Lab-on-a-Chip exam, June 23d 2014 from 8.45-12.15

You may answer the questions in English or Dutch
There is a total of eight questions. Every question is worth 10 points out of a total of 81 (Question 5 is worth 11 points).
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1. Separation methods

Describe the separation mechanism that forms the basis of each of the following separation methods:

a) electrophoresis — *2.5 pts*
b) liquid chromatography — *2.5 pts*
c) hydrodynamic chromatography — *2.5 pts*
d) capillary electrochromatography — *2.5 pts*

2. Micro- and nanofluidics

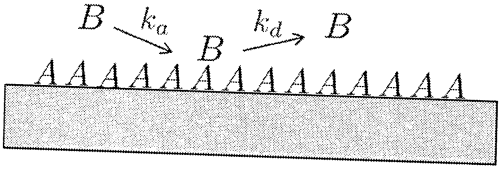
How do the flow velocity (m/s) and the volume flow rate (m^3/s) scale when we decrease the diameter d of a cylindrical microchannel from 100 micrometer to 100 nanometer while using

a) pressure-driven flow with constant applied pressure gradient — *2.5 pts*
b) electroosmotic flow with constant applied electrical field — *2.5 pts*

c) Describe the mechanism of electroosmotic flow — *2 pts*
d) How is electroosmotic flow affected by
- changing the channel diameter from 100 nm to 1 nm,
- increasing the salt concentration,
- changing the solution pH? Explain why in all three cases. — *3 pts*

3. Label-free detection methods

We have a surface that is functionalized with groups A that bind analyte molecules B as shown in the figure below



$$A + B \underset{k_d}{\overset{k_a}{\rightleftharpoons}} AB$$

a) Give the expression for the rate of formation (mol/s) of the complex AB — *1 pts*
b) Give the expression for the rate of dissociation (mol/s) of the complex AB — *1 pts*
c) Derive the relationship between the concentrations of A, B and AB once binding equilibrium has been reached, as a function of k_a and k_b . — *3 pts*
d) Describe how we can obtain a maximal equilibrium concentration of the complex AB — *2 pts*

e) Mention at least 4 label-free detection methods of AB — *3 pts*

4. Cells on Chip

I would like to develop a microfluidic device for cell biology applications, including cell culturing.

a) Which material(s) could I use to build my microfluidic device? Which materials would you particularly recommend for the present application? Discuss two particular materials in terms of pro's and con's.
4 pts

b) PDMS is widely utilized, in particular for cell biology applications. Explain why. Does this material exhibit limitations?
4 pts

c) For one particular experiment, I would like to test a range of concentrations of a soluble compound, and examine the response of my cells in a concentration-dependent manner. How can I realize this? *2 pts*

5. Surface treatment *(11 pts)*

a) a) Why can it be important to treat surfaces in a microfluidic device? Can you mention at least two applications where it is mandatory?
3 pts

b) I work with microfluidic devices made from silicon. I would like to modify covalently their surface. Which strategy can I employ?
1 pt

c) Which other strategy is available for modification of silicon surfaces? *1 pt*

d) What are the advantages and limitations of both approaches? *3 pt*

e) In my device, I have gold patterns, which I would like to functionalize. Which strategy is commonly used for gold surfaces? Which molecule(s) can I use? What is the nature of the "bond" between my molecules and the surface?
3 pts

6. Sample preparation / Cell analysis

I would like to analyze a small population of biological cells.

a) Would you recommend me to use a microfluidic device? Why? *2 pts*

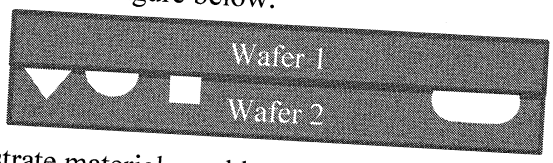
b) I would like to analyze the DNA content of my cells. Which steps do I need to implement in my microfluidic device, knowing that (i) my sample is highly diluted, and that (ii) my number of cells is too low for a direct detection of my DNA? (*hint*: 4-5 steps).
4 pts

c) Propose a complete analytical flow with specific approaches for the different steps. *2 pts*

d) Can I apply the same strategy for the analysis of proteins in my small cell population? Explain why. What are the main differences between DNA and proteins from an analytical point of view? *2 pts*

7. Microfabrication

Student X wants to make a LOC for capillary electrophoresis. Detection of the separation products will be done using fluorescence microscopy. Student X decides to use a design with 2 wafers. One for the fluidic channels, and one to cap (seal) these channels. The precise cross-sectional shape of the channel is not critical and can be any of the five shapes, as illustrated in the figure below:



a) Which substrate material would you recommend student X for this application? Explain your answer.

After some calculations, student X decides a microfluidic channel of 30 microns wide and 10 microns high is required for his application.

b) Which fabrication methods, as discussed in the microfabrication lectures or the book of Saliterman, are available to create such a channel? List as many as possible, but take your answer at (a) into account.

c) Which method would you actually recommend student X? Take your answer at (a) into account and explain your answer.

d) Which method would you recommend to bond the two wafers? Explain your answer.

Suppose student X decides to change his design to use microfluidic channels of 10 microns wide and 10 microns high.

e) Would that change in design change your answers at (a-d)? Explain your answer.

Points question 7 (10 total):

a) 2 points for suitable material

b) In total 2 points. (Depending on the answer at (a), each correct method contributes 2/(no. of all possible methods) points.)

c) 2 points for good method including good explanation.

d) 2 points for good method including good explanation.

e) *2 points for right answer with right explanation (depending on earlier answers).*

8. Electrochemical detection

$$E = E^0 + \frac{2.303 \cdot R \cdot T}{n \cdot F} \log\left(\frac{[ox]}{[red]}\right)$$

$$i(t) = n \cdot F \cdot A \cdot C^* \sqrt{\frac{D}{\pi \cdot t}}$$

$$L = \frac{F \cdot A}{l} \sum |z_i| \cdot \mu_i \cdot C_i$$

Constants:			
F	96485 coulomb/mol	μ for all ions in this exercise:	7E-8 $m^2/(V*s)$
R	8.31 J/(K*mol)	D for all ions in this exercise:	1E-9 m^2/s
T	290 K		

You have a 20mL beaker, a silver/silverchloride electrode, a platinum electrode, a (proper) reference electrode and a potentiostat available.

a) What kind of electrochemical detection method (potentiometry or conductometry) would you choose to sense the chloride ion concentration in 10mL blood, without using a separation method prior to the detection? Explain your answer.

Suppose the chloride ion concentration is 100mM in a clear aqueous solution without other interfering ions.

b) Draw the resulting current response in a graph if you would conduct an amperometric experiment, assuming an oxidative potential (i.e. the working electrode potential is 0.3V vs. NHE) and an electrode area of $1mm^2$.

Note: The reaction equation is: $Ag_{(s)} + Cl^-_{(aq)} <-> AgCl_{(s)} + e^-$

c) How can the electrical double layer affect amperometric measurements? Explain your answer i.e. by adding a second curve in the graph drawn at (b).

Points question 8 (10 total):

a) 3 points for right answer and good explanation.
b) 4 points (2 points for right curve, 1 point for axis labels, 1 point for neatness)
c) 3 points for right answer with proper explanation.