LEAP
Synthetic Biology
Leadership Excellence Accelerator Program

Metafluidics

David Sun Kong

Massachusetts Institute of Technology

dkong@MIT.EDU

Synthetic Biology LeAP Strategic Action Plan

Version 2: January 28, 2013[1]

Synopsis

Synthetic biologists need great tools to realize their creative visions. Microfluidic, or "lab-on-a-chip" instrumentation has the potential to be such a foundational tool for synthetic biology. Despite numerous examples of microfluidic devices performing complex processes central to synthetic biology, ranging from automating and miniaturizing DNA synthesis to performing single cell analyses, they are not commonly used. Microfluidics are not easy to make or use, and researchers are typically unable to leverage the designs and hardware of other groups. To help address these issues I propose in this action plan to develop metafluidics, a toolkit for microfluidics. The metafluidic toolkit leverages digital fabrication to make devices easy to manufacture, abstraction hierarchies for enabling intuitive interfaces to make them easy to use, and finally an open repository of device and hardware designs to make them easier to share and reproduce. Through metafluidics, microfluidics will hopefully become more accessible to synthetic biologists of all types, from students just learning about biology to cutting-edge innovators re-engineering organisms.

Vision

Microfluidic, or "lab-on-a-chip" instrumentation [1], has the potential to be foundational technology for synthetic biology. There have been thousands of published demonstrations of microfluidic devices performing complex biological processes central to synthetic biology, from automating and miniaturizing DNA synthesis to precisely measuring characteristics of single cells. Despite these successes, microfluidics are currently not a common tool for synthetic biologists. Typically, specialized expertise and equipment are required to both fabricate and operate the devices and the hardware/software platforms that control them. Researchers interested in microfluidics often have to "re-invent the wheel" and are unable to easily leverage the designs and hardware of other groups.

---

[1] This paper is a working version. Please contact the author at dkong@MIT.EDU to provide feedback.
For the most recent version of this strategic action plan, visit http://synbioleap.org

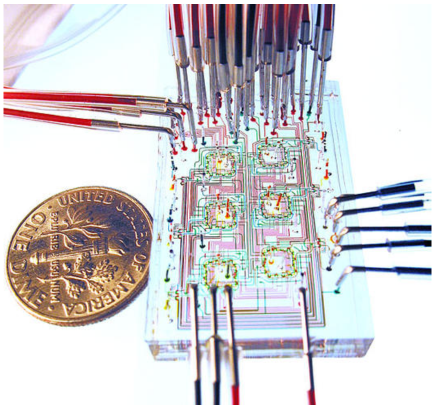

Figure 1. A microfluidic, or "lab-on-a-chip" device [1].

My goal is to create tools and organize infrastructure to help make microfluidics (1) simple to make; (2) simple to use; (3) yield experimentally reproducible results from lab to lab; and (4) enable communities of both users (synthetic biologists) and developers (microfluidic engineers) to interact, share, and improve designs.

Put most simply, I am interested in making a powerful technology more accessible to the people interested in using it, from students who have never thought about playing with biology to cutting-edge innovators re-engineering organisms. Armed with superior tools for creative expression, synthetic biologists of all types will be more empowered to fulfill their visions and unleash creative potential.

Ultimately, the public will benefit to the extent that synthetic biology's own promise of new therapies, diagnostics, energy sources, scientific discoveries, and other solutions to society's problems are achieved. With better tools we can accelerate the pace of innovation and get there faster.

Challenges

Numerous factors currently impede the widespread use of microfluidics in synthetic biology and beyond. Firstly, microfluidic devices are not easy to make. Typically specialized facilities equipped with expensive photolithography tools are required to manufacture devices. Very few people have access to such facilities. Even with access, device fabrication is an art form that requires significant training and experience.

Furthermore, there is a lack of standards for both the microfluidic devices and the hardware that control them [2]. This has led to the common occurrence of individual labs creating microfluidic technology that would be significantly enabling to the synthetic biology community, but no widespread adoption or use because of the inability to easily reproduce and operate the same device and hardware in a new setting. Given the power of the Internet to instantly share designs and the growing power of digital fabrication tools to manufacture them, we can do better.

Strategy

To overcome these challenges, I propose to develop and organize "Metafluidics," a toolkit for microfluidics. The Metafluidic toolkit has four principal goals, namely to make microfluidics: (1) easy to make; (2) easy to use; (3) easy to reproduce; and (4) easy to share.

The Metafluidic toolkit consists of three core elements:

(1) The use of digital fabrication (e.g. 3D-Printing) for the easy, reproducible manufacturing of microfluidic devices and the hardware platforms that control them.

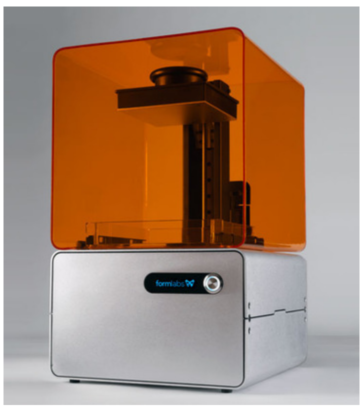

Figure 2. The Form One, a table-top 3D-printer from Formlabs.

Digital fabrication via machines like 3D-printers has emerged as a revolutionary technology for the on-demand production of tangible objects [3]. The simple transformation of data into physical objects has profound implications on how we build the world around us. Given digital designs, which can be shared and transmitted instantly via the Internet, digital fabricators can print an increasing variety of materials at faster speeds and higher resolutions. 3D printers are also increasingly affordable; a table-top 3D printer capable of making parts down to a hundred micrometer resolution can cost as little as a few thousand dollars (Figure 2).

While microfluidic device fabrication has always used digital designs as the first production step, only very recently have researchers explored using truly one-step manufacturing processes like 3D-printing for making microfluidics [4]. Using one-step printing for microfluidics eliminates the need for complex fabrication processes like photolithography for many applications, thus making it much easier for researchers and

[1] This paper is a working version. Please contact the author at dkong@MIT.EDU to provide feedback.
For the most recent version of this strategic action plan, visit http://synbioleap.org

novices alike to start making microfluidic devices. Research challenges going forward will be optimizing materials for bio-compatibility and increasing printing resolution and speed to truly compete with photolithography. However, even given current commodity 3D-printing technology, print resolutions are sufficient to produce devices for many synthetic biology applications (e.g. genetic circuit assembly) via a two-step replica molding process. As microfluidic devices are increasingly manufactured by machines that are inexpensive and easy to use, so to can the technology spread and be more widely adopted.

(2) Software abstraction hierarchies to enable intuitive interfaces for hardware and device control by non-expert users.

Most microfluidic devices are not easy to use. A typical microfluidic device requires a host of additional hardware, from pumps to valves, to execute device operations. This hardware is largely custom from lab to lab and usually requires manual, non-trivial operations. Software tools, when available, typically perform only simple operations ("open valve") as opposed to more complex commands ("mix A and B").

My goal is to make a microfluidic device as easy to use as a microwave oven. By developing software abstraction hierarchies, it is possible to deliver increasingly complex commands to a microfluidic device, building from simple operations ("open valve") all the way to biological protocols ("synthesize DNA") and ultimately to biological specification ("synthesize the genome of a microbe that can produce ethanol"). At MIT's Lincoln Laboratory we are building upon previous work [5] to abstract microfluidic device operations and make simple, intuitive interfaces that novice and expert synthetic biologists alike can use.

(3) An open repository for sharing hardware and device designs.

Microfluidic designs are currently not shared. While there have been approximately ten thousand papers published describing devices, the actual digital design files are not available, for free or purchase, and no infrastructure exists for sharing. As a consequence, researchers are unable to build upon the results and designs of others. This is a barrier that can be overcome by creating an open repository for microfluidic device designs. In the short-term, sharing the digital design files that are used for multi-step manufacturing processes like photolithography will be a considerable improvement over the status quo. Longer term, coupling one-step digital fabrication of microfluidics with an open design repository has the potential to dramatically accelerate the pace of innovation for both microfluidics and the applications they are developed for. Non-expert users would be able to re-create devices developed by leading innovators in the field, while the unexpected creation and remixing of designs could lead to all kinds of unique and interesting discoveries.

The proposed open repository will have several key features, including: (1) hardware ontology for organizing and cataloging devices; (2) meta-data associated with each design; (3) a thoughtfully constructed web environment to facilitate community interaction and encourage sharing; and (4) in a mature instantiation, advanced queries for locating designs that meet functional specifications (eg find device designs for higher-order genetic circuit assembly). Another important feature of the repository will be creating an appropriate set of licenses for uploaded designs so users have a clear set of options for how their designs can be used.

Implementation

The first two elements of the Metafluidic toolkit, digital fabrication and software abstraction, are both research areas that will be developed and supported through traditional research models. I will emphasize below analyses and tactics for creating and encouraging adoption of the proposed open repository of microfluidic designs.

Stakeholders and Incentive Analysis

Stakeholder	Incentives to download	Incentives to upload
Educators (teaching labs)	Readily available materials for course work	Curriculum sharing
Students (teaching labs)	Required for class	Recognition!
Research Labs	Don't re-invent the wheel / build from others' work	Recognition Adopt your technology
Hacker Spaces / DIY Community Bio Labs	Play and create	Recognition Adopt your technology
Government (eg DTRA)	Accelerate tool development	Accelerate tool development
Companies	Don't re-invent wheel / build from others', save $$$	In the context of "challenges"?

Figure 3. Stakeholder analysis.

The proposed open repository of microfluidic designs, which could be hosted at a public website such as http://metafluidics.org, could have a number of stakeholders, ranging from educators to government agencies to companies (Figure 3). The Metafluidics repository will have two primary forms of interaction, namely uploading new or remixed designs and downloading shared designs. Again, the over-arching benefit of this open repository is lowering the barriers of access. Educators will be able to easily incorporate microfluidics into their curriculum with a commodity 3D-printer. Do-It-Yourself (DIY) enthusiasts without formal training or access to privileged resources will similarly be able to start creating. For institutions like government agencies and research laboratories, the ability to build from others' work means an accelerated design cycle, which means better tools and more discoveries.

Tactics

Ultimately, the success of the Metafluidics repository will be measured by the vibrancy of the communities who use it. This can be quantified by metrics such as: (1) the number of users; (2) the number of designs uploaded and downloaded; and (3) the number of publications generated from repository designs. However, just because the repository is built doesn't guarantee that the stakeholders identified will find it useful or interesting. Community organizing in any context can be challenging, so building a repository with features that thoughtfully incorporate the appropriate incentives will be critical to increasing the likelihood of "success".

My first step will be to build a simple version of the repository with minimal functions but will enable basic sharing of designs. Before making this site public, I will organize an advisory board of leaders in the field of microfluidics and ask members of the board to commit to sharing designs in the future, but also crucially to seed the repository with already published designs. Seeding the repository with a curated collection of high-quality, proven, functional designs will hopefully increase the likelihood of attracting an early community of users. I will pursue internal sources at MIT's Lincoln Laboratory to fund the construction of the first version of the repository.

Additional functions of the repository can be built and refined as the community is organized. Initially, the design emphasis will be on having a simple mechanism for uploading and downloading, and also easy ways for users to attribute metadata to their designs. Building simple forms of recognition into the site (like displaying the number of design downloads) will also be important to encourage users to share. As the repository matures, it will be exciting to introduce "challenges" to the community (e.g. build the fastest cell sorter). What would the "International Genetically Engineered Machines (iGEM) competition for microfluidics" look like? Could the Metafluidics repository start as a seed for such an effort?

Conclusion

If we are as successful as we hope, beneficiaries of Metafluidics would range from society at large (who would benefit from the discoveries enabled by our tools), to researchers who want powerful tools that are simple to use, to developers who want to rapidly innovate and create newer, higher impact tools, to educators and students who simply want to teach and learn.

My dream is a world where every individual and community has access to the tools, mentoring, and resources necessary to explore and realize their creative potentials. Certainly microfluidics and synthetic biology are only a small portion of this exploration, but to the extent I can help make either more accessible to those who wish to explore and create, I will have taken steps to realize my own dream.

References

[1] Whitesides, GM. "The origins and the future of microfluidics." Nature, 442, 368-363, July 26 2006.

[2] Klapperich, CM. "Microfluidic diagnostics: time for industry standards." Expert Rev. Med. Devices 6(3), 211-13, 2009.

[3] Gershenfeld, N. "How to Make Almost Anything: The Digital Fabrication Revolution." Foreign Affairs, November/December 2012.

[4] Kitson, PJ.; Rosnes, MH., Sans, V; Dragone, V; Cronin, L. "Configurable 3D-Printed millifluidic and microfluidic 'lab on a chip' reactionware devices." Lab on a Chip, 12, 3267-3271, 2012.

[5] Thies, W; Urbanski, JP; Thorsen, T; Amarasinghe, S. "Abstraction layers for scalable microfluidic Biocomputing." Natural Computing, 7(2), 255-275, June 2008.