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Analog Circuits for BioChip - Final Exam
Thursday 24.06.2021 from 16h15 to 19h15 (INM202)

<u>Reminder of the examination rules for the course "Analog Circuits for BioChip"</u>

The written examination is organized as follows:

• The duration of the exam is 3 hours. The exam will have three parts, one for each main part of the course. Each part will consist on one exercise and three multiple choice questions linked to the course.

• Sheets of paper are provided to students. It is forbidden to bring home these sheets of paper.

• The slides in printed form of the course (which are available on Moodle) are allowed during the exam. The textbooks of the course are allowed too but in printed form only. It is allowed to have own annotations on the slides but these annotations should be only relate to the course understanding and not to exercise solutions. These documents (slides and text books) are the only documents that are allowed during the examination.

• The series of exercises and their corrections discussed during the semester are not allowed.

• A standard or scientific calculator is allowed. Thank you to take with you your calculator. No calculators will be provided during the exam. Laptops, mobile phones, tablets, or other equivalent electronic devices are prohibited during the exam.

• Each student will be placed in a predetermined position in the examination room which means it is forbidden to students to choose where to sit.

• Each student will use a pen, **not a pencil**, to solve the exercises.

• Each student will write his name and the number of exercise on each sheet and on each extra sheet he might need to complete the exercises solution.

• Space is provided on the statement to do the exercises. The final answers to each exercise should be clearly reported in that space provided. If additional sheets are required to solve exercises, the student can add extra sheets, add his name and surname, add the number of the exercise that requires this extra sheet, and declare the extra sheets when giving back to the teachers the exam solutions.

• Students need to show all the developments at best (with calculations and diagrams), by also naming the used equations and/or laws.

• Teachers will answer to questions during the examination especially if there is an error in the statement of an exercise or a problem of understanding related to a statement in the exam.

• In accordance with the rules of the EPFL, any attempt to cheat will results in the cancellation of the exam for the cheating student and he will receive a mark of zero.

C. Dehollain, A. Skrivervik, and S. Carrara

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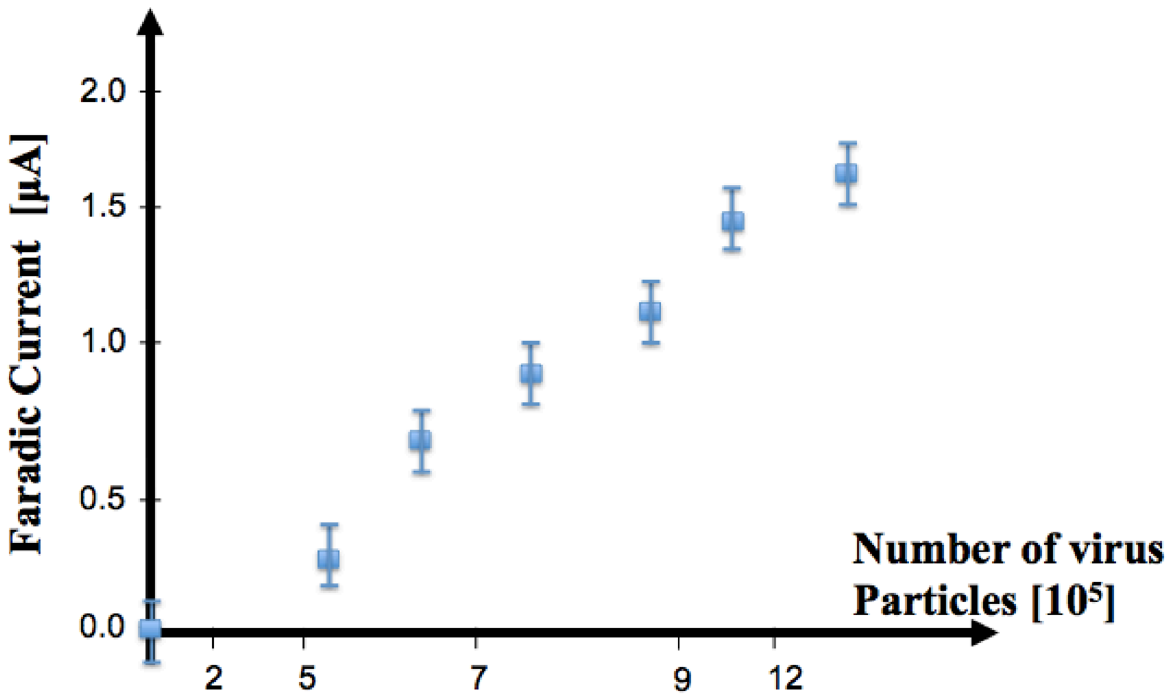
Part I: electrochemical sensors

Scenario

Coronavirus disease (Covid-19), causing a severe acute respiratory syndrome, has been classified as a worldwide pandemic in 2020. Point-of-care devices certainly increase the capability for screening, diagnosis, and monitoring by accordingly increasing the probability for saving lives of more critical patients as well. A large number of spike proteins cover the surface of the Covid-19 virus capsid (the protein shell protecting the viral RNA) and bind to the host cell receptors called Angiotensin-Converting Enzymes 2 (ACE2), mediating viral entry for cell infection. Therefore, we want to design a complete platform as a rapid electrochemical test for the detection, in patient' samples, of the Covid19 virus. Anti-Covid19 monoclonal antibodies CR3022 might be considered for the receptor-binding domain of the spike proteins present in the virus corona. Once proper functionalized and investigated, the electrochemical sensor returns a calibration curve, as acquired in chronoamperometry, following data reported here below



Calibration curves acquired in chronoamperometry experiments in the due range for detection of the Covid19 virus [bars in the graph are related to 3 times the standard deviation]

To answer the following questions and to solve the related exercises, you have also to consider that the molecular weight for the right probe protein is about 150 10^3 g/mol, while recalling that the Avogadro Number (N_A) is 6.022 10^{23}.

To solve the following exercises about the CMOS design, we also consider using unlimited number of ideal Operational Amplifiers, transistors and resistors, but only a voltage source of 1.8 V as V_{dd}.

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Question 1 (2 points)

Among the following functionalizations, which one is the correct functionalization for the working electrode (WE) to obtain an amperometric biosensor to sense the Covid19 virus?

- o We can functionalize the WE with antibodies CR3022
- o We can functionalize the WE with antibodies against the Covid19 virus
- o We can functionalize the WE with antibodies against the antibodies CR3022
- o We can functionalize the WE with enzymes named Covid19-Esterase
- o We can functionalize the WE with enzymes named Covid19-Oxidase
- o We can functionalize the WE with enzymes named CR3022-Oxidase

Comments on the chosen answer:

Question 2 (2 points)

How we need to organize the detection approach in order to acquire a Faradic current out of the interaction between the Covid19 virus and our working electrode?

- o It is enough to immobilize the enzymes named Covid19-Oxidase, which will generate hydrogen peroxide once catalyzing the virus and, thus, returning a current.
- o It is enough to immobilize the enzymes named CR3022-Oxidase, which will generate hydrogen peroxide once catalyzing the virus and, thus, returning a current.
- o By an indirect detection: immobilizing the antibodies CR3022 to trap the Covid19 virus and use further antibodies CR3022 previously functionalized with Alkine Posphatase to generate a current out of the aminophenylposphate
- o By an indirect detection: immobilizing the antibodies CR3022 to trap the Covid19 virus and use further antibodies CR3022 previously functionalized with whatever redox enzyme to generate a current out of the enzyme' substrate
- o Definitely impossible, since the interaction between the Covid19 virus and the CR3022 will never return a current

Comments on the chosen answer:

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Exercise 1(11 points)

a) Compute the <u>Sensitivity</u> and the <u>Limit of Detection</u> (LoD) obtained by the biosensors-chip envisaged by the scenario described before for the detection of the Covid19 virus in chronoamperometry. Please, also write a couple of sentences about the obtained values for the <u>Sensitivity</u> and the <u>Limit of Detection</u> with respect the picture of the above mentioned calibration curve in chronoamperometry.

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b) To bio-functionalize the above-mentioned biosensor for the Covid19 virus, we need to spread a drop of 5 μl in volume onto the working electrode with a proper protein and then let evaporate the entire amount of the solvent. Probe proteins are dissolved in Phosphate Buffer Saline solution (PBS) 0.01 M at pH 7.4 with proteins concentration of 50 mg/ml. Compute the <u>number of proteins</u> deposited on the working electrode.

c) Draw also a sketch that shows the working principle of the interface of our final biochip platform by including all the required proteins and other chemical you are planning to implement in the device.

d) Draw the simplest possible circuit that measures the Faradaic currents generated at the working electrode as per the calibration curve discussed before by through the Frequency-To-Current Conversion (FTCC) method. Add some sentences of explanation by describing the working principle of the circuit too.

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Question 3 (2 points)

Is there any other very simple circuit that might simplify the solution (d) of the previous exercise, in order to get an output analog signal that is directly proportional to the current and not to a frequency as obtained by the Frequency-To-Current Conversion (FTCC) method?

- Not really, since the output of the biosensor is always a digital signal, and it cannot be easily converted in an analog one
- Not easy, since the output of the biosensor is mainly a digital signal, which cannot be easily converted in an analog one
- It might be possible, but it is almost never done since the output of the biosensor is always better that be a digital signal, which it is not useful to convert in an analog one
- Yes indeed, even though the output of the biosensor is always better that be a digital signal, it is always possible to acquire directly the Faradic current by a voltage measure by using a transimpedance amplifier.
- Yes indeed, even though the output of the biosensor is always better that be a digital signal, it is always possible to obtain the Faradic current by adding a frequency-to-current converter.

Comments on the chosen answer:

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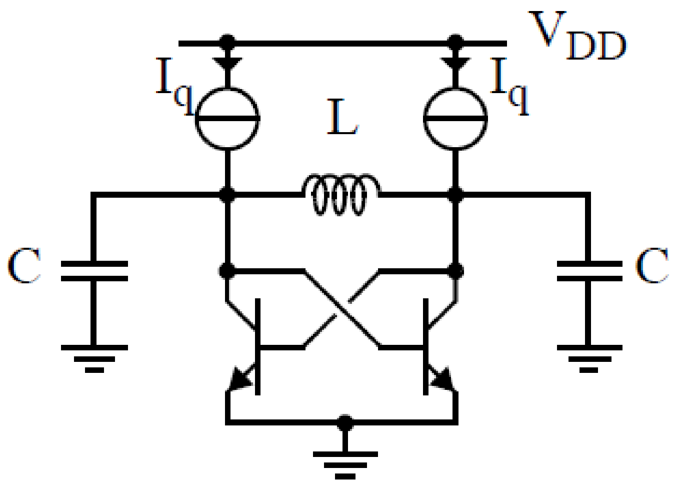
PART II: LC oscillator

Exercise 2 on LC oscillator (11 points)

The schematic of the LC oscillator is represented below.



LC oscillator.

- The LC oscillator operates at room temperature.
- The thermal voltage at room temperature is equal to $V_T = 26$ mV.
- The speed of the light is equal to 3 10^8 m/s.
- In this exercise, the Ebers and Molls small signal equivalent model of each bipolar transistor is considered by neglecting its conductance g_{be}, its output conductance g_{out}, and its parasitic capacitors.
- For the small signal equivalent model, it is considered that the variation of the voltage of the collector of one transistor is in opposite phase to the variation of the voltage of the collector of the other transistor: $\Delta V_{c1} = - \Delta V_{c2}$

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a) **Draw the small signal equivalent model of the pair of bipolar transistors** by doing the assumptions mentioned below the schematic of the LC oscillator.

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b) **Determine and prove the literal expression of the input impedance Zin of the pair of bipolar transistors** by doing the assumptions mentioned below the schematic of the LC oscillator.

c) A parallel conductance g_1 is considered in parallel to the inductance L because its quality factor Q_1 is not equal to infinity. A parallel conductance g_2 is considered in parallel to each capacitor C because its quality factor Q_2 is not equal to infinity.

- The minimum value of the collector current of each transistor and the minimum value of the transconductance of each transistor such that the circuit starts to oscillate are respectively denoted by I_{cmin} and g_{mmin}
- In first approximation, it is recalled that the oscillation frequency f_0, the capacitor C and the inductance L are linked by: $\pi f_0 C = 1 / (2 \pi f_0 L)$
- The value of the inductance L and its quality factor Q_1 are such that:
  - $L = 5$ nH and $Q_1 = 10$

Calculate the value of each capacitor C such that $f_0 = 2.4$ GHz.

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c) (continued)

Calculate the quality factor Q_2 of each capacitor C such that g_{mmin} = 4 mA/V.

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More space available to answer to question c)

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Question 4 on single turn loop antenna (2 points)

- The speed of the light is equal to $3\ 10^8$ m/s.
- The radiation resistance of the single turn loop antenna is equal to 0.02 Ohm.
- The radius of the single turn loop antenna is equal to 0.002 m.

Calculate the value of the frequency of operation

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Question 5 on electro-magnetic coupling (2 points)

- The speed of the light is equal to $3\ 10^8$ m/s.
- The distance between the RFID reader and the RFID tag in free space and in air is equal to 0.5 m.
- The two available frequencies of operation are 27 MHz and 868 MHz.

Which frequency of operation do you choose (between the two above mentioned frequencies) to have an electro-magnetic coupling between the reader and the tag ?

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Question 6 on tag (2 points)

- The impedance of the antenna of the tag is considered as a resistance R at the operating frequency.
- This resistance R is equal to 100 Ohms.
- The input impedance of the tag is considered as a resistance R_{in} at the operating frequency.
- The antenna and the tag are impedance matched at the operating frequency.
- The available input power P_{av} (which is delivered to R_{in}) is equal to 0 dBm.

Calculate the peak value of the voltage at the accesses of the input impedance of the tag

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Part III: Antennas and Propagation

Exercice 3 (10 points)

We plan to use an RF-ID tag to identify a sensor. The frequency band used is the ISM band at 2.45 GHz, and the maximal EIRP that both US and European rules allow for the application is 36dBm.

We want to assess the maximal reading distance of our RF-ID tag, and to this aim we use the power ramp method in an anechoic chamber and a calibrated reference tag. We obtain a distance of 15 m. The threshold power of the reference tag at the fixed distance D is equal to 6 dBm, while its sensitivity constant is Λ=0.5. What is the measured threshold power for the tag under test be in the following situations:

a) The antennas of reader, the reference tag and the tag under test have all a vertical linear polarization. Both RF-ID tag and reference tag have antennas that are perfectly matched to the impedance of the IC on their respective tags

b) The antenna of the reader has a polarization vector **p1** and the reference tag and the tag under test have a polarization vector **p2**, with

$$\mathbf{p1} = \frac{1}{2}\begin{pmatrix} 1+j \\ j-1 \\ 0 \end{pmatrix} \quad ; \mathbf{p}2 = \frac{1}{2}\begin{pmatrix} 1+j \\ 1+j \\ 0 \end{pmatrix}$$

Both RF-ID tag and reference tag have antennas that are perfectly matched to the impedance of the IC on their respective tags

c) The antenna on the RF-ID tag has an impedance of 50+j10Ω, while the IC on the RF-ID tag has an impedance of 60-j5Ω, the reference tag antenna is matched to the reference tag IC and the reference tag and the tag under test have both a vertical linear polarization.

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Additional space for **exercise 3**

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Additional space for exercise 3

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Question 7 (2 points)
Is free space the environment in which the pass loss is the smallest ?
A) Yes
B) No
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Question 8 (2 points)
In order to design an antenna for an implantable RF-ID, the antenna designed by first considering that the tissue into which it will be implanted is lossless (case A) and the losses are added in a second stage (case B), but keeping the same dielectric permittivity.

Please indicate which affirmation (s) is (are) right:

a) In case A, the antenna will have a broader bandwidth
b) In case A, the antenna will have a narrower bandwidth
c) In case A, the antenna will have a higher directivity
d) In case A, the antenna will have a higher gain

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Question 9 (2 points)
Consider a RF-ID system formed by a reader, and a tag fixed on targets passing randomly in front of the reader. Which configuration would you choose for your antennas?

A) Reader with linear polarization, Tag with linear polarization
B) Reader with circular polarization, Tag with linear polarization
C) Reader with linear polarization, Tag with circular polarization
D) Reader with circular polarization, Tag with circular polarization

Justification:
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