Question Set 4

Applications in fluidics

Note that this time the number of articles is quite high. The purpose is to give you an opportunity to train in extracting the essential information. It is not necessary to read the papers beyond what is indicated by the questions and what is covered by the lecture notes.

Remember to draw figures to explain your answers. This is often more efficient than just using words.

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

Questions about applications

The questions below relate to the challenges that can be addressed by microfluidics in different contexts.

1. (F) What is Global Health? Explain the requirements underlying the acronym ASSURED.
2. (F) Give examples of types of devices suitable for Global Health applications.
3. (F) Discuss differences between different health-care markets. Veterinary medicine, medicine in High-income countries, medicine in Medium and low-income countries.

Questions about nanochannels

The questions below relate to stretching of DNA in nanochanels. Most answers can be found in a review paper[1].

1. What is the underlying mechanism that forces the DNA molecule into a stretched conformation in a nanochannel?
2. What type of information can be gained using devices for stretching of DNA? What types of disease can be identified?

Questions for the "bumper" papers

The questions below relate the bumper array (a.k.a. deterministic lateral displacement, DLD) described in the original paper by Richard Huang and coworkers at Princeton[2]. Specifically, we will focus on two papers: one on sorting trypanosomes from blood based on morphology [3] and one characterizing different variants of red blood cells by their morphology and deformability [4].

4. (F) What is the basic principle governing the size separation in bumper arrays?
5. (F) What is hydrodynamic chromatography? How is it related to the paper?
6. (F) How does the DLD technique differ from the H-filter and the pinched flow separation techniques? First describe the H-filter and the pinched flow separation techniques.
7. (F) What is the key mechanism used for morphological separation?
8. (F) What is the key mechanism used for deformability-based separation?
9. What are the key performance advantages/drawbacks of DLD as compared to other microfluidic techniques for particle and cell sorting?
10. How is the critical size affected by the speed of the sorting? What could the underlying mechanisms be?
11. Why is it interesting to move particles across streams with different chemical composition? What are the requirements for it to work?

Questions for DNA sorting

Most of the questions can be answered by reading the paper by Richard Huang from Austin's group. Make sure to look at the supplementary material that comes with this paper (on the website of the Journal). There are more detailed descriptions as well as movies.

1. (F) What is the basic mechanism for sorting of ultralong (>100 kbp) DNA? How does it work in a gel (PFGE)?
2. (F) How can the approach be modified to sort the DNA in space rather than in time?

Questions for inertial focusing and sorting

Most of the questions can be answered by reading the paper by Dino di Carlo from Toner's group[5]. Make sure to look at the supplementary material that comes with this paper (on the website of the Journal). There are more detailed descriptions as well as movies. Quake's review could also be useful[6].

1. (F) What is the basic principle of the device? What is a Dean vortex? What happens at various speeds? What relationship does it have to centrifugation?
2. (F) What are the requirements to focus to one single stream?
3. (F) In which way can the technique be used to sort cells? How are the particles sorted?
4. (C) What is the benefit of this technique as compared to the bumper array? ... as compared to conventional techniques? In general, and specifically in terms of speed and throughput?

Questions single-cell measurements

Most of the questions can be answered by reading the paper from Luke Lee's group[7]. (There is also an overview paper from the same group[8]. A similar paper has also been published in Lab on a Chip[9]. At the website, a movie is available showing trapped individual cells in an array.)

1. (F) What is the basic idea of the single-cell trapping approach? In which way does the design ensure that only one cell is trapped in each trap?
2. (F) Why is this approach better than the alternatives? What are the alternatives? How can droplet fluidics be used for studying single cells? What are the challenges?
3. (C) Why is it interesting to study single cells?

References

1. Persson, F. and J.O. Tegenfeldt, *DNA in nanochannels - directly visualizing genomic information*. Chemical Society Reviews, 2010. **39**(3): p. 985-999.
2. Huang, L.R., et al., *Continuous Particle Separation Through Deterministic Lateral Displacement*. Science, 2004. **304**(5673): p. 987-990.
3. Holm, S.H., et al., *Separation of parasites from human blood using deterministic lateral displacement*. Lab on a Chip, 2011. **11**(7): p. 1326-1332.
4. Beech, J.P., et al., *Sorting cells by size, shape and deformability*. Lab on a Chip, 2012. **12**(6): p. 1048-1051.

5. Di Carlo, D., et al., *Continuous inertial focusing, ordering, and separation of particles in microchannels*. Proceedings of the National Academy of Sciences of the United States of America, 2007. **104**(48): p. 18892-18897.
6. Squires, T.M. and S.R. Quake, *Microfluidics: Fluid physics at the nanoliter scale*. Reviews of Modern Physics, 2005. **77**: p. 977-1026.
7. Di Carlo, D., N. Aghdam, and L.P. Lee, *Single-cell enzyme concentrations, kinetics, and inhibition analysis using high-density hydrodynamic cell isolation arrays*. Analytical Chemistry, 2006. **78**(14): p. 4925-4930.
8. Di Carlo, D. and L.P. Lee, *Dynamic single-cell analysis for quantitative biology*. Analytical Chemistry, 2006. **78**(23): p. 7918-7925.
9. Di Carlo, D., L.Y. Wu, and L.P. Lee, *Dynamic single cell culture array*. Lab on a Chip, 2006. **6**(11): p. 1445-1449.