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

Prof. C. Guiducci

FUNDAMENTALS OF BIOSENSORS AND ELECTRONIC BIOCHIPS
EE-515

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Wednesday JANUARY 13th 2020 Exam Fall Term 2019/2020

Duration: 2:15 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.

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EXERCISE 1

Your job is to design a population screening assay for colon cancer. The data below are provided.
Figure 1 shows ROC curve for your biomarker. Figure 2 represents the incidences of such disease for 10'000 people in a given age group (eg. in age group 70+ there will be 1000 incidences (cancer cases) per 10'000 people).

A. Your initial target is to diagnose 100% of the patients affected by the disease. You will first consider the option to screen the entire population. In this case the maximal precision is around 13%. What is the corresponding screening performance (sensitivity, specificity and prevalence)? Discuss the consequences of low precision.
B. In the same hypothesis of wanting to diagnose 100% of the patients affected by the disease, how can you maximize the precision using the same biomarker? What value would this be?
C. In order to increase precision of the test, you decide to accept that some cancer patients in the population won't be detected. Which parameters and conditions of the assay should be modified to achieve a better precision? Please, provide one numerical example for each parameter. Comment on these options.

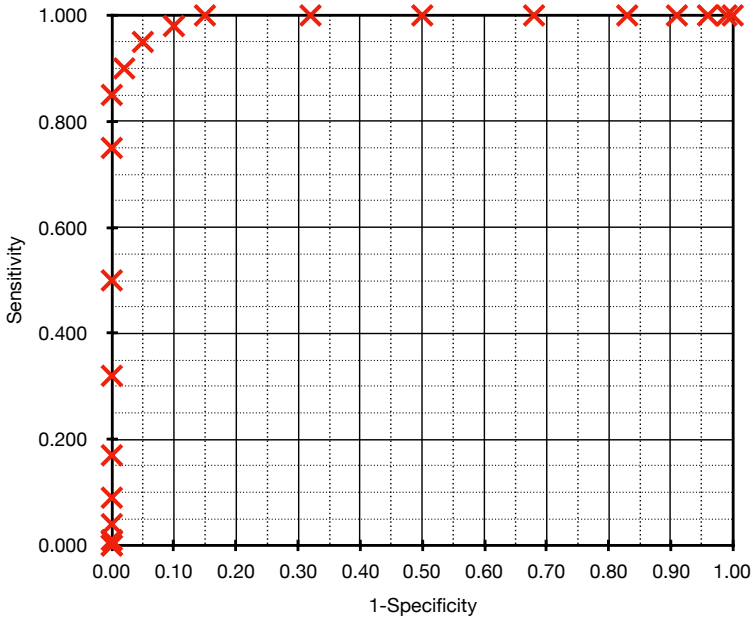

Figure 1.

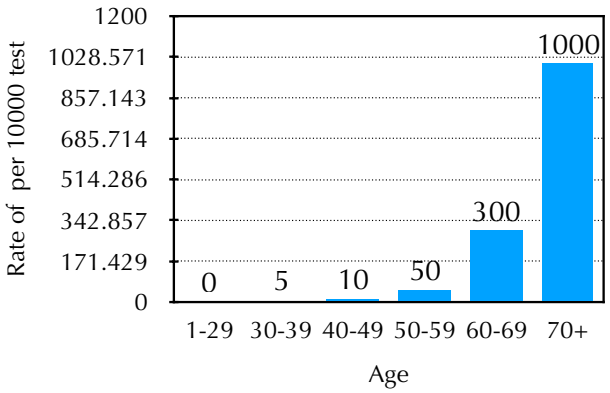

Figure 2.

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EXERCISE 2

A single rectangular-shaped surface biosensor is placed at the bottom of a channel having rectangular section. Consider the following parameters:
Length of the channel L_C : 500 μm
Height of the channel H_C : 20 μm
Width of the channel W_C : 100 μm
Diffusion coefficient D of the target molecule in the sample: $10^{-10}\ m^2$/sec
Length of the sensor L_S : 100 μm
Width of the sensor W_S : 20 μm
Density of binding sites on the sensor: Γ_0= 4 × 10^{11} molecules/cm^2
Dissociation constant K_D = 5 × $10^{-8}\ M$
Flow rate in the channel: Q = 1 $\mu L/s$

A. Calculate the associated Peclet number Pe_H and comment whether either convection or diffusion is dominating in the device
B. Calculate the height of the depletion region
C. The concentration of the target biomolecule in the channel has been maintained at 1 nM until equilibrium is reached. At t = 0 s, a new solution at a concentration of 100 nM is injected. How long will it take to reach the new equilibrium?
D. We assume now that the biomolecules are captured on the surface of 2 μm-diameter beads having the same surface density as the previous planar sensor. How many beads do we need in order to capture the same number of molecules as on the planar channel? (Reminder: Area of a sphere with a radius *r* : $A = 4\pi r^2$)
E. What is, in terms of mass transport, the advantage of using such beads?

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EXERCISE 3

Empty graphs and tables are provided on the following pages.

Two different antibody-antigen interactions are performed on sensing surfaces during two separate experiments. During the first 100 s, the analyte is injected in the chamber above the sensor and at time 100 s the chamber is filled with a rinsing buffer solution.

In both cases, we make the hypothesis of full sensor coverage by the antibodies.

A. Based on the given data,
    1. Fill the table (including missing units in the table header). Calculate the surface density Γ_0 considering the footprint of each antibody given in the table and no spaces between them.
    2. Draw the two Langmuir binding isotherms corresponding to the two different antigen-antibody interactions experiments for the interval 0-200 s. Do calculate at least two points for the association, equilibrium and dissociation phases respectively (at least 6 points), indicating them on the plots. Complete the plot with the label of the Y axis.

B. Discuss the difference between the two affinity binding experiments. In particular, comment on the role of the concentration of the antigen.

C. Draw calibration curve for each antibody for concentrations values 10 nM, 30 nM, 100 nM, 300 nM and 1000 nM, and discuss whether it is possible to quantify the concentration of each antigen in this range. Complete the plot with the label of the Y axis.

D. For these two antigens, what could be modified to change the interval of concentration corresponding to the linear range in the calibration curves?

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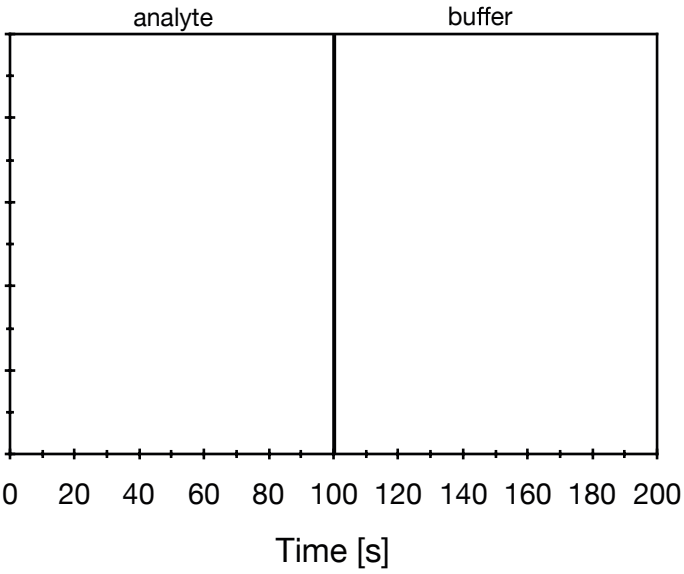
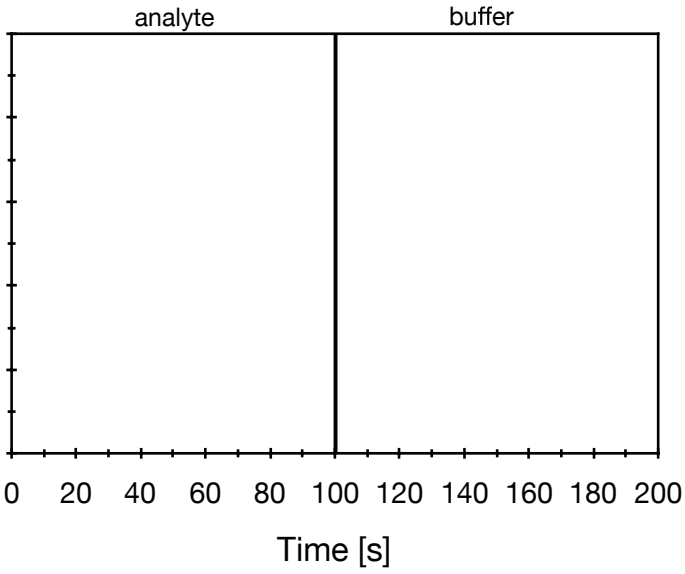
3.A.1.

Antigen/ Antibody	K_D [M]	Concentration of antigen [M]	Γ_{eq} [ ]	Γ_o [ ]	k_{on} [$M^{-1}s^{-1}$]	k_{off} [ ]	Antibody footprint [nm^2]
PSA/PSA-Ab	$10x10^{-12}$	$100x10^{-12}$			$2.5x10^{9}$		4
CA125/ CA125-Ab	$250x10^{-9}$	$2500x10^{-9}$			$100x10^{3}$		4

3.A.2.





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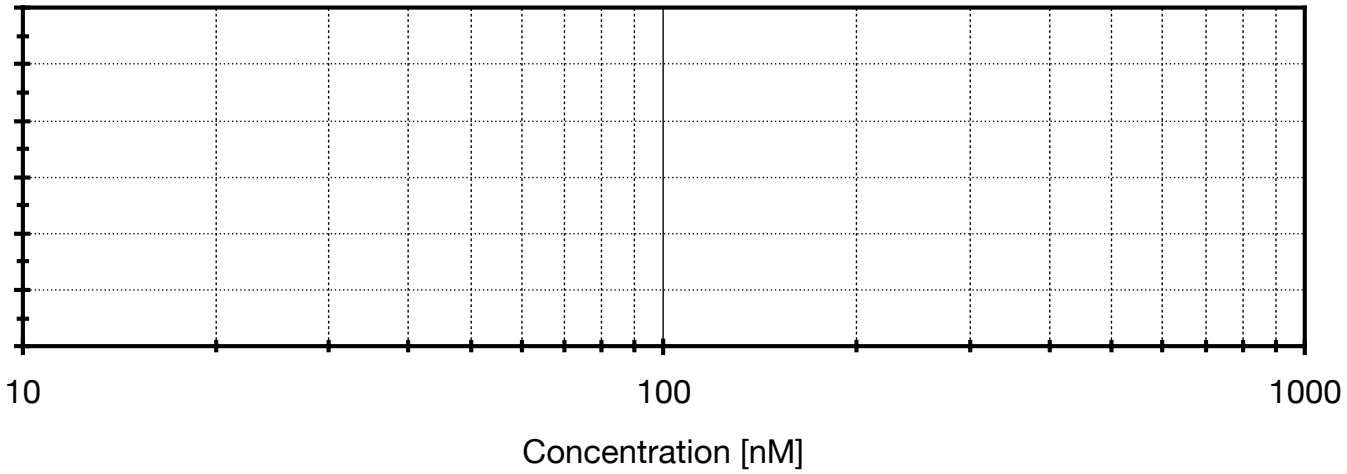
3.C.



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