Application to Graduate with Honors

Student ID: _

I plan to defend in: FALL / [illegible] of 20 11

Personal Information:

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I am an: (IN-STATE) / OUT-OF-STATE student

Academic Information:

☒ I plan to graduate with *Departmental Honors* in:

☐ I plan to graduate with *General Honors*

Cumulative GPA:

Please attach a brief **PROSPECTUS**, **BIBLIOGRAPHY**, and **TIMELINE** of your thesis project to this application. When summarizing your work, consider the following:

- What is the problem you are investigating?
- What is the hypothesis you are testing?
- What is the focus of your study?
- What is your goal in this study?

Primary thesis advisor: Name: Matt Glaser Dept: Physics

List the other members of your committee:
Name: Joel Eaves Dept: Chem.
Name: _____ Dept: _____
Name: _____ Dept: _____
Name: _____ Dept: _____

Departmental and General Honors Committee Checklist:

Applicant has a total of at least three committee members.
At least one Honors Council Representative is included on committee.
At least one committee member from an outside department.

APPLICATION CONTINUED ON BACK OF THIS SHEET

Please initial if you are pursuing Departmental Honors:

JKV I have consulted with my department and have completed (or am completing) the requirements they have established.

For Honors Council Representative:

I have met with applicant and approve him/her for departmental honors.

Printed Name: John Cumalat Signature: John P. Cumalat

Please initial if you are pursuing General Honors:

_____ I have completed (or am completing) the requirements for graduating with General Honors.
Please list the courses you have or are taking toward General Honors:

_____ _____

_____ _____

For General Honors Council Member:

I have met with applicant and approve him/her for general honors. I agree to be on his/her defense committee.

Printed Name: _____ Signature: _____

For the Thesis Advisor:

I have met with the applicant to discuss the proposed work and agree to provide the necessary help and direction for this thesis project.

Printed Name: Matt Glaser Signature: _____

For the Student:

I have read the requirements for graduating with honors at the University of Colorado. I also understand that my designation will be sent to the CU email address that I have provided and will not be given out over the phone.

Signature: _____ Date: Dec 1, 2010

For additional graduation information including requirements, guidelines and deadlines, you can download them online at www.colorado.edu/honors

Prospectus

Josh Kelly

Introduction and Goals

The goal of my project is to sort liquid crystal droplets using electric fields and automated optical detection. The type of liquid crystal my project aims to sort is special, it is a fluid containing liquid crystal domains made from stacked DNA[6]. A second sub project has evolved from the main project, where we aim to create smectic phase shells. I am working on these two projects under Matthew Glaser and Noel Clark in the Liquid Crystal Materials Research Center (LCMRC).

Microfluidics are a rapidly expanding technology, that have applications in many areas of science and engineering, as well as pure science. Most applications are in biomedical research, and can be used to do chemistry on a very small scale, and in doing so reduce the amount of rare or expensive reagents. It also provide a very fine degree of control over very small amounts of fluid. This can accomplish as vast array of tasks, some common ones are high speed sorting and analysis of individual cells [1]. Liquid crystal shells presently only have applications to pure science as far as I know [3]. However similar designer emulsions have applications in medicine, such as targeted drug delivery.

Our particular project has applications to understanding the origins of life. Specifically it may give insight into how dsDNA (short for double stranded DNA) could have self assembled from the "primordial soup".

Background

There is more to DNA than encoding genetic information. It has interesting structural properties, such as the ability to form liquid crystal phases. A liquid crystal, like what its name suggests, has properties of both liquids and crystalline materials. It flows like a liquid, however it retains a certain amount of orientational order. For example, a liquid crystal could be made of molecules that flow, however all the molecule may be pointing in the same or nearly the same direction on average (assuming the molecules are longer in one direction). This has many uses, especially in optics. Most modern computer screens use liquid crystals, thus the name "Liquid Crystal Display", or LCD.

One common optical property is called birefringence. This is property of liquid crystals comes from having an anisotropic index of refraction. Because the molecules in liquid crystal are usually rod shaped, and have an average orientation (called a director) the index of refraction will be non uniform. This optical anisotropy can create elliptical polarization of incoming light.

Birefringence is useful for many reason, however it gives me a very convenient way to detect small amounts of DNA in solution. The LCMRC did an experiment where they put short complementary (10-20 base pair) segments of dsDNA helix halves in solution. As expected, some of these helix halves found their complement and formed short segments of dsDNA. There short segments are rod like in shape and stiff. This property gives them liquid crystal behavior. Their ends are also hydrophobic. These factors allow the segments to stack like soup cans. An open question is whether stacking in this manner aids the segments to fuse into longer chains, forming a possible basis for DNA synthesis from simpler components.

I can inject the solution into a microfluidic device. The device forms small (picoliter) droplets of water in oil, where each droplet could contain DNA. Using a laser and crossed polarizers to detect birefringence in the droplets, I can detect liquid crystal and steer the droplet down one of two exit channels using electric fields (as water is polar).

Most of the components of this system are currently working, however I am having trouble with 5-10 micron diameter dust particles jamming my devices, and it has taken a surprising amount of engineering to minimize this issue.

Methods

The techniques for building mircrofluidic devices are quite involved, so I will only give a brief overview. There are two basic types of devices, glass capillary and PDMS. PDMS is a soft polymer that is transparent, and feels a lot like rubber. I will start with describing glass capillary devices, as they are simpler.

Glass capillary microfluidic devices work by injecting a fluid into another fluid that it is immiscible in, such as oil in water. If you do this in such a way to generate a shearing flow on the fluid you are injecting, it will pinch off a droplet. Just think of a leaky faucet. The surrounding fluid is air, and the injecting fluid is water. There is no shear flow needed in this case, however you can imagine you could form smaller water droplets if there was one.

Glass capillary devices are made from glass micro-needles. These are formed with a tool called a pipette puller, which heats the glass in the middle and pulls the pipette apart, forming two very sharp needles. The tips of the needles can be precisely broken off to create apertures of the appropriate size (about 10 to 100 microns) and then assembled into a microfluidic device. The downside of glass capillary devices is they are linear, there is only one path droplets can take through them. The positive is that glass is chemically resistant, and the cylindrical symmetry allows for a 3D flow.

PDMS microfluidic devices are fabricated using a complicated multi step procedure, involving lithography. Essentially a mold of the fluid channels is patterned in a photosensitive epoxy called SU8. UV lights and standard photolithography procedures are used, although this is a very sensitive process.

After a mold is created, PDMS is poured on the mold and allowed to cure in an over. Then the PDMS is peeled off the mold and bonded to glass using an oxygen plasma bonding process. This forms rectangular channels at a very small channel. Some of the devices have channels as narrow as 10 microns. The benefit is these devices can be nonlinear. Channels can branch is any way possible in 2D (as in left or right, there is of course height to the channels), and 3D if you are clever. The disadvantage is PDMS is more chemically active than glass, and rectangular channels tend to squeeze the droplets. In glass devices the droplets tend to stay in the middle of the channel.

For analysis I am using crossed polarizers and a laser shining through a refraction microscope. This allows me to detect droplets, as the crossed polarizers only allow light through the optical path when birefringent material passes between them. I use a photodiode mounted over an eyepiece of the microscope to detect changes in laser intensity. This is connected to a micro-controlled for automated detection/control. The electrodes are made of low melting temperature solder injected into specially made fluid channels. These are brought to about 1kV at 100kHz AC by a simple transformer. Steering droplets this way is called dielectrophoresis. By combining all this, I can potentially steer droplets down a channel left or right, although I have not yet integrated all these components successfully to be totally operational.

Timeline

- Year of 2009 – This was the first year of my project. A lot of it was learning the basics of my project and literature. I spent a fair amount of time building glass microfluidic devices and getting emulsions formed properly. Then I spent some time building PDMS devices and trying to get them to work. It was not always easy or straightforward, although I did make progress. I think the largest accomplishment I made was the creation of my optical sensor for detecting droplets. I was rather pleased it had good enough sensitivity and frequency.
- Summer 2010 - Worked on fabricating electrodes. Built ITO electrodes, eventually used solder electrodes. Attempted to use 100 micron scale fluid channels. This did not work, the flow was turbulent. Designed and made 20 micron scale devices. I also spent a lot of time trying to get the lithography process to work at higher resolutions (it is easy to make 100 micron features, less so to make 10), which I eventually did. I had built the optical sensor previously, however over the summer I set up the laser detection system, as well as designed and began programming the micro-controller.
- Fall 2010 – After having many devices destroyed by dust, I took a diversion to create dust free systems. I used glass capillary devices as a test bed as they are around 10x as fast to build vs PDMS devices. This led to a couple side projects. One is to create blue phase liquid crystal emulsions, which I have done successfully, although it needs to be a little refined. Also our group has been interested in creating double emulsions of liquid crystals, which is one of the things I am currently working on. I also recently built a temperature controlled microfluidic device to study phase transitions.

References

1. Baret JC, et al. (2009) Fluorescence-activated droplet sorting (FADS): efficient microfluidic cell sorting based on enzymatic activity. (Translated from English) Lab on a Chip 9(13):1850-1858 (in English).
2. Bates MA (2008) Nematic ordering and defects on the surface of a sphere: A Monte Carlo simulation study. (Translated from English) Journal of Chemical Physics 128(10):4 (in English).
3. Fernandez-Nieves A, et al. (2007) Novel defect structures in nematic liquid crystal shells. (Translated from English) Physical Review Letters 99(15):4 (in English).
4. Shah RK, et al. (2008) Designer emulsions using microfluidics. (Translated from English) Materials Today 11(4):18-27 (in English).
5. Siegel AC, Bruzewicz DA, Weibel DB, & Whitesides GM (2007) Microsolidics: Fabrication of three-dimensional metallic microstructures in poly(dimethylsiloxane). (Translated from English) Advanced Materials 19(5):727-+ (in English).
6. Zanchetta G, Nakata M, Buscaglia M, Bellini T, & Clark NA (2008) Phase separation and liquid crystallization of complementary sequences in mixtures of nanoDNA oligomers. (Translated from English) Proceedings of the National Academy of Sciences of the United States of America 105(4):1111-1117 (in English).2007).