Answers to Question Set 3

Fluidics - Basics

These answers are not always complete, but they do indicate what are the important points in the papers.

If you have any questions feel free to send an email: jonas.tegenfeldt@ftf.lth.se.

The suggested literature for this theme is quite extensive. However, the papers are overlapping and not everything in the papers is included in the course. Remember that the main task is to extract some key pieces of information as well as a general understanding of the basic principles of fluidics from the given literature.

Read the question and try to find the answer in the papers: Beebe's paper[1], Weigl's paper[2], and Quake's review[3]. The lectures also key information for the questions.

For a more comprehensive discussions on microfluidics there are at least two books that may be useful:

1. Nam-Trung Nguyen, Steven T Wereley: Fundamantals and Applications of Microfluidics (2006).

2. Henrik Bruus: Theoretical Microfluidics (Oxford Master Series in Physics) - (2007)

For the homework questions, note that they can be divided into two categories: Some mostly concern listing a few facts. These are labeled (F) and the expected answer should fit within five rows of text. Some are more focused on calculations or a qualitative argument. These are labeled (C). Here the answer may become more extensive due to the space taken up by equations.

The question labeled ** is more challenging than the others.

QUESTIONS ON MICROFLUIDICS

1. (F) What is the major difference between fluidics in the macro scale and fluidics in the micro scale? What are the implications for microfluidics?

The major differences between fluidics on the macro and micro scales arise from the fact that the different observables do not scale equally when we change the dimensions of a device. Various phenomena depend on ratios between different observables such as volume and surface area, or inertial and viscous effects. Note that the properties of the liquid do not change for typical water-based liquids unless the channel size approach the size of the molecules involved.

• The Reynolds number for microchannels is typically < 1 which indicates laminar flow (no turbulence).

• Diffusion: the average time it takes a particle to diffuse a given distance is proportional to the square of that distance: $x^2=Dt$. The small distances involved in micro- and nanochannels can thus be covered in very small time periods, whereas on the macro scale the effects of diffusion can often be neglected.

• The surface area to volume (SAV) ratio grows rapidly when we shrink dimensions. This affects, for example friction between liquid and channel walls, increasing the fluidic resistance drastically for smaller channels. Heat dissipation also depends on the SAV ratio.

• Surface tension forces become important for small channels. On the other hand, the flow velocity scales with the radius of the channels so that the velocity decreases with radius of the channel.

The main change in going down in size is that the surface-to-volume ratio increases. This makes effects that are associated with surfaces more important: Pressure driven fluid flow is slower due to viscous drag (friction) of the walls. Electroendosmotic flow is possible.

Advantages of running experiments in microfluidic devices include: (1) less sample and reagents are needed, (2) parallel operation is possible for high-thoughput screaning, (3) faster analysis, (4) more sensitive analysis, (5) integration of different analytical techniques on a single chip, (6) single-cell measurements are possible giving additional information as compared to standard bulk measurements.

2. (C) What is the Reynolds Number? What is the Reynolds Number in a typical microfluidic channel (assume water, velocity ~ 1mm/s, channels of size 10µm and room temperature)? What type of flow do you have in that case?

$$\mathrm{Re} = \frac{inertial\ terms}{viscous\ terms} = \frac{\rho u D}{\eta} = \frac{1000 kg\, m^{-3}\ 10^{-3} ms^{-1} 10 \cdot 10^{-6} m}{10^{-3} kg m^{-1} s^{-1}} = 0.01 << 1 \quad \Rightarrow$$

Laminar flow. Using the Reynolds number instead of solving the differential equations is a very simple way to predict behaviors in fluids. Compare with the discussion about the bacterium and dolphin swimming in water.

Note that water has the viscosity of 1 centiPoise = 1cm^{-1} g sec^{-1}=1 kg m^{-1}s^{-1}

3. (F) What are the major means of moving sample and/or liquids in small channels? How do they scale with size of the channels?

The typical dimension of the channel is given by *a* (radius).

- Pressure driven flow (v~a^2)
- capillary forces (v~a)
- electrophoresis (independent on size)
- electroendosmosis (works well for *a*~<100µm)
- dielectrophoresis (typically *a*~1µm-10µm).
- Centrifugal forces (www.gyros.com).
- Acoustic forces (Thomas Laurell group in Lund)

4. (C) A pressure difference can be applied between one free end and one end connected to vacuum or to an overpressure. What are the practical differences between these two approaches?

Overpressure: Device can break apart. Liquid leaks out of device. Risk that the particles cannot stand the pressure.

Vacuum: bubbles can form in the device; maximum pressure difference is 1 atm. Air can be sucked into device. Increased evaporation. Device is held together.

Questions 5 to 7 are all connected - Think first above a general strategy to address these questions before trying to solve them. It is a good idea to calculate the ultimate expression for each question before introducing the actual numerical values. This way, one can benefit from the fact that some of the variables cancel out. On the other hand, calculating intermediate values can be useful as a way to check for inconsistencies.

To what extent can you treat these types of problems analogously to electronics problems involving resistances, currents and voltages?

For the serial case (q. 5), the flows, Q_0, in both sections are the same (assuming incompressible fluid). Calculate the total pressure difference:

$$\Delta P_{total} = P_1 + P_2 \Leftrightarrow R_{total}Q_0 = R_1Q_0 + R_2Q_0 \Rightarrow R_{total} = R_1 + R_2$$

In the parallel case (q. 6), the pressure drops (ΔP) across the channels are the same. Calculate the total flow rate:

$$Q_{total} = Q_1 + Q_2 \Leftrightarrow \frac{\Delta P_0}{R_{total}} = \frac{\Delta P_0}{R_1} + \frac{\Delta P_0}{R_2} \Rightarrow \frac{1}{R_{total}} = \frac{1}{R_1} + \frac{1}{R_2}$$

This is in analogy with how networks of passive components (resistors, capacitors, inductances) are treated. In our case, Q corresponds to the current, R to resistance and ΔP to the voltage.

Numerical values:

ΔP=1 atm = 10^5 Pa [=$\mathrm{kgm^{-1}s^{-2}}$]

$\eta = 10^{-3}\mathrm{kgm^{-1}s^{-1}}$

For the wide channel (w=50μm, h=5μm, L=1mm):

$$R_{wide} = \frac{12\eta L}{wh^3}\left[1-0.63\frac{h}{w}\right]^{-1} = \frac{12.8\eta L}{wh^3} = 12.8\,\frac{10^{-3}kgm^{-1}s^{-1}\cdot 10^{-3}m}{50\cdot 10^{-6}m\left(5\cdot 10^{-6}m\right)^3} = 2.0\cdot 10^{15}kgm^{-4}s^{-1}$$

For the narrow channel (w=5μm, h=5μm, L=1mm) use the expression for a square cross section:

$$R_{narrow} = \frac{29\eta L}{wh^3} = 29\,\frac{10^{-3}kgm^{-1}s^{-1}\cdot 10^{-3}m}{\left(5\cdot 10^{-6}m\right)^4} = 46\cdot 10^{15}kgm^{-4}s^{-1}$$

5. (C) A 50μm wide channel is connected in series with a 5μm wide channel. Assuming that each channel is 1mm long and 5μm deep, what is the expected flow rate of water through the channels at a pressure difference of 1 atm? What are the expected velocities?

Total fluidic resistance: $R_{total} = R_{wide} + R_{narrow} = 48\cdot 10^{15}kgm^{-4}s^{-1}$

Flow rate Q_0 is constant along the device (incompressible fluid and conservation of mass):

$$Q_0 = \frac{\Delta P}{R_{total}} = \frac{10^5 kgm^{-1}s^{-2}}{48\cdot 10^{15}kgm^{-4}s^{-1}} = 2.1\cdot 10^{-12}m^3s^{-1} = 2.1nLs^{-1}$$

Velocity in the wide part is given by

$$v = \frac{Q}{A} = \frac{\Delta P}{w\,h\,R_{total}} = \frac{2.1 \cdot 10^{-12} m^3 s^{-1}}{50 \cdot 10^{-6} m\, 5 \cdot 10^{-6} m} 8.4 mm\, s^{-1}$$

and in the narrow part by

$$v = \frac{Q}{A} = \frac{\Delta P}{w\,h\,R_{total}} = \frac{2.1 \cdot 10^{-12} m^3 s^{-1}}{5 \cdot 10^{-6} m\, 5 \cdot 10^{-6} m} = 84 mm\, s^{-1}$$

6. (C) Same channels as in question 5, only that this time the channels are parallel. What are the expected flow rates through the channels at an applied pressure difference of 1 atm? Velocities?

Flow rates Q_{wide} and Q_{narrow} and corresponding velocities are given by:

$$Q_{wide} = \frac{\Delta P}{R_{wide}} = \frac{10^5 kgm^{-1}s^{-2}}{2.0 \cdot 10^{15} kgm^{-4} s^{-1}} = 50 \cdot 10^{-12} m^3 s^{-1} = 50 nL\, s^{-1}$$

$$v_{wide} = \frac{Q_{wide}}{wh} = \frac{50 \cdot 10^{-12} m^3 s^{-1}}{50 \cdot 10^{-6} m\, 5 \cdot 10^{-6} m} = 200 mm\, s^{-1}$$

and

$$Q_{narrow} = \frac{\Delta P}{R_{narrow}} = \frac{10^5 kgm^{-1}s^{-2}}{46 \cdot 10^{15} kgm^{-4} s^{-1}} = 2.2 \cdot 10^{-12} m^3 s^{-1} = 2.2 nL\, s^{-1}$$

$$v_{narrow} = \frac{Q_{narrow}}{wh} = \frac{2.2 \cdot 10^{-12} m^3 s^{-1}}{5 \cdot 10^{-6} m\, 5 \cdot 10^{-6} m} = 87 mm\, s^{-1}$$

Doublecheck!

Total fluidic resistance: $\dfrac{1}{R_{total}} = \dfrac{1}{R_{wide}} + \dfrac{1}{R_{narrow}} \Rightarrow R_{total} = 1.92 \cdot 10^{15} kgm^{-4} s^{-1}$

$$Q_{total} = \frac{\Delta P}{R_{total.}} = \frac{10^5 kgm^{-1}s^{-2}}{1.92 \cdot 10^{15} kgm^{-4} s^{-1}} = 52 \cdot 10^{-12} m^3 s^{-1} = Q_{wide} + Q_{narrow}$$

OK!

7. (C) This time the device of questions 5 is connected to a device of question 6. Explain briefly how to calculate the flow rates and velocities in the channels.

Total fluidic resistance is (use values from above):

$$R_{serial} + R_{parallel} = 48 \cdot 10^{15} kgm^{-4} s^{-1} + 1.92 \cdot 10^{15} kgm^{-4} s^{-1} = 50 \cdot 10^{15} kgm^{-4} s^{-1}$$

Total rate Q_0 is:

$$Q_0 = \frac{\Delta P}{R_{total}} = \frac{10^5\, kgm^{-1}s^{-2}}{50\cdot 10^{15}\, kgm^{-4}s^{-1}} = 2.0\cdot 10^{-12}\, m^3 s^{-1} = 2.0\, nL\, s^{-1}$$

Velocity in the first wide part is given by

$$v_{wide} = \frac{Q_0}{A_{wide}} = \frac{Q_0}{w\,h} = \frac{2.0\cdot 10^{-12}\, m^3 s^{-1}}{50\cdot 10^{-6}\, m\; 5\cdot 10^{-6}\, m} = 8.0\, mm\, s^{-1}$$

and in the first narrow part by

$$v_{narrow} = \frac{Q_0}{A_{narrow}} = \frac{Q_0}{w\,h} = \frac{2.0\cdot 10^{-12}\, m^3 s^{-1}}{5\cdot 10^{-6}\, m\; 5\cdot 10^{-6}\, m} = 80\, mm\, s^{-1}$$

For the section with the parallel channels we calculate the flow rates and the velocities. Note first that

$$\Delta P_{parallel} = Q_0 R_{parallel} = \frac{\Delta P}{R_{total}} R_{parallel}$$

which is used to calculate the flow and velocities for the wide channel of the parallel section:

$$Q_{wide}^{parallel} = \frac{\Delta P_{parallel}}{R_{wide}} = Q_0 \frac{R_{parallel}}{R_{wide}} = 2.0\cdot 10^{-12}\, m^3 s^{-1} \frac{1.92\cdot 10^{15}\, kgm^4 s^{-1}}{2.0\cdot 10^{15}\, kgm^4 s^{-1}} = 1.9\cdot 10^{-12}\, m^3 s^{-1} = 1.9\, nL\, s^{-1}$$

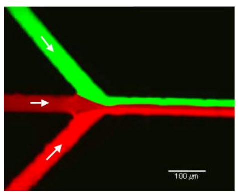
$$v_{wide}^{parallel} = \frac{Q_{wide}^{parallel}}{A_{wide}} = \frac{Q_{wide}^{parallel}}{w\,h} = \frac{1.9\cdot 10^{-12}\, m^3 s^{-1}}{50\cdot 10^{-6}\, m\; 5\cdot 10^{-6}\, m} = 7.6\, mm\, s^{-1}$$

and for the narrow channel of the parallel section:

$$Q_{narrow}^{parallel} = \frac{\Delta P_{parallel}}{R_{narrow}} = Q_0 \frac{R_{parallel}}{R_{narrow}} = 2.0\cdot 10^{-12}\, m^3 s^{-1} \frac{1.92\cdot 10^{15}\, kgm^4 s^{-1}}{46\cdot 10^{15}\, kgm^4 s^{-1}} = 84\cdot 10^{-15}\, m^3 s^{-1} = 84\, pL\, s^{-1}$$

$$v_{narrow}^{parallel} = \frac{Q_{narrow}^{parallel}}{A_{narrow}} = \frac{Q_{narrow}^{parallel}}{w\,h} = \frac{84\cdot 10^{-15}\, m^3 s^{-1}}{5\cdot 10^{-6}\, m\; 5\cdot 10^{-6}\, m} = 3.3\, mm\, s^{-1}$$

8. (C) In a diffusive mixer (see figure to the right) the entrance velocities are 100μm/s for the outer channels and 1μm/s for the center channel. With 50μm wide channels, what is the expected mixing time for a small protein dissolved in the buffer solution entering in the center channel?



To simplify things, assume plug-like flow (no parabolic flow profile!). Also, assume incompressible flow and conservation of mass.

The question is quite open-ended! In the following, we calculate the time it takes on average for the protein to traverse the central, very narrow, stream. On the other hand, in fact what may be the most relevant is the time for the water to diffuse into the central stream and mix with the protein. Note that the protein will diffuse so that the protein stream will widen along the channel. This means that the measurements must be adapted accordingly. To measure the protein, different regions of interest (ROI) must be selected along the channel. Shortly after the mixing point, the ROI can be small with a size roughly corresponding to the width of the stream. Further down the channel, the ROI should be made long (laterally) to cover most of the protein.

First, calculate the width of the central stream, x, in the exit channel. We have

$$h\,x\,v_{final} = Q_{central} \Rightarrow x = \frac{Q_{central}}{h\,v_{final}}$$

Here h is the depth of the channel, v_{final} is the velocity of the mixed stream in the exit channel and $Q_{central}$ is the flow rate of the central entry channel.

Calculate v_{final}. This is basically the total flow coming in from the three channels on the left, divided by the cross-sectional area of the exit channel.

$$v_{final} = \frac{Q_{top} + Q_{central} + Q_{down}}{w\,h}$$

Combine the above two equations to obtain:

$$x = \frac{Q_{central}}{Q_{top} + Q_{central} + Q_{down}} w = \frac{v_{central}\ A_{central}}{v_{top}\ A_{top} + v_{central}\ A_{central} + v_{down}\ A_{down}} w$$

$$A_{top} = A_{central} = A_{down} \Rightarrow$$

$$x = \frac{v_{central}}{v_{top} + v_{central} + v_{down}} w = \frac{1\mu m/s}{100\mu m/s + 1\mu m/s + 100\mu m/s} 50\mu m = 250nm$$

Note, that we used the fact that the cross-sectional areas of all entry channels are equal.

We have

$$\langle r^2 \rangle = 2Dt \Rightarrow t = \frac{\langle r^2 \rangle}{2D}$$

For the diffusion coefficient, D, we have (Stokes-Einstein relation)

$$D = \frac{k_B T}{6\pi\eta a}$$

and for a typical protein (radius a=5nm) under typical conditions (25°C water solution) we have

$$D = \frac{k_B T}{6\pi\eta a} = \frac{4 \cdot 10^{-21} J[= kgm^2 s^{-2}]}{6\pi 10^{-3} kgm^{-1} s^{-1} 5 \cdot 10^{-9} m} = 42.4 \cdot 10^{-12} m^2 s^{-1} = 42 \mu m^2 s^{-1}$$

For a diffusion length of 250nm we therefore get

$$t = \frac{\langle r^2 \rangle}{2D} = \frac{\left(250 \cdot 10^{-9} m\right)^2}{2 \cdot 42.4 \cdot 10^{-12} m^2 s^{-1}} = 740 \mu s$$

which is on the order of the typical time scale of these types of devices.

For water diffusing in, the time would be an order of magnitude less.

Alternative:

One can also consider the equalities of the incoming and outgoing flows. This is more straight-forward!

$$\sum_i Q_i = v_{final} A = v_{final} h \sum_i w_i = v_{final} hW$$
$$Q_i = v_{final} A_i = v_{final} hw_i$$

Divide the two equations!

$$\frac{Q_i}{\sum_i Q_i} = \frac{vhw_i}{vh\sum_i w_i}$$
$$\Rightarrow \frac{v_i}{\sum_i v_i} = \frac{w_i}{W}$$

9. (F) Taylor diffusion is due to the combined effect of a parabolic flow profile and diffusion. Explain how it improves the integrity of a sample plug in a flow system. Under some circumstances the flow behaves as if the spreading due to the parabolic flow profile is not there. Explain!

In a situation with pressure driven flow, but no diffusion, the parabolic flow profile will result in a spreading of a small sample plug, $W \sim ut$. Adding ***lateral*** diffusion, the spreading due to the parabolic flow profile is in fact *decreased* to something that scales with the square root of time, $W^2 \sim t$. It is quite odd, but we have a situation where diffusion *reduces* the spreading.

At sufficiently small Péclet numbers and/or in sufficiently shallow channels, Taylor diffusion will ensure that the sample moves in a plug-like fashion.

Note that for Taylor diffusion to be applicable, sufficient time needs to pass for the sample molecules to diffuse across the channel width, $t >> w^2/D$ or the sample plug needs to move a sufficient distance along the channel $L >> Pe\, w$.

10. ** (C) Derive the expression for the velocity as a function of time of the fluid as it fills a small channel by capillary action. Consider a channel with open ends. Qualitatively, what happens if the end of the channel is closed?

Viscous-drag forces balance forces due to surface energy (assume low Reynolds number, *i.e.* no inertial effects).

$$F_{drag} = F_{surface}$$

Viscous forces are given by the expression for flow and the fluidic resistance (in our case for a circular cylinder, radius a).

$$Q = \frac{\Delta P}{R} \Leftrightarrow vA = \frac{F_{drag}}{AR} \Rightarrow F_{drag} = vA^2R = v\pi^2 a^4 \frac{8\eta x}{\pi a^4} = 8\pi\eta v x$$

Surface forces are simply the circumference ($2\pi a$) times the surface energy.

$$F_{surface} = 2\pi a \gamma_{LG} \cos\theta$$

We now have

$$F_{viscous} = F_{surface}$$
$$\Rightarrow 8\pi\,\eta\, v x = 2\pi a\,\gamma_{LG}\cos\theta$$
$$v = \frac{a\,\gamma_{LG}\cos\theta}{4\,\eta\, x} = \frac{a0.0728Nm^{-1}\cos 20°}{4\;10^{-3}kgm^{-1}s^{-1}\;x} = 17ms^{-1}\frac{a}{x}$$

Calculate position and velocity as a function of time.

$$v = \frac{dx}{dt} = \frac{\gamma_{LG}\cos\theta}{4\,\eta}\frac{a}{x}$$
$$\Rightarrow \int x\,dx = \int \frac{\gamma_{LG}\cos\theta}{4\,\eta}a\,dt$$
$$\Rightarrow \frac{x^2}{2} = \frac{\gamma_{LG}\cos\theta}{4\,\eta}a\,t + const$$
$$x(t=0) = 0 \Rightarrow const = 0$$
$$\Rightarrow x^2 = \frac{\gamma_{LG}\cos\theta}{2\eta}a\,t$$
$$\Rightarrow v^2 = \left(\frac{\gamma_{LG}\cos\theta}{4\,\eta}\right)^2\frac{a^2}{x^2} = \left(\frac{\gamma_{LG}\cos\theta}{4\,\eta}\right)^2\frac{a^2}{\frac{\gamma_{LG}\cos\theta}{2\cdot 2\eta}a\,t}\frac{1}{2} = \frac{\gamma_{LG}\cos\theta}{8\,\eta}\frac{a}{t}$$

or equivalently simply from $v = \dfrac{dx}{dt}$ etc.

The capillary number is given by (low Ca -> surface energies dominate; high Ca -> viscous forces dominate)

$$Ca = \frac{\eta v}{\gamma} \sim v$$

So that

$$Ca^2 = \frac{\eta^2 v^2}{\gamma^2} = \frac{\eta^2}{\gamma^2}\frac{\gamma\cos\theta}{8\eta}\frac{a}{t} = \frac{\eta\cos\theta}{8\,\gamma}\frac{a}{t}$$
$$\Rightarrow Ca = \sqrt{\frac{\eta\cos\theta}{8\,\gamma}\frac{a}{t}}$$

Viscous forces dominate close to t=0, basically because the velocity is large initially but falls off as the channel is filled with liquid. Note that the capillary stress γ/a is constant as a function of time where the shear stress, $\eta U/h$ falls off as velocity falls off.

For a closed channel we have a counteracting force due to the pressure exerted by the enclosed air volume in addition to the interfacial force and the drag force. From the ideal gas law we have $PV=nRT$. Taking into account that we operate at air pressure we now have:

$$PV = nRT$$

$$\Rightarrow \Delta P(x) = \frac{nRT}{V(x)} - P_0 = \frac{nRT}{V(x)} - \frac{nRT}{V(x=0)} = P_0\left(\frac{V(x=0)}{V(x)} - 1\right)$$

$$F_{air} = A\Delta P(x) = AP_0\left(\frac{V(x=0)}{V(x)} - 1\right)$$

$$V(x) = A(L_0 - x)$$

$$\Rightarrow F_{air} = AP_0\left(\frac{AL_0}{A(L_0 - x)} - 1\right) = AP_0\left(\frac{L_0}{(L_0 - x)} - 1\right)$$

Note that the air will eventually absorb into the water. In the long run the air bubble is expected to disappear[4].

References

1. Beebe, D.J., G.A. Mensing, and G.M. Walker, *Physics and Applications of Microfluidics in Biology*. Annual Review of Biomedical Engineering, 2002. **4**: p. 261-286.
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4. Phan, V.N., et al., *Capillary Filling in Closed End Nanochannels*. Langmuir, 2010. **26**(16): p. 13251-13255.