sensor is less. Lastly the figure shows that for the large ion concentrations in which we are most interested, the potential stays below 1.
The next two subsections will be about making approximations which enable us to solve for $\Psi_b$ analytically. The two approximations are $\Psi_b \ll 1$ and $\Psi_b \gg 1$. Although it was seen in figure 3.4 that the approximation $\Psi_b \gg 1$ is a poor approximation for biomolecule sensing, the results for this approximation will be given in section 3.1.2 for completeness, and a better understanding of the system. In the end of these subsections the results of the two approximations are plotted as a function of the surface charge, together with the numerical solution (figure 3.7).

3.1.1 Small potentials

Assuming that the surface potential is small, $\Psi_b \ll 1$, equation (3.9) can be approximated by

$$- \frac{\alpha}{\tau_{\text{ox}}} \Psi_b + \lambda_S - \alpha k_b^\text{flat} \Psi_b = 0. \quad (3.10)$$

This equation can easily be solved for $\Psi_b$, yielding

$$\Psi_b = \frac{\lambda_S}{\alpha k_b^\text{flat} + \alpha/\tau_{\text{ox}}}. \quad (3.11)$$

Substituting this result back into equation (3.4), and multiplying by the width of the device, we obtain the charge per unit length induced in the FET

$$\lambda_{\text{FET}}^\text{flat} = - \frac{\alpha}{\tau_{\text{ox}}} \Psi_b$$

$$= - \frac{1}{1 + \frac{k_b^\text{flat}}{\tau_{\text{ox}}}^\text{flat}} \lambda_S. \quad (3.12)$$
This equation shows that the charge induced in the FET is linearly dependent on the surface charge. The slope of this proportionality depends on the physical variables via $\frac{1}{\kappa_{\text{ox}}} \text{ and } \tau_{\text{ox}}$. If the slope is large, a small increase in the surface charge induces a large amount of charge in the FET, and the sensitivity of the biosensor is high. This suggests the device will perform optimal for a small oxide thickness, a large screening length in the electrolyte, small dielectric constant of the electrolyte solution, and a large dielectric constant of the covering oxide.

For $\frac{\tau_{\text{ox}}}{\tau_{\text{ox}}}$ equation (3.12) becomes $\lambda_{\text{FET}} = -\lambda_S$. The charge on the surface is then completely compensated by the charge induced in the nanowire, and the effect of screening is negligible. This is the upper limit of the charge induced in the FET. In this region the charge induced in the nanowire is independent of the inverse Debye screening length, $\frac{1}{\tau_{\text{ox}}}$, and the relative oxide layer thickness. This dependence is shown in the left of figure 3.5 (a.).

For $\frac{\tau_{\text{ox}}}{\tau_{\text{ox}}}$ equation (3.12) becomes $-\lambda_S/\tau_{\text{ox}}$, where the denominator is large. The charge induced on the FET vanishes, indicating that the surface charge is (almost) completely compensated by the double layer. The dependence on the inverse Debye screening length and the relative oxide thickness is now simple, namely it is proportional to the inverse of these variables, as seen in the right of figure 3.5 (a.).

A large value of $\frac{\tau_{\text{ox}}}{\tau_{\text{ox}}}$ can be achieved by increasing the ion concentration of the electrolyte. This decreases the induced charge in the FET, and reduces the sensitivity of the sensor. It is therefore often said that screening by the ions in the electrolyte solution is a large problem for biosensing, and that the ion concentration should be kept as low as possible. In biological systems however, this is not always possible. The value of $\frac{\tau_{\text{ox}}}{\tau_{\text{ox}}}$ for the biosensing system of interest is large, and therefore the approximation $\frac{\tau_{\text{ox}}}{\tau_{\text{ox}}}$ is the appropriate one here. Figure 3.5 (b.) shows this dependence of the induced charge in the FET on $\frac{\tau_{\text{ox}}}{\tau_{\text{ox}}}$. The dependence on $\tau_{\text{ox}}$ is the same, as was seen in equation (3.12), and will therefore not be shown here.

Using equations (3.7), (3.8), and (3.12), the explicit dependence of the induced charge in the metallic FET on physical variables is obtained

$$\lambda_{\text{FET}}^{\text{flat}} = -\frac{1}{1 + \kappa_{\text{ox}}(t_{\text{ox}}/r_{\text{w}}) \tau_{\text{ox}}} \lambda_S. \quad (3.13)$$

The dependence on the inverse Debye length $\kappa$, can be easily understood by realizing that screening plays a larger role when the ion concentration is larger.

To understand the dependence on $t_{\text{ox}}$ one should realize that the potential drop across the FET oxide and in the electrolyte double layer is the same. The two regions have the same boundary conditions, zero potential on one side, and $\Psi_b$ on the other side, at the oxide-electrolyte interface. Now imagine a situation in which the amount of charge induced in the FET is
THE SURFACE CHARGE MODEL

3.1.2 Large potentials

In figure 3.4 we saw that for decreasing ion concentrations or increasing values of the surface charge, the potential at the sensor surface increases. In this subsection the induced charge will be derived assuming a large potential.
In the large potential approximation, $\Psi_b \gg 1$, equation (3.9) becomes

$$\lambda_S - \alpha \kappa_{bf}^\text{flat} \exp \left( \frac{\Psi_b}{2} \right) = 0,$$

(3.14)

where the first term in equation (3.9) was left out, since $\exp(\Psi_b) \gg \Psi_b$ for large $\Psi_b$, and it was assumed that $\kappa_{bf}^\text{flat} \neq 0$. Note that $\Psi_b$ was assumed to be positive, for a large negative potential some signs will be different. If we solve the above equation for $\Psi_b$, we get

$$\Psi_b = 2 \ln \left( \frac{\lambda_S}{\alpha \kappa_{bf}^\text{flat}} \right),$$

(3.15)

Substituting this into equation (3.4), and multiplying with the width of the device, we obtain the charge induced on the flat FET per unit length as a function of $\lambda_S$,

$$\lambda_{\text{FET}}^\text{flat} = \frac{2\alpha}{\tau_{\text{ox}}} \ln \left( \frac{\lambda_S}{\alpha \kappa_{bf}^\text{flat}} \right)$$

$$= \frac{4\pi b_0 \varepsilon_{\text{ox}} k_B T}{e \varepsilon_{\text{ox}}} \ln \left( \frac{\lambda_S e}{2\pi b_0 \varepsilon_{\text{ox}} k_B T K} \right),$$

(3.16)

It is seen that for larger $\kappa_{bf}^\text{flat}$, so for a larger ion concentration, the charge induced in the FET is smaller, showing again that screening decreases the sensitivity. The dependence on $\kappa_{bf}^\text{flat}$ and $\tau_{\text{ox}}^\text{flat}$ is shown in figure 3.6(a) and (b) respectively. The value of the surface charge was taken to be 10 times larger than one would expect for biosensing, otherwise the approximation that was used, $\Psi_b \gg 1$, would not hold. It is seen that also in this limit screening has a negative effect on sensing, and that it is beneficial to have a small value of $\tau_{\text{ox}}^\text{flat}$, which corresponds to having a device with a large capacitance.

### 3.1.3 Comparing the small and the large potential regime

In the previous sections is was shown that for small potentials the dependence of the charge induced in the FET, $\lambda_{\text{FET}}$, on the surface charge, $\lambda_S$, is linear (equation 3.12), while for large potential this dependence is logarithmic (equation 3.16). This can be explained by the fact that the effect of screening is exponential in the large potential limit, and therefore has more influence in this limit. Sensing is thus affected more by screening in the large potential limit than in the small potential limit. A small change in the linear regime causes a much larger change in the charge induced in the FET, than in the logarithmic regime. This means that the sensor is more sensitive in the small potential regime.

The charge induced in the FET both in the approximation $\Psi_b \ll 1$ and in the approximation $\Psi_b \gg 1$ is plotted in figure 3.7 as a function of the
surface charge. The green line is the result which was found numerically. The black dots indicate a realistic value of the surface charge. As can be seen, this value is well within the regime where the small potential approximation holds, and the sensor is expected to operate in its sensitive regime.

The crossover point between the region where the small and where the large surface potential result is more applicable can be found by considering the ratio of the two results

\[
\frac{\lambda_{FET,\text{large}}^{\text{flat}}}{\lambda_{FET,\text{small}}^{\text{flat}}} = \frac{2(1 + \frac{\tilde{\rho}^{\text{flat}}}{\tilde{\rho}^{\text{flat}}_{\text{ox}}}) \ln \left[ \frac{\lambda_{S}}{\alpha \tilde{\rho}^{\text{flat}}_{\text{ox}}} \right]}{\tilde{\rho}^{\text{flat}}_{\text{ox}}},
\]

(3.17)

taking the derivative with respect to \( \lambda_{S} \), and setting this equal to zero. This gives an estimated crossover point at \( \lambda_{S} = \alpha \tilde{\rho}^{\text{flat}}_{\text{ox}} e \), with \( e \) the base of the natural logarithm.

The dependence on the two variables \( \tilde{\rho}^{\text{flat}}_{\text{b}} \) and \( \tau_{\text{ox}}^{\text{flat}} \) in the regime \( \Psi_{b} \ll 1 \) is different from that in the regime \( \Psi_{b} \gg 1 \). In both cases however it is

\[ \text{Figure 3.6: The charge induced in the flat FET, } \lambda_{FET}, \text{ as a function of (a.) } \tilde{\rho}^{\text{flat}}_{\text{b}} \text{ and (b.) } \tau_{\text{ox}}^{\text{flat}}, \text{ in the regime where } \Psi_{b} \gg 1. \text{ The surface charge is taken to be 100 times larger than realistic, to make sure the approximation is valid. The values of the other variables are chosen to be standard (see table at the end of chapter 2).} \]
Figure 3.7: The numerical result of the charge induced in the flat FET, $\lambda_{\text{FET}}$, as a function of the charge on its surface, $\lambda_S$, and the analytical results using the approximations $\Psi_b \ll 1$ and $\Psi_b \gg 1$, for two values of the ion concentration. Left: 0.001 M. Right: 0.1 M, which is more realistic for biosensing. All other variables are taken to be standard (see the table at the end of chapter 2). The realistic value of the biomolecule surface charge, $\lambda_S$, is indicated by the black dots.

beneficial to have a small value of $\lambda_{\text{flat}}$, and a small value of $\tau_{\text{ox}}$, implying a small ion concentration and a thin oxide layer.

3.2 The Surface Charge Model for the cylindrical sensor

In this section the charge induced in the cylindrical FET sensor will be calculated in the Surface Charge Model. The system is shown in figure 3.8

Figure 3.8: The nanowire sensor in the SCM model. The biomolecule charge is shown as a blue layer on the sensor surface. The green layer represents the charge induced in the FET. The ions in the double layer charge are shown with red and blue dots, representing the negative and the positive ions respectively.

The charge induced in the cylindrical FET as a function of the surface potential was given in the previous chapter (equations (2.9) and (2.11)).
With the FET surface potential $\Psi_b$, the charge in the FET is

$$\sigma_{\text{FET}} = \frac{C_{\text{cyl}} k_B T}{e} \Psi_b,$$  \hspace{1cm} (3.18)

The charge in the double layer is given by equation (2.26), and gives

$$\sigma_{\text{DL}}^{\text{cyl}} = \frac{-2 \alpha \epsilon_r \kappa k_B T}{e} \kappa \sinh \left( \frac{\Psi_b}{2} \right) \left[ 1 + \frac{(\gamma(\kappa b))^{-2} - 1}{\cosh^2 \left( \frac{\Psi_b}{4} \right)} \right]^{\frac{1}{2}}.$$  \hspace{1cm} (3.19)

To calculate the charge per unit length of FET device, the surface charge densities have to be multiplied by different factors, one factor for the charge induced in the FET, $\sigma_{\text{FET}}$, and a different factor for the charge in the double layer, $\sigma_{\text{DL}}^{\text{cyl}}$. This is due to the fact that the area where the charge induced in the FET is located is smaller than the area of the electrolyte interface. Multiplying equation (3.18) by $2\pi a$, equation (3.19) by $2\pi b$, and rewriting these expressions we obtain

$$\lambda_{\text{FET}} = -\frac{\alpha}{\tau_{\text{cyl}}^{\text{cyl}}} \Psi_b,$$  \hspace{1cm} (3.20)

and

$$\lambda_{\text{DL}}^{\text{cyl}} = -2 \pi b \tau_{\text{flat}}^{\text{flat}} \sinh \left( \frac{\Psi_b}{2} \right) \left[ 1 + \frac{(\gamma(\kappa b))^{-2} - 1}{\cosh^2 \left( \frac{\Psi_b}{4} \right)} \right]^{\frac{1}{2}},$$  \hspace{1cm} (3.21)

with $\alpha$ and $\tau_{\text{b}}^{\text{flat}}$ defined in equations (3.6) and (3.8), and

$$\tau_{\text{cyl}}^{\text{cyl}} = \frac{-\epsilon_0}{\alpha C_{\text{cyl}}},$$

$$= \frac{\ln(1 + \tau_{\text{cyl}}^{\alpha} \tau_{\text{cyl}}^{\gamma})}{\epsilon_r \tau_{\text{cyl}}^{\gamma}}.$$  \hspace{1cm} (3.22)

Substituting this into equation (3.1), we obtain

$$-\frac{\alpha}{\tau_{\text{cyl}}^{\alpha}} \Psi_b + \lambda_S - 2 \pi b \tau_{\text{flat}}^{\text{flat}} \sinh \left( \frac{\Psi_b}{2} \right) \left[ 1 + \frac{(\gamma(\kappa b))^{-2} - 1}{\cosh^2 \left( \frac{\Psi_b}{4} \right)} \right]^{\frac{1}{2}} = 0,$$  \hspace{1cm} (3.23)

This equation can be solved numerically for $\Psi_b$. The result is given in figure 3.9. It can be seen that also for the cylindrical sensor the potential remains small for the relevant value of the ion concentration and the surface charge. It is seen that for lower ion concentrations, the large potential regime, $\Psi_b \gg 1$, is a valid approximation.

The numerical solution for $\Psi_b$ can be used to find the induced charge in the FET as a function of the surface charge. In the following sections
approximations will be used, such that an analytical solution of the above equation is possible. The two approximations are $\Psi_b \ll 1$ and $\Psi_b \gg 1$. Like for the flat FET in the previous section, both the numerical and the two approximate results are plotted at the end of this section in figure 3.10.

### 3.2.1 Small potentials

Under the assumption $\Psi_b \ll 1$ equation (3.23) can be approximated by

$$-\frac{\alpha}{\tau_{ox}^{cyl}} \Psi_b + \lambda_s - \frac{\alpha \kappa_b^{flat}}{\gamma(\kappa b)} \Psi_b = 0.$$  \hspace{1cm} (3.24)

The potential $\Psi_b$ can then be expressed as

$$\Psi_b = \frac{\lambda_s}{\alpha/\tau_{ox}^{cyl} + \alpha \kappa_b^{flat}/\gamma(\kappa b)}.$$ \hspace{1cm} (3.25)

Substituting this in equation (3.18) and multiplying this by the circumference, $2\pi a$, we find the charge per unit length induced in the cylindrical FET to be

$$\lambda_{FET}^{cyl} = -\frac{1}{1 + \frac{\kappa_b^{cyl}}{\kappa_b^{flat}}/\gamma(\kappa b)} \lambda_s = -\frac{1}{1 + \frac{\kappa_b^{cyl}}{\kappa_b^{flat}} \lambda_s},$$ \hspace{1cm} (3.26)

where

$$\kappa_b^{cyl} = \frac{\kappa_b^{flat}}{\gamma(\kappa b)}.$$ \hspace{1cm} (3.27)
This result is similar to the result for the flat FET (equation (3.12)).
The difference is that \( \tau_{\text{ox}}^{\text{cyl}} \) and \( \kappa_b^{\text{cyl}} \) are replaced by \( \tau_{\text{ox}}^{\text{flat}} \) and \( \kappa_b^{\text{flat}} \).

Using equations (3.22), (3.27) and (3.8), the charge induced per unit length in the cylindrical FET can be written explicitly as

\[
\lambda_{\text{FET}}^{\text{cyl}} = -\frac{1}{1 + (\epsilon_{r,\text{ox}}/\epsilon_{r,\text{ox}})(\kappa_b/\gamma(\kappa b))\ln\left(1 + \frac{L}{a}\right)} \lambda_S. \quad (3.28)
\]

This simple expression shows that in order to get a large induced charge in the cylindrical FET, just as for the flat FET, it is beneficial to create a device in which the dielectric constant of the surrounding medium is comparable to that of the oxide, the Debye screening length is large compared to the device radius, and the oxide thickness is small compared to the inner FET radius.

### 3.2.2 Large potentials

Under the assumption that \( \Psi_b \gg 1 \) equation (3.23) becomes

\[
-\frac{\alpha}{\tau_{\text{ox}}^{\text{cyl}}} \Psi_b + \lambda_S - \alpha \kappa_b^{\text{flat}} \exp\left(\frac{\Psi_b}{2}\right) \left[1 + \frac{(\gamma(\kappa b))^{-2} - 1}{\exp\left(\frac{\Psi_b}{2}\right) / 4}\right]^{1/2} = 0. \quad (3.29)
\]

Assuming \(((\gamma(\kappa b))^{-2} - 1) \ll \exp(\Psi_b/2)/4\), which is a realistic assumption when \( \Psi_b \gg 1 \), the part between the square brackets will be approximately equal to one. Also for large potentials \( \Psi_b \) is much smaller than \( \exp(\Psi_b) \) and the first term drops out, leading to [2]:

\[
\lambda_S - \alpha \kappa_b^{\text{flat}} \exp\left(\frac{\Psi_b}{2}\right) = 0. \quad (3.30)
\]

The solution of this equation gives the expression for \( \Psi_b \), as also found by Nair and Alam [2]:

\[
\Psi_b = 2 \ln\left[\frac{\lambda_S}{\alpha \kappa_b^{\text{flat}}}\right], \quad (3.31)
\]

Substituting this in the expression for the charge induced in the FET, equation (2.8), we obtain the result for the charge induced on the cylindrical FET per unit length

\[
\lambda_{\text{FET}}^{\text{cyl}} = -\frac{2\alpha}{\tau_{\text{ox}}^{\text{cyl}}} \ln\left[\frac{\lambda_S}{\alpha \kappa_b^{\text{flat}}}\right] = -\frac{4\pi \alpha \epsilon_{r,\text{ox}} k_BT}{\ln(1 + \frac{L/a}{e}) e} \ln\left[\frac{\lambda_S e}{2\pi \beta \epsilon_{r,\text{ox}} k_BT K}\right]. \quad (3.32)
\]

This is again similar to the result of the flat FET. The dependence on \( \kappa_b^{\text{flat}} \) is the same, and the role of \( \tau_{\text{ox}}^{\text{cyl}} \) is the same as that of \( \tau_{\text{ox}}^{\text{flat}} \) in equation (3.26).
3.2.3 Comparing the small and the large potential regime

The numerical solution, and the approximate solutions are shown in figure 3.10 for two different values of the ion concentration. It is seen that, just as for the flat FET, the relevant regime is the small potential regime. For smaller values of the ion concentration, the large potential approximation becomes more important. The result in equation (3.26) showed that the induced charge in the FET has a linear dependence on the surface charge in the small potential regime, and equation (3.32) showed a logarithmic dependence in the large potential limit. Therefore the small potential regime is also the sensitive regime for the cylindrical FET.

![Figure 3.10: The numerical results of the charge induced in the cylindrical FET, λ_{FET}, as a function of the charge on its surface, for two different values of the ion concentration. The value 0.1 M is realistic for biosensing. The analytical results for the approximations Ψ_{b} < 1 and Ψ_{b} > 1 are also shown. The values of the other variables are the standard values (see table at the end of chapter 2).](image)

3.3 Comparing the effect of surface charge for the flat and the cylindrical sensor

In the previous section it was seen that for both the small potential approximation as the large potential approximation the expression of the induced charge in the FET per unit length has the same form in the cylindrical system as it has in the flat system. The only differences are due to the fact that the variables τ_{cyl} and τ_{flat} are not the same, and that \kappa_{cyl} and \kappa_{flat} are not the same. These differences are caused by the differences in capacitance and the difference in the double layer of the two geometries respectively. In this section these differences will be studied.

Comparing equation (3.27) to equation (3.8), we find that the difference between \kappa_{cyl} and \kappa_{flat} is only a factor \( (\gamma(kb))^{-1} \). As was seen in chapter 2, figure 2.18, \( (\gamma(kb))^{-1} \) never reaches values below one. We find \( \kappa_{cyl} / \kappa_{flat} = \ldots \)
\[(\gamma(\kappa b))^{-1} \geq 1\], which makes the charge induced in the cylindrical FET, \(\lambda_{\text{FET}}^{\text{cyl}}\), smaller than the charge induced in the flat FET, \(\lambda_{\text{FET}}^{\text{flat}}\).

Comparing equation (3.22) to equation (3.7), we find that the difference between \(\tau_{\text{ox}}^{\text{cyl}}\) and \(\tau_{\text{ox}}^{\text{flat}}\) is due to the difference in the capacitance per unit length of the devices. \(C_{\text{flat}} = 2\pi b C_{\text{flat}}\) and \(C_{\text{cyl}} = 2\pi a C_{\text{cyl}}\). In figure 2.13 it was seen that the capacitance per unit length of the cylindrical FET is smaller than that of the flat FET. We find \(\tau_{\text{ox}}^{\text{cyl}} / \tau_{\text{ox}}^{\text{flat}} = C_{\text{flat}} / C_{\text{cyl}} \geq 1\), which also makes \(\lambda_{\text{FET}}^{\text{cyl}}\) smaller than \(\lambda_{\text{FET}}^{\text{flat}}\).

So in general a certain amount of surface charge will induce less charge in the cylindrical FET than in the flat FET. This means that the cylindrical FET is less sensitive to the attachment of a uniform surface charge.

\[\text{Figure 3.11: The charge induced in a flat (green line) and a cylindrical (red line) FET due to adsorption of the same amount of surface charge as a function of (a.) } t_{\text{ox}} / a, \text{ and (b.) } \kappa b. \text{ In figure (c.) and (d.) the ratio of these two results is shown.}\]

The difference between the results of the two geometries for the case that \(\Psi_b \ll 1\) is shown in figure 3.11. The first figure shows the charge induced in the flat (green line) and the cylindrical (red line) FET as a function of \(t_{\text{ox}} / a\), which represents the difference in capacitance. A realistic value of \(t_{\text{ox}} / a\) is 1/2. The charge induced in the flat FET is seen to be only 77% of that induced in the cylindrical FET. The plot as a function of \(\kappa b\) shows the difference due to the different double layers in the two geometries. It should be noted that for small values of \(\kappa b\) the analytical result of the cylindrical geometry is not accurate due to the fact that the assumption was used in the derivation that this was large [13]. Therefore the left of the plot is not accurate. For biosensing we are usually not interested in this regime, and no further investigation is necessary.

It was shown in section 2.5 that for the relevant value of \(\kappa b\) there was only a small difference in the double layer charge, and in fact the difference
between the two geometries is therefore mainly caused by the difference in capacitances. This can be seen in figure 3.12 where in figure (a.) the expression of the double layer in the cylindrical geometry was set equal to that in the flat geometry by imposing $\gamma = 1$. A realistic value of $t_{ox}/a$ is $1/2$. It can be seen in figure 3.12 that for this value $20\%$ less charge is induced in the cylindrical FET than in the flat FET, even without taking into account the effect of the difference in double layer.

In figure 3.12 (b.) the capacitance of the cylindrical FET was assumed to have the value of the capacitance of the flat FET. A realistic value of $\kappa b$ is 15.5. For this value the difference between the charge induced in the flat FET and the charge induced in the cylindrical FET is seen to be only $6\%$. This was without including the effect of the difference in capacitance.

Considering the case that $\Psi_b \gg 1$, it is seen that the only difference between the results of the two geometries is in the capacitances of the two different FETs. The ratio of the charge induced in the cylindrical sensor and the charge induced in the flat sensor exactly follows the ratio of the capacitances given in figure 2.13 (b.), $\Lambda_{\text{FET}} / \Lambda_{\text{FET}} = C_{\text{cyl}} / C_{\text{flat}}$. In this regime the difference in the charge in the double layer of the two geometries has no influence.

It can be concluded that electrostatically, the cylindrical FET sensor is less sensitive to a uniform biomolecule surface charge than the flat FET sensor. This is due to both the difference in capacitance and the fact that screening of the double layer in the cylindrical geometry has a stronger influence than in the flat geometry. However, for a nanowire with realistic dimensions in a physiological solution, the difference in double layer charge is only small. In this realistic biosensing regime the difference therefore is mainly caused by the different capacitances.
3.4 Applying a voltage to the sensor

In the previous sections it was always assumed that the FET was grounded. When the FET is not grounded the results change, since the charge induced in the FET is no longer only dependent on the surface potential, but also on the FET potential. The expression for the induced charge is then for the flat FET

$$\lambda_{\text{FET}} = 2\pi b C (\Psi_b - \Psi_a) \frac{k_B T}{e}. \quad (3.33)$$

Since the capacitance of the FET now has to be multiplied with the potential difference across the FET oxide (equation (2.8)), the equation for the flat FET becomes (equation (3.9))

$$\frac{\alpha}{\tau_{\text{ox}}^\text{flat}} (\Psi_b - \Psi_a) + \lambda_S - 2\alpha \kappa_b^\text{flat} \sinh \left( \frac{\Psi_b}{2} \right) = 0, \quad (3.34)$$

The above equation can be rearranged to find the following expression

$$\frac{\alpha}{\tau_{\text{ox}}^\text{flat}} \Psi_b + \lambda_S - 2\alpha \kappa_b^\text{flat} \sinh \left( \frac{\Psi_b}{2} \right) = 0, \quad (3.35)$$

with

$$\lambda_S = \lambda_S + \frac{\alpha}{\tau_{\text{ox}}^\text{flat}} \Psi_a. \quad (3.36)$$

Equation (3.35) is similar to equation (3.9), with the difference that $\lambda_S$ is replaced by $\lambda_S$. The effect of the FET potential is seen to be equivalent to the effect of a surface charge. In figure 3.13 it is shown that for a FET voltage of 0.7 V the effect of the potential is just as large as the effect of the surface charge.

![Figure 3.13: The effect of a FET potential is equivalent to that of the surface charge. The value of $\alpha \Psi_a / \tau_{\text{ox}}^\text{flat}$ is equal to the value of the surface charge for a FET potential of 0.7 V.](image)
Replacing \( \lambda_S \) by \( \lambda_S \) leaves all the calculations the same. We can therefore simply take all the previously derived results, and use equation (3.36) to obtain the dependence on \( \Psi_a \).

In the small potential limit, \( \Psi_b \ll 1 \), we obtain (equation (3.12))

\[
\lambda_{\text{FET}}^{\text{flat}} = -\frac{1}{1 + \frac{\alpha}{\varepsilon_{\text{ox}}^{\text{flat}}}} (\lambda_S + \frac{\alpha}{\varepsilon_{\text{ox}}^{\text{flat}}} \Psi_a).
\]  

(3.37)

It is seen that the charge induced in the FET is still linearly dependent on the surface charge when \( \Psi_b \ll 1 \). However, the FET potential \( \Psi_a \) determines in which regime the FET is operating, and it can no longer be assumed that the biosensing system is in the small potential regime. The FET potential can be used to shift between the small and the large potential regime.

In the large potential approximation, \( \Psi_b \gg 1 \), we obtain (equation (3.16))

\[
\lambda_{\text{FET}}^{\text{flat}} = -\frac{2\alpha}{\varepsilon_{\text{ox}}^{\text{flat}}} \ln \left[ \frac{(\lambda_S + \frac{\alpha}{\varepsilon_{\text{ox}}^{\text{flat}}} \Psi_a)}{\alpha \lambda_b^{\text{flat}}} \right].
\]  

(3.38)

In figure 3.14 this result is illustrated. Depending on the value of the FET potential, \( \Psi_a \), a certain change in surface charge, \( \lambda_S \), will induce a different amount of charge in the FET. The FET potential can thus be used to tune the sensor to be more sensitive.

In the article written by Nair and Alam (2) the large potential approximation is calculated. It was shown in this chapter that for reasonable biomolecule densities and charge the value of the surface charge density is such that the biosensor operates in the small potential regime. For larger surface charge densities or if the FET potential is not equal to zero, the operation of the biosensor moves towards the large potential regime. The large potential regime is, however, not the most sensitive regime of operation of the biosensor, and it is recommended that the sensor operates in its small potential regime.

The above results (equations (3.37) and (3.38)) are also valid for the cylindrical case, but then \( \lambda_{\text{cyl}}^{\text{flat}} \) and \( \lambda_{\text{cyl}}^{\text{flat}} \) are replaced with \( \varepsilon_{\text{cyl}}^{\text{flat}} \) and \( \varepsilon_{\text{cyl}}^{\text{flat}} \).
Figure 3.14: The charge induced in the FET upon attachment of a surface charge, $\lambda_0$, is dependent on the FET potential, $\Psi_a$. The position on the x-axis is determined by the FET potential $\Psi_a$. The interval on the x-axis is given by $\lambda_0$. It is seen that for larger values of the FET potential less charge is induced in the FET upon attachment of surface charge.
Chapter 4

The Excluded Volume Model

The field-effect transistor (FET) sensor detects changes of the potential on its surface. In the previous chapter it was shown how attachment of charged molecules affects the FET surface potential. In this chapter it will be shown how another property of the biomolecules, their volume, influences this potential [3].

When biomolecules attach to the sensor surface, they push away a certain amount of electrolyte. This effect is illustrated in figure 4.1. The presence of the biomolecules excludes the presence of the electrolyte, therefore this model is called the Excluded Volume Model (EVM).

By including the volume of the biomolecules in the model, two effects have to be taken into account. The first one is a change in the dielectric constant. Since the dielectric constant of the biomolecule is different from that of the electrolyte, attachment of biomolecules changes the dielectric constant in a thin layer around the FET.

A second effect is a decrease of the amount of ions close to the sensor surface. Ions in the electrolyte in the region close to the sensor surface are pushed away by the biomolecules. If a double layer is formed in a thin layer close to the sensor surface (for example due to a fixed surface charge, a different FET potential, or a back gate), the removal of these ions will cause a rearrangement of the charges in the vicinity of the sensor.

These two effects are independent of the charge of the biomolecule, so hypothetically in this way even the presence of neutral biomolecules can be detected. The question remains whether the influence of the volume of the biomolecules is strong enough to detect the attachment of biomolecules? Is this a strong effect or can it be neglected compared to the effect of biomolecule charge?

In this and the following chapter the effects of the biomolecule volume will be studied, and the results will be compared to the results of the Surface Charge Model (chapter 3). This chapter will be dealing with a dense biomolecule layer in which all the volume in a thin layer on the sensor sur-
face is occupied by biomolecules. This will provide an upper limit of the effect of biomolecule volume. In this chapter most results can still be derived analytically. In the next chapter a partial occupation of this layer is studied using numerical calculations.

**Figure 4.1:** The effect of the volume that is occupied by biomolecules. When the molecules attach to the sensor surface, they push away the electrolyte in a thin layer around the sensor, thereby changing the local dielectric constant and the ion concentration.

The results of the model can be applied to two situations. In the first case the charge on the surface charge is due to attachment of biomolecules. The results will answer the question how big the error is when the biomolecules are modelled as point charges, instead of molecules with a certain size. In figure 4.2 a biomolecule is shown and how it is modelled when both the effect of charge and the effect of volume are taken into account.

**Figure 4.2:** A biomolecule modelled as a big volume with a point charge close to the sensor surface.

In the second case the biomolecule is modelled as a volume without a charge, while there are some charges present in the system on the sensor surface that are fixed (see figure 4.3). If a device is made with a fixed surface charge, biomolecules can be detected even without taking into account the effect of the biomolecule charge. We want to answer the question whether this effect is more pronounced than the charge effect in certain cases.

The charge induced in the FET is related to the other charges in the
system by an equation that is similar to equation (3.1), with the difference that \( \lambda_S \) is no longer necessarily attributed to the charge of the attached biomolecules, but it can also be a fixed surface charge (e.g. oxide or capture molecule charge)

\[
\lambda_{\text{FET}} + \lambda_S + \lambda_{\text{DL}} = 0. \tag{4.1}
\]

This equation can be used to find the charge induced in the FET, \( \lambda_{\text{FET}} \). Changing any of the three above surface charges influences the whole system, thereby changing the charge induced in the FET. Recall that in the previous chapter the attachment of biomolecules changed the surface charge, \( \lambda_S \), while leaving the expression for the charge in the double layer the same. Including the volume of the biomolecules will have an influence on the charge in the double layer, \( \lambda_{\text{DL}} \).

### 4.1 The Excluded Volume Model for the flat sensor

In this section an analytical expression is derived for the charge induced in the flat FET when a surface charge and a dense biomolecule layer are present on the surface of the FET (see figure 4.4). In the dense biomolecule layer no ions are present, and the dielectric constant is \( \varepsilon_{\text{bio}} \). The thickness of the layer will be represented by \( t_{\text{bio}} = c - b \), and again the FET is grounded, \( V_a = 0 \).

In chapter 2 expressions were derived for the charge in the FET and the charge in the double layer. In figure 4.4 it can be seen that now the surface potential that determines the charge induced in the FET is \( \Psi_b \), and that the potential of the electrolyte interface, that determines the charge in the double layer is \( \Psi_c \). Equation (4.1) then becomes

\[
\lambda_{\text{FET}}(\Psi_b) + \lambda_{\text{DL}}(\Psi_c) + \lambda_S = 0, \tag{4.2}
\]

which can not be solved without an extra relation between \( \Psi_b \) and \( \Psi_c \). This relation is found by the following calculation.
The electric field inside the dense biomolecule layer is

\[ E = \frac{\sigma_{\text{FET}}(V_b) + \sigma_s}{\epsilon_0 \epsilon_{r,\text{bio}}} \]. (4.3)

Integration over \( x \) from \( b \) to \( c \) yields

\[ V_c - V_b = -\frac{\sigma_{\text{FET}}^\text{flat} + \sigma_s}{\epsilon_0 \epsilon_{r,\text{bio}}} \]. (4.4)

or

\[ \Psi_c - \Psi_b = -\frac{\lambda_{\text{FET}}^\text{flat} + \lambda_s}{2 \pi b \epsilon_0 \epsilon_{r,\text{bio}}} \left( \frac{t_{\text{bio}}(c)}{k_B T} \right). \] (4.5)

Inserting into this equation the relation between the charge induced in the FET and the FET surface potential (equation (2.9)),

\[ \Psi_b = \frac{e}{k_B T} \frac{\lambda_{\text{FET}}^\text{flat}}{2 \pi b C_{\text{FET}}^\text{flat}} \] (4.6)

and solving for \( \lambda_{\text{FET}}^\text{flat} \), an expression for \( \lambda_{\text{FET}}^\text{flat} \) is obtained that is dependent on \( \Psi_c \) instead of \( \Psi_b \)

\[ \lambda_{\text{FET}}^\text{flat} = -\frac{\lambda_s + \frac{k_B T}{e} \Psi_c 2 \pi b \epsilon_0 \epsilon_{r,\text{bio}}/t_{\text{bio}}}{1 + \frac{\tau_{\text{bio}}^\text{flat}/t_{\text{bio}}}{\tau_{\text{ox}}^\text{flat}}} \] (4.7)

with \( \alpha \) and \( \tau_{\text{ox}}^\text{flat} \) defined in equation (3.6) and (3.7), and

\[ \tau_{\text{bio}}^\text{flat} \equiv \frac{t_{\text{bio}}}{b \epsilon_{r,\text{bio}}} \] (4.8)
As mentioned before, the double layer charge depends on the interface potential which is $\Psi_c$. The charge in the double layer is

$$\lambda_{DL} = \frac{-4\pi b_M e \kappa_T}{e} \kappa \sinh \left( \frac{\Psi_c}{2} \right)$$

$$= -2\alpha \kappa_b \sinh \left( \frac{\Psi_c}{2} \right),$$

(4.9)

with $\kappa_b$ defined in equation (3.8). Substituting equations (4.7) and (4.9) into equation (4.1) we obtain

$$\lambda_S + \frac{\alpha \kappa_b}{1 + \sqrt{\kappa_b \kappa_{in}}} \Psi_c + \lambda_S - 2\alpha \kappa_b \sinh \left( \frac{\Psi_c}{2} \right) = 0.$$

(4.10)

In figure 4.5 the numerical solution of this equation is given as a function of the surface charge for different values of the biolayer thickness. It is seen that the value of the dimensionless potential, $\Psi_c$, is smaller than 1 for any surface charge value that is realistic for a biomolecule charge. The values of the variables were also chosen to have values that are realistic for biosensing experiments. If other charges are present in the system the value of the surface charge may be much larger. For increasing surface charge the potential increases rapidly, and the potential will reach values larger than one. For larger biomolecule layer thicknesses the large potential regime will be reached less rapidly. Note that in the figure the potential at position $c$ is plotted, while in the previous chapter the potential at position $b$ was considered. For increasing biomolecule layer thickness, the potential at position $c$ decreases, while the potential at position $b$ increases.

![Figure 4.5](image)

**Figure 4.5**: The numerical solution of equation (4.10) is given as a function of the surface charge for different values of the biolayer thickness. It is seen that $\Psi_c$ stays well below 1. The values of the other variables are chosen such that they are realistic for biosensing applications (see standard values in the table at the end of chapter 2).

In the following sections equation (4.10) will be solved analytically for $\Psi_c$ using the approximations $\Psi_c \ll 1$ and $\Psi_c \gg 1$ respectively. As discussed
above, $\Psi_c$ will be small in the case of a surface charge due to biomolecule attachment and under these circumstances the approximation $\Psi_c \ll 1$ will be a good one. The other approximation, $\Psi_c \gg 1$, will be given since it may be beneficial to design the sensor with a much larger surface charge for volume detection, as will become clear later on, and this gives rise to large potentials. Besides that, a FET that is not grounded can also give rise to large potentials.

### 4.1.1 Small potentials

Applying the approximation $\Psi_c \ll 1$ to equation (4.10), we get

$$-rac{\lambda_S + \alpha_{\text{flat}} \Psi_c}{1 + \tau_{\text{ox}} / \tau_{\text{bio}}} + \lambda_S - \alpha_{\text{flat}} \Psi_c = 0,$$

for which the solution of $\Psi_c$ is

$$\Psi_c = \frac{\tau_{\text{ox}} / \alpha}{1 + \tau_{\text{bio}} (\tau_{\text{flat}} + \tau_{\text{ox}})} \lambda_S.$$  \tag{4.12}

Substituting this back into the expression for $\lambda_{\text{FET}}$ (equation (4.7)) the following expression is obtained

$$\lambda_{\text{FET}} = -\frac{\lambda_S}{1 + \tau_{\text{ox}} / \tau_{\text{bio}}} \left(1 + \frac{\tau_{\text{ox}} / \tau_{\text{bio}}}{1 + \tau_{\text{bio}} (\tau_{\text{flat}} + \tau_{\text{ox}})}\right).$$  \tag{4.13}

This can be rewritten as

$$\lambda_{\text{FET}}^{\text{flat}} = -\frac{1}{1 + \tau_{\text{bio}} / \tau_{\text{ox}}} \left(1 + \frac{\tau_{\text{bio}} (\tau_{\text{flat}} + \tau_{\text{ox}})}{1 + 1/(\tau_{\text{bio}} (\tau_{\text{flat}} + \tau_{\text{ox}})}\right) \lambda_S.$$  \tag{4.14}

It is now easily seen that in the limit $\tau_{\text{bio}}^{\text{flat}} = 0$ the result of the calculations of the Surface Charge Model are obtained (equation (3.12)). Just as in the Surface Charge Model, again $\lambda_{\text{FET}}^{\text{flat}}$ is linearly dependent on the surface charge, $\lambda_S$, and decreases for increasing $\tau_{\text{bio}}^{\text{flat}}$. This means that less charge is induced in the FET when screening is enhanced. In the case of the excluded volume model this effect however is less strong. The ions are excluded from the region close to the surface, reducing the effect of screening. This is explained below.

The second term in brackets in equation (4.13) is much smaller than 1. This can be seen since the value of $\tau_{\text{bio}}^{\text{flat}}$ is large ($\tau_{\text{bio}}^{\text{flat}} \approx 1200$, equation (3.8)) compared to the values of $\tau_{\text{bio}}^{\text{flat}}$ ($\approx 1/15$, equation (4.8)) and $\tau_{\text{ox}}^{\text{flat}}$ ($\approx 1/12$, equation (3.7)), while $\tau_{\text{bio}}^{\text{flat}}$ and $\tau_{\text{ox}}^{\text{flat}}$ have the same order of magnitude. Therefore $\tau_{\text{ox}} / \tau_{\text{bio}}^{\text{flat}}$ is much smaller than $\tau_{\text{bio}}^{\text{flat}} (\tau_{\text{bio}}^{\text{flat}} + \tau_{\text{ox}}^{\text{flat}})$. The second
term in brackets is much smaller than 1 and can be neglected compared to the first term. Equation (4.13) therefore becomes

\[
\lambda_{\text{FET}}^\text{flat} \approx -\frac{\lambda_s}{1 + \tau_{\text{ox}}/\tau_{\text{bio}}} \tag{4.15}
\]

for the values of the physical parameters relevant for biosensing. Note that if \(\tau_{\text{bio}} \ll \tau_{\text{ox}}\), the above relationship no longer holds. The dependence on \(\tau_{\text{bio}}^\text{flat}\) was located in the second term in brackets of equation (4.13). This term was shown to be negligible, and therefore it can be concluded that the influence that \(\tau_{\text{bio}}^\text{flat}\) has on \(\lambda_{\text{FET}}^\text{flat}\) is very small. The influence of screening is shown to be reduced.

The dependence on the biomolecule layer thickness, and the oxide thickness is also clear in the above equation. If the biomolecules layer thickness is increased the charge in the FET increases. For increasing oxide thickness the charge in the FET decreases.

Now the two applications of the Excluded Volume Model result will be studied. In the first case (EVM1), where all the surface charge is attributed to the biomolecules, there was no charge on the sensor surface before biomolecule attachment. The induced charge upon attachment of the biomolecules is

\[
\Delta \lambda_{\text{FET}}^{\text{EVM1, flat}} = \lambda_{\text{FET}}^{\text{EVM, flat}} - \lambda_{\text{FET}}^\text{flat} \\
= -\frac{\lambda_s}{1 + \tau_{\text{ox}}/\tau_{\text{bio}}} \left(1 + \frac{\tau_{\text{ox}}/\tau_{\text{bio}}}{1 + \tau_{\text{ox}}/\tau_{\text{bio}} (\tau_{\text{bio}}^\text{flat} + \tau_{\text{ox}}^\text{flat})}\right) \\
\approx -\frac{\lambda_s}{1 + \tau_{\text{ox}}/\tau_{\text{bio}}} \tag{4.16}
\]

The dependence of the exact result above on the relative biomolecule layer thickness, \(\tau_{\text{bio}}^\text{flat}\), is shown in figure 4.6 (a.). It is seen that for increasing biomolecule layer thickness more charge is induced in the FET upon biomolecule attachment. The dependence on \(\tau_{\text{bio}}^\text{flat}\) is shown in figure 4.6 (c.). It is seen that, as noted before, when the ion concentration in the electrolyte is larger, less charge is induced in the FET. For increasing biomolecule layer thickness the influence of the ion concentration is less and less. For realistic values of the ion concentration the value of \(\tau_{\text{bio}}^\text{flat}\) is 1250 (equation 3.8), and it is seen that in this part of the graph the lines are almost horizontal, and small fluctuations in the ion concentration are not noticeable compared to the effect of the excluded volume. Figure 4.6 (e.) shows that for increasing oxide thickness less charge is induced in the FET. A realistic value of \(\tau_{\text{ox}}^\text{flat}\) is 0.08. This all suggests that just like for the SCM, for the EVM the sensor will respond best if the ion concentration is small and the oxide layer is thin.

Figures 4.6 (b.), (d.), and (e.) show the ratio of the charge induced upon biomolecule attachment if the biomolecules are modeled as a surface charge
and a volume layer, and if the biomolecules are only modeled as a surface charge. The former is the result of the Excluded Volume Model. The latter is the Excluded Volume Model result when \( \tau_{\text{bio}}^{\text{flat}} = 0 \), and is equivalent to the Surface Charge Model result. Using equation 4.14 the corresponding expression is found to be:

\[
\frac{\Delta \lambda_{\text{FET}}^{\text{EVM}}}{\Delta \lambda_{\text{FET}}^{\text{SCM}}} = 1 + \frac{\tau_{\text{flat}}^{\text{flat}} \tau_{\text{bio}}^{\text{bio}}}{1 + 1/(\tau_{\text{flat}}^{\text{bio}} \tau_{\text{ox}}^{\text{flat}}) + \tau_{\text{bio}}^{\text{bio}} / \tau_{\text{ox}}^{\text{flat}}} \tag{4.17}
\]

In this equation the second term is large compared to the first. Realizing that \( \tau_{\text{bio}}^{\text{flat}} / \tau_{\text{ox}}^{\text{flat}} \approx 1 \), and that \( \tau_{\text{flat}}^{\text{flat}} \tau_{\text{bio}}^{\text{bio}} \) and \( \tau_{\text{flat}}^{\text{bio}} \tau_{\text{ox}}^{\text{flat}} \) are large and have a value of about 100, it can be concluded that the second term has a value of about 50. This means that if the attached biomolecules are modeled as only a surface charge, while in fact they do not only have a charge but also form a dense surface layer on the sensor surface, the result that is found is about a factor 50 too small. The error in modeling the biomolecule as a point charge without including any volume effect could therefore lead to a serious underestimation of the charge induced in the FET, and therefore of the sensor signal.

In figure 4.6 (b.) equation (4.17) is plotted as a function of the layer thickness. It is seen that for a layer thickness of 10 nm (corresponding to \( \tau_{\text{bio}}^{\text{flat}} = 0.33 \)), the error is a factor 84, for a layer thickness of 2 nm (corresponding to \( \tau_{\text{bio}}^{\text{flat}} = 0.067 \)) the error is a factor 47, and for a layer thickness of 0.94 nm (corresponding to \( \tau_{\text{bio}}^{\text{flat}} = 0.031 \)) the error is a factor 29. This last thickness is chosen such that the excluded volume in the surface layer is the same as the total volume of the biomolecules, when a surface charge density and a biomolecule volume is chosen as derived in section 2.2 (see the table at the end of chapter 2). Or put differently, this is the total volume of the biomolecules spread out over the sensor surface. In figure 4.6 (d.) it can be seen that the error increases for increasing \( \tau_{\text{bio}}^{\text{flat}} \), which is for increasing ion concentration. This could explain (part of) the mysterious sensitivity of nanowire sensors at large ion concentrations [3] [14]. In figure 4.6 (f.) it is seen that the error is larger when the oxide layer is thicker, and this dependence is stronger for larger biolayer thicknesses, meaning that the negative effect of a large oxide thickness is less pronounced when a biomolecule layer is present on the surface.

The results of the second application of the model, in which we interpret the result in equation (4.13) as the effect of the attachment of neutral biomolecules on top of a fixed surface charge, will be discussed now. We want to know how much charge will be induced in the FET upon attachment of a dense layer of neutral biomolecules. We are interested in the difference between the result of the SCM and the EVM, since the SCM gives the situation before attachment, and the EVM gives the situation after attachment of the dense biomolecule layer on the sensor surface. This charge induced in
The charge per unit length induced in the flat FET, \( \lambda_{\text{FET}}^{\text{flat}} \), in the approximation \( \Psi_c \ll 1 \) for the first application of the model. The result is plotted as a function of (a.) the relative biolayer thickness, \( t_{\text{bio}}^{\text{flat}} \), (c.) as a function of \( t_{\text{ox}}^{\text{flat}} \), and (e.) as a function of the relative oxide thickness, \( t_{\text{ox}}^{\text{flat}} \). The ratio of these results and the results of the Surface Charge Model are shown to their right in figures (b.), (d.), and (e.). These figures show that the influence of the biomolecule volume can be very large, and that for increasing ion concentration the effect of an excluded volume increases. The values of the variables are given in the table at the end of chapter 2.

\[
\Delta \lambda_{\text{FET}}^{\text{EVM2}} = \lambda_{\text{FET}}^{\text{EVM}} - \lambda_{\text{FET}}^{\text{SCM}} = \frac{1}{1 + \frac{t_{\text{bio}}^{\text{flat}}}{t_{\text{ox}}^{\text{flat}}}} \left( \frac{1}{1 + \frac{t_{\text{bio}}^{\text{flat}}}{t_{\text{ox}}^{\text{flat}}}} + \frac{t_{\text{bio}}^{\text{flat}}}{t_{\text{ox}}^{\text{flat}}} \right) \lambda_S (4.18)
\]

where the surface charge is for example an oxide charge or a capture molecule charge. The induced charge upon biomolecule attachment is large for a sensor with a thin oxide layer, and a thick biomolecule layer, just like in the other models. The dependence on the value of \( t_{\text{bio}}^{\text{flat}} \) requires some further investigation. It was seen that the result of the EVM is almost independent
of the ion concentration. It was also seen that according to the SCM the induced charge decreases for increasing ion concentration. This suggests that the difference between the two increases for increasing ion concentrations.

Equation (4.18) can be rewritten to obtain

$$\Delta \lambda_{\text{FET}}^{\text{EVM}2} = -\frac{\lambda_S}{2/(\kappa_{b}^{\text{flat},\text{bio}}) + \pi_{\text{ox}}/\pi_{\text{bio}} + 1/(\kappa_{b}^{\text{flat}} \pi_{\text{ox}}^{\text{flat}} \pi_{\text{bio}}^{\text{flat}}) + 1/(\kappa_{b}^{\text{flat}} \pi_{\text{ox}}^{\text{flat}}) + 1},$$

(4.19)

which shows that for increasing $\kappa_{b}^{\text{flat}}$ the charge induced in the FET upon biomolecule attachment indeed increases. This time a large value of $\kappa_{b}^{\text{flat}}$ has a positive influence on the amount of charge induced in the FET upon biomolecule attachment! This is illustrated in figure 4.7. It can be explained by the increased ion concentration, which increases the charge density close to the sensor surface which is moved away by the biomolecules. This implies that the "problem" of a large ion concentration could be used as an advantage in biosensing. This can have large implications for sensor design.

![Figure 4.7: The charge per unit length induced in the flat FET upon biomolecule attachment in the Excluded Volume Model, $\Delta \lambda_{\text{FET}}^{\text{EVM}2} = \lambda_{\text{FET}}^{\text{EVM}} - \lambda_{\text{FET}}^{\text{SCM}}$, for $\Psi_c \ll 1$. For an ion concentration of 0.1 M the value of $\kappa_{b}^{\text{flat}}$ is 1250.](image)

It was seen in equation (4.18) that the dependence of $\Delta \lambda_{\text{FET}}^{\text{EVM}2}$ on the surface charge is linear. This means that when the sensor is charged with more surface charge, the presence of the volume of the biomolecules is detected more strongly. Therefore, one can increase the fixed surface charge on the surface for a good use of this excluded volume sensing mechanism.

To compare the effect of neutral biomolecules with a volume to that of charged biomolecules without a volume, the ratio of the above result and the result of the Surface Charge Model is considered,
This expression is similar to that of $\frac{\lambda_{EVM}^{\text{FET}}}{\lambda_{SCM}^{\text{FET}}}$ (equation (4.17)). Only a constant value of 1 has to be subtracted, and then all the results are applicable, and also figure 4.6 can be used to study the trends. It is seen that for large ion concentrations the effect of a neutral biomolecule layer is about 50 times larger than the effect of a surface charge. This implies that for biosensing, the effect of the volume of the biomolecules may have a large influence on sensing.

4.1.2 Large potentials

In the previous section it was shown that increasing the fixed surface charge, can enhance the properties of the biosensor when an excluded volume layer is included in the model. A large surface charge increases the potentials, and at some point the small potential approximation will no longer be valid. In this section the charge per unit length induced in the flat FET for the Excluded Volume Model will be derived under the assumption that the potentials in the system are large ($\Psi_c \gg 1$).

Applying the approximation $\Psi_c \gg 1$ to equation (4.10), we get

$$-\lambda_S \frac{1}{1 + \tau_{\text{bio}}^{\text{flat}}} + \lambda_S - \alpha \lambda_b^{\text{flat}} \exp \left(\frac{\Psi_c}{2}\right) = 0,$$

where the second term in equation (4.10) was neglected since $\exp(\Psi_c) \gg \Psi_c$. Solving the above equation for $\Psi_c$ yields

$$\Psi_c = 2 \ln \left[ \frac{\lambda_S}{\alpha \lambda_b^{\text{flat}}} \left( \frac{1}{1 + \tau_{\text{bio}}^{\text{flat}} / \tau_{\text{ox}}^{\text{flat}}} \right) \right],$$

which reduces to the result of the Surface Charge Model (equation (3.15)) in the limit $\tau_{\text{bio}}^{\text{flat}} = 0$. Inserting this result in equation (4.7) the charge induced in the FET per unit length is obtained

$$\lambda_{\text{FET}}^{\text{flat}} = -\frac{\lambda_S \tau_{\text{bio}}^{\text{flat}} / \tau_{\text{ox}}^{\text{flat}}}{\tau_{\text{bio}}^{\text{flat}} + \tau_{\text{ox}}^{\text{flat}}} - \frac{2\alpha}{\tau_{\text{bio}}^{\text{flat}} / \tau_{\text{ox}}^{\text{flat}}} \ln \left[ \frac{\lambda_S}{\alpha \lambda_b^{\text{flat}}} \left( \frac{1}{1 + \tau_{\text{bio}}^{\text{flat}} / \tau_{\text{ox}}^{\text{flat}}} \right) \right].$$

Just like in the case of small potentials the second term in this equation is much smaller than the first term. This is because in order for the large potential approximation to be valid the surface charge must be large. Since the first term has a linear dependence on this surface charge and the second
only a logarithmic dependence. Since the second term is negligible compared to the first, the influence of the ion concentration is small. The above expression can therefore be approximated by

\[
\lambda_{\text{FET}}^\text{flat} \approx -\frac{\lambda_S\tau_{\text{bio}}^\text{flat}}{\tau_{\text{bio}}^\text{flat} + \tau_{\text{ox}}^\text{flat}},
\]

which is the same as the result for the small potential in equation 4.15. The behavior of the charge in the flat FET for small potentials and large potentials is therefore the same as long as the surface charge is large. Note that without the effect of volume, or \(\tau_{\text{bio}} = 0\), the dependence on the surface charge was logarithmic in the large potential regime, as also shown by Nair [2]. We have found here that the effect of a volume layer gives a linear term.

In the first application of the model we have

\[
\Delta \lambda_{\text{FET}}^\text{EVM1,flat} = \Delta \lambda_{\text{FET}}^\text{EVM,flat} \\
\approx -\frac{\lambda_S\tau_{\text{bio}}^\text{flat}}{\tau_{\text{bio}}^\text{flat} + \tau_{\text{ox}}^\text{flat}}.
\]

It is seen that the result of the large potential approximation is similar to that of the small potential approximation, and its behavior will not be studied here. The above expression has to be compared to the result without the volume effect, the SCM, to obtain the error of not including the effect of volume. This SCM expression is different in the large potential approximation than in the small potential approximation. The SCM has a result that is linear in \(\lambda_S\) for small potentials and a result that has a logarithmic dependence on \(\lambda_S\) for large potentials. This error does therefore not have the same behavior in the large potential approximation as in the small approximation, and must be studied.

\[
\frac{\Delta \lambda_{\text{FET}}^\text{EVM1,flat}}{\Delta \lambda_{\text{FET}}^\text{SCM}} = \frac{\Delta \lambda_{\text{FET}}^\text{EVM,flat}}{\Delta \lambda_{\text{FET}}^\text{SCM}} \\
= \frac{\lambda_{\text{EVM}}}{\lambda_{\text{SCM}}} \\
= \frac{\tau_{\text{biot}}^\text{flat} + \tau_{\text{ox}}^\text{flat}}{2\alpha \hbar \frac{\lambda_S}{\alpha R_b^\text{flat}}} \left( \lambda_S \frac{\tau_{\text{bio}}^\text{flat} + \tau_{\text{ox}}^\text{flat}}{\tau_{\text{bio}}^\text{flat} + \tau_{\text{ox}}^\text{flat}} \left( \frac{1}{1 + \frac{1}{\tau_{\text{bio}}^\text{flat} / \tau_{\text{ox}}^\text{flat}}} \right) \right) \\
\approx \frac{\lambda_S \tau_{\text{bio}}^\text{flat} \tau_{\text{ox}}^\text{flat}}{(\tau_{\text{bio}}^\text{flat} + \tau_{\text{ox}}^\text{flat}) 2\alpha \hbar \frac{\lambda_S}{\alpha R_b^\text{flat}}}.
\]

In figure 4.8 (a.) the dependence of the result on \(\tau_{\text{bio}}^\text{flat}\) is shown. The dependence on the surface charge \(\lambda_S\) is given in figure 4.8 (b.) It is seen that in order for this approximation to be true, the surface charge has to be large, and the dependence of the ratio on the surface charge is dominated.
by the linear term on top. The factor can be varied by changing this value of the surface charge.

In the second application of the model the charge induced in the FET upon biomolecule attachment is

\[
\Delta \lambda_{\text{FET}}^{\text{EVM2, flat}} = \lambda_{\text{FET}}^{\text{EVM, flat}} - \lambda_{\text{FET}}^{\text{SCM, flat}} \\
\approx -\frac{\lambda_{\text{S}}^{\text{flat}}}{\tau_{\text{bio}}^{\text{flat}}} + \frac{2\alpha}{\tau_{\text{ox}}^{\text{flat}}} \ln \left(\frac{\lambda_{\text{S}}}{\alpha R_{b}^{\text{flat}}}\right). \tag{4.27}
\]

For an increasing ion concentration the second term becomes smaller. Therefore there is more negative charge induced in the FET upon biomolecule attachment if the ion concentration is large. So just like in the small potential regime, it is also beneficial to have a large ion concentration in the large potential regime.

To compare the charge that is induced in the FET by the attachment of neutral biomolecules to the charge induced by the attachment of charged biomolecules modelled as point charges, we need the ratio

\[
\frac{\Delta \lambda_{\text{FET}}^{\text{EVM2, flat}}}{\Delta \lambda_{\text{FET}}^{\text{SCM, flat}}} = \frac{\lambda_{\text{FET}}^{\text{EVM, flat}} - \lambda_{\text{FET}}^{\text{SCM, flat}}}{\lambda_{\text{FET}}^{\text{SCM, flat}} - 1}. \tag{4.28}
\]

This is again almost the same as equation 4.26. It is seen that the effect of an excluded volume layer can be much larger than the effect of a surface charge, and can be tuned by varying the surface charge.

\[\text{Figure 4.8: The ratio of the charge induced in the flat FET, } \lambda_{\text{FET}}^{\text{flat}}, \text{ upon attachment of a surface charge and a volume layer, and the charge induced in the flat FET upon attachment of only a surface charge layer, in the approximation } \Psi_{c} \gg 1. (a.) \text{ The result is plotted as a function of the relative biomolecule layer thickness, } \tau_{\text{bio}}^{\text{flat}}. (b.) \text{ The result is plotted as a function of the thickness of the surface charge, } \lambda_{\text{S}}. \text{ Note that the surface charge is taken to be 100 times larger than before, since this way the potential is large and the condition } \Psi_{c} \gg 1 \text{ is satisfied. The values of the other variables are as stated in the table at the end of chapter 2.}\]
4.1.3 Comparing the small and the large potential regime

In Figure 4.9 the numerical result and the result of both approximations $\Psi_c \ll 1$ and $\Psi_c \gg 1$ are shown as a function of $\lambda_S$. The dependence was shown to be approximately linear, but it is shown on a log scale here to show the whole range of possible values of the surface charge and thus the potential $\Psi_c$. It is seen that for realistic values of the physical parameters both approximations give the same result. Only for very thin biomolecule layers do the two approximations give different results.

This implies that for the applications of interest, in the EVM we do not have to distinguish between the regime where $\Psi_c \ll 1$ and $\Psi_c \gg 1$. For the results of the SCM, however, the behavior is different in the $\Psi_b \ll 1$ and $\Psi_b \gg 1$ regime. Therefore, when comparing the results of the EVM to the results of the SCM we have to distinguish between two regimes, namely $\Psi_b \ll 1$ and $\Psi_b \gg 1$.

**Figure 4.9:** The numerical result of the charge induced in the flat FET sensor, $\lambda_{\text{FET}}$ (green line), as a function of the charge on its surface, $\lambda_S$, and the analytical results using the approximations $\Psi \ll 1$ (black dots) and $\Psi \gg 1$ (black dashed line), for two values of the biomolecule layer thickness. Thickness of the biomolecule layer 2 nm (left), and 0.1 nm (right).

In general it was seen that including the effect of volume in the model, thereby modelling the biomolecules as a surface charge and a volume instead of a surface charge only, increases the charge induced in the FET upon attachment of biomolecules drastically.

The first application of the model is assuming that both the surface charge and the volume layer are not present before biomolecule attachment, and are present after biomolecule attachment. When comparing this with the SCM in which no volume effect was included we found the following (EVM1). In the small potential approximation the charge induced in the FET upon biomolecule attachment is about 50 times larger in a model in which the biomolecules are modelled as a surface charge and a surface volume layer than in a model in which the biomolecule is described as a surface charge.
charge only. In the large potential approximation it was shown that the ratio of the results of the two models was dependent on the surface charge. For larger biomolecule surface charge the difference between the two models is larger. The error of ignoring the volume of the biomolecule when calculating the effect of attachment of biomolecules on the sensor can therefore be very large.

The second application of the model assumes that the biomolecules are neutral. In this model the surface charge is already present before biomolecule attachment, and after biomolecule attachment both the surface charge, and the surface volume layer are present. It was seen that in the small potential regime the effect of volume only was 50 times larger than the effect of surface charge only, irrespective of the value of the surface charge. In the large potential regime the difference is even larger, and the ratio is dependent on the value of the surface charge. The effect of a volume surface layer is therefore tunable by tuning the surface charge of the sensor before biomolecule attachment.

4.2 The Excluded Volume Model for the cylindrical sensor

![Figure 4.10](image)

In this section the charge induced in the cylindrical FET is derived when both a surface charge and a dense biomolecule layer are located on the sensor surface (see figure 4.10).

As for the flat sensor, a relation between the potential at the position $b$ and at position $c$ is necessary. This is obtained by first finding the electric field in the biomolecule layer with the use of a Gaussian surface in the biomolecule layer, and integrating from $b$ to $c$. This yields the relation between the two potentials,
\[ V_c - V_b = -\frac{\lambda_{\text{FET}} + \lambda_S}{2\pi \epsilon_0 \epsilon_{r,\text{bio}}/\ln \left(\frac{c}{b}\right)}, \]  
(4.29)

or

\[ \Psi_c - \Psi_b = -\frac{e}{k_B T} \frac{\lambda_{\text{FET}} + \lambda_S}{2\pi \epsilon_0 \epsilon_{r,\text{bio}}/\ln \left(\frac{c}{b}\right)} \cdot \]  
(4.30)

The relation between the charge induced in the FET and the surface potential is given by the capacitance (equation (2.9)), inverting this relation we obtain

\[ \Psi_b = \frac{\lambda_{\text{FET}}^\text{cyl}}{2\pi \alpha C_{\text{cyl}}} \frac{e}{k_B T}. \]  
(4.31)

Inserting this into equation (4.30) and solving for \( \lambda_{\text{FET}}^\text{cyl} \) the following result is obtained for the charge induced in the FET as a function of the potential at position \( c \):

\[ \lambda_{\text{FET}}^\text{cyl} = -\frac{\lambda_S + \frac{k_B T}{e} \Psi_c}{\frac{\epsilon_0 \epsilon_{r,\text{bio}}}{-\alpha C_{\text{cyl}} \ln(c/b)} + 1} \]
\[ = -\frac{\lambda_S + \alpha/\tau_{\text{bio}}^\text{cyl} \Psi_c}{1 + \tau_{\text{bio}}^\text{cyl}/\tau_{\text{bio}}}, \]  
(4.32)

where

\[ \tau_{\text{bio}}^\text{cyl} = \frac{\ln \left(\frac{c}{b}\right)}{\epsilon_{r,\text{bio}}}, \]  
(4.33)

and \( \alpha \) and \( \tau_{\text{bio}}^\text{cyl} \) are defined in equations (3.6) (3.22).

The expression for the charge in the double layer is given in equation (2.26). Multiplying by the circumference, \( 2\pi c \), and noting that the double layer interface potential, \( \Psi_0 \), is \( \Psi_c \) here, and that the radius of the cylindrical potential, \( R \), is \( c \), we obtain the charge in the double layer per unit length of the FET

\[ \lambda_{\text{DL}} = -2\alpha \kappa_c^\text{flat} \sinh \left(\frac{\Psi_c}{2}\right) \left[ 1 + \frac{(\gamma(\kappa c))^{-2} - 1}{\cosh^2 \left(\frac{\Psi_c}{4}\right)} \right]^{1/2}. \]  
(4.34)

Putting this together with equation (4.1) we obtain the equation that needs to be solved for \( \Psi_c \) in order to obtain an expression for \( \lambda_{\text{FET}}^\text{cyl} \):

\[ -\frac{\lambda_S + \alpha/\tau_{\text{bio}}^\text{cyl} \Psi_c}{1 + \tau_{\text{bio}}^\text{cyl}/\tau_{\text{bio}}} + \lambda_S - 2\alpha \kappa_c^\text{flat} \sinh \left(\frac{\Psi_c}{2}\right) \left[ 1 + \frac{(\gamma(\kappa c))^{-2} - 1}{\cosh^2 \left(\frac{\Psi_c}{4}\right)} \right]^{1/2} = 0. \]  
(4.35)
In Figure 4.11, the numerical solution of the above equation is shown as a function of the surface charge for two different thicknesses of the biomolecule layer. It is seen that, if the surface charge is due to the charge of the attached biomolecules, it is reasonable to assume $\Psi_c \ll 1$. If other charges are present on the sensor surface, or when the FET is not grounded, the potential can be much larger. Therefore the results for the approximation $\Psi_c \gg 1$ are also given.

**Figure 4.11:** The numerical solution of equation (4.35) is given as a function of the surface charge for different values of the biolayer thickness. It is seen that $\Psi_c$ stays well below zero. The values of the other variables are chosen such that they are realistic for biosensing (see table at the end of chapter 2).

### 4.2.1 Small potentials

Assuming $\Psi_c \ll 1$, equation (4.35) becomes

$$-rac{\lambda_S}{1 + \frac{\lambda_c}{\lambda_{\text{ox}}}} + \lambda_S - \frac{\lambda_c}{\lambda_{\text{ox}}} = 0,$$

with

$$\lambda_c = \frac{\tau_{\text{flat}}}{\gamma(\kappa_c)}.$$  

(4.37)

This equation has exactly the same form as the equation for the flat geometry (equation (4.11)). The calculations are therefore also the same, and yield the charge per unit length induced in the FET

$$\lambda_{\text{FET}} = -\frac{\lambda_S}{1 + \frac{\lambda_c}{\lambda_{\text{ox}}}} \left(1 + \frac{\lambda_c}{\lambda_{\text{ox}}} \frac{\tau_{\text{ox}}/\tau_{\text{bio}}}{1 + \frac{\lambda_{\text{ox}}}{\lambda_{\text{bio}}}}\right),$$

(4.38)

or

$$\lambda_{\text{FET}} = -\frac{\lambda_S}{1 + \frac{\lambda_{\text{ox}}}{\lambda_{\text{bio}}} \left(1 + \frac{\lambda_{\text{ox}}}{\lambda_{\text{bio}}} \frac{\tau_{\text{ox}}/\tau_{\text{bio}}}{1 + 1/(\frac{\lambda_{\text{ox}}}{\lambda_{\text{bio}}} + \frac{\lambda_{\text{ox}}}{\lambda_{\text{bio}}})}\right)\lambda_S.}$$

(4.39)
The dependence on the variables is the same as for the flat case, only the variables themselves are different. Also in this case the order of magnitude of the variables is such that the second term in brackets is small compared to the first term. The difference between the cylindrical results and the flat results will be discussed in section 4.3.

Since the values of the variables are not the same, some results are given here. For a cylindrical FET with standard surface charge, the charge in the FET in the EVM with a layer thickness of 10 nm is 93 times larger than the charge in the FET in the SCM. The charge in the FET in the EVM with a layer thickness of 2 nm is 50 times larger than the charge in the FET in the SCM. The charge in the FET in the EVM with a layer thickness of 0.91 nm is 30 times larger than the charge in the FET in the SCM.

4.2.2 Large potentials

In the approximation $\Psi_c \gg 1$ equation (4.35) becomes

$$\frac{\lambda_S}{1 + \tau_{\text{cyl}} / \tau_{\text{bio}}} + \lambda_S = 0 - \alpha \kappa_{\text{cyl}} \exp \left( \frac{\Psi_c}{2} \right) ,$$

which has the same form as equation (4.21). The same calculations can be done, and all the results are the same as those in subsection 4.1.2. Also when comparing the small and the large potential regime, the results of subsection 4.1.3 can be used. The difference is only due to the fact that the variables have different values, and different dependencies on the physical variables. The charge per unit length in the FET is

$$\lambda_{\text{FET}}^{\text{cyl}} = - \frac{\lambda_S \tau_{\text{bio}}^{\text{cyl}}}{\tau_{\text{bio}}^{\text{cyl}} + \tau_{\text{bio}}^{\text{cyl}}} - \frac{2 \alpha}{\tau_{\text{bio}}^{\text{cyl}} + \tau_{\text{bio}}^{\text{cyl}}} \ln \left[ \frac{\lambda_S}{\alpha \kappa_{\text{cyl}}^{\text{flat}} \left( \frac{1}{1 + \tau_{\text{bio}}^{\text{cyl}} / \tau_{\text{bio}}^{\text{cyl}}} \right)} \right] .$$

In figure 4.12 the result of this approximation is shown together with the result of the small potential approximation and the numerical result. Is is shown that, just like in the flat geometry, the result of the small and the large potential approximation are very similar. The difference in the results of the flat and the cylindrical FET are discussed in section 4.3.

4.3 Comparing the excluded volume effects in the flat and the cylindrical geometry

The dependence of the induced charges on the system parameters, $\tau_{\text{bio}}^{\text{cyl}}$ and $\kappa_{\text{cyl}}^{\text{flat}}$, and the variables, $\lambda_S$ and $\tau_{\text{bio}}^{\text{cyl}}$, is the same for the flat as for the cylindrical geometry, both for the small potential regime (equations (4.13), (4.38)) as for the large potential regime (equations (4.23) and (4.41)). The difference is only due to the fact that these parameters and variables have
a different dependence on the physical quantities, and therefore a different value.

For the first application a plot of the charge induced in the flat and in the cylindrical FET is given in figure 4.13(a.) as a function of the surface charge, and in figure 4.13(b.) as a function of the biomolecule layer thickness. It is seen that more charge is induced in the flat FET than in the cylindrical FET.

In figure 4.13(c.) the ratio of the EVM and the SCM result is shown as a function of the biomolecule layer thickness $t_{\text{bio}}/b$. The effect of the excluded volume is seen to be large. Already for a small biomolecule layer thickness the induced charge in the FET is many times larger when a biomolecule layer is present on top of the surface charge than when there is only a surface charge present. For both geometries this effect is substantial. It is seen that the error in considering only the charge, instead of considering a charge and a dense biomolecule layer, is larger in the cylindrical than in the flat geometry.

For the second application the difference with the model without the volume is considered. In figure 4.13(d.) this difference is plotted again as a function of $t_{\text{bio}}/b$. It is seen that the cylindrical geometry is more sensitive to the presence of a surface layer.

It should be noted that setting the thickness of the biomolecule layers equal in the two geometries implies excluding more volume in the cylindrical geometry. Therefore a comparison was made in which the excluded volume was the same, and the layer thickness differs. For the flat geometry 29 times more charge was induced in the FET in the Excluded Volume Model with a layer thickness of 0.94 nm than for the Surface Charge Model. In the cylindrical geometry with a layer thickness of 0.91 nm this factor was shown...
to be 30. This is still more than in the flat geometry. It can be concluded that omitting the effect of the volume leads to a slightly larger error in the cylindrical case. It was seen before that screening had more effect in the cylindrical geometry than in the flat geometry. The fact that the cylindrical geometry is more sensitive to the volume effect, or that it is more sensitive to the effect of removal of screening, is therefore an intuitive result.

The above results were obtained for the small potential regime, since for realistic values of the surface charge, the sensor operates in this regime. The results for the large potential regime are similar, but all the values, fractions and differences are larger.

In this chapter it was seen that the dense biomolecule has a strong effect on the induced charge in the FET, both for the flat and the cylindrical sensor. The excluded volume could therefore very well be a sensing mechanism in biosensing. It should be noted, that the biomolecule layer will not be completely dense in reality. Some ions will be present in the layer, and also the dielectric constant is likely to be somewhat larger than the dielectric constant of the biomolecules. Further research is necessary to investigate the charge induced in the FET when the biomolecule volume only partially occupies the surface layer. A model of a uniform partial excluded volume layer will be discussed in the next chapter.
Figure 4.13: The charge induced in the cylindrical FET sensor (red line), and in the flat sensor (green line) as a function of the charge on the FET surface, $\lambda_S$, and the biomolecule layer thickness $t_{bio}/b$. The values of the variables are taken to be the standard values given at the end of chapter 2.
Chapter 5

The Partially Excluded Volume Model

In the previous chapter the volume of the biomolecules was included in the calculations as a dense layer. In a thin layer on top of the sensor surface the electrolyte was completely replaced by biomolecules, removing the presence of ions and changing the dielectric constant in that region to the value of the dielectric constant of the biomolecules. The picture sketched is a somewhat extreme situation, since the density of attached biomolecules depends on the concentration of ions in the solution. Also between the biomolecules some space needs to be present to allow attachment in the first place. Therefore another model is presented in this chapter, in which the volume of the biomolecules is taken into account by considering a surface layer on the sensor in which only a fraction of the volume is occupied by the biomolecules (see figure 5.1). In this surface layer only a fraction of the ions is pushed away by the biomolecules, and the dielectric constant is replaced by a new dielectric constant, $\varepsilon_{r,\text{new}}$. This new dielectric constant will be taken to be a combination of the dielectric constant of the electrolyte, $\varepsilon_{r,\text{w}}$, and the dielectric constant of the biomolecules, $\varepsilon_{r,\text{bio}}$. This model is called the Partially Excluded Volume Model (PEVM).

In this system there are four charges we need to take into account. The charge in the FET, $\sigma_{\text{FET}}$, the surface charge, $\sigma_{\text{S}}$, the ionic charge in the biomolecule surface layer, $\sigma_{\text{DL,I}}$, and the charge in the electrolyte solution, $\sigma_{\text{DL,II}}$. The charge neutrality condition now is

$$\sigma_{\text{FET}} + \sigma_{\text{S}} + \sigma_{\text{DL,I}} + \sigma_{\text{DL,II}} = 0.$$  (5.1)

The expressions for most of these charges were already derived in chapter 2, only the expression for the charge in the surface layer was not derived yet. For the flat sensor this will be derived in this chapter, and the results will be calculated numerically. The cylindrical results will be derived using a finite element computer simulations (COMSOL).
Figure 5.1: The biomolecules exclude the electrolyte from part of the volume in the surface layer. In the Partially Excluded Volume Model this is modelled by a surface layer with adjusted dielectric constant and ion concentration.

5.1 The partially Excluded Volume Model for the flat sensor

The flat sensor is shown in figure 5.2. Region I is the surface layer in which a fraction of the volume is occupied by the biomolecules, and the remaining volume by the electrolyte. Region II is taken as an electrolyte only region, in which the biomolecule concentration can be neglected. The part of the volume that is occupied by the biomolecules contains no ions and has a dielectric constant $\varepsilon_{\text{r,\,bio}}$. The part of the surface layer that is occupied by the electrolyte has dielectric constant $\varepsilon_{\text{r,\,w}}$, and has the same ion concentration as the bulk electrolyte, only altered by the local potential.

Figure 5.2: The flat biosensor in the Partially Excluded Volume Model. In the surface layer part of the volume is occupied by biomolecules and part by the electrolyte.

To be able to model this layer as a uniform surface layer a new dielectric constant, $\varepsilon_{\text{r,\,new}}$, is used, which can be calculated using the values of $\varepsilon_{\text{r,\,bio}}$ and $\varepsilon_{\text{r,\,w}}$ (equation (2.1) or (2.2)). Furthermore the discrete nature of the ion
concentration is removed by taking a new uniform charge density, $\rho_{\text{new}}(\Psi)$, which is only a part of the charge that would be present if the biomolecules did not exclude a certain fraction, $f$, of the volume $\rho_{\text{new}}(\Psi) = (1 - f)\rho(\Psi)$. The dependence of the charge density on the ion concentration in the bulk electrolyte, $I_0$, is

$$\rho_{\text{new}}(\Psi) = (1 - f)eI_0(\exp[-\Psi] - \exp[+\Psi]). \quad (5.2)$$

The charge density has a linear dependence on the ion concentration in the bulk. Taking only a certain fraction of the charge density, can be modelled as taking only a fraction of the ion concentration in the bulk, $I_{0,\text{new}} = (1 - f)I_0$. The inverse Debye screening length in region I of the model, $\kappa_I$, is therefore adapted in order to take this excluded volume effect into account, by taking a both a new dielectric constant and a new ion concentration.

The charge of the ions in both region I and II can be found by taking a Gaussian surface enclosing both the biomolecule surface layer and the double layer in the electrolyte

$$\sigma_{\text{DL},I} + \sigma_{\text{DL},II} = \epsilon c_{r,\text{new}} k_B T \frac{d\Psi^1(b^+)}{dx}, \quad (5.3)$$

with $\sigma_{\text{DL},I}$ and $\sigma_{\text{DL},II}$ the surface charge per unit area of FET device in region I and region II respectively, and $\Psi^1(x)$ the potential in region I. This gives the amount of charge in these two layers as a function of the electric field just at the outside of the sensor surface. The above expression shows that the PEVM introduces an additional variable to the charge neutrality condition (5.1). To find the derivative of the potential at position $b$ in terms of the potential at position $b$ and the potential at position $c$, we consider the Poisson-Boltzmann equation that specifies the potential in region I,

$$\frac{d^2\Psi^1(x)}{dx^2} = \kappa_I^2 \sinh\left(\Psi^1(x)\right). \quad (5.4)$$

The left hand side can be rewritten to obtain

$$\frac{1}{2} \frac{d}{d\Psi} \left(\frac{d\Psi^1(x)}{dx}\right)^2 = \kappa_I^2 \sinh\left(\Psi^1(x)\right). \quad (5.5)$$

By integrating both sides over $\Psi^1$ from $\Psi^1(x)$ to $\Psi^1(c)$ we obtain

$$\left(\frac{d\Psi^1}{dx}(c^-)\right)^2 - \left(\frac{d\Psi^1}{dx}(x)\right)^2 = 2\kappa_I^2(\cosh(\Psi^1(c^-)) - \cosh(\Psi^1(x))). \quad (5.6)$$

This can be solved for $d\Psi^1(x)/dx$ to get

$$\frac{d\Psi^1}{dx}(x) = \pm \sqrt{-2\kappa_I^2(\cosh(\Psi^1(c^-)) - \cosh(\Psi^1(x))) + \left(\frac{d\Psi^1}{dx}(c^-)\right)^2}. \quad (5.7)$$
At position \( c \) there is no surface charge present, so the electric fields in region I and II are related the following way

\[
\frac{d\Psi^I}{dx}(c^-) = \frac{\epsilon_{r,w}}{\epsilon_{r,\text{new}}} \frac{d\Psi^{II}}{dx}(c^+).
\]

(5.8)

We also know that

\[
\frac{d\Psi^{II}}{dx}(c^+) = -2\kappa_{II} \sinh \left( \frac{\Psi_c}{2} \right),
\]

(5.9)

since the result for the double layer charge from chapter 2 is valid in region II (see equation (2.18)). Combining equations (5.7), (5.8), and (5.9) we obtain

\[
\frac{d\Psi^I}{dx}(x) = \pm \sqrt{-2\kappa_I^2(\cosh(\Psi_c) - \cosh(\Psi(x))) + \left( \frac{2\kappa_{II}\epsilon_{r,w}}{\kappa_I \epsilon_{r,\text{new}}} \right)^2 \sinh^2 \left( \frac{\Psi_c}{2} \right)}
\]

\[
= \pm 2\kappa_I \sqrt{\sinh^2 \left( \frac{\Psi(x)}{2} \right) + \left( \frac{\kappa_{II}\epsilon_{r,w}}{\kappa_I \epsilon_{r,\text{new}}} \right)^2 - 1} \sinh^2 \left( \frac{\Psi_c}{2} \right)
\]

\[
= \pm 2\kappa_I \sqrt{\sinh^2 \left( \frac{\Psi(x)}{2} \right) + C},
\]

(5.10)

where

\[
C = C(\Psi_c) = \left( \frac{\kappa_{II}\epsilon_{r,w}}{\kappa_I \epsilon_{r,\text{new}}} \right)^2 - 1 \sinh^2 \left( \frac{\Psi_c}{2} \right).
\]

(5.11)

Choosing \( x = b \) and substituting the result of equation (5.10) into equation (5.3) we obtain an expression which is only dependent on the potentials at positions \( b \) and \( c \),

\[
\sigma_{DL,1} + \sigma_{DL,II} = (-\text{sgn} \Psi_b) \frac{2\epsilon_{r,\text{new}} k_B T \kappa_I}{e} \sqrt{\sinh^2 \left( \frac{\Psi_b}{2} \right) + C(\Psi_c)}.
\]

(5.12)

In the above equation the sign has been fixed. Since we know that the potential in the bulk of the electrolyte is zero, the charges with sign opposite to that of the potential, \( \Psi_b \), will flow towards the sensor. Therefore the total net charge in the double layer, \( \sigma_{DL,1} + \sigma_{DL,II} \), must have a sign opposite to that of \( \Psi_b \). This has been indicated with \(-\text{sgn} \Psi_b\). Throughout this thesis the potential is positive, since the surface charge was taken to be positive, therefore the negative sign is appropriate here. It can be seen that for \( f = 0 \), or \( \kappa_I\epsilon_{r,\text{new}} = \kappa_{II}\epsilon_{r,w} \), the above result becomes equal to the result of the charge in the double layer without an excluded volume (equation 3.3).
It can also be shown that in the limit $\kappa_1 = 0$, or $f = 1$, the result for the excluded volume model is retrieved (equation (4.9)).

Equation (5.12) is dependent on both $\Psi_b$ and $\Psi_c$. Therefore also equation (5.1) is dependent on both $\Psi_b$ and $\Psi_c$

$$\sigma_{\text{FET}}(\Psi_b) + \sigma_S + (\sigma_{\text{DL},1} + \sigma_{\text{DL},2})(\Psi_b, \Psi_c) = 0. \quad (5.13)$$

In order to solve the problem, a relationship between $\Psi_b$ and $\Psi_c$ has to be derived. This can be obtained by rewriting equation (5.10), and performing the integration

$$\int_b^c dx = (-\text{sgn} \Psi_b) \int_{\Psi_b}^{\Psi_c} \frac{d\Psi}{2\kappa_1 \sqrt{\sinh^2 \left( \frac{\Psi}{2} \right) + C}}, \quad (5.14)$$

which is equal to

$$c - b = \frac{1}{(-\text{sgn} \Psi_b)2\kappa_1 \sqrt{C}} \int_{\Psi_b}^{\Psi_c} \frac{d\Psi}{\sqrt{1 - \frac{1}{C} \sinh^2 \left( \frac{\Psi}{2} \right)}} \quad (5.15)$$

This equation provides the relation between $\Psi_b$ and $\Psi_c$. Recall that the constant $C$ also depends on $\Psi_c$.

Using this result, for a given value of $\Psi_b$, the corresponding value of $\Psi_c$ can be found numerically. The values of $\Psi_b$ and $\Psi_c$ can be used together with equation (5.12), to find the total net double layer charge for that specific value of $\Psi_b$. Doing this for many values of $\Psi_b$, a plot can be made of the total double layer charge as a function of $\Psi_b$, this is shown in figure 5.3. Plotting $-\sigma_{\text{FET}}(\Psi_b) - \sigma_S$ in the same figure, the intersection tells us what the solution is, or for what value of $\sigma_{\text{FET}}$ the equation

$$\sigma_{\text{DL},1} + \sigma_{\text{DL},2} = -(\sigma_{\text{FET}} + \sigma_S) \quad (5.16)$$

is satisfied (equation (5.1)). The surface charge is multiplied with $2\pi b$ in order to get the surface charge per unit length of the device, which is the quantity shown in the plot.

This is a cumbersome method, and the results will be analyzed further with the use of elliptic functions. The elliptic integral of the first kind is defined as

$$F(\theta, m) \equiv \int_0^\theta \frac{d\alpha}{\sqrt{1 - m \sin^2 \alpha}} = u, \quad (5.17)$$

and its inverse is the Jacobian Amplitude

$$Am(u, m) = \theta. \quad (5.18)$$
Figure 5.3: The solid line indicates the charge of the ions both in region I and in region II of the flat FET, $\lambda_{DL,1} + \lambda_{DL,II}$, as a function of the sensor surface potential, $\Psi_b$. The dashed line shows the negative of the charge induced in the FET and the charge on the surface, $-\lambda_{FET}(\Psi_b) - \lambda_S$. The intersection shows the solution of the problem.

To rewrite equation (5.15) in terms of elliptic integrals a few steps have to be made. We start by defining the following function

$$G(\phi, m) \equiv \int_0^\phi \frac{d\mu}{\sqrt{1 + m \sinh^2 \mu}},$$

which obeys the following relation

$$G(\phi, m) = \frac{1}{m} G \left( \frac{1}{m} \right),$$

with $\theta = \text{arcsinh}(\sqrt{m} \sinh \phi)$. If the value of $m$ is larger than one, this relation can be used to obtain the same function where the prefactor of the square of the hyperbolic sine is smaller than 1. Once a function with a prefactor smaller than one is obtained the following relation can be proven

$$G(\phi, m) = F(\theta, 1 - m),$$

where $\theta = \text{arctan}(\sinh \phi)$, and $m < 1$ (see appendix B).

Taking a function $G(\phi, m)$, with $m > 1$, and using the two above equations we obtain

$$G(\phi, m) = \frac{1}{\sqrt{m}} F \left( \text{arctan}(\sqrt{m} \sinh \phi), 1 - \frac{1}{m} \right).$$

With this relation equation (5.15) can be rewritten in terms of Elliptic integrals if $C < 1$. This is true for the physical variables that are realistic for biosensing. For $C > 1$ equation (5.21) can be used immediately.
\[ c - b = \frac{1}{-(\text{sgn} \psi_b)\kappa_1 \sqrt{C}} \left( G \left( \frac{\psi_c}{2}, \frac{1}{C} \right) - G \left( \frac{\psi_b}{2}, \frac{1}{C} \right) \right) \]
\[ = \frac{1}{-(\text{sgn} \psi_b)\kappa_1} \left[ F \left( \arctan \left( \frac{1}{\sqrt{C}} \sinh \left( \frac{\psi_c}{2} \right) \right), 1 - C \right) \right. \]
\[ - F \left( \arctan \left( \frac{1}{\sqrt{C}} \sinh \left( \frac{\psi_b}{2} \right) \right), 1 - C \right] \]. \tag{5.23} \]

This can be inverted with the use of the Jacobian amplitude to obtain the relation between \( \psi_b \) and \( \psi_c \):

\[ \psi_b = 2 \arcsinh \left( \sqrt{C} \tan \left[ \text{Am} \left\{ F \left( \arctan \left( \frac{1}{\sqrt{C}} \sinh \left( \frac{\psi_c}{2} \right) \right), 1 - C \right) \right. \right. \]
\[ + (c - b)(\text{sgn} \psi_b)\kappa_1, 1 - C \left. \right\} \right) \]. \tag{5.24} \]

Using this relation we can eliminate \( \psi_b \) from equation (5.13). This yields an equation with only one unknown, and the problem can be solved. So the above result combined with the results for \( \sigma_{\text{FET}}(\psi_b) \) (equation (2.9)), \( (\sigma_{\text{DL,1}} + \sigma_{\text{DL,II}})(\psi_b, \psi_c) \) (equation (5.12)), the value of the surface charge, \( \sigma_S \), and equation (5.13), can be used to calculate the value of \( \sigma_{\text{FET}} \) numerically.

In figure 5.4 the numerical solution of the charge in the FET is given as a function of the excluded volume fraction, \( f \). To be able to compare the charge induced in the flat FET with that induced in the cylindrical FET, the results are multiplied with \( 2\pi b \) to obtain the charges per unit length of the device. For \( f = 0 \) the figures show the result when the volume of the biomolecules has not been taken into account, which yields the result of the SCM. For \( f = 1 \) the surface layer is a dense layer, here the figure shows the result of the EVM.

Figure 5.4 (a.) shows two different lines. The bottom line shows the result in case the biomolecules lie flat down on the surface. The surface layer thickness is the diameter of the biomolecules, which was taken to be 2 nm. The dielectric constant of the surface layer changes with \( f \) according to equation (2.2). The top line in figure 5.4 shows the results assuming that the biomolecules are oriented perpendicular to the sensor surface. The influenced surface layer thickness is the length of the biomolecules, which was assumed to be 10 nm. Here equation (2.1) is used to find the dielectric constant.

The dependence on \( f \) is different for the two biomolecule orientations. This is caused by the fact that the dielectric constant has a different dependence on \( f \) for the two orientations (see figure 2.11). Since \( \kappa_1 \) is dependent on the dielectric constant, also this parameter has a different dependence...
on \( f \) for the two orientations. It is seen that for both orientations for large excluded volume fractions, \( f \), the charge induced in the FET changes very rapidly. Such large values of \( f \) are not realistic, however. For smaller values of \( f \) the induced charge changes more rapidly with \( f \) when the molecules lie flat on the surface. It should be noted that in addition to this effect, also the value of \( f \) is different for the two orientations. When the biomolecules are oriented flat on the sensor surface the value of \( f \) was shown to be about 0.5. In case the biomolecules are positioned straight on the sensor surface the value is about \( f = 0.1 \). This increases the difference in the charge induced in the FET for the two orientations even more.

![Figure 5.4](image)

**Figure 5.4:** (a.) The dependence of the induced charge per unit length in the FET in the case the biomolecules lie flat on the sensor surface (bottom line, \( t_{\text{bio}} = 2 \text{ nm} \)) and in the case the biomolecules stand straight on the surface (top line, \( t_{\text{bio}} = 10 \text{ nm} \)), for different surface layer thicknesses. (b.) The ratio of this result and the SCM result.

There are different applications of this result. In the first application (PEVM1) we want to find what the error is of modelling the biomolecule as a surface charge, ignoring any effects of volume. The expression of interest is

\[
\frac{\Delta \lambda_{\text{PEVM}}^{\text{FET}}}{\Delta \lambda_{\text{SCM}}^{\text{FET}}} = \frac{\lambda_{\text{PEVM}}^{\text{FET}}}{\lambda_{\text{SCM}}^{\text{FET}}}. \tag{5.25}
\]

Note that the result of the SCM is independent of volume, so independent of the surface layer thickness, or the excluded volume fraction.

In figure 5.4 (b.) again both the result assuming the biomolecules are oriented flat on the sensor surface (line at the top), and that assuming the biomolecules stand up straight (line at the bottom) are shown. There are two different points to distinguish in this figure.

The first point of interest lies on the bottom line, corresponding to the straight orientation, and \( f = 0.1 \). The induced charge per unit length of device is 1.1 times than that of a model without volume taken into account (or \( f = 0 \)). The second point lies on the curve on top corresponding to the flat orientation, and \( f = 0.5 \). For this value of the excluded volume fraction the induced charge per unit length in this model is 5.6 times that of the model where the effect of volume was not taken into account.
Not taking into account the effect of volume gives an underestimation of the induced charge, which is larger if the biomolecules lie flat on the sensor surface than when they stand straight. It is expected that in reality the orientation is not flat or straight, but somewhere in between. The result is therefore also expected also to be in between the results of the two orientations.

In the second application (PEVM2) we compare the result of modelling the biomolecule as a surface charge only, with the result of modelling it as a volume only. The expression of interest is

\[
\frac{\Delta \lambda_{\text{PEVM2}}}{\Delta \lambda_{\text{FET}}} = \frac{\lambda_{\text{PEVM}}}{\lambda_{\text{SCM}}} - 1.
\]  

This is the same expression as for the first application, only with a value of 1 subtracted. It is seen that the induced charge in the PEVM in the second interpretation is 4.6 and 0.1 times that of the SCM, for the case the biomolecules lie flat and stand up straight respectively. It should be noted, however, that these results were derived when the device was not especially designed for volume detection. When the surface charge is increased in order to increase the influence of the volume of the biomolecules, this factor becomes larger. This way the sensor can be designed to be more sensitive to the presence of a surface charge layer.

The dependence on the biomolecule layer thickness is shown in figure 5.5. The value of the charge induced in the FET is shown at different values of the excluded volume fraction. It is seen that the influence of the biolayer thickness is large for small biolayer thicknesses. For larger biolayer thicknesses the value of the induced charge in the FET stabilizes. Both in the case that the biomolecules lie down and in the case the biomolecules stand up straight, the value of the biolayer thickness is in this stabilized regime for a realistic biolayer thickness (10 nm for top line, 2 nm for bottom line).

This can be understood as follows. If all the fields are screened within the surface layer, then there are no fields present in the electrolyte solution (region II). The charge density of the electrolyte is zero in the regions where there are no fields present. Therefore, replacing part of the electrolyte in this region with neutral biomolecules does not change the charge density in this region. Also the change in the dielectric constant of this region does influence the problem since no fields are present in this region. Extending the thickness of the biomolecule surface layer in this case therefore has no influence on the charge induced in the FET.
The distance from the sensor surface at which all the fields are screened is characterized by the screening length in that layer. This is the screening length, \( \kappa^{-1} \), with an adjusted ion concentration and dielectric constant. In case the biomolecules are oriented parallel to the sensor surface his length is about 0.3 nm. When the biomolecules are oriented perpendicular to the sensor surface this is about 1 nm. At distances larger than this adjusted screening length, the value of the induced charge in the FET is the same as the value of the charge induced in the FET for infinite layer thickness. It can be concluded that the results of the PEVM are then the same as the result of the SCM, with adjusted dielectric constant and adjusted ion concentration. This means that the less complex, and more insightful formulas of chapter 3 can be used to describe partial occupation of the surface layer by the biomolecules.

The fact that the system is in the stable regime also means that there is no difference in the sensitivity of the sensor to a biomolecule with dimensions as discussed here and a biomolecule that is twice as long. A biomolecule with a larger diameter, one that lies flat on the sensor surface or one that is curled up, will give a larger excluded volume fraction and therefore a larger sensitivity. In order to increase the ease of detection of a certain biomolecule therefore one could try to attach additional groups to the biomolecule of interest that increase the volume of the biomolecule, or influence the orientation of the biomolecule.

**Figure 5.5:** The charge induced in the FET in the PEVM as a function of the surface layer thickness. The bottom line gives the result for an excluded volume fraction of \( f = 0.5 \). A realistic value of the surface layer thickness is \( t_{\text{bio}} = 2 \) nm. In the top line the excluded volume fraction was taken to be that of biomolecules standing up straight, \( f = 0.1 \), and the realistic surface layer thickness is \( t_{\text{bio}} = 10 \) nm.

When considering the influence of the ion concentration on the volume effect we look at figure 5.6. We compare three different cases with the same total excluded volume. The first case is a result of the EVM, where the layer thickness is 0.94 nm and the excluded volume fraction is 1. The second case is the result when the biomolecules lie down, giving a layer thickness of 2 nm and an excluded volume fraction of 0.5. The third case is the result for biomolecules that stand straight on the sensor surface, corresponding to a
surface layer thickness of 10 nm and an excluded volume fraction of 0.1. The black dashed line corresponds to the SCM result where no volume effect is taken into account. In figure 5.6(a) the total charge in the FET is shown. It is seen that screening has a negative influence on the charge induced in the FET. In the first application (PEVM1), where the biomolecules are modelled as having both a charge and a volume, it is therefore beneficial to have a small ion concentration.

In the second application (PEVM2) the sensor surface itself is charged due to for example oxide charge, and the biomolecules are neutral. The charge induced in the FET upon biomolecule attachment in this model is shown in figure 5.6(b). The EVM result is the line at the bottom. For a larger ion concentration the difference between the EVM and the SCM increases. When looking at the results of the PEVM (middle and top line), however, the opposite behavior is shown. This is due to the fact that for very large ion concentrations only a small available volume for the ions is already large enough for the ions to completely dominate the system. Almost all of the surface charge is compensated by the ions and the charge induced in the FET is small.

In figure (c) the top line of figure (b) is shown again, showing that there is an optimum value of the ion concentration. For biosensing, the ion concentration is not a variable, and the ion concentration imposed by the system is not likely to be at this optimum. When comparing these results to those of the SCM (figure 5.6(d)), we see that the charge induced in the FET upon attachment of neutral biomolecules with a volume is much larger than the charge in the FET in a model without an excluded volume. It is seen that although the effect of the volume decreases for increasing ion concentration, the ratio of this result and the SCM result increases. For larger ion concentrations therefore the presence of the biomolecule volume is easier to detect than the presence of the biomolecule surface charge.

Adding 1 to the result in figure 5.6(d) we obtain \( \lambda_{\text{PEVM}}^{\text{FET}} / \lambda_{\text{SCM}}^{\text{FET}} = \Delta \lambda_{\text{PEVM}}^{\text{FET}} / \Delta \lambda_{\text{SCM}}^{\text{FET}} \). The error in modelling the biomolecules as a charge layer only, without taking into account the effect of the volume, is seen to be larger for larger ion concentrations. For biosensing the ion concentration is large, therefore it is important that the effect of the volume is taken into account.

The dependence of the excluded volume effect on the surface charge, \( \lambda_{S} \), is shown in figure 5.7. The results are shown both for the case the SCM is in the small potential regime (a) and for the case it is in the large potential regime (b). It is seen that increasing the surface charge increases the excluded volume effect.

This can be understood the following way. For increasing surface charge, \( \lambda_{S} \), the surface potential increases, which increases the charge density of the electrolyte close to the sensor surface. Replacing part of this charged electrolyte solution with neutral biomolecules changes the charge distribution.
in the vicinity of the sensor. The larger the charge density in the electrolyte close to the sensor surface, the larger the change in the charge distribution in the vicinity of the sensor upon biomolecule attachment. This causes again a larger change of the charge induced in the FET.

**Figure 5.7:** The charge induced in the FET upon attachment of neutral biomolecules as a function of the surface charge, in the small potential regime (a.) and in the large potential regime (b.).
5.2 The Partially Excluded Volume Model for the cylindrical sensor

The cylindrical geometry as discussed in this section is shown in figure 5.8. Just like in the flat model the surface layer is now modeled as a layer in which part of the volume is occupied by the electrolyte solution, and part by the biomolecules. The layer is taken to be a uniform surface layer with dielectric constant \( \epsilon_{\text{r,new}} \), and adjusted screening length \( \kappa_1 \). Both \( \epsilon_{\text{r,new}} \) and \( \kappa_1 \) are dependent on the excluded volume fraction, \( f \). The problem can not be solved analytically. Therefore the results presented in this section were derived using a finite element method (COMSOL).

In figure 5.10 (a.) the charge induced in the cylindrical FET is shown as a function of the biomolecule layer thickness, both for the case that the biomolecules are oriented flat on the sensor surface and for the case that they stand straight on the sensor surface. It is seen that, just as for the flat case, the charge induced in the FET is larger when the biomolecules lie flat on the sensor surface and the values of the charges induced in the FET stabilize. This implies that for biomolecule layer thicknesses larger than the distance of stabilization, the results of the SCM can be applied, reducing the complexity of the calculations.

![Figure 5.8: Schematic of the nanowire biosensor in the PEVM. The biomolecules exclude the electrolyte from a certain fraction of the volume in the surface layer.](image)

It should be noted that, in contrast to the flat geometry, the excluded volume fraction in the cylindrical geometry varies with distance, \( f = f(r) \), when modeling the biomolecules as rigid rods(see figure 5.9). This implies that also the dielectric constant and the screening length vary with distance. Taking the layer to be a uniform layer, with a fixed excluded volume fraction, leads to excluding a larger total volume in the cylindrical geometry than in the flat geometry. In order to account for the fact that the sensor is cylindrical, the the excluded volume fraction at the surface is the value of the excluded volume fraction of the uniform surface layer, \( f(b) = f \), while in the remainder of the biomolecule layer the excluded volume fraction is...
calculated as follows:

\[ f(r) = f^b_r \]  \hspace{1cm} (5.27)

The results of this distance dependent partially excluded volume model (distance dependent PEVM) are presented in figure 5.10(b). It is seen that the result also stabilizes in this model for layer thickness larger than a couple of nanometers.

\[ \text{Figure 5.9: Schematic of the cylindrical nanowire biosensor in the PEVM. The fraction of the volume occupied by the biomolecules is largest close to the surface of the sensor.} \]

It is expected that for small values of the biolayer thickness the difference between the cylindrical uniform PEVM and the cylindrical distance dependent PEVM is small, since the difference in the value of the excluded volume fraction \( f \) is in that case small. In figures 5.10(c) and (d) this can indeed be seen. For larger biolayer thicknesses we see that the difference between the curves increases. Due to stabilization of the curves, at a certain distance from the sensor surface, the difference between the two models remains the same.

Depending on the biological system of interest, the first or the second model described here gives more realistic results.

In the next section the second model, the distance dependent PEVM, will be used to compare the flat and the cylindrical sensor. This was chosen because the total excluded volume is the same in the cylindrical distance dependent PEVM as in the flat distance dependent PEVM.

5.3 Comparing the effects of a partially excluded surface layer for the flat and the cylindrical geometry

In this section the flat and the cylindrical geometry will be compared in the PEVM. To be able to compare the cylindrical results with the results of the flat sensor, the value \( f \) is used with a somewhat different meaning. Before it was the fraction of the volume of the biomolecule surface layer that
Figure 5.10: The charge induced in the cylindrical FET as a function of the biomolecule layer thickness for (a.) a uniform surface layer, (b.) a surface layer with an excluded volume fraction dependent on the distance to the surface, \( f = f(r) \). These results are compared in (c.) for the case that the biomolecules are oriented perpendicular to the sensor surface, and in (d.) for the case the biomolecules are oriented parallel to the sensor surface.

was occupied by biomolecules, here it is the fraction of the sensor surface occupied by biomolecules. In the case of the flat sensor this is equal to the excluded volume fraction, in the cylindrical case this is only equal to the excluded volume fraction at the sensor surface. Comparing the flat and the cylindrical results with the same value of \( f \) then implies comparing the results for the same surface density of biomolecules and the same total excluded volume.

In figure 5.11 (a.) the charge induced in the FET is shown as a function of the excluded volume fraction for both the cylindrical (black dots) and the flat sensor (green line), and for the two biomolecule orientations. It is seen that, according to the PEVM, more charge is induced in the flat sensor than in the cylindrical sensor just like in the SCM. When dividing the results by the SCM result we obtain the results in figure 5.11 (b.). Since the result of the SCM was different for the two geometries, it is seen that the error in modelling the sensor without volume, for realistic values of \( f \), is comparable for the flat and for the cylindrical sensor.
Figure 5.11: (a.) The charge induced in the FET is shown as a function of the excluded volume fraction for both the cylindrical (black dots) and the flat sensor (green line). The upper line and dots are the results when the biomolecules are oriented perpendicular to the sensor surface, the lower line and dots are the results when the biomolecules are oriented parallel to the sensor surface. (b) The result in (a.) divided by the SCM result.
Chapter 6

Discussion and Conclusion

The question that raised interest to start this thesis was: How is it possible that nanowire biosensors give such good results in the lab, while in theory screening is expected to prohibit this? This was the starting point for this thesis. Different steps are taken to achieve better understanding of the sensing mechanism.

First a simplified metallic nanowire sensor was studied, where the biomolecules were modelled as a surface charge. As predicted by many others, it was found that screening reduced the sensitivity of the sensor. It was also found that the dielectric constant of the sample solution has a large effect. A large dielectric constant decreases the sensor sensitivity. In many biological samples the solution is based on water, with a large dielectric constant. These solutions contain a large amount of ions, which is necessary for the stability and attachment of the biomolecules. The ion concentration and the dielectric constant of the biological sample cannot be chosen, but are dictated by the biological system of interest. Both the ion concentration and the dielectric constant of the solution close to the sensor surface can be influenced by the presence of biomolecules. The biomolecule volume, that is usually ignored, can therefore have a large effect on the sensitivity. The question was raised whether this surface charge model described the real system good enough.

To test whether the biomolecule volume indeed has a considerable effect a model was studied in which a thin layer on the sensor surface was occupied by biomolecules. This excludes the ions from this region and the dielectric constant of the layer is taken equal to the value of the dielectric constant of the biomolecules. It was shown that in a model where the biomolecules are modelled as a surface charge and a surface volume, instead of only a surface charge, the charge induced in the sensor increases greatly. Rough estimations show this can be as large as a factor 80. The problem of screening is shown to be reduced due to the biomolecule volume. If the effect of volume is not taken into account in the calculations this can lead to a strong
underestimation of the sensor sensitivity. This study showed that even a neutral biomolecule layer can be detected by the nanowire sensor. The effect of this neutral biomolecule layer exceeds many times the results of the biomolecule surface charge. The screening due to the presence of ions is not actually a problem when considering the biomolecule volume, but a necessity for the volume effect.

These results showed that the volume of the biomolecules can have a large influence on the detection of the molecules. However, a uniform biomolecule layer excluding all ions is not that realistic. Therefore the surface layer was considered being partially occupied by biomolecules. It was shown that the results depend greatly on the surface layer characteristics. The orientation of the biomolecules determines the fraction of volume occupation at a certain distance from the sensor surface, which in turn determines the dielectric constant.

Understanding this large influence of the biomolecule volume, allows for fine tuning of the sensor. Adding a fixed surface charge to the sensor surface for example increases the volume effect. Also one could think about attaching groups to the biomolecules of interest to increase their volume, or making sure the biomolecules lie flat on the sensor surface. Another more complex use of this volume understanding can be depositing a certain material on the sensor after biomolecule attachment.

The strong dependence on the precise characteristics of the biomolecule volume suggests that a model in which the biomolecule layer is taken to be a uniform layer probably will not yield correct predictions. It is recommended that the system is studied further, taking into account the discreteness of the biomolecules.

The before mentioned studies have been done both for a cylindrical nanowire sensor, and for a flat sensor. The cylindrical geometry is more similar to the realistic geometry, but the flat sensor was included since the calculations are more insightful in this geometry. Both the flat and the cylindrical sensor gave similar results. It was shown that the models for both geometries can be described using the same equations, with a different dependence of the variables on the physical quantities. The results showed that the cylindrical sensor induced less charge than the flat sensor. This does not imply that the flat sensor is more sensitive than the cylindrical sensor, since the discreteness of the biomolecules was not taken into account. Pinching for example is only possible in the cylindrical geometry, and can result in single molecule detection.

The material of the sensors was taken to be metal and not a dielectric. If one is interested in including dielectric properties, the simple capacitance that was used in this thesis can be replaced with the capacitance of a dielectric sensor.

The values of the charges of the biomolecules and their attachment to the sensor that were used were rough estimations. For each biomolecule system
this will be different. Depending on the local potential the attachment of biomolecules and the local ion concentration varies. This in turn can have an influence on the charge of the biomolecules and the sensor surface. This potential dependence was not taken into account in the models described in this thesis.

To conclude, we can answer the question: Is the influence of volume important for biosensing or is it negligible compared to the effect of the charge of the biomolecules? It was shown that the effect of volume cannot be neglected, and in all future studies this topic should be addressed. This can explain why nanowire biosensing experiments show a much higher sensitivity than one would expect from simple charge calculations.
Bibliography


