1. **Bio-Molecule Detector**

We've already seen how to build a bio-molecule detector where bio-molecules change the resistance between two electrodes. In this problem, we will explore a different scheme, where bio-molecules change the capacitance between two electrodes.

![Diagram of Bio-molecule Detector](image)

As shown in Figure 1, the detector works by flowing a liquid that may or may not contain the biomolecules through a region in the device that has electrodes on the top and bottom of the liquid channel. The electrodes (E1/E2 in Figure 1) are chemically “functionalized” (using e.g. some appropriately designed antibodies), so that if the specific bio-molecule of interest is present in the fluid sample, one or more of the molecules will get physically trapped between the two electrodes (bottom right of Figure 1). After all of the fluid has been cleared out of the device (i.e., so that if there are bio-molecules present, there is only air in between the two electrodes E1/E2), we can then figure out whether or not one or more bio-molecules were trapped by measuring the capacitance between the two electrodes.

(a) If no bio-molecules are present, what should the capacitance between E1/E2 be? Assume that the electrodes are 10µm on each side and that the electrodes are 100nm apart. Leave your answer in terms of $\varepsilon_0$.

**Answer:**

$$C = \varepsilon_0 \left(\frac{10\mu m}{100nm}\right)^2 = 0.001\varepsilon_0\mu m$$

(b) As shown in Figure 1 if each bio-molecule is a cylinder with diameter $d = 2\mu m$, height $h = 100nm$, and permittivity $\varepsilon_b = 4\varepsilon_0$, what would the capacitance between E1 and E2 be if only a single bio-molecule is trapped? Note that you can assume that the trapped molecule is exactly vertically oriented when it is trapped – i.e., the top and bottom faces of the molecule are both aligned with surfaces of the electrodes.

**Answer:**
With biomolecules trapped in between the electrodes, we will model the entire structure as two capacitors in parallel.

The first capacitor is the region on the electrode where no molecule is trapped. This capacitor has air between its plates, so we use \( \varepsilon_0 \) for the permittivity. The second region is where the bio-molecule is located. This region has the bio-molecule between its plates, so we use \( \varepsilon_b \) for the permittivity.

\[
C = \varepsilon_0 \frac{100\mu m^2 - \pi (1\mu m)^2}{100\text{nm}} + 4\varepsilon_0 \frac{\pi (1\mu m)^2}{100\text{nm}}
\]

(c) Using the same numbers for \( d \), \( h \), and \( \varepsilon_b \) as in part (b), as a function of the number of trapped biomolecules \( N_{\text{molecules}} \), what is the capacitance between E1 and E2? (Note that you can assume that \( N_{\text{molecules}} \) is small enough that all of the molecules fit within the electrode area and that all of the molecules are still trapped in exactly vertical orientation.)

Answer:

\[
C = \varepsilon_0 \frac{100\mu m^2 - N\pi (1\mu m)^2}{100\text{nm}} + 4N\varepsilon_0 \frac{\pi (1\mu m)^2}{100\text{nm}}
\]

(d) The presence of bio-molecules changes the capacitance between the two electrodes. We would like to turn this change in capacitance into a change in voltage. Suppose that you design the circuit shown below to accomplish this, where \( C_e \) is the capacitance between the electrodes. If the value of \( C_e \) changes, does \( V_{\text{out}} \) change?

Answer:

Regardless of the capacitance of \( C_e \), \( V_{\text{out}} = V_s \).

(e) In order to measure the change in capacitance, we might try to use charge sharing with another capacitor whose capacitance we already know. Let’s call this capacitor \( C_{\text{ref}} \). Charge-sharing circuits generally have more than one phase. In the first phase, one set of switches might be closed, and in another phase, a different set of switches might be closed. Switches labeled \( \phi_x \) are closed in phase \( x \). We also need to know in what phase to measure the output voltage.

Re-draw the circuit shown below in each phase. Does the voltage \( V_{\text{out}} \) depend on \( C_e \)? Suppose that we measure \( V_{\text{out}} \) in phase 2.
We can redraw the circuit is phase 1 when the switch is open.

In phase 2, when we measure $V_{\text{out}}$, the switch is closed.

Regardless of the capacitance of $C_e$, $V_{\text{out}} = V_s$.

(f) Now we add another switch and come up with the circuit below. Re-draw the circuit in each phase. Assume that we measure $V_{\text{out}}$ in phase 2 once again. Does $V_{\text{out}}$ depend on the capacitance $C_e$?

Answer:
In phase 1, the left switch is closed while the right switch is open.
In phase 2, the left switch is open while the right switch is closed.

In phase 2, $V_{out}$ is not directly connected to $V_s$. $V_{out}$ is the voltage across the capacitor $C_{ref}$. To find the voltage across the capacitor, we need to know the charge on the capacitor since $Q = CV$.

Let’s assume that the capacitors are initially uncharged. In phase 1, the capacitor $C_e$ has a voltage of $V_s$ across it and thus has a charge $C_e V_s$. We assumed that the capacitors were uncharged initially, so $C_{ref}$ still has no charge on it.

In phase 2, the capacitors $C_e$ and $C_{ref}$ are in parallel and have some $V_{out}$ voltage across them. The total charge is then $(C_e + C_{ref})V_{out}$.

We know the charge in each phase, but we need some way to relate the charges. Using conservation of charge, we know that the charges must be the same in both phases in this circuit. Therefore,

$$Q_1 = Q_2$$

$$C_e V_s = (C_e + C_{ref})V_{out}$$

$$V_{out} = \frac{C_e}{C_e + C_{ref}} V_s$$

(g) In the above circuit, how many times can you measure $C_e$? Suppose that the circuit cycled through phase 1 and 2 again, could we measure $C_e$ again? Modify the circuit, such that you can repeatedly use the circuit to measure $C_e$.

**Answer:**

We assumed in our analysis above that all capacitors were initially uncharged, i.e., the charge on $C_{ref}$ was zero. However, once we complete a cycle, the charge on $C_{ref}$ is no longer zero, but we need the charge to be zero. To do this, we use a clean switch that shorts both plates of $C_{ref}$ during phase 1.
(h) Finally, we have a circuit that can be used to measure $C_e$. Suppose that we now want to output 5V when there are at least 5 biomolecules present. Otherwise, we want to output 0V. Design a circuit that accomplishes this using a comparator, a voltage source, and your circuit from part (g).

**Answer:**

Before we start building a circuit, let’s analyze what actually happens to $V_{out}$ when more molecules are trapped in the detector. As the number of molecules in the detector goes up, the capacitance $C_e$ goes up. This results in an increase in $V_{out}$.

Now, we consider the comparator. Recall that when configured as a comparator, an op-amp will output the voltage at the top rail when $V^+ > V^-$ and the voltage at the bottom rail when $V^+ < V^-$. Since we want a 5V output when $V_{out}$ is high, we will connect $V_{out}$ to $V^+$. Since we need to compare $V_{out}$ against some other voltage $V_{ref}$, we connect $V_{ref}$ to $V^-$. 

Let’s now find values for $V_{ref}$ and $C_{ref}$. Since $N_{molecules} = 5$ is the threshold, let’s set $C_{ref} = C_{e4} = 12.19\,\text{fF}$.

We can now calculate $V_{out}$ for $N_{molecules} = 4$ and $N_{molecules} = 5$. 

$$N_{molecules} = 4 \implies C_{e4} = 12.19\,\text{fF} \implies V_{out4} = 2.5\,\text{V}$$

$$N_{molecules} = 5 \implies C_{e5} = 13.02\,\text{fF} \implies V_{out5} = 2.58\,\text{V}$$

Therefore, we can set $V_{ref} = 2.54\,\text{V}$.