Graduate ChBE 8803 / Undergraduate ChBE 4803
Micro- and nanofluidics
Fall 2008
Professor Hang Lu, ChBE

Course outline:
- Fabrication processes and designs
- Flow at small scale
- Mass transfer at small scale
- Field effects
- Applications in biology and medicine

The course focuses on the fluid and flow aspects of micro and nano devices. It will cover basic micro/nanofabrication techniques, introduce transport of momentum and materials (including charged and magnetic materials) in small scale, and the applications in biology and medicine. The grade will be based on a cumulative design project (45%), homework (20%), class discussion and paper presentation (15%), one mid-term (10%), and a final during finals' week (10%). The class targets graduate students and the upper class undergraduates in engineering and sciences.

Prerequisites:

- Undergrad transport or consent of instructor is required.

- Ideally students should be proficient in one of the following areas and introductory background in another area: biology, biochemistry, ChBE or ME fluid dynamics and mass transfer, ECE device technology or MEMS.

Instructor:

Dr. Hang Lu.
Contact info: hang.lu@chbe.gatech.edu, 404-894-8473.
Office hours: by appointment; ES&T 2228.

Course resources:

T-square:

I will use t-square extensively to post papers, references, supplemental information, and grades, etc. I expect you to check it periodically, at least once a week.

Library:

Georgia Tech Library has extensive electronic and hardcopy resources. You may find many of the electronic resources extremely useful. Remember for this class, you need to provide references that are ISI listed, i.e. not from Wikipedia or Google for example.

Some useful search engines and electronic journals:

Pubmed
Web of Science
INSPEC
Google scholar (note that if you use Google scholar to search, be sure the citation is correct; it's a great search engine but it makes a lot of mistakes)
Nature (and other Nature journals)
Science
J. MEMS
Analytical Chemistry
Lab on a Chip
EEE publications

Textbooks:

There is no formal textbook for this class. However, you may find the following books useful as references:

- Analysis of Transport Phenomena, by William M. Deen. Publisher: Oxford University Press, USA (March 12, 1998), ISBN-10: 0195084942

- Fundamentals of Momentum, Heat, and Mass Transfer, by James Welty, Charles E. Wicks, Robert E. Wilson, Gregory L. Rorrer. Publisher: Wiley; 4 edition (2000), ISBN-10: 0471381497

- Microsystem Design, by Stephen D. Senturia. Publisher: Springer; 1 edition (2000), ISBN-10: 0792372468

- Fundamentals of Microfabrication, by Marc J. Madou. Publisher: CRC; 2 edition (2002), ISBN-10: 0849308267

- Molecular Cell Biology, by Harvey Lodish, Matthew P. Scott, Paul Matsudaira, James Darnell, Lawrence Zipursky, Chris A. Kaiser, Arnold Berk, Monty Krieger. Puslisher: W. H. Freeman; 5th edition (2003), ISBN-10: 0716743663

Academic integrity:

Students in this class are expected to abide by the Georgia Tech Honor Code. All work turned in for grading must be original. Collaborations between students in the class are allowed but have to be acknowledged. References need to be cited explicated if ideas are borrowed.

The complete text of the Honor Code and other resources are available at http://www.honor.gatech.edu/, http://www.deanofstudents.gatech.edu/integrity, and http://www.deanofstudents.gatech.edu/codeofconduc

Rough outline of the class (order of lectures may still change depending on guest lectures and other constraints):

Lecture date topics

1 19-Aug intro/fab/MEMS
2 21-Aug standard IC
3 26-Aug standard IC
4 28-Aug nonstandard fab
5 2-Sep review Navier-Stokes; dimensional analysis
6 4-Sep low Re number flow
7 9-Sep pressure driven flow; electroosmotic effects
8 11-Sep chaotic flow; surface effects; body forces (gravitational)
9 16-Sep capillary effects/evaporative effect; thermal effects
10 18-Sep mixing; multiphase flow
11 23-Sep pumps and valves
12 25-Sep diffusion, Taylor dispersion; multiphase mass transfer
13 30-Sep nonelectrolyte mass transfer, reactive mass transfer
14 2-Oct coupled diff-migr, membrane potential; ionic mass transfer
15 7-Oct colloidal behavior; macromolecule behavior
16 9-Oct electrokinetics; double layer
17 14-Oct ..... fall recess.....
18 16-Oct EOF, electrophoresis
19 21-Oct midterm
20 23-Oct appl: DNA/protein sep
21 28-Oct material compatibility
22 30-Oct dielectric effects; dielectric spectroscopy
23 4-Nov magnetic effects; micro rheology on cells
24 6-Nov optical effects
25 11-Nov bioapplications
26 13-Nov applications: separations; chromatography
27 18-Nov applications: cell based assays; tissue engineering
28 20-Nov applications: material synthesis; colloidal assembly; chemical synthesis
29 25-Nov applications: HTS; catalyst screening; photonics
30 27-Nov ..... thanksgiving.....
31 2-Dec design project presentations
32 4-Dec design project presentations

ChBE 4803/8803
Design projects

Team A: single-cell genomics on-chip
(Adriana, Chris, Seung-Dae)

Team B: high-throughput screening of compound library on-chip
(Ekapop, Letian, Hyo, Jan)

Team C: cell signaling dynamics on-chip
(Thuy, Hyewon, Catherine)

Rules to follow:
There is no right or wrong answer to the design projects. There are only creative engineering approach and elegant solution to problems. You may consult the instructor (or outside experts but acknowledge them) at any stage of the design.
Everyone should contribute to the project in whatever way they can. The evaluation of your performance on the design project will come from the instructor, your peers (other people who are in the class but not on the project), and the team members.
Late assignments will have points deducted: up to 3 hours late 5% deduction and each day late 15% deduction.
Quick questions and requests for feedback (by email to the instructor) sufficiently ahead of the deadline are always welcome.

350 points total for the design project

* Literature review – "state-of-the-art" report
50 points, due Nov. 9 (Sunday) 11:59 PM
This report should review the state-of-the-art technologies related to your design project. You should search both journal and patent sources, and sometimes finding out existing commercial products and services. Your review does not need to be exhaustive, but should identify major technological breakthroughs and limitations of the existing methods if appropriate. It is to your advantage to find the existing work as early as possible. You may wish to divide up the reading and summary. The report should be 5-10 pages excluding references but including figures (you may crop out figures from published work and provide references), 1.5 line space, and 11-12 point font.

* Meeting with the instructor to discuss overall system layout
Nov. 12 (Wed) -Nov. 17 (Monday) noon
Each team should arrange a group meeting with the instructor to discuss the progress of the project during this time – a single email with a few options is preferred. At this point, the team should have a vision of the overall system architecture, materials requirement, fabrication limitations, and how the device will be used. Cartoons or sketches would be helpful for the discussion. Back-of-the-envelope calculations should support the design ideas. Remember you are not limited to a single core technology platform.

* Initial design, including overall system layout, fab sequence, and experimental protocol
100 points, due Nov. 23 (Sunday) 11:59 PM

Each team is to implement the design and to incorporate input from the instructor. The overall system layout and top views and cross-sectional views of the fabrication sequence should be in graphics form. If you so choose, hand-drawn and scanned-in images are acceptable. The fabrication sequence and experimental protocol should be simple and concise (e.g. list in bullet form). You would also want to submit numerical simulations or calculations to support certain design decisions. In some projects, you will also need to perform economic analysis. *This is not a report, but a progress update, so the goal is to demonstrate concepts and progress clearly and concisely for feedback purposes.*

* Draft of the project report
50 points, due Dec. 2 (Tuesday) in class
The report should not just be an explanation of the design. It should also include explanations of design trade-offs, material choices, justifications of design decisions, interpretation of the simulation results, evaluations of whether the design meets the specs, and comparisons to existing technology if appropriate. Deficiencies identified from the initial design but addressed by the draft stage can earn additional points.

* Project presentation
50 points, Dec 2 and Dec 4
The instructor will assign up to 30 points, and the rest of the 20 points will be assigned by the rest of the class.

* Team member review
25 points, due Dec 2 by email to the instructor
You will evaluate the rest of your team on a 25 point basis (and give reasons for your scores); you will receive an average score from the rest of your team.

* Submission of questions for the final
25 points, due Dec 4 by email to the instructor
You are to submit a question related to your design project and provide the solution to this question. It should be quantitative and it should address either a clever design feature, or a general concept, or a fabrication trick that enables your design. It should be solvable in ~15-20 min. The instructor will select questions to use on the final exam. If you do a good job, you will end up answering an easy question on the final.

* Final project report
50 points, due finals week
The final report should put everything together, from the design, to fabrication, to operation, to economic analysis (if necessary), and also address issues that are pointed out during the feedback stages of the project and the final presentations. If you had done a good job with the draft, this should not be difficult.

Project descriptions:
Team A: single-cell genomics on-chip
Your goal is to design an integrated system that will be used in single-cell genomics applications. The microbial communities in the environment and in the human gut are complex. One of the challenges is to know what kind of bacteria actually live in these environments and in what fraction; therefore single-cell genomic identification is important. Your job is to design a system that (1) takes a microbial sample containing ~10^5 microbial

cells as a 0.1-mL suspension and separates them into single-cell entities; (2) cleans up the naked contaminating DNA in the solution; (3) lyses the cells and prepares the sample for high-throughput DNA sequencing (such as by the 454 sequencer, Roche), i.e. the concentrations of DNA and of interfering molecules - enzymes (e.g. DNase) and salts - need to be ready for sequencing, which means you may need to run certain reactions and perform DNA amplifications. The final prepared samples should be in 384- or 1536-well format, and the probability of more than one cell in the sample should be less than 0.01%, and that of no cell in the sample should be less than 0.1%. Although cost is not an issue, please perform an economic analysis to ensure that the entire system and operation cost no more than $10,000 (or 10 cents per single cell).

Team B: high-throughput screening of compound library on-chip

Your goal is to design an integrated system to perform a fluorescence cell-based compound screen. Small molecule compound libraries are typically available in 384-well (or smaller) format, and these are candidate drugs for diseases that pharmaceutical companies would like to use to discover new therapeutics. Assume you have at your disposal a cell line HL60 (non-adherent cell) expressing a green fluorescent protein marker that can be seen using a 63x objective on a compound microscope. The compounds of interest are those that can knock down the fluorescence by 3-fold or more. Your job is to design a system that can (1) take 100-nl of each compound from the library (i.e. in the 384-well format) and mix with 1-1000 cells in 0.1-1 μl of medium; (2) culture the cells for 2-48 hours; (3) allow fluorescence microscopy on standard microscopy tools (e.g. compound microscope with an x-y-z stage or confocal microscope). The volume variation should be less than 0.1% from sample to sample, and the variation in the number of cells should be less than 2%. The compounds obviously cannot cross-contaminate each other. The entire preparation (starting with compound library in 384-well plates and cells in suspension, and ending with cell-compound mixture ready for culture) should be less than 1hour for a 100,000-compound library. The cost of the sample preparation system should have a disposable cost of less than $1,000 per screen; this includes things like pipette tips, pins, tubing, and plates, i.e. whatever you cannot wash and re-use and still maintain the no-cross-contamination requirement.

Team C: cell signaling dynamics on-chip

Your goal is to design a chip for studying cell signaling dynamics on-chip. Some cancer cells are thought to use a mechanism called autologous chemotaxis to migrate towards the lymphatic system, where small flow of interstitial fluids can generate a gradient of signaling molecules secreted by the cancer cells themselves. An alternative hypothesis is that the autocrine signal sensitizes the cells towards the flow (or shear), which induces the chemotaxis. In order to understand the mechanism better, you are to design a chip system that can (1) generate a range of flow and shear, (2) deliver or control the autocrine signals to test the hypotheses, and (3) deliver antibodies, RNAi reagents, or drugs to perturb the system. The chip/system needs to be able to handle parallel experiments such that combinations of conditions can be tested and controls can be run on the same chip simultaneously. You need to design both the chip/system and the experimental protocol. Another requirement is that because this assay is potentially used to study primary cells, fluorescence microscopy is likely not going to work, so you need to device methods to track cellular polarization and migration. The final foot print of the device should not be bigger than 1 inch by 1 inch, and the disposable chip should be less than $10 each