NAME: **FIRST NAME:** **SECTION:**

Prof. C. Guiducci

FUNDAMENTALS OF
BIOSENSORS AND
ELECTRONIC BIOCHIPS
EE-515

Saturday JANUARY 30th 2021 Exam Fall Term 2020/2021 Duration: 2:30 hours

- Please don't turn the cover page until authorized to do so.
- Please place the StudentID card visible before you.
- Please write your name on **all the response sheets.**
- Authorized material: copies of lessons slides, all material relevant to the exercises, your notes, other papers.
- Please answer directly on the sheets provided using a black or a blue pen. Do not use red or green pens (which are used for corrections).
- Please use legible handwriting and make clear diagrams/drawings etc. Illegible parts won't be corrected.
- Please make clear schemes and diagrams of an appropriate size. All units - either calculated or used - have to be clearly indicated.
- All communication with other students is strictly forbidden.
- Please detail the procedures followed to obtain any results.
- The use of pocket calculators is permitted. Computers, mobiles phones or tablets are forbidden.

NAME: **FIRST NAME:** **SECTION:**

EXERCISE 1

This exercise aims at evaluating the applicability of the Covid-19 PCR test for various scenarios of prevalence of the disease. The specificity of the considered PCR test is 99% and the sensitivity is in the range of 56-83%. The data are extracted from a study performed by Unisanté (Centre universitaire de médecine générale et de santé publique), Lausanne. [Note: in this exercise some answers have to be given as a range.]

A. Each of the three hypothetical scenarios (Tables 1-3) is characterized by a different prevalence of Covid-19 disease, namely 10%, 20% and 50%. For each case, you can consider a statistical sample of patients who are infected (Covid positive) and not infected (Covid negative): calculate how many patients among the Covid positive group would be tested positive or negative with the considered PCR test; calculate also how many patients among the Covid negative group would be tested positive or negative. Please fill the Tables 1-3 with the obtained results.
B. For each scenario calculate the probability that a patient has been infected in the case that the PCR test resulted positive (i.e. calculate the precision, also known as positive predictive value, PPV). Comment on the obtained values.
C. In order to better evaluate the test performance, also calculate for the three cases the probability that the patient is not infected in the case that the test resulted negative, known as negative predictive value, NPV. Comment on the obtained values.
[Hint: NPV=TN/(TN+FN)]
D. The current prevalence of positive Covid-19 tests over the total amount of tests performed in Lausanne is about 16%. On the other side, if you consider as statistical sample only patients who show multiple Covid-19 symptoms the prevalence can be as high as 50%. Comment qualitatively on the relevance of the PCR test given the considerations from the previous points.

Table 1.

Scenario 1		
	Covid positive (100 patients)	**Covid negative** (900 patients)
Test positive		
Test negative		

Prevalence:	**10%**
PPV(precision):	
NPV:	

Table 2.

Scenario 2		
	Covid positive (100 patients)	**Covid negative** (400 patients)
Test positive		
Test negative		

Prevalence:	**20%**
PPV(precision):	
NPV:	

Table 3.

Scenario C		
	Covid positive (100 patients)	**Covid negative** (100 patients)
Test positive		
Test negative		

Prevalence:	**50%**
PPV(precision):	
NPV:	

NAME: **FIRST NAME:** **SECTION:**

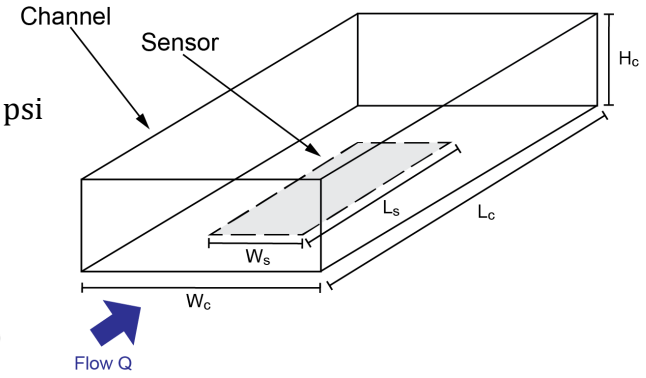
NAME: **FIRST NAME:** **SECTION:**

NAME: **FIRST NAME:** **SECTION:**

EXERCISE 2

A single rectangular-shaped biosensor is placed at the bottom of a microfluidic channel having rectangular section. The surface is sensitive to the solution's pH since it binds variable amounts of hydrogen H^+ ions, depending on their bulk concentrations. Consider the following parameters:

Length of the channel $L_C = 1\,mm$
Height of the channel $H_C = 50\,\mu m$
Width of the channel $W_C = 100\,\mu m$
Maximal pressure across the channel $\Delta P_{max} = 100$ psi
Diffusion coefficient of H^+ ions $D = 8 \times 10^{-5}\,cm^2/s$
Length of the sensor $L_S = 500\,\mu m$
Width of the sensor $W_S = 70\,\mu m$
Viscosity of the solution $\eta = 10^{-3}\,Pa \cdot s$
Elementary charge $e^- = 1.60 \times 10^{-19}\,C$
Boltzmann constant $K = 1.38 \times 10^{-23}\,m^2/(kg^2 \cdot K)$
Temperature $T = 298\,K$



A. Calculate the flow rate Q associated with a Peclet number Pe_H of 10^3. Comment on the correlation between a large Pe_H and the mass transport phenomena (convection and diffusion).
B. Does the flow rate calculated at question (A) comply with the maximal pressure that the microfluidic channel can withstand? [Hint: $1\,psi = 6.9$ kPa]

For the following points please consider a flow rate equal to $Q = 6\,\mu L/min$, regardless of what calculated at point A.

C. Calculate the new Peclet numbers Pe_H, Pe_S and the size of the depletion region.
D. For a bulk pH value of 5.5, calculate the collection rate J_D of hydrogen H^+ ions at the sensing surface.
E. Considering that at the sensor surface the charged target molecules form an electrical double layer and that the hydrogen ions concentration at the surface $[H^+]$ is equal to $2.5\,\mu M$, calculate the surface potential Ψ_0.

NAME: **FIRST NAME:** **SECTION:**

NAME: **FIRST NAME:** **SECTION:**

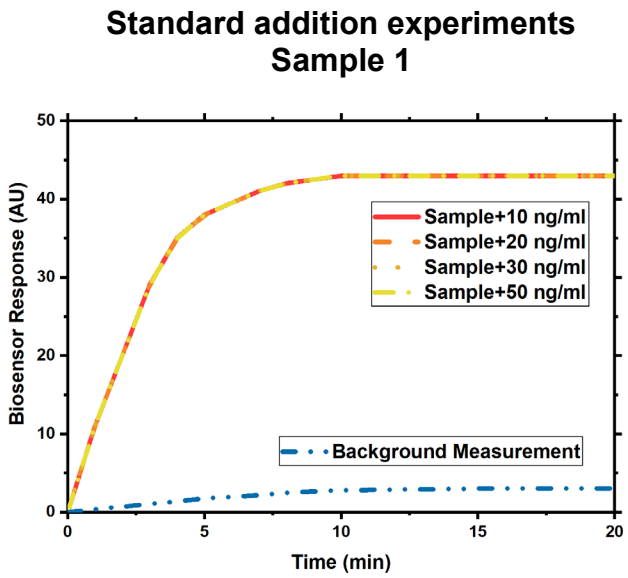
NAME: **FIRST NAME:** **SECTION:**

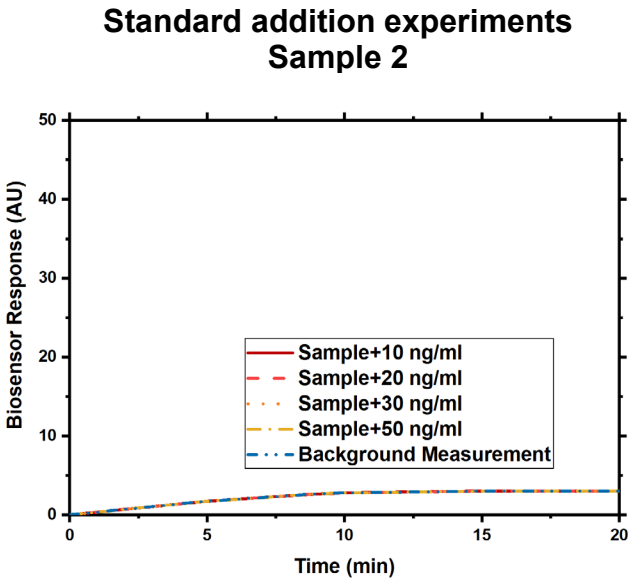
NAME: **FIRST NAME:** **SECTION:**

EXERCISE 3

A biosensor is employed to determine the concentration of an antigen molecule dissolved in two distinct samples of phosphate buffered saline (PBS). The molecules of antigen are captured on the surface of the sensor by ligand molecules (direct assay configuration). The concentrations of the antigen in the two samples are measured in experiment 1 and 2, using the standard additions method.

The reference (background) measurements are depicted in blue, whereas the other kinetics correspond to separate additions of several different concentrations (+ 10, 20, 30, 50 ng/mL) of the antigen to separate aliquots (the final concentrations obtained are the unknown concentration from the sample + the added concentration).





A. Are those experiments useful to determine the antigen concentrations in the two samples? You can complement your explanations by drawings. Discuss what is the issue of the experiments above (Standard addition experiments 1 and 2) and how it could be solved.
B. Comment on the proportion between the density of the bound ligands at equilibrium (Γ_{eq}) and the total density of ligands (Γ_0) in the two experiments.
C. Given the standard addition experiments for sample 2, discuss whether a competitive assay instead of a direct assay would be preferable.
D. What would need to be considered if the measurements were conducted in a different sample matrix, e.g., saliva?

NAME: **FIRST NAME:** **SECTION:**

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