Control Challenges in Micro Fluidic Systems and Nanoscale Transport Phenomena
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Over the last three decades, the number of available micro devices, actuators, and sensors has grown in leaps and bounds. Moreover, newly emerging nano-technology and nano-sized patterning techniques are enabling even more capabilities in micro fluidic systems. The micro community is now moving from component creation to system design, optimization, and control. Hence there is a real opportunity for controls researchers, who are steeped in system dynamics and control, to contribute to the maturing field of micro systems, and also to the emerging field of nano systems. This paper presents a brief description of my groups research efforts in this direction, and outlines our perspective on the available control opportunities and emerging system integration and control challenges.

Introduction
The paper begins by presenting two representative control applications, one passive and one active. For each application, the key design tasks, the current solutions, and the remaining open questions are discussed. The devices considered in each case are micro scale, but the second application involves transport of nanoscale bio-molecules such as DNA, RNA, and proteins. The paper closes with our perspective on the grand challenges for control of micro fluidic systems.

Application 1: Passive Control of Fluid Filling in Multi-Channel Fluidic Networks
The motivation for this project comes from joint work with Nanostream (www.nanostream.com). Nanostream Inc. has the ability to fabricate cheap, disposable, plastic chips in a matter of hours. By changing the shape and surface coatings of components in their micro fluidic networks, they can ensure that surface tension forces will cause component A to fill before component B but only after component C (see Figure 1). Placing such passive surface tension valves in key locations, it is possible to create packets of fluid of that have known volumes, and that will mix with each other in a prescribed order and stoichiometry. Thus the Nanostream surface tension valves enable accurately prescribed, ordered chemical reactions in cheap disposable plastic chips. This is clearly useful for lab-on-a-chip type applications where we wish to chemically test minute amounts of liquid.

Figure 1: Left: Conceptual diagram of the prescribed channel filling technology. Fluid is forced into a chip by a steadily increasing pressure or prescribed volume. The micro fluidic network then fills in a pre-designed order due to carefully engineered surface tension forces. Right: A photograph of a Nanostream Inc. passive, disposable, plastic chip. Fluid is forced into the center and fills the network.

Tasks: My group was called upon to help control the fluid flow in these networks. Instead of the 5 components shown on the right of Figure1, Nanostream would like to control networks with thousands of components as shown on the left of the figure. Right now Nanostream designs these networks by hand, which each component is individually crafted based on empirical experimental intuition. The reason for this is that using available off-the-shelf numerical tools like CFDRC or Coventor which discretize the 2-phase liquid/gas Navier Stokes equations, it takes hours of computer runtime to simulate a single component. In other words, it takes Nanostream longer to simulate one component then it takes
to build and test an entire network. Thus our first challenge was efficient “design ready” modeling of liquid filling in multi-channel fluidic networks. The next challenge would be to design networks containing thousands of components that would fill in a desired manner, even under small but unavoidable practical variations in geometry, temperature, humidity, and chemical composition.

**Current Solutions:** To date we have solved the modeling problem and are currently working on the robust network design problem. Three crucial observations enable effective modeling of the networks. 1) The amount of fluid in the network is small, and the network is being filled slowly, thus fluid momentum effects are negligible and we can focus on an equilibrium quasi-steady approach. 2) To first order, surface tension can be modeled by assigning an energy to each interface, this energy is given by a material dependent surface tension coefficient times the area of the interface: $E_{\text{mat1/mat2 \ interface}} = \sigma_{\text{mat1/mat2}} A_{\text{mat1/mat2}}$. 3) To find an equilibrium solution, we must find an energy minimum where the energy is given by a summation of weighted interface areas. This must be done subject to the constraint that there is a given amount of liquid volume in the component/network.

**Hydrophobic T junction**  
**Hydrophyllic chamber**  
**Hydrophobic elbow**

Corresponding energy versus filled volume curves …

Figure 2: Top row: Equilibrium (i.e. minimum energy) liquid/gas fronts for three planar micro fluidic components (a top view is shown). From left to right, the 3 components are a T junction, a rounded chamber, and an elbow. Each component is filled from the bottom with a prescribed and increasing amount of liquid. Only the critical curves are shown in the figure. So for example, the T junction first displays horizontally oriented shallow circular front shown at the bottom of the T junction. This front moves up as the volume is increased. When the front meets the 2 bottom corners of the T junction it begins to bow out until it takes the shape of the ¼ circle shown, etc.  
Bottom row: The energy of the equilibrium front as a function of volume is shown for each component: the edges of the graph and the vertical bars correspond to shown fronts in the top row. Since the middle component is hydrophylic (the solid attracts the liquid), then the energy of the component decreases as the front progresses through the device. (These results are due to Neil Fortner at University of Maryland. He used the Surface Evolver constrained energy minimization solver written by Ken Brakke at Susquehanna University [2].)

Figure 2 shows solutions for three different components. The solutions are attained by numerically solving a minimum energy problem subject to a prescribed volume constraint. A solution for each device is attained in minutes instead of the hours it was taking Nanostream using off-the-shelf micro-fluidic simulation tools. More importantly, each of the energy versus volume curves $E_j(V_j)$, $j=1,2$ or 3, shown at the bottom of Figure 2 completely describes that component. So in order to simulate a network, we must now find the energy minimum across all components subject to a prescribed volume constraint in the network. Namely, we must solve $\min E(V)=E_1(V_1)+E_2(V_2)+\ldots+E_N(V_N)$ subject to $V_1+V_2+\ldots+V_N=V$.
prescribed for the filled component volumes $V_1, V_2, \ldots, V_N$. Here the $E_j(.)$ curves are known (based on the type of analysis shown in Figure 2) and $N$ is large. This problem can be solved efficiently using standard optimization tools, such as the gradient descent tools contained in the Matlab optimization toolbox.

![Figure 3: Solution of channel filling problem for 10,000 channels. Three snapshots are shown for three different volumes of liquid in the network. The horizontal axis shows the amount of volume per component, the vertical axis corresponds to the component number. Each component in the network is described by a (randomly generated) energy versus volume curve $E_j(V_j)$, see Figure 2. This solution took 10 seconds on Matlab.](image)

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In the above, the component solutions have been validated against experiments. We are currently in the process of validating network solutions against experiments also.

**Open Problems:** Our next goal is to control the fluid flow by designing the networks. There are three essential open questions. 1) How do we shape components to make sure they fill in a precisely designed order. This implies we need to shape the components to generate the right $E_j(V_j)$ curves. Stability of the solutions must also be considered because unstable solutions do occur, and there exist bifurcation diagrams and bi-stable solutions. 2) A related question is how to create components so that no fluid is left behind and no bubbles are created. This is a major problem in micro fluidic devices (for example, a bubble can be seen at the top left of the elbow component in Figure 2) because if an unknown quantity of fluid is left behind then not only is precious fluid wasted, but in addition, instead of mixing 20 nanoliters with half a microliter, we will instead be mixing maybe 14.3 nanoliters with 1/3rd of a microliter and that will defeat the whole purpose. 3) Robustness: the networks must work even if there are slight variations in manufactured geometries, surface tension coefficients, and chemical composition.

**Application 2: Active Control of Electro-Wetted Driven Flows with Bio-Chemicals**

The control problems described below arise out of the Electro-Wetting-On-Dielectric (EWOD) devices made at UCLA by CJ Kim [3]. Here, applied electric fields can effectively change the local surface tension properties of solids (see Figure 4), and this can be used to move, split, merge, and mix small quantities of fluid in active micro devices (Figure 5). This technology enables infinitely re-programmable bio-chip devices: the same device can perform multiple fluidic processing functions.

![Figure 4: Illustration of fluid motion induced by an electrical potential applied across dielectric-coated electrodes above and below a liquid droplet. By switching on the voltage at an electrode adjacent to the droplet, the surface tension is lowered locally causing the droplet to move to the right. It returns to its original shape when the potential is switched off.](image)
Tasks: The basic task is active control of the liquid motion and the chemicals and bio-molecules inside it. We would like to insure that the proteins in droplet one are split 32% to 68% and tested against two chemical concoctions contained in droplets 3 through 9. The sub-tasks are numerous.

Current Solutions (Modeling): As in the filling problem, in order to design controllers we must have appropriate models. The modeling effort was split into two parts. Equilibrium behavior was once again described by minimum energy methods subject to volume constraints. Except this was done in three dimensions, and it included the dominant physical effects that we identified after many months of research. These are, in order of importance, surface energies, dielectric energies in the solid, electrolysis, and liquid resistance. Our equilibrium modeling results are summarized in [4].

The dynamic behavior of the droplets clearly includes viscous effects, along with other physical effects that we have yet to identify, but fluid momentum effects are negligible. Current open issues include: 1) The correct boundary conditions to apply at the vicinity of the solid/liquid/gas triple line: see [5] for a discussion of why this is still an open research area. 2) Tracking of the liquid/gas interface during splitting and merging. Theoretically, splitting requires that two material points (one on each side of the neck) must meet in finite time, this cannot happen with continuous velocity flow fields. Hence for the Stokes flow plus volume-of-fluid interface tracking simulations shown in Figure 5, the splitting time depends on the mesh density, the finer the mesh the longer the droplet takes to split, and this is obviously not correct. 3) Predicting the local concentration in the liquid and adhesion/desorption to the Teflon surface of bio-molecules such as DNA, RNA, and proteins. This has two parts. One, the concentration of chemicals must be tracked in the droplet as it undergoes motion, splitting, merging, and convoluted internal fluid dynamics due to imposed tortuous droplet paths (this is how we achieve mixing on the micro scale). Second, the adsorption/desorption to the surface per concentration must be understood, this depends on the chemistry of the bio-molecules and also on the nature of the applied electric fields.

Current Solutions (Control): The control schemes currently implemented in the devices are simple. To move a droplet left, we turn on the electrode to the left; to split a droplet we turn on electrodes on either side. More sophisticated control is required for one of three reasons: to deal with uncertainty, to improve performance, or to enable tasks that are not possible without sophisticated control.

Of these three, dealing with uncertainty is most important from a practical point of view. For example, a single grain of dust can prevent droplets from splitting. But in the field these devices will be used with dirty fluids, in uncertain conditions, and in messy environments; not in pristine laboratory environments. We are heading towards addressing these problems, but first we need to tackle the simpler control problems associated with improved performance and task enabling.

Precision splitting and embedded particle control are two good examples of control for improved performance. Right now, we can move a droplet from one electrode to the next, but we cannot precisely control the position of embedded particles (like cells) inside the drop. Similarly, we can split a droplet
50%/50% give or take 15% but we have no tools to split droplets into precisely known volumes. Our current approach to these two problems is shown in Figure 6 and Figure 7. Another good example is droplet trajectory planning for optimal chemical mixing: what path should the droplet be forced to take to maximize mixing rate. We have not addressed this problem yet.

Figure 6: Framework for precision control of droplet splitting and embedded particle control. Turning on an electrode lowers the pressure on the liquid/gas boundary locally, this creates pressure gradient forces inside the liquid droplet. For embedded particle control, like precision control of cell positions to sensor locations, we must apply the right sequence of pressures that will create the right underlying fluid velocities and will move a finite number of particles to the desired direction. For control of splitting we create two artificial material points on the liquid/gas boundary, and we then make those two points collide along a set path – this enforces accurate splitting. Thus the two problems can be cast in the same framework. See also Figure 7.

Figure 7: Control of forces at key internal or external points within an arbitrarily shaped droplet. The right figure shows a droplet with 4 embedded particles (at the root of the arrows). The question is: what voltages should we apply to create the desired (blue) forces at each of these particles? The answer is as follows: the applied electric voltages change the pressure on the liquid/gas boundary locally, this creates pressure gradient forces inside the liquid droplet. At low Reynolds number, the pressure inside the droplet is described by the Laplace equation \( \nabla^2 P(\Omega) = 0 \) which is linear. Hence there is a linear mapping between the applied voltages and the achieved pressure gradient field (the forces) at the 4 particles. To find the best possible applied voltages we solve a least squares problem that minimizes the error between the achieved forces and the desired forces. The resulting pressure field is shown on the left. Contours of that field are shown on the right, along with the achieved forces (red arrows).

Particle collision control and control of bio-chemical adsorption/desorption are good examples where control is enabling. For any kind of non-trivial forcing, the link between the applied electrode voltage, the path of the droplet, and the internal fluid dynamics inside the droplet is too complex to be described empirically. Hence if we want to understand how to apply voltages so that cell A hits cell B without touching bacteria C, D, and E, or if we want to control the distribution of chemical inside a drop to deposited them on a sensing surface only when we so desire, we must turn to advanced control design.
Open Problems: There are many remaining open issues, both in terms of modeling and in terms of control design. In terms of modeling, we need to create 2-phase liquid/gas flow simulations that capture droplet splitting and that can be used to design controllers. Simulations with millions of free variables cannot be inserted into any kind of control design methodology. In terms of control design, we are essentially concerned with control of partial-differential-equations (PDEs) that have time varying domains, that include topology changes (from 1 droplet to 3 droplets or vice versa), that display instabilities, and that are forced by only partially known constant changing boundary conditions. The good news is that we do not have to concern ourselves with momentum effects (there is no turbulence). Instead we must handle a myriad of coupled effects including electric fields, chemical species, viscous effects, surface tension effects, and interface chemistry and dynamics.

(Our Perspective on) Challenges in Control of Micro Systems
The most serious challenge involves modeling. My group spends easily 85% of its time doing modeling, and the remaining time is split between control design and control validation. Micro and nano researchers are experts in creating devices, they do not have the time (and sometimes the interest) to learn the tools they would need to create control ready models. The same problem is true, though less so, for micro fluidic modeling tools created by fluids researchers. These tools, be they commercial or academic, are currently geared for device validation, fabrication process design, device design (somewhat). They have not been created for control design. For instance, almost all available codes are too big to fit into control design methodologies. Right now, if the control researcher does not create the models that he or she needs, no one else will do it for him or her.

A related difficulty is one of technical language. To control bio-chemical micro fluidic devices, and to also control devices with nano technologies, requires that the control researcher be able to understand information given to him by physicists, chemists, and biologists and to translate it into quantitative models and control design goals. Bridging this language gap takes time and effort.

Micro flow control is very different from macro flow control. Macro flow control is difficult essentially because it includes turbulence. Micro flow control is difficult because there are so many competing physical effects (chemical, electrical, biological, and interfacial), because it is still so new, and because there is such a large degree of uncertainty (things that do not effect macro systems, like dust, can destroy micro systems), and because that uncertainty is so hard to limit and measure. Yet once dominant physics have been identified, there are some beautiful control problems hiding inside micro (and probably nano) systems. For example, trajectory control of embedded cells can be reduced to control of Laplaces equation over topologically changing boundary conditions. In short, micro fluidics is a gold mine for the mathematically oriented dynamics and control community, but only if they are willing to spend the time and effort to learn the physics that is required to extract these problems.

References