Sensors and Microsystems Technology
Project : Design of a sensor to measure COVID-19 in air and saliva

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COVID-19 is detected in saliva, blood and urine. It is detected in saliva very early, while in blood and urine it is detected in very advanced stages. It is also found in very high density in saliva. So if we want to detect a case validly and in time, the use of saliva is very efficient. In fact, with coughing and breathing, coronavirus particles can be detected in the area where a carrier is.

1 Measurement in air

Figure 1: *Capacitor*

One approach to detect COVID-19 and indeed any virus is to detect antibodies. Every virus also has an antibody with which it attaches itself. The unique antibody of COVID-19 is ACE2. This peptide is derived from the ACE peptide and is stabilized in the ACE2 form. It is found in the myocardium and the lungs, and it is on this that COVID-19 attaches itself (1).

These oligopeptides have very good dielectric properties. In short, the dielectric constant (ε) changes with the contact of COVID-19 and ACE2. That is, a capacitor device with varying capacitance can be used to detect COVID-19.

The "comb" shown in Figure 1 can be used to have more capacity in a smaller space. In other words, conductive roads are constructed, one of which goes inside the other without joining each other, thus creating a parallel array of capacitors.

This can be made either microelectronically or hybridly with thousands of such capacitors or tens respectively. In any case it can be in such a form that the COVID-19 molecules that come into contact with the sensor will pair with the peptides.

More specifically, this sensor can be implemented as follows:

1. ACE2: A known number of ACE2 is placed on the capacitor of capacity C_0. ACE2 changes the dielectric constant and thus the capacitance of the capacitor which becomes C_1.

2. COVID-19: The virus is deposited on the capacitor which binds to ACE2 changing again the dielectric constant and therefore the capacity of the capacitor which becomes C_2.

3. Measurement: Knowing the capacities in each phase of the capacitor, calculate the number of coronas stuck on it. So the measurement is not only qualitative but also quantitative.

An oscillating device with this capacitor and a coil of known inductance L is used to measure the capacitances (Figure 3). The oscillation eigenfrequency of the circuit LC_i is:

$$\omega_i = \frac{1}{\sqrt{LC_i}}$$

Thus, by calculating the natural oscillation frequency ω_i, the value of the capacitor's capacitance is also found. Obviously the values of ω_i depend on the values of the oscillating circuit (coil and capacitor).

1.1 Geometric characteristics of the sensor

This arrangement can be implemented in various ways such as hybrid technology (thick film technology-screen printing layout 10m) or thin films evaporation (PVD with arrangement of metal sublimation using 1m masks). As more accessible, the use of PCB (printed circuit board) is chosen, i.e. a printed copper board on which the capacitance is engraved. PCB limits are 0.1 cm = 100 μm. For material economy, dimensionally we prefer to move close to these limits for material economy. We want the dimensions of the capacitor to be in the order of 1 cm^2 = 10000 μm.

So we choose for this (Figure 2):

- $L_1 = 10000\mu m$: total capacitor width
- $w = 100\mu m$: height and thickness of capacitor plates
- $d = 100\mu m$: capacitor plate spacing

So it is calculated that $L_1 = l + 2w + 2d \Rightarrow l = L_1 - 2w - d \Rightarrow l = 9600\mu m$. In order to have the length L_2 $10000\mu m$ of the capacitor, the number N of the plates must be such that:

$$L_2 = N * w/2 + (N/2 - 1)(2d + w) + d + w \Rightarrow$$
$$N = \frac{L_2 + d}{d + w} = 50.5$$

N is obviously an integer so $N = 50$ is chosen so $L_2 = 9900mm$. The capacitance of the comb capacitor is calculated by the formula: (2)

$$A_1 = 4.409 \tanh[0.55(w/w)^{0.45}]pF/m = 2.20pF/m$$
$$A_2 = 9.92 \tanh[0.52(w/w)^{0.5}]pF/m = 4.73pF/m$$
$$C_0 = (\varepsilon_r + 1)l[(N - 3)A_1 + A_2]pF = 4.68pF$$

Where $\varepsilon_r = 3.5$ the dielectric constant of the PCB (3)

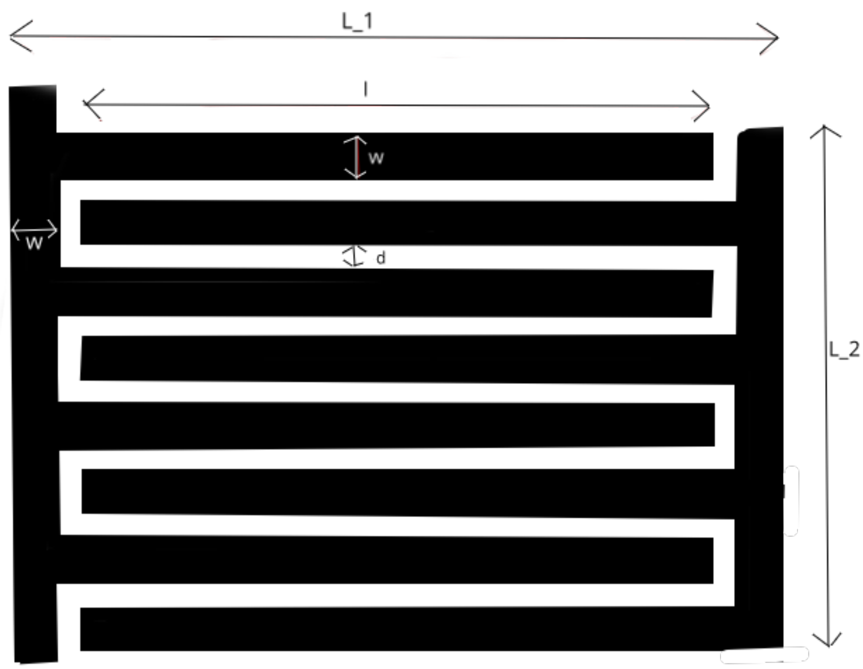

Figure 2: *Capacitor*

We want the coil of the oscillating circuit to be dimensionally of the same size as the capacitor, so we choose:

- $D = 0.01m$: coil diameter
- $l = 0.02\mu m$: coil length

- $d = 40\mu m$: copper wire diameter

Also, to make it possible to measure the resonant frequency with conventional electronics, $\omega_0 < 1Mr/s$ so:

$$\frac{1}{\sqrt{L_{min}C_0}} = 10^6 \Rightarrow$$
$$L_{min} = \frac{1}{10^{12}C_0} = 213.42mH$$

From the inductance formula we have that:

$$L = \frac{\mu\mu_0 N^2 S}{l} > 213.42mH \Rightarrow$$
$$\mu_{min} = \frac{lL_{min}}{\mu_0 N^2 S}$$

Where $S = \pi D^2/4 = 78.53mm^2$ the cross-section of the copper wire, $N = 2l/d = 500$ the number of turns, μ the relative permeability of the core, $\mu_0 = 0.001257mH/m$ the vacuum permeability The dimensions of the coil must be corresponding to the capacitor, so the diameter of the coil should be chosen $D = 0.01m$. So its cross section is:

$$S = \pi * D^2/4 = 78.53mm^2$$

It is therefore calculated that $\mu_{min} = 43.23$.

Ferrite has at least $\mu = 350$ for frequencies up to $4MHz$ so it is a good choice of material for a (4) core. Ferrite is a better choice than iron as iron can reach a magnetic permeability $\mu = 10^6$ for low frequencies (close to $100Hz$). Its specific resistance is of the order of $\mu\Omega cm$ with the result that at higher frequencies very strong eddy currents are created and the magnetic permeability decreases rapidly. On the contrary, ferrite has a specific resistance of the order Ω or $K\Omega$ with the result that the eddy currents are very small and the magnetic permeability is maintained at high frequencies (although lower than iron). By choosing ferrite for the core the inductance of the coil has a value of:

$$L = \frac{350\mu_0 N^2 S}{l} = 1727.68mH$$

The copper wire has a specific resistance $\rho = 1.72x10^{-8}\Omega m$ the coil has a resistance which must also be taken into account.

$$R_L = \frac{\rho Length}{cross-section-area}\frac{\rho_{fer}N\pi D}{\pi d^2/4} = 430\Omega$$

1.2 Electronic excitation circuit and electronic measuring circuit for the sensor

The sensor will be placed at the air outlet (air conditioner) to trap the airborne coronavirus peptides. To calculate the number of coronas but also to adjust the excitation, we need to know the density $a\%$ of ACE2 on the capacitor. Initially, the surface of the capacitor must be dry from water (with peltier heating) and then $\varepsilon_r = \varepsilon_{ACE2} * \alpha/100$, where $\varepsilon_{ACE2} = 15$. The peptides are apparently limited and can bind a specific number of coronaviruses. Then a suitable $\alpha\%$ must be entered so that a coronavirus is not caught by 2 peptides. This will only happen if each peptide is at a distance of $1\mu m$ from its neighbor. The peptides have a diameter of about $10nm$. Either now we fill the surface with ACE2 ($\alpha = 100$) or we put one peptide per $1\mu m^2$ then in both cases we expect 1 corona at most per μm^2. For simplicity we consider $\alpha = 100\%$. So in the presence of the peptide the capacitance has become:

$$C_1 = (\varepsilon_{ACE2} + 1)C_0 = 74.96pF$$
$$f_1 = \frac{1}{2\pi\sqrt{LC_1}} = 13984Hz$$

That is, on the $1cm^2$ surface we have 10^8 coronaviruses at most. Since both the ACE2 and the corona have dimensions dramatically smaller than the teeth of the comb we are confident that the dielectric constant will add to our capacitance. Up to 10^8 coronaviruses can be bound and knowing that $er_{COVID-19} = 16$ then catching $X < 10^8$ it follows that $er = e_{COVID-19} * X/10^8$. So in the presence of the coronavirus, the capacity has become:

$$f_2 = \frac{1}{2\pi\sqrt{LC_2}}$$
$$C_2 = (\varepsilon_{COVID-19} * X/10^8 + \varepsilon_{ACE2} * \alpha/100 + 1) * C_0 \Rightarrow$$
$$X = \frac{C_2/C_0 - \varepsilon_{ACE2}\alpha/100 - 1}{\varepsilon_{COVID-19}} 10^8$$

In this linear way X is calculated through the measurement of f_2. The difference of f_1 from f_2 will be relatively small as it is obviously impossible for the space to be full of coronaviruses.

For the range we are looking for, f_2 is from the smallest value that f2 can take, that is, when the surface is filled with coronas up to the value of f_1.

$$C_{2_{max}} = (\varepsilon_{COVID-19} + \varepsilon_{ACE2} + 1) * C_0 = 149.93pF$$
$$f_{2_{min}} = \frac{1}{2\pi\sqrt{LC_{max}}} = 9888Hz$$

If X starts and approaches the value 10^8 then we have to have a backup and with an automation we open its surface and it makes new measurements. Then we have to wash the coronavirus from the filled surface using an organic solvent such as ethanol which is able to wash the coronavirus but not the ACE2.

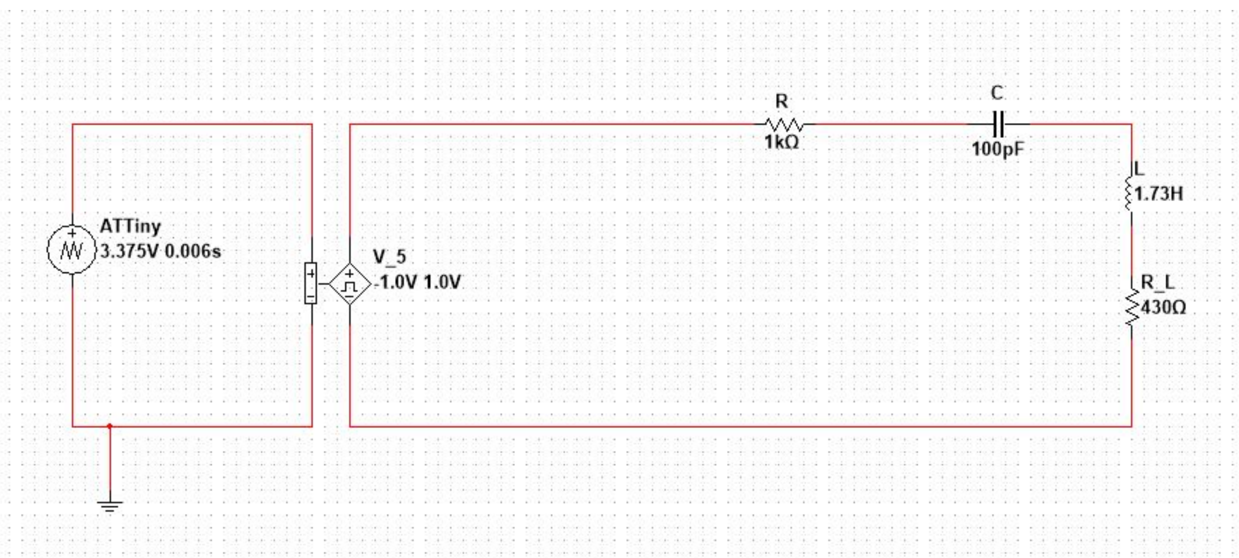

Figure 3: *Κύκλωμα συντονισμού*

The overall circuit is R, C, L with generator in series or in parallel (Figure 3). So a variable frequency signal generator is needed for excitation. The range of resonant frequencies of R, L, C is determined by the values of the capacitor and is:

$$\omega_2 = 62132r/s, f_2 = 9888Hz, \text{ for } C = C_2$$
$$\omega_1 = 87868r/s, f_1 = 13984Hz \text{ for } C = C_1$$

Therefore the sine excitation generator should be swiping from about 9kHz to 15kHz. To implement this we use an LM566c square wave crystal oscillator (Figure 4) with $duty - cycle = 50\%$. For the frequency of square pulses we have(5):

$$f = 2.4\frac{V_{CC} - V_5}{R_6 C_7 V_{CC}}$$

Where $2k\Omega < R_6 < 20k\Omega$. So we choose $R_6 = 20k\Omega, C_7 = 6nF$ so that with a power supply $V_{CC} = 4.5V$ we have a bandwidth: $5kHz - 20kHz$.

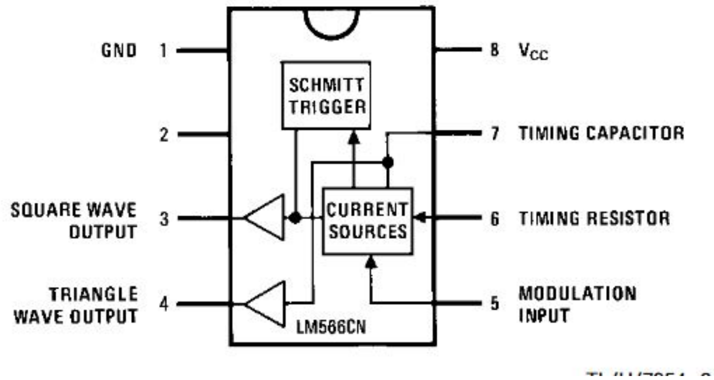

Figure 4: *LM566c Connection Diagram*

In this way, a circuit is made which excites with a frequency f which is controlled by the polarization of the LM566c. The bias voltage of the LM566c must be changed to modulate f respectively. Practically, a voltage is applied which will correspond to the change in resistance. This could also be done with small DC steps per $msec$ using binary search. To locate the maximum value of V_R with an accuracy of $0.5Hz$ you must:

$$\Delta f = 2.4\frac{DV_5}{R_6C_7V_{CC}} < 0.5Hz \Rightarrow$$
$$\Delta V_5 = 0.1mV$$

An ATTiny85 microprocessor can be used to drive the ramp or the steps, Figure 5 (code: covid.txt). The computing power of ATTiny85 is enough for the function we need.

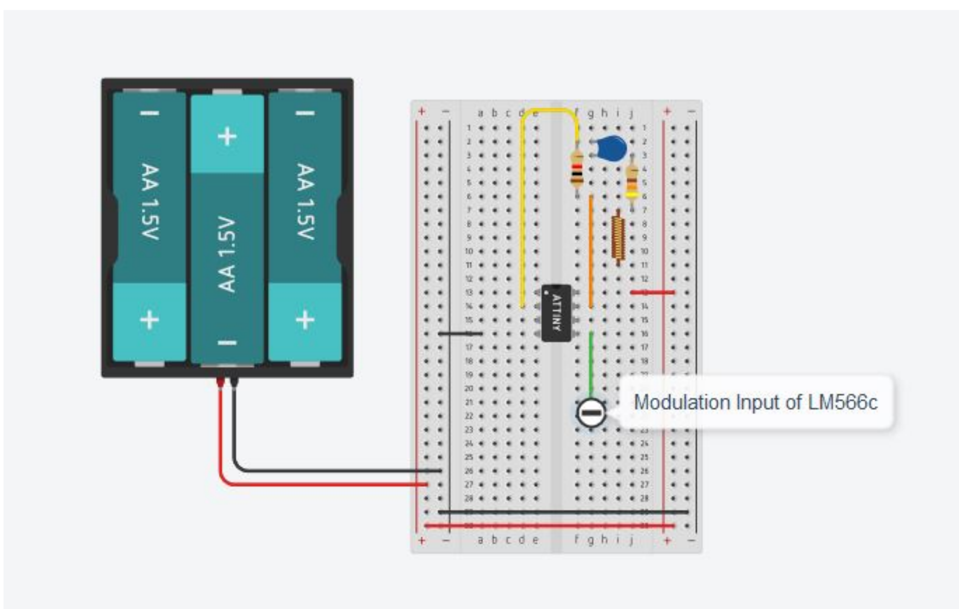

Figure 5: *ATTiny85 connectivity*

The ATTiny85 is programmed using Arduino as shown in Figure 6 (6).

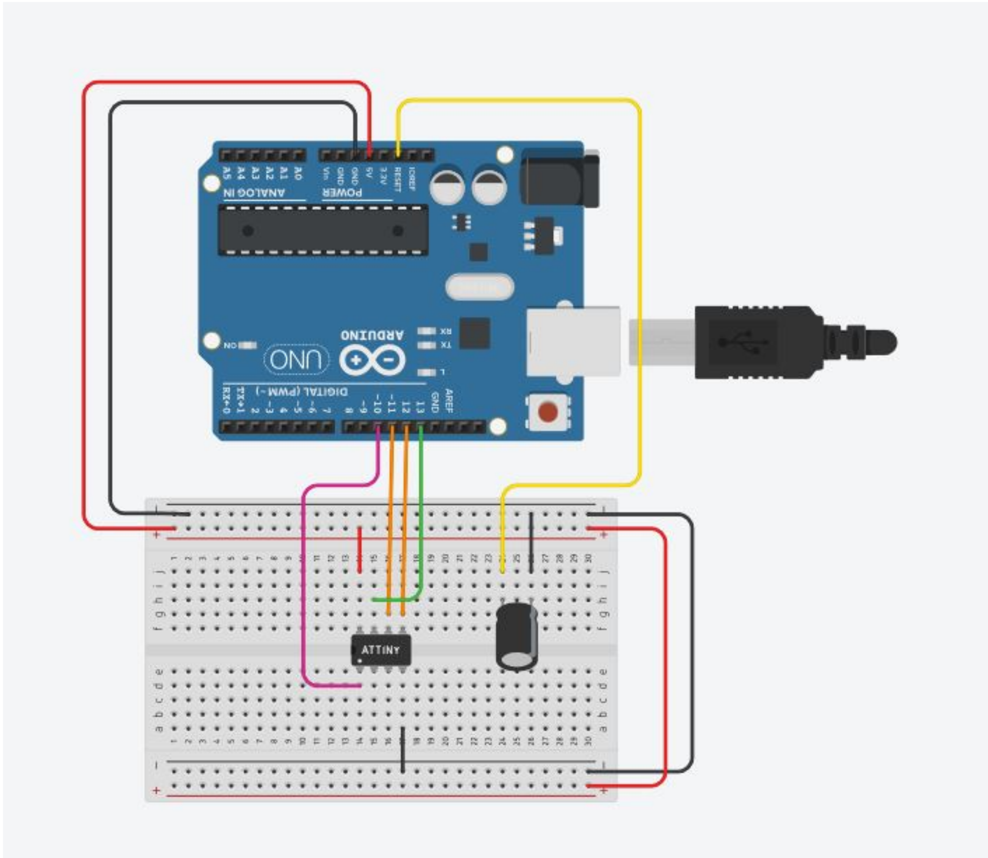

Figure 6: *ATTiny85 and Arduino wiring for ATTiny85 programming*

Unfortunately the multisim tool does not have a simulation model for this LM566c and for Arduino or ATTiny. So the square wave was simulated with a "Voltage Controlled Square Wave Oscillator" object and the ATTiny's output with a "Triangular Voltage". The results are shown in Figure 7.

By measuring in a small resistor $R = 1000\Omega$ the output voltage and finding for which value of V_5 it is maximized, the resonant frequency is calculated:

$$f_2 = 20000 - \frac{15000}{3.375} V_5$$

For example in Figure 7 we have a maximum amplitude of V_R for $V_5 = 1.59V$. So $f_2 = 12933Hz$ so $C = \frac{1}{4\pi^2 L f^2} = 98pF$ and the number of wires is $X = \frac{98/4.68 - 15 - 1}{16} 10^8 = 0.3087 * 10^8$.

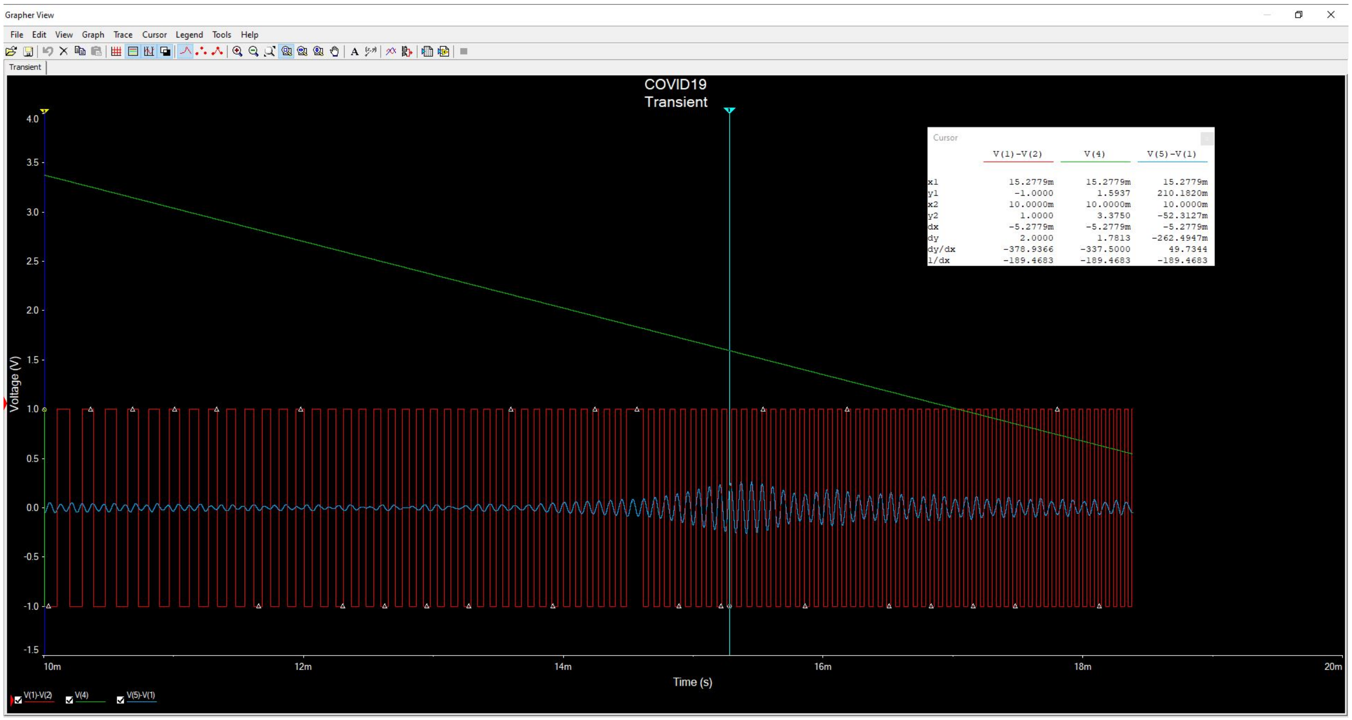

Figure 7: *Green:* V_5 *bias, Red: LM566c square output, Blue:* V_R *voltage*

1.3 Fabrication techniques for the sensor and the required electronics.

As discussed above the capacitor $1cm^2$ with the resin with capacity C_0. To make the circuit functional we equip the upper surface of the capacitor with ACE2. Using an aqueous solution of ACE2 with a % ace 2 content. I put a drop and rotate the capacitor to have an even distribution of peptide on its surface. Then you remove the water from the surface of the capacitor by heating with a peltier.

As mentioned above, the capacitor is implemented with a PCB (printed circuit board) printed copper board on which the capacitance is engraved. If the copper thickness is 10μ in an A4 then the thickness must increase to 100μ copper height. The simplest that can be done is electrolysis - electrodeposition with oxygen free copper. This will be done before it is engraved and the material cost is very small. So for an A4 you will need $90m * 21cm * 29cm * 10kg/m^2$ grams of copper.

If the dimensions of the capacitor are $0.01x0.0099m^2$ and the solder margins $0.005m$ and 0.005 294 capacitors with dimensions $0.015x0.014m^2$ can be made from a PCB A4 surface.

Finally, the excitation circuit requires an ATTiny85 microprocessor and an LM566c crystal oscillator, the whole circuit can be powered by a 4.5V battery.

2 Measurement in saliva

2.1 Detect the virus in saliva using (a) magnetism, or (b) optics

In the case that the COVID-19 cells are not in the air but are dissolved in liquid (most likely saliva) capacitive sensor is not functional. This is because the dielectric constant of water is $\varepsilon_{water} = 80$ while that of COVID-19 is $\varepsilon_{COVID-19} = 16$. This means that the water masks the information from the resonance frequency change since it has a much greater effect than the COVID-19 cells.

However, it is possible to utilize other natural phenomena for the detection of COVID-19 which are not affected by the presence of water. Such sensors will be very useful for detecting COVID-19 in saliva.

The detection of COVID-19 magnetically can be done if we bind it to some material that can give a magnetic response. This binding can be done by covering a small paramagnetic (without magnetic hysteresis) particle with a polymer (glycol). The polymer acts as a glue for ACE2 and so we put a specific number of ACE2 on it. Finally, we place the break with the coronavirus which is bound by ACE1. Thus knowing the number of ACE2 on each magnetic particle is enough to know the number of magnetic particles to calculate the number of COVID-19.

More specifically, this sensor can be implemented as follows:

1. Ferrofluid: We construct a break with magnetic particles which are covered with ACE2. For better properties, superparamagnetic iron oxides SPION nanoparticles are chosen which are covered with polyethanol glycol (PEG).

2. Planar Coil: On a planar coil of capacity $L = \mu L_0$ (L_0 = coil inductance in vacuum) I place a saliva sample with X coronas.

3. Execution: Dip the coil into the magnetic particle break. For convenience we use a solution with excess magnetic particles so that each coronavirus bound to an ACE2 in a nanoparticle.

4. Measurement: These particles have a magnetic permeability much greater than one. That is, then we will have a change of $L' = \mu' L_0$. We measure L' again by connecting it in series with a capacitor of known capacity to get our response as in the previous sensor.

References

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