Exercises with leads for EEMN21, fall 2017

Note that the leads **indicated by bold text** are not the full solution but only hints or answers. In the exam, if it says *calculate*, then you need to write up the equation(s), motivate, rearrange etc. and then produce a number and a unit. If it says *express* then you need to produce an expression, if it says *show* or *derive* then you need to highlight the important steps in getting to the final expression. If it is not clear, then you ask Per or Pelle. Note that the document may have errors, if you think you find one, contact Per or Pelle.

Use these exercises to facilitate understanding of the key concepts and the physics of microfluidic systems. The exercises are ordered approximately according to their order of appearance in the course. Make necessary assumptions to support your argumentation and insert relevant values for constants when required. For some exercises the answer or a full solution will be provided. Please provide feed-back on errors, inconsistencies or things that are unclear so that we can improve this document.

0. Warm up by converting some units

All research fields have their own conventions regarding what units are used. For instance in microfluidics flow rates are relatively small and flow is therefore expressed in µL/min or µL/h. Pressures on the other hand can be expressed in units of psi, Pa or bar. One safe way of getting things right is to convert all units to SI units (kg, s, m, m^2, m^3, Pa, Pa·s) etc before entering values into expressions. Take the opportunity to practice some conversions.

0.1. What is the volume of a cube of side-length 1 mm? Express the volume in µL and in m^3. **1 $(mm)^3$ = 1µL = 1E-9 m^3**

0.2. Write an expression to convert from a flow rate expressed in µL/min to m^3/s. **1µL/min = 1/6*10^{-10} m^3/s**

0.3. Express the pressure 1 bar in Pa and in psi. **1 Bar = 100000 Pa = 14.5 Psi**

0.4. The diffusion constant of a small ion in water is ~$2 \cdot 10^{-9}$ m^2/s. Express the diffusion constant in the unit $(cm)^2/h$. **1 m^2 = 10^4 $(cm)^2$, 1 s = 1/1200 h -> $2 \cdot 10^{-9}$ m^2/s = $2 \cdot 10^{-9} \cdot 10^4 \cdot 1200$ $(cm)^2/h$ = $2.4 \cdot 10^{-2}$ $(cm)^2/h$**

1. Surface tension, capillaries and droplets

1.1. Why are small droplets spherical?

1.2. Why is there an over-pressure inside a spherical droplet?

1.3. Write an expression for the Laplace pressure inside a spherical droplet?

1.4. Write an expression for the pressure drop at the liquid-air interface inside a glass capillary.

1.5. Derive an expression for the capillary fill-height of a vertical capillary that has been dipped into liquid?

1.6. Ignoring gravity, redo the experiment (1.5) for the same capillary. When does the capillary filling stop? **- At the end of the capillary**

1.7. Explain why the liquid-air interface slows down with increasing fill level. **Lead: Flow resistance scales with the length of a pipe.**

1.8. Based on Washburn's equation, derive an expression for the fill velocity of a capillary as a function of time. **Lead: u = dx/dt**

1.9. What happens when the liquid-air interface reaches the far end of the capillary?

1.10. Why does not the liquid follow the glass surface and wet the outside of the capillary? **Lead: contact angle.**

1.11. To think about: Can wetting outside the capillary occur if the opening is very rounded? It depends. No calculations are necessary.

Imagine a hydrophilic (0 deg contact angle) circular surface (radius (a)) on a hydrophobic (180 deg contact angle) surface. Inside the hydrophilic circle there is a tiny hole through which you can pump liquid using a syringe pump. First, the liquid will cover the hydrophilic surface in a thin sheath and then the droplet will grow as a spherical cap (https://en.wikipedia.org/wiki/Spherical_cap) with increasing radius (r) but with a fix sized base radius (a).

1.12. For what drop radius (r) do you need to supply the highest pressure to sustain the droplet? For r = a

1.13. Neglecting gravity, what is the theoretical maximum size of a droplet that can be anchored in this hydrophilic circle, and what would be the Laplace pressure inside that droplet? **Infinite**

1.14. **Not** neglecting gravity, can you figure out for what drop-height gravity will deform the sphere. Assume for instance a = 0.5 mm. **Gravity forces dominate for Bond number higher than 1 (Bo = $\rho g r^2/\gamma$). Then the droplet would be deformed. Alternatively, if we imagine we flip the surface so that the drop is hanging we know from the lab how to calculate the drop size when it falls from $\gamma 2\pi a = \rho g 4\pi r^3/3$ -> r = 1.8 mm. At this point it has definitely deformed due to gravity. Then one could calculate the corresponding cap height or just argue that the cap height would be close to 2a.**

2. Viscosity and laminar flow

2.1. What is the side length of the smallest cube of water that can be modelled as a continuum according to this model? Assume that you need 10^4 molecules to get stable statistics, that water molecules weigh 18 g/mol and that there are 6 x 10^{23} molecules in a mole.

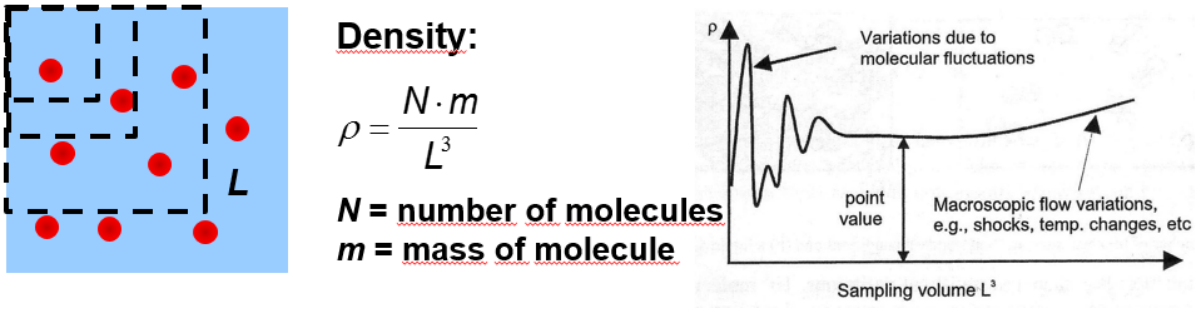

Figure 1: Fluid modelled as a continuum.

2.2. What two effects/forces influences the Reynolds number (Re)?

2.3. Write an expression for Re.

2.4. What is the Re below which the flow can be considered to be laminar in circular cross section channels?

2.5. Estimate Re for the following

2.5.a. Water flowing at 100 µL/min through a circular microfluidic channel with a diameter of 100 µm

2.5.b. Drinking water through a straw

2.5.c. Blood flowing at 5 mL/min through aorta (diameter: ~2.5 cm)

2.6. Draw microfluidic channels of different cross sections. Assume that h = r = 100 µm.

2.6.a. Circular [r]

2.6.b. Square [h:w = 1:1]

2.6.c. Rectangular [h:w = 1:20]

2.6.d. Rectangular [h:w = 1:2]

2.6.e. Trapezoidal [h:w1:w2 = 1:2:3]

2.6.f. What dimension is most influential for the different channels (a-e) above?

2.7. What is the formula for the hydraulic diameter?

2.8. The hydraulic diameter is sometimes, but not always, a decent estimation of the dimension that can go into the formula for Re. When and why is it a particularly bad estimation? Is the hydraulic diameter actually a necessary concept in this context?

2.9. What is hydraulic resistance and what is it useful for?

2.10. For the abovementioned (2.6.a) circular and (2.6.c) parallel plate geometries there exist analytical solutions to the hydraulic resistance (Rh). What are the equations for Rh in these cases? (Note that in the Folch-book the channel height and width is defined as 2h and 2w, respectively).

2.11. The hydraulic resistance of the rectangular channels (2.6.b) and (2.6.d) can be described by infinite sums. This is rather tedious. Further, for the trapezoidal channel (2.6.e)

we have no expression. Employ instead the concept of hydraulic diameter to calculate the hydraulic resistance for channels (2.6.b), (2.6.d) and (2.6.e).

2.12. Calculate the flow resistance and the necessary pressure drop to push water at 1 mL/min through the following channels:

2.12.a. A 20 cm long tube with an inner diameter of 200 µm. **$R_1 = 8\eta L/(\pi r_1^4)$, $\Delta p = Q \cdot R$**

2.12.b. A 20 cm long tube with an inner diameter of 400 µm. **$R_2 = 8\eta L/(\pi r_2^4)$, $\Delta p = Q \cdot R$**

2.12.c. The two tubes connected in series: **$R = R1 + R2$, $\Delta p = Q \cdot R$**

2.12.d. The two tubes connected in parallel: **$1/R = 1/R1 + 1/R2$, $\Delta p = Q \cdot R$**

2.12.e. What will be respective the flow rates in the two branches in the parallel configuration? **Lead: Get Δp from 2.12.d, same pressure drop over each channel branch, $Q1 = \Delta p/R1$, $Q2 = Q-Q1$.**

2.13. You want to use the chip shown in Figure 2 to separate bacteria from blood cells in a 2 cm long, 375 µm wide and 150 µm deep rectangular separation channel. You have connected each of the four inlets and outlets of the chip to 20 cm long pieces of tubing of inner diameter 200 µm and you can control the pressures in the liquid sample containers.

2.13.a. Calculate the fluidic resistance for the main separation channel

2.13.b. Draw the equivalent circuit ignoring all other fluidic resistances except the tubing and the main separation channel

2.13.c. Calculate the pressures to set at the end of each tube, relative to atmospheric pressure, to get a flow of 100 µL/min through each inlet and outlet in the direction of the arrows. (Hint: identify the point of lowest pressure and set this pressure to 0 and work your way stepwise through the model.)

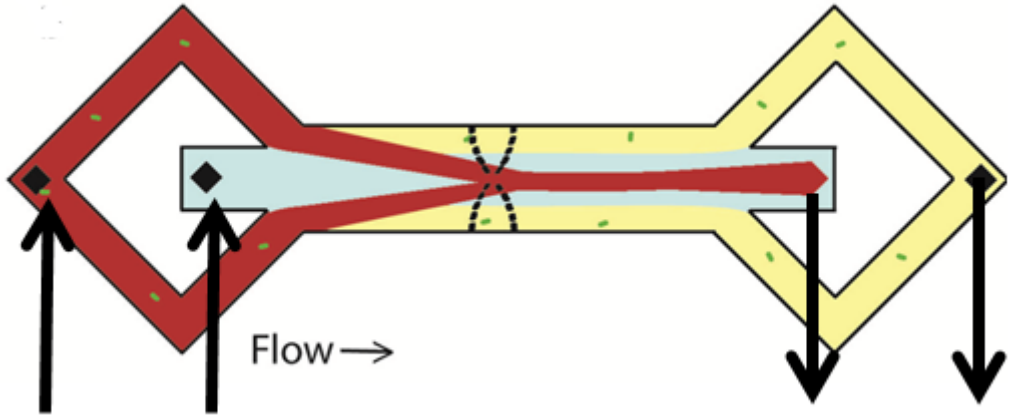

Figure 2: A chip to separate bacteria.

2.14. How do the flow velocity profiles look for the different channel geometries in 2.6? Draw schematically as viewed from above, from the side and from along the flow (in the last case, use contour lines to indicate velocity regimes).

Imagine now two plates of area A with a thin film of thickness y of water between them. One plate is fixed and the other one move with some velocity u due to some applied shear force ***F*** and the water will move with so called Couette flow. Try to draw the velocity flow profile as viewed from the side.

2.15. Search online: Relating to the above. What is the definition of viscosity η? (en.wikipedia.org/wiki/Viscosity)

2.16. What is the dynamic viscosity of water?

2.17. Let A = 1 m2, y = 100 µm, u = 1 m/s. What is the shear force ***F***?

2.18. (**Tip: Do this after Lab 1**) In the Lab 1 exercise you have noted that the relative flow rates of two laminated liquids will affect the widths of the two streams. Additionally some of you have noted that the differences in viscosity of two laminated liquids can affect the relative widths of the two streams. To exemplify: even if the two flow rates are set to the same value the stream widths are not the same unless the viscosity is the same. See Figure 3.

In this exercise you will try to show how this can be explained. Try to work with variables in the expressions. Here is the setting:

Two liquids of different viscosities η_1 and η_2 flow side by side in a low aspect ratio channel ($h << w$) at flow rates Q_1 and Q_2. How broad (w_i) will the respective streams be? We assume here for simplicity that the side walls as well as the interface between the two liquids have no effect on the flow so that the resistance to flow can be described by the formula for a parallel plate geometry, $R = 12\eta\, L/(h^3 w)$. Since the liquids have different viscosities we will need to treat them as two individual parallel channels of a combined width $w = w_1 + w_2$. But we do not know the position of the interface.

a) Try to derive an expression that indicates the position of the interface between the two liquids (e.g. w_1/w_2). Remember that the pressure drop $p = p_1 = p_2$ along the channel must be the same for the two liquids because there is no rigid wall separating them. What factors determine the widths of the streams?
We can express the pressure *p* at the inlet of each channel as $p_i = Q_i R_i = Q_i 12\eta_i L/(h^3 w_i)$. Even if we would not really care what the pressure is at the inlet of the channel we can at least say that the pressure for the two flows must be the same at all points along the channel, because there is no rigid wall separating them. By setting $p_1 = p_2$ a lot of things cancel out and we arrive at the result that $Q_1\eta_1/w_1 = Q_2\eta_2/w_2$. A higher viscosity leads to a broader stream.

b) Try to figure out a way to derive the pressure at the inlet as a function of the two inlet flow rates, the channel dimensions and the two viscosities.
If we do care about the pressure at the inlet we can use that $w = w_1 + w_2$ is known and that $w_2 = w_1 Q_2\eta_2/(Q_1\eta_1)$. Solving for w_1 leads to $w_1 = w / (1 + Q_2\eta_2/(Q_1\eta_1))$ and inserting this into Ohm's law of laminar flows for one of the flow streams leads to $p = Q_1 R_1 = 12L(Q_1\eta_1 + Q_2\eta_2)/(h^3 w)$.

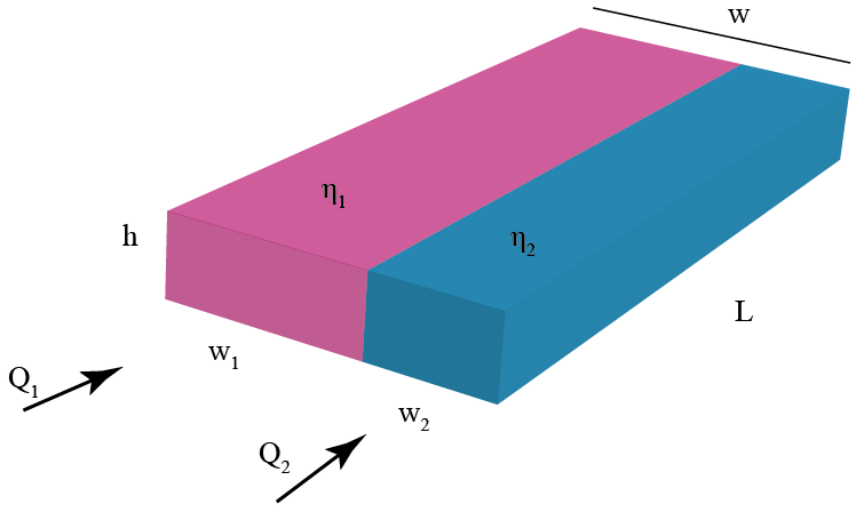

Figure 3: Two liquids of different viscosities are laminated side by side.

3. Diffusion

3.1. Diffusion is driven by the random motion of colliding molecules. The speed of individual molecules is on the order of 500 m/s, but due to being closely packed and constantly crashing into each other they traverse longer distances very slowly. Draw concentration profiles for some different cases. Draw four lines: one line for time zero, one for intermediate times, one for long times, and one for infinite time. (We imagine here a channel which has three dimensions, but due to flow along the length-axis and because of a flat geometry, we assume 1D diffusion directed along the width-dimension only.)

3.1.a. A finitely wide rectangular channel uniformly filled with molecules on one half and with no molecules on the other half.

3.1.b. An infinitely wide channel, with a finite number of molecules in a thin vertical lamina at the channel center.

3.2. How long time does it take before molecules are significantly spread over the whole 1 mm wide channel, if they are initially in a thin band in the center of the flow in a channel.

3.3. Assume you have a 1 mm wide channel half-filled with a dye ($D \approx 10^{-9}$ m^2/s), see Figure 4.

3.3.a. How long will it take for the dye to completely fill the channel through diffusion?

3.3.b. What is the maximum distance that a slow protein ($D = 10^{-7}$ cm^2/s) will be able to move during 1 min? **x = sqrt(2Dt)**

3.3.c. How long would it take a neurotransmitter ($D = 20\,000$ (µm)^2/s) to move the same distance? **Convert unit for D, $x^2 = 2D_{protein}t_{protein} = 2D_{transmitter}t_{transmitter}$ solve for $t_{transmitter}$.**

3.4. Model the following objects as spheres and estimate their diffusion constant.

3.4.a. A sphere of diameter 1 µm, **$D = kT/(6\pi\eta a) = 4.4 \cdot 10^{-13}$ m^2/s**

3.4.b. A bacteria (look up size)

3.4.c. A cell (look up size)

3.4.d. A large molecule (5 nm), **$8.8 \cdot 10^{-11}$ m^2/s**

3.4.e. A small molecule (https://en.wikipedia.org/wiki/Small_molecule)

Figure 4: Dye molecules are flow laminated along one side of a microfluidic channel.

4. Separating cells and particles

Relating to exercise **2.17**. Another way to measure viscosity is to study a sphere sedimenting through a liquid. Then you measure the velocity u of a sphere of radius r that sinks through a liquid of known density. The buoyant density ($\Delta\rho = \rho_{sphere} - \rho_{medium}$) of a sphere leads to a gravity force ***F***g that makes it sink at terminal velocity counteracted by the hydrodynamic drag force ***F***d.

4.1. What is the gravitational force acting on the sphere? **$F_g = \Delta\rho 4\pi r^3 g/3$, I get 0.26 pN.**

4.2. What is the drag force acting on the cell? **Lead: The net force is zero at constant velocity. Fg=Fd**

4.3. Write the expression for the Stokes' drag force on the particle?

4.4. Derive an expression for the viscosity based on the sedimentation rate of the sphere.

4.5. How long time does it take for a cell to sediment 100 µm in isotonic water of density 1005 kg/m^3 and viscosity 1 mPas? This cell is spherical and 10 µm in diameter and we can assume it to have a density of 1055 kg/m^3. **Rearrange the formula for viscosity that you derived in 4.4 so that you get the sedimentation velocity. The sedimentation time is $t_{sed} = H_{sed}/u_{sed}$. I got 36 s.**

4.6. A cell suspension is pumped through a horizontally aligned microchannel. Given your calculated sedimentation time for the cell and for a flow rate in a channel of 5 µl/min. For a channel of width 1 mm and height 100 µm, how far into the channel will the cell reach before it starts tumbling along the channel floor? Assume for simplicity a uniform flow velocity distribution in the channel (i.e. a plug flow). **Most extreme case: The cell starts out at the channel ceiling at z = 100 µm. Time to sediment = 36 s equals expression for the time to flow. -> cell hits bottom at L = 30 mm.**

4.7. **In preparation for Lab 2. Acoustic cell wash**

You are constructing a chip (see Figure 5) to wash away unbound dye molecules (blue) from cancer cells (white) after labelling. You want to use acoustophoresis to move the labelled cells from buffer a sample inlet and transfer them into a clean buffer (white) that enters from a central inlet. At the end of the channel the labelled cells exit through a central outlet and free dye molecules exit through the sides. The main separation channel is 20 mm long. Assume slip conditions at the walls (i.e. plug flow). Assume that all liquids have the same properties as water. The flow of liquid is 100 µL/min through all four inlets and outlets respectively.

a. An acoustic standing half wave across the width (375 µm) of the separation channel is used to move the tumor cells from the labelling buffer to the cell-free medium. Write an expression and calculate the actuation frequency that should be used? **2MHz**

b. What is the time that it takes for a cell to flow through the separation channel? **Since the height is not given I assume it to be 100 µm and then I get 0.45 s.** During this time the cell must be deflected sideways from one of the walls and reach the center of the channel?

c. What is the average acoustic radiation force ***F***r that is required to push a cell this distance within the time frame of passing the separation channel? **F_r must balance with stokes drag. The cell moves W/2 in 0.45 s. That gives us the acoustically induced sideways velocity that will go into the equation for Stokes' drag force. I get F_r = 39 pN.**

d. Compare ***F***r to ***F***g in exercise 4.1. What flow rate would you need to use to manage the separation based on gravitational sedimentation? (assume here the chip has been flipped sideways in the gravitational field so that cells sediment from the top-most inlet towards the central outlet). **First I think we should assume that we have blocked the lower cell inlet. Calculate the time for gravity to sediment the cell a distance of W/2. The corresponding flow rate is the volume of one channel length divided with the sedimentation time. Alternatively, Fg = Fr/150 so the flow must be set to 100/150 µL/min = 0.67 µL/min.**

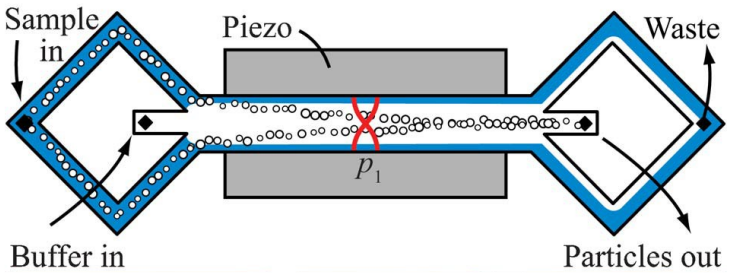

Figure 5: An acoustic cell washing channel.