Interactive Biology through Remote Control

Introducing a web interface for remotely controlling a digital microfluidics device in life sciences education

Thesis Media Technology
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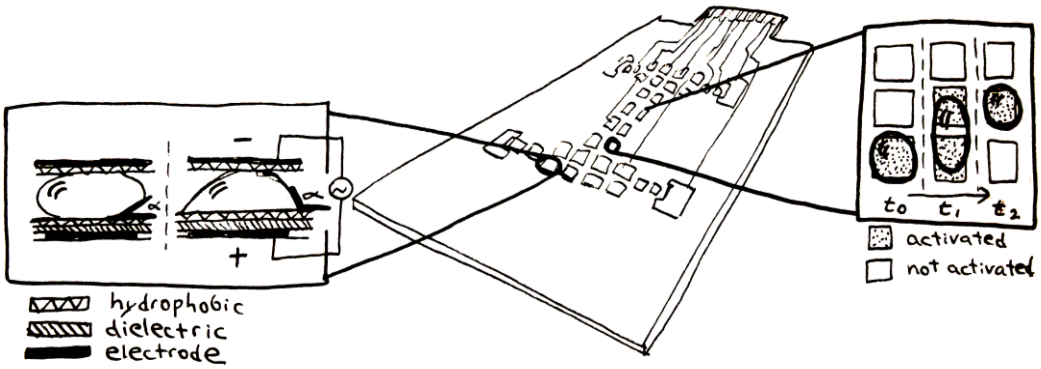

Abstract

Programmable, automated devices and remote laboratories are changing the way biochemistry research is done. As one of the promising lab automation technologies, Digital Microfluidics (DMF) allows the controlled movement of droplets on a surface, translating laboratory protocols to droplet operations. The DIY Biology community, that fosters cheap digital fabrication tools and the accessibility of biology research through hands-on practice, has shown interest in this technology. This study harnesses these developments for education. An online remote DMF laboratory is developed and a simulation is tested with undergraduate and graduate Biology students, with the goals of providing a framework for learning technical as well as conceptual skills, while questioning what such an interface should look like. The value of this also lies in the observation that remote laboratory studies, although rare in biology education, are yet a growing trend. Moreover, the usability of user interfaces for digital microfluidic control environments is previously mostly ignored in literature.

Introduction

Digital tools in biology

The methods and technologies used in biochemical research are rapidly changing. Measurements are stored in unprecedentedly big data bases, and processed with powerful computational tools that can analyse data, build models, and assist the formation of new hypotheses. On the experimentation side, technologies are developed that allow for the automatization of laboratory protocols. Cloud biology companies are building centralized facilities that lets researchers outsource the running of experiments[1,2]. Visual design tools are being developed that offer an easy method to construct DNA parts (e.g. Edinburgh Genome Foundry, Autodesk Bio/Nano Research & Groban, 2016) and compose laboratory protocols (Sadowski, Grant & Fell, 2010), which can then be executed on different machines, such as pipetting robots.[3] According to Perello (2015), the developments of these tools requires a new breed of "biocoders", multidisciplinary individuals that are skilled in programming as well as have a basic understanding of biology. Training these broadly skilled individuals is one of the major challenges in the development of the bio-automation field.

Besides changing the workflow of laboratory procedures, another trend in hardware and software aimed for biology is geared towards making experimentation more accessible. The availability of cheap microcontrollers such as Arduino[4] and microcomputers such as Raspberry Pi[5] has enabled a community building research equipment with open source hardware and software (Pearce, 2012), using increasingly available fabrication techniques such as laser cutting and 3D-printing (Baden et al., 2015). From this community, accessible, portable tools have been developed, such as Bento Lab[6], for DNA analysis, and Amino Bio[7], for bioengineering micro-organisms. In recent presentations, multiple researchers and makers at the forefront of these developments have drawn a comparison between current developments in biotechnology and

[1] Emerald Cloud Laboratories, "Emerald Cloud Lab", accessed October 3, 2016, http://emeraldcloudlab.com/
[2] Transcriptic, "Transcriptic: The Robotic Clout Laboratory", accessed October 3, 2016, https://www.transcriptic.com/
[3] OpenTrons, "Robots for Biologists", accessed October 3, 2016, http://opentrons.com/
[4] Arduino, "Arduino", accessed October 3, 2016, https://www.arduino.cc/
[5] Raspberry Pi, "Raspberry Pi – Teach, Learn and Make with Raspberry Pi", accessed October 3, 2016, https://www.raspberrypi.org/
[6] Bento Lab, "Bento Lab – experience genetics everywhere", accessed October 3, 2016, https://www.bento.bio/
[7] Amino Bio, "Amino Labs", accessed October 3, 2016, http://www.amino.bio/

the history of computing. A room-sized mainframe computer, that could only be controlled by specialists, was been replaced by a desktop computer for home use, and more recently by smartphones and a variety of portable micro-computers that are highly accessible, easy to use and connected. After a "fifty years lag", similar developments are now revolutionizing biology, where portable devices, and online accessible resources, are making it possible to take biology out of the lab, or outsiders into the lab.[8,9,10]

This study focuses on Digital Microfluidics (DMF), a promising lab automation technology that allows the movement of small droplets. The goal is to investigate whether DMF can be used to create a remotely accessible, real-time controllable laboratory environment for biology education through conceptualizing, implementing and testing a remote DMF system, while at the same time researching the usability aspects of user interfaces of a DMF control environment, and questioning what such an interface could look like. Thirdly, this study reflects upon the development of the DMF technology within the context of a DIY Biology community outside of academia or corporations, both through being developed as part of it, and through observation and inquiry from an outsider perspective. The main research goal is to study whether an online interface for a remote DMF device can allow users to control and observe experiments so as to be part of a remote laboratory for biology education. In utilizing this lab automation technology, which is still in development phase, in the novel context of remote laboratories for education, this study is a first step towards assessing the possibilities, partly within the paradigm of research-through-design. In the following Background section, a review of relevant topics is provided, giving a short background on DMF and previous studies on remote laboratory studies in university education, and introducing the context of DIY Biology.

Background

Digital Microfluidics

A majority of laboratory protocols within biology and chemistry research can be viewed as sequences of liquid handlings. Materials dissolved in water are transferred, mixed and incubated within containers such as Eppendorf tubes, using common tools such as pipettes for liquid transfers. This manual laboratory process is very time-consuming, occupying a great share of the time and energy of highly educated researchers. Moreover, it is prone to errors; variances in execution can cause slight differences in results, which negatively influence the reproducibility of scientific results. In an effort to overcome these disadvantage, technologies are being developed for laboratory protocol automation. Digital Microfluidics (DMF) is a promising technology that allows the controlled manipulation of liquids in the form of individual water droplets on a flat surface (Fair, 2007). This enables the execution of miniaturized versions of laboratory protocols, consisting of a series of standard liquid handlings such as mixing, splitting and moving small volumes of liquid. Discrete droplets can be moved by activating and deactivating individual addressable pads, an architecture bearing similarities to that of digital microelectronics, hence the adjective 'digital' (Srinivasan, Pamula & Fair, 2004). The relatively tiny volumes reduce the cost of material such as reagents in biochemical analysis, while the digital programmability of the device allows the manual laboratory work to be greatly reduced. In DMF, fluids are moved by means of electricity. Droplets are placed on electrodes covered by a dielectric (i.e. insulating) and

[8] Trojok, R. & Alistar, M. (BioFlux), "Bioflux – A Personal Laboratory for everyone", accessed October 3, 2016, https://voicerepublic.com/talks/bioflux-a-personal-laboratory-for-everyone
[9] Riedel-Kruse, I. H. "Interactive Biotechnology: Cloud Labs, Biotic Games, DIY kits, and more", accessed October 3, 2016, https://www.youtube.com/watch?v=HM5zFq9HWzw
[10] Wolfendsen, B. "(Open) Hardware for Engineering Biology.", accessed October 3, 2016, https://vimeo.com/180914536

a hydrophobic layer. Putting high voltages on the electrodes results in an electrostatic force that changes the wettability of the surface, i.e. its ability to reduce the surface tension of the droplet and, as a result, increase both the spreading of the droplet over the surface increase and the contact angle between the droplet and the surface (Figure 1). This process is described in literature as electrowetting-on-a-dielectric (EWOD), and can be used to control the movement of droplets over a surface by the activation and deactivation of electrodes.

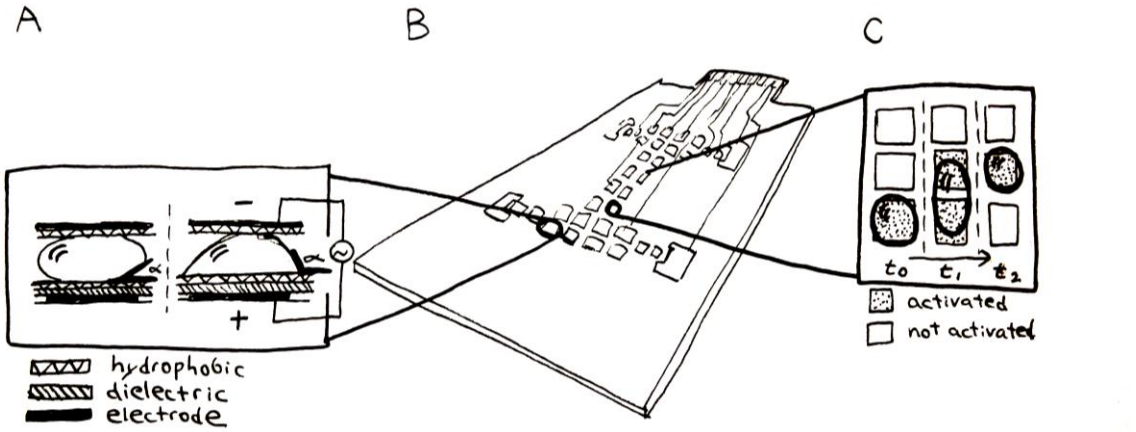

Figure1. Electrowetting-on-a-dielectric and overview of a digital microfluidics biochip. A) A side view of electrowetting. When an electrode is activated, the contact angle (α) between the droplet and the surface increases. Different layers are indicated. B) Schematic view of a DMF biochip, the small end can be plugged in an edge connector C) Droplet movement between three steps in time. The activation state of tiles is indicated.

Advantages of DMF, compared to other lab automation techniques, include its configurability and flexible control, especially when compared to microfluidic channel systems that are generally more application-specific (Rackus, Shamsi & Wheeler, 2015). It costs comparably little effort to create and implement new DMF chip designs, and the translation from protocols to droplet movements on a surface is relatively straightforward. DMF devices could increase the experimental throughput in laboratories, while at the same time their relative compact architecture allow makes DMF systems suitable for portable operations (Gong, Fan & Chang-Jin, 2004; Yang, Hsu & Fan, 2008). On the other hand, the advancement of Wi-Fi-connected microcontrollers enables the remote control of a DMF system over the web, a possibility that is not yet previously harnessed in implementation studies, to the knowledge of the authors.

A wide range of proof-of-concept applications of DMF is covered in the literature. Demonstrated applications for clinical diagnostics include the extraction of molecules such as estrogen from blood (Gong et al., 2009), and analysis of molecules from dried blood samples (Jebrail et al., 2011), where DMF biochips are integrated with sensors such as photospectrometers for on-chip readout. DMF is expected to play a role in a diverse set of human clinical diagnostic situations in the future (Pollack et al., 2011). In the area of cell research, DMF has been used for cell lysing (Fair, 2007), cell-based toxicity assays (Choi et al., 2012) and cell culture (Au, Shih & Wheeler, 2011). In the areas of genetics and synthetic biology, researchers in DMF related studies have performed techniques such as plasmid formation, DNA assembly and electroporation (Shih et al., 2015), pyrosequencing (Fair et al., 2007), real-time polymerase chain reaction (Hua et al, 2010), and have automated experimental pipelines for genetic engineering (Gach et al., 2016).

Notable DMF devices include the NeoPrep System sold by Illumina[11], developed specifically for library preparation for next-generation sequencing and the only DMF product beyond development phase that is currently commercially available for research labs, the automated molecular biology platform by Sandia (Kim et al., 2013), and the DropBot, an open source DMF device developed mainly by Ryan Fobel as part of his PhD at the Wheeler laboratory at the University of Toronto (Fobel, Fobel & Wheeler, 2013), which has recently been field-tested in Kenya, performing ELISA tests for measles and rubella detection.[12] The open source nature of the DropBot inspired different communities of open biotechnology and DMF enthusiasts outside of academic or industrial circles to start experimenting with the technology themselves, further enabled by the availability of cheap and fast prototyping methods, such as printing electrodes with conductive ink on paper (Fobel et al., 2014), electrode fabrication through photolithography (Abelgawad & Wheeler, 2007), or the use of standard printed circuit board (PCB) production methods, and the availability ubiquitous plastic wraps and oils as coating (Li, Chen & Baker, 2014).

Remote laboratories in education

Remote laboratories are laboratory environments controlled by an experimenter over a network, where there is a distance between the experimenter and the experiment. There have been numerous implementations of remote laboratories in education, especially for the topics of engineering and physics, with subjects ranging from robotics, to chemistry, and, recently, biophysics (Ma & Nickerson, 2006; Alkhaldi, Pranata & Athauda, 2016). There are multiple online repositories of remote and virtual laboratories, including links to request direct access to such laboratories, with varying education goals. These include iLabs[13], a project run by MIT, Go-Lab[14], a portal maintained by Twente University focuses on virtual and remote environments for inquiry based learning, and LabShare[15] by the University of Technology Sydney's remotelabs group, that focuses on remotely controlling engineering tools.

In their review of remote laboratories, Ma & Nickerson (2006) sum up the benefits of remote laboratory experiments, including the potential to provide affordable experiments and experimental data, the extension of conventional laboratories' capability, the flexibility in performing experiments at different times and places for students, the motivating effects on students. Disadvantages, on the other hand, include the limited equivalence of remote laboratories with conventional laboratories, the likelihood of distraction and impatience in the students, the uncertainty of the remote experiment's value and the lack of realism experienced by some students. In their review of contemporary remote laboratory implementations, Alkhaldi, Pranata and Athauda (2016) add to the list of advantages the aspects of safety, accessibility, the potential of newer opportunities for learning not available in conventional laboratories, and the possibility to create environments that allow a greater focus on the pedagogical goal then conventional laboratory settings, by abstracting away from the complexities of real-world experiments and their troubleshooting aspects. The latter advantage is also pointed out by Hossain et al. (2015), who argue that the remote laboratory setups they devised allowed students

[11] NeoPrep library system (Illumina, 2015), "Neoprep library system", accessed October 6, 2016, http://www.illumina.com/systems/neoprep-library-system.html
[12] DropBot, "Measles and Rubella field trial in Kenya", accessed October 6, 2016, http://microfluidics.utoronto.ca/dropbot/2016/05/17/measles-and-rubella-field-trial-in-kenya/
[13] MIT iLabs, "iLabs Around the World", accessed January 23, 2017. https://wikis.mit.edu/confluence/display/ILAB2/iLabs
[14] Go-Lab, "Go-Lab", accessed January 23, 2017, http://www.golabz.eu/
[15] LabShare, "Remote Labs. Enriching digital education", accessed January 23, 2017, http://www.labshare.edu.au/

to concentrate on biology experimentation by abstracting away the hands-on skills and logistics needed for wet-lab protocols.

Compared to disciplines such as engineering, remote laboratories for biology are rare. The Riedel-Kruse Interactive Biotechnology Laboratory at Stanford University recently described specially designed implementations. Originally motivated by the prospect of using digital games and interfaces for biology education, their research developed to include studies into "Human Biology Interaction", as well as the architecture of such systems. Initially, the lab created Biotic Games, which allow players to interact with micro-organism or biological processes, an experience that can be enhanced by an additional virtual game layer on top of the video stream (Riedel-Kruse et al., 2011). Recently, the research group started bringing current trends in cloud biology and lab automation technologies into natural sciences education. Hossain, Chung & Riedel-Kruse (2015) describe two different platform designs: one for biological processes on short time scales, requiring a single user to have direct access to the experiments, and another for longer processes that due to the longer duration allow for batch-processing of instructions by multiple users on a limited number of machines. As an example of the first category, they build a platform for phototaxis experiments with euglena, remotely accessible by anyone via the cloud.[16] As an example of the second category, Hossain et al. (2015) built a cloud experimentation platform that let a small group of graduate students experiment with the effect of fluid food placement on the growth of Physarum polycephalum (slime mould). On an interface that showed a time-lapsed video of the slime mould growth, students could draw the locations of fluid droplets to be dropped by a pipetting robot. Students could access the web interface at any time, as the researchers designed an architecture that controlled the scheduling and processing of programmed actions and the storage and output of data.

In their comparison of papers on the topic of remote laboratory implementations, Ma & Nickerson (2006) observed that there is no common foundation to evaluate the effectiveness of labwork. However, they argued that remote laboratory implementations would benefit from explicitly stating the learning goals, which are often implicitly held. Therefore, they proposed a four-dimensional model for laboratory education goals, taking the education goals proposed by the Accreditation Board for Engineering and Technology (ABET) as a starting point (Table 1).

Table 1. Laboratory education goals, adapted from Ma & Nickerson, 2006. A learning based on design skills is in recent literature often described as inquiry based learning (e.g. Hossain et al., 2015). These definitions are used here intermittently.

Laboratory goals	**Description**
Conceptual understanding	Extent to which laboratory activities help students understand and solve problems related to key concepts taught in the classroom
Design skills	Extent to which laboratory activities increase student's ability to solve open-ended problems through the design and construction of new artefacts or processes
Social skills	Extent to which students learn how to productively perform engineering-related activities in groups

[16] Riedel-Kruse Lab, "Realtime Online Euglena Lab. Interactive Biology Online", accessed January 23, 2017, http://euglena.stanford.edu

Professional skills	Extent to which students become familiar with the technical skills they will be expected to have when practicing the profession.

Table 1 shows different categories of educational goals related to labwork, as formulated by Ma & Nickerson (2006). These categories might not be completely fixed and display a degree of overlap. However, they can serve as a tool to formulate and evaluate specific learning goals related to the four categories. Respectively, different implementations of remote laboratories might evaluate the design with respect to the potential of the remote laboratory to teach the students to contemplate and illustrate scientific principles (conceptual understanding), to set up experiments and investigations (design skills), to show productive cooperation (social skills) or to apply specific technical skills (professional skills). As an example, the labs within the Go-Lab project all share the use of inquiry based learning, whereas the remotely controllable measurement equipment available at ShareLab have the goal of learning professional skills.

The learning goals of the digital microfluidics control interface developed in this study are chosen to be conceptual understanding and professional skills, because these are first steps to be taken in developing the DMF technology in the context of education. Cooperation skills and inquiry based learning require the controls and concepts to be clear. Another consideration is the current flexibility of the DMF chip and control system used, which do not yet allow for the degrees of freedom desirable for inquiry based learning goals. With regards to the conceptual understanding goals in this study, students should be able to comprehend what happens at different steps in a biochemical protocol. With regards to professional skills, students acquire an understanding of how to use digital microfluidics for bioassays. Moreover, they get an intuition for the challenges of controlling the liquid movement technology, especially with regards to droplet routing. We hypothesize the proposed interface can function to make biology engaging, while also sketching an experience of one of the possible futures of biology research. At least it is a hands-on method to explore the possibilities of DMF for remote laboratories in university education.

The combination of conceptual and applied learning goals bears resemblance bifocal modelling approach developed by Blikstein and Wilensky, where computer models (concept-driven) are connected with physical real-time systems (phenomenon-driven). According to them, Bifocal modelling in education allows for a better transition from theory to technology, introduced fundamental issues coming from the connection between simulated and physical models, and created content-driven connections with science learning (Blikstein & Wilensky, 2007; Blikstein, 2010). It builds upon Papert's "constructionism", which focuses "forms of knowledge based of working with concrete materials rather than abstract prepositions", replacing for example mathematics classes with classes in programming languages such as Logo, guided by a vision of "soap-sculpture math" and bottom-up, hands-on education (Papert & Harel, 1991). The aforementioned research of the Riedel-Kruse Lab aims to combine the hands-on engineering or computer science paradigm with living materials such as euglena or slime mould. There implementations are consciously designed to be domain-specific. The benefit of instead using a DMF chip in a remote lab setup is that it is much more adaptable to new experiments and different organisms, compounds and media. A platform using DMF could overcome the constraints of prior biology related remote laboratory setups by providing a more general technology for a wide array of experiment types.

DIY Biology

The DIY Biology or "biohacking" movement aims to make biotechnology accessible, fosters bottom-up innovation and sharing of knowledge and designs, and offers spaces for alternative

research (Sanchez, 2014). It is a distributed network of independent laboratories, where people gather to work on biology related projects. One of the main drives is the desire to open up science and technology through the development and sharing of designs for devices and hands-on experiments. Agents often operate outside of academia, in for example hackerspaces, maker spaces, and open labs. Trojok (2016) sees DIY biologists or biohackers as an alternative to traditional biology labs, becoming on equal terms when it comes to equipment and knowledge, and expects more bio related companies to arrive out of the biohacking scene. The freedom to do projects because they are enjoyable to do is at the core of the scene, allowing the freedom to learn and to explore.

Waag Society in Amsterdam is an NGO that focuses on opening up new technologies to enable societal engagement, discussion and creative use, and also organizes events around the Open Wetlab, specifically aimed towards opening up biotechnology to a broader public, and allowing people to be creative with biology. To this end, it organizes open evenings, workshops, the BioHack Academy, where students build their own lab equipment[17], a microbial Petshop[18], among other things. Besides making published biology related experimentation more accessible, the space is also used for research and innovation, where people from different backgrounds and disciplines come together to develop new ideas.

At an event called Rock'n'Roll Biotech in 2015 at the University of Helsinki system present in Helsinki inspired Pieter van Boheemen of Waag Society to start tinkering with digital microfluidics, while Rüdiger Trojok and Mirela Alistar sketched out the outlines what would become BioFlux.[19] Urs Gaudenz, founder of GaudiLabs and co-founder of the Hackteria Network, created the OpenDrop, a portable DMF device made of PCBs, of which the design files are openly accessible.[20] As can be seen on the OpenDrop website, a number of "wild" variants have been developed by researchers building upon their design. Auryn (formerly BioFlux) is a Berlin-based startup that develops DMF building upon the OpenDrop technology (Trojok, Volpato, Alistar, & Schubert, 2016).[21] Digi.bio came from the community around Waag Society's wetlab and Fablab. Digi.bio is a project initiated by the core group of Federico Muffato, Frido Emans and Jelmer Cnossen, who have the intention developing a startup out of their DMF system in the future. Around the group, a web of enthusiasts have gathered who regularly meet and tinker, some of which have been present in a brainstorm session for this study. It is a project that develops DMF hardware and software. The hardware setup and DMF chips used in this study were designed or created in cooperation with Digi.bio, who use paper printed chips with conductive silver ink and a custom made board with DC high voltage output.

Although these initiatives outside of academia or major industries are connected in their interest in the development of the DMF technology, the nuances within their vision on this development are slightly different. Auryn's Rüdiger Trojok foresees the future use of DMF devices as a personal toolkit for personalized medicine, as a portable device for synthetic biology prototyping that allows e.g. personalised phage therapy (Trojok, 2016). The OpenDrop is developed in the midst of a bigger shift towards open source science hardware, which recently has been described in the

[17] BioHack Academy, "BioHack Academy Syllabus", accessed November 11, 2016, http://biohackacademy.github.io/
[18] Petshop,"Tiny relations in a big world. Microbes for Sale", accessed November 11, 2016, https://www.petshop.bio/
[19] Trojok, Ruediger, "Rock'n Roll Bio, Biofilia Laboratory 2015, Helsinki", accessed January 20, 2016, https://www.synenergene.eu/blog/rockn-roll-bio-biofilia-laboratory-2015-helsinki
[20] Gaudi. "OpenDrop V2", accessed October 6, 2016, http://www.gaudi.ch/OpenDrop/?p=17
[21] BioFlux, "BioFlux – launching digital biology ", accessed October 30, 2016, http://www.bioflux.eu/

Global Open Science Hardware (GOSH) manifesto.[22] Most recently, OpenDrop has also been coupled to blockchain technology, which could enable the development of the technology in a radical novel open format.[23] Digi.bio aim is to develop the lab automation tool specifically for (synthetic) biologists, although they are investigating the potential of open creation and innovation in makerspaces in the process. All of these DMF initiatives are connected, and knowledge is shared between them. OpenDrop is unique in sharing all PCB files and Arduino code openly online.[24]. The DMF DIY biology scene also organizes occasional events, two of which fuelled the conception of this study. Frido Emans and Federico Muffatto of digi.bio organized a Microfluidics Hackathon in November 2015, where participants created and printed biochip designs, assessed different coatings, and worked on a control interface.[25] Rüdiger Trojok and Mirela Alistar of BioFlux (now Auryn) organized a seminar on Digital Biology in Berlin in January 2016, revolving around Doing It Together (DIT), assessing the challenges of digital microfluidics, and the options of developing the technology across borders.[26]

The study of DIY Biology from a sociological perspective is a scholarly field on its own. Although a majority of published studies focus on American spaces and role of ethics within their work, which is due to legislative differences with other countries more genetically focused, there is also academic, political and artistic interest in the field in Europe, exemplified by the BioFabbing Convergence event in May 2017.[27] This study does not aim to be a review of articles on DIY Biology in Europe, but collaterally it reflects on the local practice from a first-hand perspective. Besides, the development of DMF within this open movement is touched upon in communication with actors in the field, especially focusing upon the view on users from the perspective of active developers.

In the following section the methods used for conceptualizing, developing and testing the remote DMF laboratory setup and interface are outlined. First, the technical system architecture is detailed, followed by an overview of the interface design methods and tactics to get feedback used in the development process. Finally, the rationale for and setup of user testing is detailed.

Methods

Technical system architecture

The general architecture of the system can be split up between the user side and the remote laboratory, communication between which flows via the cloud (see a simplified sketch of the

[22] GOSH, "GOSH Manifesto", accessed October 30, 2016, http://openhardware.science/gosh-manifesto/
[23] Cryptoking, "[FLUXEL] OpenDrop is an open source microfluidics platform tied to a crypto asset and a DCO", accessed November 5, 2016, http://cryptocentral.info/topic/239/fluxel-opendrop-is-an-open-source-microfluidics-platform-tied-to-a-crypto-asset-and-a-dco
[24] OpenDrop Github repository, "Gaudilabs/OpenDrop", accessed November 5, 2016, https://github.com/GaudiLabs/OpenDrop
[25] Frido, "Software improvements since the hackathon", accessed November 5, 2016, https://digi.bio/2016/01/software-improvements-since-the-hackathon/
[26] BioFlux, "DIT Seminary in Berlin", accessed November 5, 2016, http://www.bioflux.eu/activities.html
[27] BioFabbing http://citizensciences.net/biofabbing/

architecture in Figure 2).

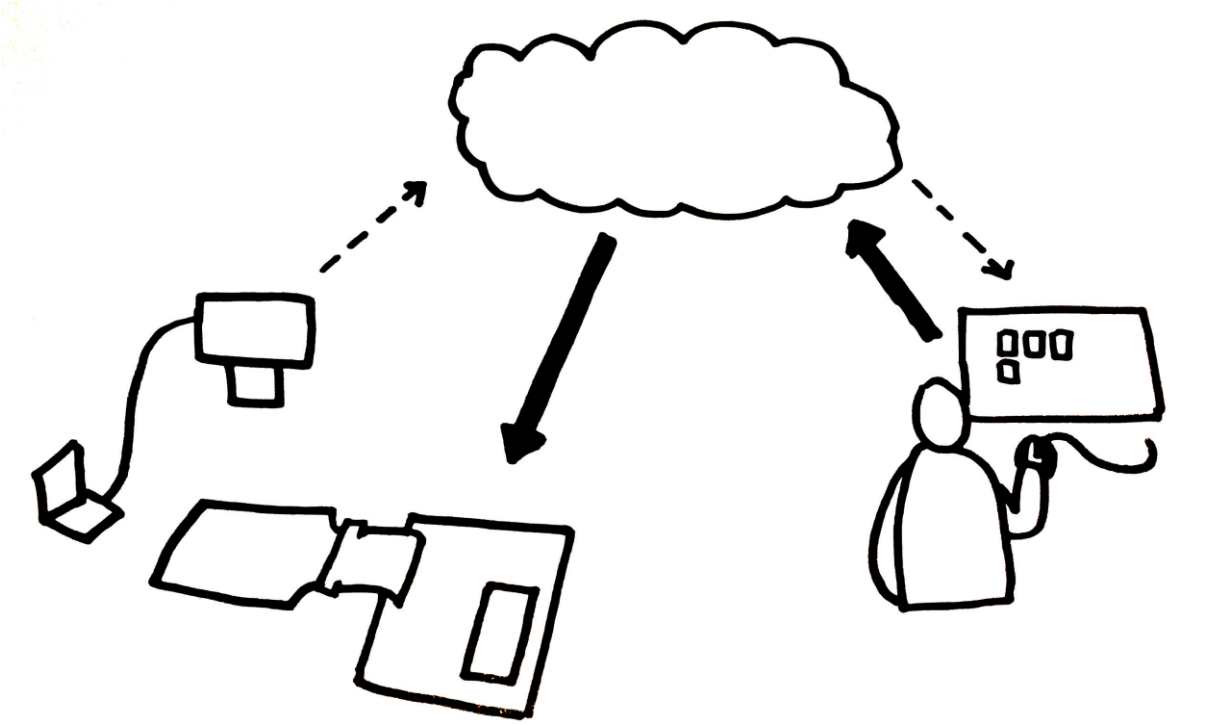

Figure 2. Simplified layout of the system architecture. A user controls the voltage control board via the cloud, which is connected to a DMF chip. The action on the DMF chip is caught by an HD camera and transmitted live to the user interface via the cloud.

In this setup, digi.bio's DB2 board (hardware design by Jelmer Cnossen, digi.bio/ biotronics) is used for voltage switching. It main parts include a Nixi power supply circuit, and the HV507 64-channel voltage switching chip. The state of the HV507 is controlled by a Photon micro-controller (Particle), which is he micro-controller is flashed with Arduino code co-written by Frido Emans, Jelmer Cnossen and the author. The DB2 board output pins are connected to the DMF biochip using a 38-channel, two sided edge connector, where the DMF chip can be stuck in like a USB drive in a USB port.

The DMF biochip is fabricated by printing ink containing silver nanoparticles (AgIC) on glossy photo paper with an Epson ET-2500 inkjet printer (Epson). The print is coated with mineral oil, 20 µm polytetrafluorethylene (PTFE, or Teflon) foil. For the spacer, 1 mm thick silicon is used. As the top layer, polyethylene terephthalate (PET) pre-coated with Indium tin oxide (ITO) is spin coated with CYTOP (AGC Chemicals Europe). Vector files created in Inkscape are exported to DXF formats for cutting with a laser cutter (BRM). Out of 2mm PMMA (acrylic), a bottom layer is cut, on which the photo paper chip is attached using laser cut double sided tape. The stack of layers is tightly screwed with four 3mm screws and bolts in the corners.

The C920 HD webcam (Logitech) is attached above the DMF chip, with a 24-LED Ring (Neopixel) around the lens for lighting. The video is streamed using a laptop, using the node module stream-server.

The web interface is created using HTML5, CSS3 and JavaScript. Code is written in the Atom text editor, and stored on Github. Using the web server provider Heroku, the node module http-server is used to serve the web application. On a Heroku created URL, users log in on a laptop to access the interface. In the interface, an Ajax call calls on a voltage switching function on the Particle microcontroller, a command that is send via the native Particle cloud. The stream server's address

is integrated in the JavaScript code to show the video stream. For the test situation, all users control the interface using a separate screen and mouse connected to a laptop computer, as is schematically drawn in the figure.

Interface Design Methods

The development of the web interface was a layered process, consisting of multiple steps and input moments. Requirements were conceptualized, initial concept designs were tested in a group brainstorm session, and information on DMF interface usage and development was gathered in exploratory interviews with DMF engineers and users. Although these different steps are presented linearly, the actual process was non-linear, with feedback loops between the different stages of developing and questioning the interface.

Design considerations

To investigate which requirements are of importance with regards to the interface developed within this specific study, a PACT-analysis was used as a tool to get an insight into users and their context (Benyon, 2005). Based on the derived requirements, a number of solutions were sketched out.

Session

These initial design considerations were tested in a 90 minutes, semi-structured session with a group of participants with background knowledge in digital microfluidics, biology research, or web design. The session was aimed at discussing key requirements from a user perspective for a web interface that allows biology or biochemistry students to remotely control a digital microfluidics device. The session was constructed to maximize the individual and group input, preventing an echo-chamber of ideas presented in its introduction. In Table 2, the session structure is outlined. It started with a short presentation about this study, which explained the focus of the system in allowing students to acquire conceptual skills (e.g. which droplet movement step corresponds to which step in the protocol, and what is happening at the biological level) and professional skills (e.g. how to execute an experiment), but consciously left out an analysis of requirements and possible solutions. The example of a enzymatic colorimetric reaction for glucose level detection in blood samples was described, after which participants were asked to think about the interface for executing such a protocol on the proposed digital microfluidics platform, what requirements such an interface has, and which solutions could be thought of. This thinking was first done individually, then in duos, and then in groups. Hereafter I presented my own assessment of the system's requirements, and ideas that could help fulfilling these. The presented concepts led to more discussion. Eventually, I showed some "wild" interface and control ideas, and discussed these, and summarized the session's conclusion together with help of the participants.

Table 2. Session structure

Part	Duration (min)	Summary
I	10	Introduction thesis and research question
II	5	Introduction glucose concentration example
III	30	Hands-on session and discussion
IV	10	Discussion: interface ideas
V	10	Wild ideas discussion
VI	10	Open-ended discussion

Explorative interviews

To gain knowledge on the interface design choices and user philosophy made by DMF developers as well as users, semi-structured interviews were executed with people in the field (Appendix A): Ryan Fobel (developer of the DropBot at Toronto Univeristy), Sebastian von der Ecken (DMF researcher, DropBot User, PhD at KIT Karlsruhe), Urs Gaudenz (biohacker, OpenDrop developer), Gowtham Sathyanarayanan (DropBot user, PhD at Helsinki University). The goal of these interviews to gather information on a user perspective on DMF: how would DMF be described, how is it currently used, what are the problems with current software, what types of interaction could be used. Moreover, the interviews provide a bigger context to the designs, developments and tests in this study, to shine a light on the secondary goals of a user perspective on DMF in general, and the development of DMF within the DIY Bio or open source community. In analysis, parts of the interviews were grouped in four categories. The first one being a description of DMF as a technology, its applications and its users. The second one the user interface to control a DMF system, including ideas on that topic as well as problems encountered while using such an interface, and possible solutions. Technical statements on the software are grouped in this category as well. The third category was the DIY Biology community and open source hardware, and the relationship with these fields. The fourth and last group consists of statements on the future challenges and vision. Statements within the interviews were colour coded with blue, orange, yellow and green left borders for category one to four, respectively.

A summary is given of statements per topic, focusing on shared views as well as differences, using inline quotes or block quotes to support the argumentation and to highlight statements particularly interesting for this study.

The information gained from both the session and the explorative interviews was used towards developing the main goal of developing and testing a DMF interface. However, it also brought data for the broader analysis of this study's secondary goal, getting insight into a user perspective for DMF applications. Moreover, through the interaction with agents within the open source and biohacking communities, information was gathered on the DMF development within the biohacking community.

User test

The method for designing the user test questions followed a common paradigm within the Human Computer Interaction research field: the ISO usability standard 9241 (1988) offers guidelines for usability categories, separating effectiveness (can a user fulfil his/her goals using the system?), efficiency (how fast can actions be performed using the system?) and satisfaction (does the user enjoy using the system?). As from the requirements analysis and group session was reasoned that, in this specific case study, efficiency in terms of time for completing an action is not important, the focus lies on effectiveness (i.e. assessing whether protocols can be controlled using the interface) and satisfaction, where the first is part of the technical skills, and the second included in conceptual understanding.

Because this is the first known attempt to formalize a user test with DMF, the System Usability Scale (SUS, Digital Equipment Corporation, 1986) is included, to achieve a general indication of the system's usability. Besides testing this specific implementation, this also feeds into the secondary goal of questioning the usability aspects of a user-controlled DMF system in general. The SUS questions were introduced by a text that positions this system as a possible implementation of a learning environment for life science students, as an addition to their regular curriculum, by introducing them with a text that reads: "Imagine being able to use the system you just used in one of your study's courses that involve laboratory work. How would you rate the following statements?"

In the user test, two design solutions concerning input were tested, analysing their impact and asking the participants to rate them. The first is direct activation, where users control the droplets immediately by activating and deactivating electrodes through clicking on them. The second is droplet routing, where users draw and save the droplet movement in multiple steps, before execution. In both cases, other factors such as the camera feed, the protocol, and the actuation parameters are held constant.

In summary, the user evaluations aims to test the system's general usability, two alternatives for user input, and understanding.

User test outline

The user tests consisted of three phases. After watching a movie clip, participants, all undergraduate and graduate Biology students at Leiden University, performed tasks with the user interface, and filled in a questionnaire. During the user interface part, the users were shadowed, i.e. silently observed. Remarks made by the participants during and after testing were written down.

Because the hardware was not stable enough to be used in user tests, we opted for simulating the droplet movement. However, users are under the impression that they are controlling a real-time remote device, to exclude the influence of different expectations and to fulfil the research goal. To attain this goal, students first watch a compilation of movies of droplet moving on the DMF device. A 1:54 long movie clip was played to the participants. The movie was a combination of text and moving images, the content being as follows.

"Digital Microfluidics is a technology used to control the movement of fluids, by means of electricity. It can be used to execute laboratory protocols. The following clip is an example of a microfluidics system by Illumina", followed by five seconds from Illumina's NGS Library Prep video.[28]

"We have printed and coated microfluidic chips", followed by clips of silver ink printed, and hydrophobic coating. "To move little droplets for simple experiments", followed by short clips from Arjen Pit and digi.bio.[29,30]

"In this experiment, you will control a remote microfluidics device through a real-time internet connection", followed by a sketched diagram of the cloud connection.

"Droplets are tracked by the camera, and the chip is shown graphically. On the chip there are two input reservoirs, a mixing area, and a readout output for measurements. You will merge two droplets and move them to the readout spot", followed by a representation of the chip.

Thus, students get informed that the interface they are using is simplified but based on a live connection, that the droplet movement is analysed and visualized real-time graphically by the changing colour of the tiles: tiles with water are coloured blue. Participants are informed that the red line surrounding a tile represents the activation of electricity on that spot. They were asked to move droplets from both of the input reservoirs to the output square, first in direct actuation mode, and then in routing mode. In routing mode, it was explained that the route had to start at

[28] Illumina Inc, "NeoPrep NGS Library Prep with Digital Microfluidics | Illumina", accessed January 23, 2017, https://www.youtube.com/watch?v=F_Hks6OnSKM
[29] Arjen Pit, "Automated EWOD (Spliting, double droplet transport, high speed)", accessed January 23, 2017, https://www.youtube.com/watch?v=4FDbC5Opv2w
[30] Digi.Bio, "splitting from reservoir", accessed January 23, 2017, https://www.youtube.com/watch?v=TT44H-MXyh8

the reservoir, saved with the save button after finishing the route, and started with the start button after drawing all routes.

First users control droplet movements by clicking on the tiles directly, and then then they do the same protocol by drawing routes. Afterwards, users fill in the questionnaire. In table 3 the steps of the test are outlined. The total duration of the test is around 30 minutes.

Table 3. Outline user test (Step II and III are swapped in half of the participants' tests)

Part	Duration (min)	Summary
I	2	Introductory talk and setup
II	2	Introductory video
III	4	Use interface
IV	20	Fill in questionnaire
V	2	Debriefing talk

Students get an introduction, both spoken and in the form of a movie, before using the system, as would be the case when it were implemented in an online available learning environment. Moreover, this introductory information results in an equal pre-test knowledge of participants, and thus enables a better analysis of gathered user data. As was suggested during preliminary interviews, participants are shadowed, i.e. observed when they use the system intuitively, without interfering with their thought process.

Protocols consist of two inputs (blue tiles), that have to be moved, merged, split, and moved to an end position. For the context of the protocol, the assay is based on a colorimetric glucose assay, where a droplet, said to contain blood, is mixed with another droplet, said to contain reagents, and a readout is done on a dedicated spot, as an endpoint. This protocol was selected, because it has been shown to be implementable from start to end on a DMF chip (contrary to for other sets of protocols in which steps on a DMF device function as preparatory steps in a bigger plan). Moreover, it requires no extra technological features, unlike for example PCR, which would require heating elements to create a thermal gradient. The layout of the chip is designed to suit this protocol, with two inputs, a mixing area, and a readout spot (Figure 3).

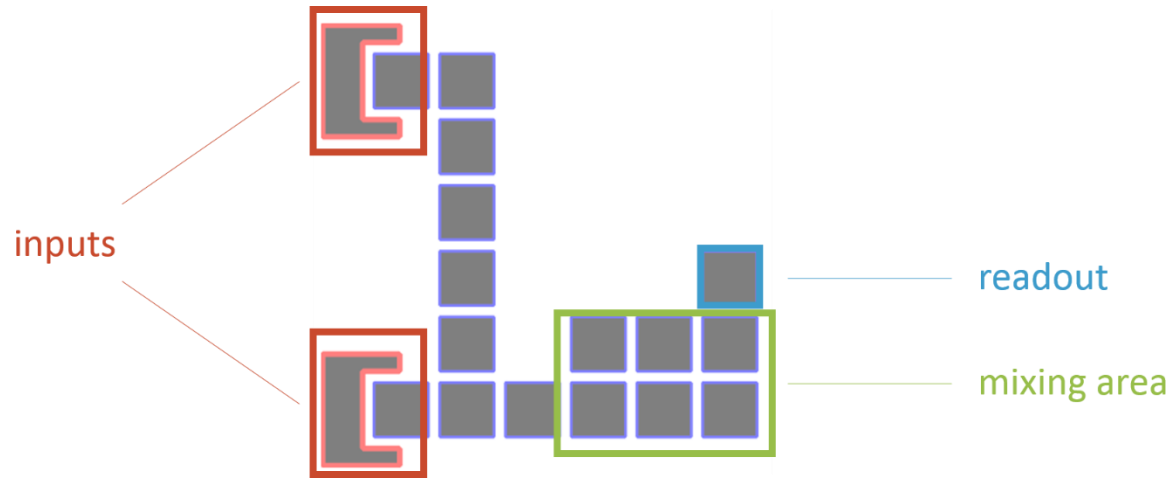

Figure 3: Layout of the DMF biochip used in user tests

The questionnaire is designed using the Likert scale from 1 to 7, with multiple questions per category (understanding, technical skills and implementation). These are often phrased in the same direction (negative to positive), so scores can be added to give a global score per theme per

user. The questionnaire is followed by SUS questions, and ends with a number of open questions. The user test questionnaire can be found in Appendix B.

Results

Initial design considerations

As guidelines for assessing the first conceptual design, a PACT analysis was used, focusing on the people, activities, context and technology of this specific case study (Benyon, 2005), see Table 4.

Table 4. PACT analysis

People	Undergraduate and graduate life science students. No coding experience.
Activities	Walk through protocols on a remote DMF lab
Context	Distant from actual DMF device, which is viewed via a webcam
Technology	Interface built using modern web standards (HTML5, CSS3, JS). Users can live control the actuation of electrodes on DMF device

Several requirements were considered based on these requirements. A graphical interface ensures the users do not need to learn programming skills to use the system. Users need to be able to know at where the protocol is at intermediate moments, or which steps have already been taken. The control has to be intuitive, and interactive. Droplet movements have to be independently schedulable. The sequence of droplet movement has to be stored and retrieved.

Different solutions for these requirements were considered. Regarding options for droplet control, the following three: direct clicking on tiles to activate or deactivate them, moving droplet end-to-end by clicking on the route, and selecting the tile where the droplet is, before moving the droplet by clicking buttons (left, up, right, down, split left-right, split up-down). Regarding the scheduling of routes, a timeline solution was considered, similar to in for example movie editing programmes. When clicking and dragging a route for a droplet, blocks are filled in a lane of a timeline consisting of discrete blocks of time, of which the sizes are adjustable, but constant. Alternatively, when clicked on next electrode, the timeline could automatically move to the next square, unless user presses a key to select multiple electrodes. These ideas are captured in sketches (Figure 4 and 5).

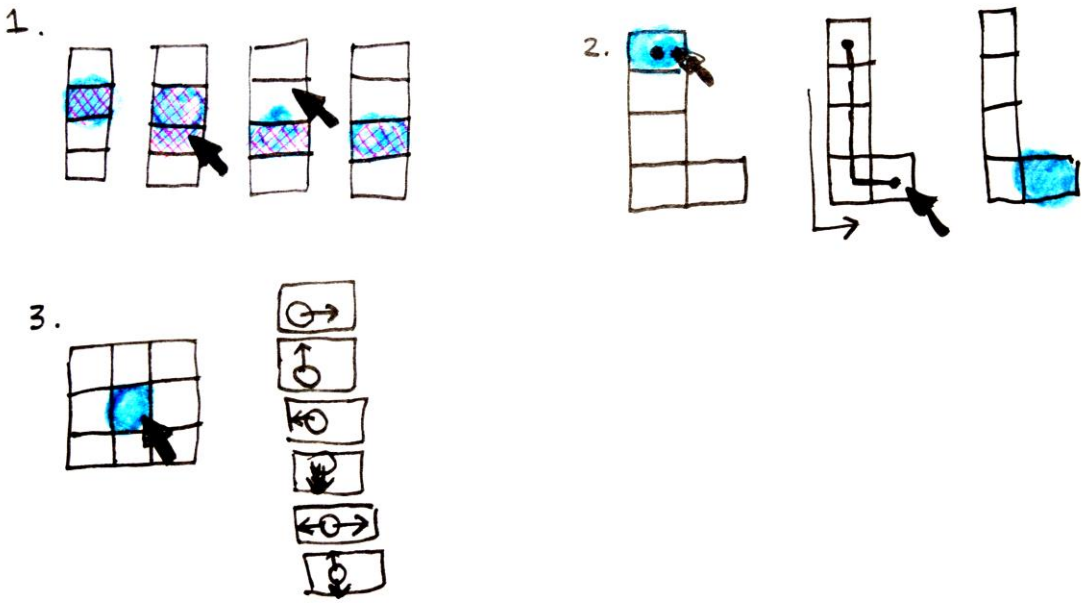

Figure 4. Three types of control. (1) Direct clicking on tiles to activate or deactivate them. (2) Click and draw line from end-to-end. (3) Use buttons to move droplet from starting point.

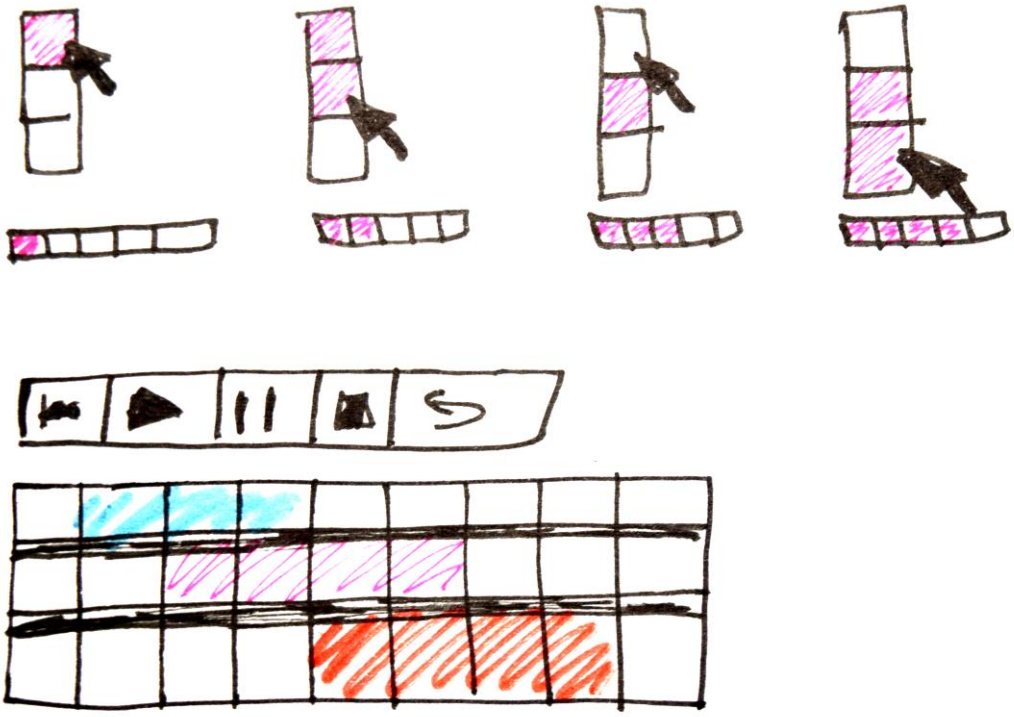

Figure 5. Timeline interaction idea

Subsequently, the designs and requirements resulting from these analyses were put to test in an expert session, the results of which are condensed below. Each header indicates a major theme of the debate. While some are relevant to the current specific implementation space and thus the primary research, others are entering the terrain of a user perspective on controlling DMF devices

in general. The session is summarized boldly. Statements were carried by a majority of participants, unless uncertainties are shown.

Results session

Learning biology: it is not about technology

The focal point of the interface should be to teach biology, not to teach how DMF works. Students need to understand the experiments, they do not need to know how to get a droplet from A to B. In the translation from protocol to liquid handling, students can write steps and queue these, and determine the start and end position.

Levels of abstraction: the pro and cons of manual routing

A matter of debate was at which level students using such a system in a remote laboratory setup should be able to control it. Instead of the lowest level of activating individual electrodes, students can also drag and drop, click or draw the path of droplets on the tiles; this would be a level of abstraction on top of the system. On top of this functionality, control and abstraction layers can be added to control the system at a higher level, allowing the user to concentrate on the biological protocol. From a user perspective, this might be much easier to control. A user is not interested in moving droplet, it is interested in what happens when samples mix. A user interface at this level could for example hold dilutions and sample names, which users can drag and execute. The software will figure out which steps are necessary to get there. On the other hand, it is not necessarily bad for a student to do manual work. When things break, when mistakes happen, one learns. In an abstract system, it is hard to see at what stage mistakes or errors occurred. In this aspect, manual control is better. In the end, it makes little sense to replace a pipette with a digit al system only if the user still has to control it as if it were a pipette. However, for the student case study it does make sense to let droplet routing be handled by individual users.

Scheduling of actions: step-by-step

The easiest way to schedule operations is one step at a time: set which parts you want to activate, and press *save* to go the next step, similar to turn based games. Time line ideas similar to music programmes or movie editing software were considered to have a too steep learning curve. Also, for this specific use case, time does not sound like an important variable.

User interface controls for moving droplets

It would be best if users could control the droplets, and not be bothered with the actuation technology. Hence, this abstraction level needs to be built in. Users could draw arrows for droplet movement. Or click and drag. For splitting, the concept of drawing a line straight through a droplet was introduced, similar to the game “Fruit Ninja”.

Additions beyond the case study: macros, visual programming and error-handling

For eventual future users of DMF systems, in the presently defined context and outside of it, it makes sense to have the possibility to easily save and reuse protocols. This could be done in macros. These could be nested in each other in similar ways to for example macros in Photoshop, where you can call the set of instructions of one macro inside of the other one. Another thing considered was visual protocols, like the Blockly-based Bioblocks initiative and Petrinets. A suggestion was to have an interface where you can zoom in into blocks, to show other blocks inside of them, to make for a clearer overview.

The system is error-prone. If one wants to save an electrode actuation sequence to use another time, it might as well not function the second time. Because of this, a system of checks has to be built into the software. The computer has to check where the droplets are, because they do not always behave similarly. The tracking can be done via object sensing of the webcam feed, or capacitive sensing. In the software, there can be checks for operations. This auto-feedback is not

that important for this case study, but is inevitable in future implementations. Ideally, the computer does everything, and the user only checks in case of an error message.

Conclusion: next steps for the interface development

Summing up, the next iteration of the environment built in this study will have a step-based control system, where users control the movement of droplets, for example by clicking and dropping. It is going to be connected to the digi.bio API to move actual droplets.

Analysis of exploratory interviews

The transcribed interviews are added in Appendix A, with per interview a short list of details concerning time and place, the goal of the interview, a background of the interviewee, the rationale the transcription and the transcribed text. Statements on (1) DMF, how it works, its applications and users, (2) the user interface and software, also concerning problems and possible solutions, (3) the development of DMF within the context of DIY Bio and open source hardware and (4) future challenges and vision are colour coded with blue, orange, yellow and green, respectively. These four topics are analysed below.

Digital Microfluidics

Digital microfluidics is seen as a general purpose laboratory automation tool, the goal of which is to replace the pipette as a workhorse for laboratory work. Its general use follows from its ability to digitally store and precisely steer basic liquid movements corresponding to common protocol steps, such as mixing, merging and moving fluids. The programmability of it alludes to the vision of a "personal computer for digital biology" (Urs Gaudenz). This vision on DMF is described as follows by Ryan Fobel:

> *"People that work in biology and chemistry labs, they spend a lot of their time with pipets just moving liquids around from tube to tube, splitting liquids into smaller tubes and mixing them together. What this system is trying to do is to take a small, card-sized chip, and be able to perform those same operations in tiny droplets. All controlled by a computer. Basically people can then press a button and walk away and the experiment will just do itself. Which ideally would allow people to do a lot more things in parallel, to get an increased productivity." (Ryan Fobel)*

With regards to more specific applications, the interviewees mention sample preparation, point-of-care testing and optimizing the synthetic biology pipeline. The interviewees have used DMF to prepare samples to be used in mass spectrometer to separate pharmaceutical components (cf. Gowtham Sathyaranayan), diagnosing rubella and measles in a field station in Kenya (cf. Ryan Fobel) and TALEN synthesis (cf. Sebastian von der Ecken).

Three of the interviewees are engineers that besides using DMF devices are foremost working on their development. Their view is the user pool of the current devices is limited to technically minded users, as the technology at this stage requires the capability to troubleshoot hardware errors and apply technical know-how to get it running. The solitary user of a DMF system interviewed was Gowtham Sathyaranayan, who thought the functionality of the DropBot was perfect for the basic sample preparation steps he is using it for.

There is a shared view of the need to get in contact with users in order to develop the technology further. The engineers that develop the system do not have the background knowledge to investigate all possibilities on what to use it for, and the consequences of these uses for the development. This contact between developers of different kinds with all possible users and enthusiasts is wished for most fiercely by Urs Gaudenz, who realizes a project needs to be fun to

engage people to join in it. He even build in a synthesizer in the OpenDrop, to ease the contact between people over the device:

> *"Because when people first see the device, and it's quite a futuristic device, it moves stuff like magic, they think 'what is this?' And when they hear it makes music they think 'ok, I know, it makes music'. So then you kind of connect. You say 'I like it, because I like music'. And then you have a first bond. Because when you know the thing, you can explore. Because it's not just music, it's also these water droplets. And these water droplets actually represent the music! It's not just for music, it's also for biology"(Urs Gaudenz)*

In summary, DMF is seen as a general purpose, programmable liquid handling device that could enable the automation of protocols that are currently executed manually by pipetting. Specific application areas include mass spectrophotometry sample preparation, point-of-care testing and synthetic biology. Due to the level the technology is at, current users are largely engineers, but in order to develop the technology's functionality and accessibility, contact between users and developers is needed.

User interface and software

A commonly shared view is that a graphical user interface is needed to control DMF devices, because this feature allows users to do complex things with the system. In the interviews, questions were focused specifically on the MicroDrop software used for the DropBot and OpenDrop. A video overlay was one of the first aspects made by Ryan Fobel and his colleagues at Wheeler Lab, because it was more efficient then looking back and forth from interface to chip. The graphical interface lets users click to activate tiles, with a recent version of the software allowing to draw a path by dragging from start to finish, while an algorithm searches for the shortest path. In the current version, different droplet movements can be scheduled to happen at the same time.

Positive remarks about the MicroDrop software were its ease of use, its 'point and click, copy and paste' functionality, and the fact that it is free to use and open source, so both affordable and customizable. The ability to switch between the graphical interface and a box that allows to program the device was also mentioned as a plus.

Features that could be improved in the current version include the instalment time due to its large file size, the clarity of the menus, the availability using logical operators in programming, and a smarter automatic mode, wherein parameters such as the height of the voltage can be automatically adapted based on measurements.

Two of the biggest requirements for DMF control software are first of all a flexible communication with other devices and their software, for example integrate a sensor module on the DMF device, and second the monitoring of certain constraints to aid smart routing and scheduling of the various droplet operations, for example to avoid problems such as unwanted collision or imperfect splitting of droplets.

The tools at hand for the user, and the level at which they grant him control over the device, vary in different scenarios. The current version of MicroDrop is at a relatively low level, where users are preoccupied with programming droplet movements. However, there are several computer science groups studying the algorithmic optimization of droplet movements on DMF devices, which would allow the user to control the devices from a top-down perspective. Ryan Fobel hopes that through continuing work on implementing the aforementioned control systems to the current functionality, the engineers and computer scientists can meet in the middle.

The visions on the ideal user interface by Urs Gaudenz and Ryan Fobel are radically different. Ryan Fobel envisions future software to abstract away from the actual droplet movement, letting the user focus more on the steps in the protocols, the input they require and the data that is outputted. Urs Gaudenz, however, appreciates that a user can be right on top of the action. He disliked the video stream option on a computer screen, and stated that the electrode array of the OpenDrop is the interface a user wants to see (Urs Gaudenz).

Another issue that divides the interviewees is the knowledge a final user would have to have in order to control the system. Sebastian von der Ecken and Ryan Fobel both hint towards a moment where control is largely eased and aided by smart software, where a researcher that uses the interface does not have to worry about its inner workings. A user would not have to know what is going on, as the software takes care of many parameters and the execution, it could be as simple as press and play. Urs Gaudenz, however, believes it is important that the user has an understanding that it has been designed by engineers. To ease communication between users and makers, he advocates "design for collaboration", based around the idea that the interface is not between the user and the machine, but between people. According to Gaudenz, it is required that users have insight into the technology's functionality to be able to correctly interpret results and spot errors at an early stage. In other words, he would not like the system becoming a "black box" behind the interface.

In summary, the MicroDrop software for the DropBot and OpenDrop is graphical and relatively easy to use, but the control interface could include more logical controls. Software for DMF systems would need to be open for integration with other modules, and offer monitoring and optimization functionalities. These could allow the interface to abstract away from the actual droplet movement and focus on the experiments, although Urs Gaudenz favours the direct contact to the electrode array.

DIY Bio and open source development

Inspired by hackerspaces and the DIY Bio movement, Ryan Fobel hopes that the DropBot gets to a level where it is affordable for people in these places to play with it and prototype with it in their own time. However, a main difference between the academic (and corporate) research environments and outside spaces is the availability of money and resources. Sebastian von der Ecken and Ryan Fobel both work in an academic environment with a primary goal to develop decently working DMF devices, where affordability is a second thought. With the OpenDrop, however, the aim was to make it work, but not necessarily perfect. It also had be affordable, and the functionality could incrementally be improved in collaboration with others. The hacker mentality in the DIY Bio community was experienced as liberating to Sebastian von der Ecken, used to the university environment where he did his PhD:

> *"I was fascinated with what the people are capable of in one day, what we were able to do there. And I realized my thinking is wrong to make a perfect working machine in the end. You just have to have a fun, one or two times working, with a good idea behind it in the end" (Sebastian von der Ecken)*

The goals of academic researchers and what are sometimes called biohackers are different. The researchers want to either research questions important in the development of the technology, or make steps towards putting it on the market. For Urs Gaudenz however, the motivation for developing the OpenDrop was not to become an expert in electrowetting. He saw it is a vehicle to challenge new technologies, meanwhile trying new collaborations. Therefore, he is open to ideas that link its development to other new technologies, such as the Blockchain technology.

As detailed in the previous section, a major difference between the development of DMF within academic or corporate environments and within the DIY Bio scene is its view on the knowledge the end user has to have. For Urs Gaudenz, opening up technology and releasing it as open source also includes a commitment of the user to partly become the engineer. This hacker mentality is apparent in the open source hardware scene, where openness and sharing of designs is valued. Although released at open source, Ryan Fobel's development hints more at a black boxing of the device, and accessibility of the interface.

Both open source hardware, the DropBot and the OpenDrop are aimed at becoming a common platform. Using these standards, knowledge can be built on top of previous knowledge, so interested researchers or tinkerers do not have to start anew. It opens up the possibility of collaborating on a common technology, sharing designs and solution, and according to Sebastian von der Ecken the DIY Bio community might also foster the meeting of users and developers, to combine the ideas of engineers with the needs of laboratory researchers.

In summary, differences between the academic world and the DIY Biology environment are to be found in money and resources, but also in mentality; the first striving for reproducibility and robustness, the second for fun, affordability and openness. The DropBot and OpenDrop both aim to be a common platform for others to build upon.

Future challenges and vision

Concrete areas that were mentioned to harbour challenges in the development trajectory of DMF devices were biochip fabrication, the integration with sensors and the deployment of smart feedback systems. Smart feedback is required in order to reduce the attention required to perform an assay on the device. Currently, the DropBot requires one person to observe, having a monitoring system that signals when errors occur would already decrease the number of observers needed to control a number of devices. Another feature mentioned by Ryan Fobel is the settings of voltage, frequency and timing. Currently these parameters have to be set manually through trial-and-error, but sensing systems might be able to perform a characterization of the fluids. In general these kind of hardware and software improvement would allow the development of the system into areas that are increasingly complex and abstract.

In contrast, Urs Gaudenz envisioned the tangible control of the droplets on the electrode array, mentioning a gesture chip that would allow using hand movements as input.

Ryan Fobel envisioned two roads of development for DMF, the first leading towards a small and portable device, the second to automated laboratories:

> *"The power requirements are not high, so it's quite easy having one that can be even battery powered. And I for applications where you want to have something portable this technology is probably well suited to that. (…) I can also imagine situations where you'd have these in a bigger lab. Maybe you could even have multiple systems, stacked together in a rack. We've talked about interfacing these types of systems with liquid handling robots. So you could imagine one big liquid handling robot with smaller DMF systems inside of it, and the pipetting robot is just loading the liquid, or moving liquid from one chip to another chip. So I think this technology could work in both portable applications and more established laboratory environments." (Ryan Fobel)*

In summary, challenging areas include biochip fabrication, sensor integration, and feedback systems and sensing capabilities in the software. The future DMF device is envisioned to be controlled in a tangible manner by Urs Gaudenz. Ryan Fobel's vision of future DMF devices include both portable and lab based versions, the first being small and battery-powered, the

second having the potential of being part of a bigger automation ecosystem with pipetting robots to load samples on the chips

DMF chip and interface design

The following paragraphs describe the design choices made within the development of the DMF chip and the user interface.

DMF chip design

The DMF chip was connected to the voltage switching board via an edge connector. This put a constraint on the number of connections, as per side only 15 connections were available. Multiplexing of routes to connect more tiles to an input was tested, but caused a burning of the paper due to the high density of parallel lines and made it impossible to split large droplets due spreading caused by opposite attracting forces. The final DMF chip design was therefore limited to 15 tiles, all connected to an individual input. Connection lines were spread across the print to diminish their attraction force on the area with droplets (see Figure 6).

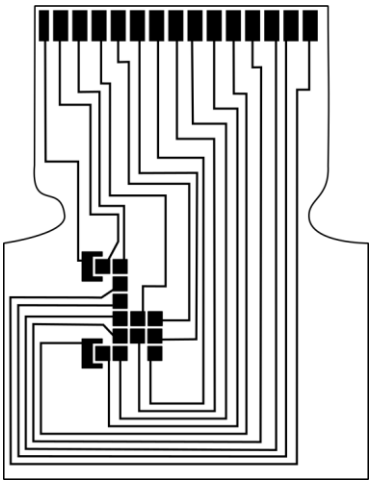

Figure 6. DMF chip design. SVG created in Inkscape.

The layout was designed to two input reservoirs, a mixing area and an end point. This design was guided by the protocol of a simple enzymatic colorimetric assay, where for example a droplet of blood is mixed with reagents to measure the glucose concentration, based on a change of colour, sensed by a LED and photodiode sensor combination. Among other options, this type of protocol was chosen because it has relatively little steps, and fits on the small chip layout. The placing of reservoirs were determined by the placing of input holes on a before made DMF chip stack, to be able to reuse coated top layers. Distances between tiles and the size of tiles was determined by the author and members of digi.bio, through iterative testing at Waag Society in Amsterdam.

Interface and interaction design

As a major goal of this study is to explore the interactive control of an actual DMF device, and as the current state of the technology does not yet allow for optimized translations between protocols and voltage actuation (cf. Analysis of exploratory interviews), directness and simplicity were favoured in design decisions regarding the interface and interaction. In the centre of the user interface are the tiles of the DMF chip. As can be seen in Figure 7A, the reservoirs are coloured blue to simulate the presence of water (cf. User Test Design).

Two input solutions were implemented: direct actuation and routing. In the interface these modes could be switched through clicking on the button “Change actuation style”. In direct

actuation mode, electrodes could be switched “on” or “off”, signalled by a red outline (Figure 7B). In routing mode, a path of tiles could be added through clicking on each tile. Each path had a distinctive colour. When hovering the mouse, tiles which could be added to the path, i.e. which were adjacent to the last added tile, were coloured green (Figure 7C).

A mistaken addition of a tile to a path could be reversed with the button “Remove last click”. After finishing a route, it could be saved through the “Save route” button. “Start droplet movement” started the actuation of tiles in the paths. Tiles in the route were activated in the order “1 – 1,2 – 2 – 2,3 – 3 – etc.”, and the resulting, simulated water movement reacted visually live. Water droplet movement based on tile actuation was simulated in JavaScript, the script and movies of droplets moved using both modes can be found in the Supplementary Information.

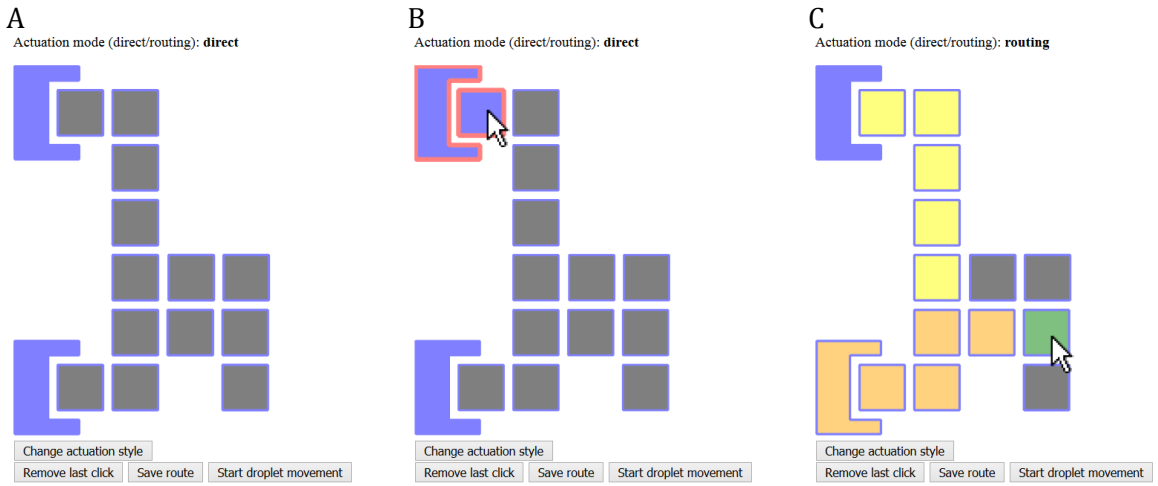

Figure 7. The user interface. A) The layout or the user interface. B) A snapshot in direct actuation mode. C) A snapshot in routing mode. The mouse pointer image was added afterwards, as the mouse pointer was absent from screenshots.

User Test Results

This section includes the results of the user tests, starting with observations and an analysis of the questionnaire results, followed by remarks users made during or after testing.

Participants

Eight users participated in the user tests, of which three were doing the BSc. Biology, and five were Master students, all based at the Biology faculty of Leiden University. Out of the eight students, one Bachelor student accidently did not submit his questionnaire results, and is excluded from the following analysis of participants and questionnaires, but included in the section about observations and user remarks. A majority of the participants was between 18 and 25 years old. The average number of hours performing lab work per week varied widely, with four participants scoring four or less, and three scoring nine hours or more. The type of lab work they did varied. The master students reported in more detail, they were doing bacterial cell culturing, PCR, zebra fish immunology, bioessays and in situ hybridization. The bachelor students reported more generally drawing specimen and lab work.

Observations

In Table 4, the effectiveness of both control modes is display, as well as observations noted down when shadowing users using the system. What I called “water bridge formation” was the situation wherein all tiles in and between both input reservoirs would blue coloured. The code then did not allow the tiles to return to their normal state, due to lines in the simulation function. This is a

behaviour that could not have occurred in a real DMF chip, and it caused the failure of a number of participants to successfully complete the task in direct actuation mode. Besides the variance in success caused by this software bug, the oral explanation of button functionality was received and handled differently by different users, which made impossible to take the time until completion as a proxy measure for efficiency.

Table 4. Success of the interface testing. Defined as whether the participants were able to move a droplet of each input reservoir to the output tile. Y = Yes; N = No. In the last column are observations made while shadowing the participants using the interface.

Participant	**Success Direct Actuation Mode?**	**Success Routing mode?**	**Observations**
1	Y	Y	The participant finished the task in both direct and routing mode successfully without errors.
2	N	N	In direct routing, the simulation failed to deliver a good results because of water bridge formation. In routing mode, it was not clear to the user that it is possible to draw a second route.
3	Y	Y	The participant was not very pleased with the quality of the simulation, and appeared to doubt its authenticity
4	Y	N	The routing mode fared less well then direct control. The participant stays calm, and discovers the functionality of the direct control option by trial and error.
5	N	N	The participant expected an option to construct the routes by clicking on the start and end.
6	Y	Y	In the direct mode, the participant was really waiting for something to happen. The routing mode appeared to be more intuitive. A bug in the code resulted in a blue tile jumping diagonally.
7	N	Y	The participant expected the drop to get through in one time using the direct actuation mode. It is not intuitive.
8	N	Y	In direct actuation mode, bridge formation prevented the user to be able to succeed.

Questionnaire Results

The ten questions of the Systems Usability Scale (Table 5) were scored on a range from 55 to 95, with a mean of 71.8 (n = 7) on a scale from 0 to 100, with a standard error of 5.1. Opinions on the usability were divided, with three out of seven participants scoring 65 or less and two scoring 80 and higher.

On average, the statement that people would quickly learn the system was rated highest (mean = 3.29, S.E. = 0.29, n = 7), and the statement expressing a frequent hypothetical use was rated the lowest (mean = 2.29, S.E. = 0.36).

Table 5. Scores on the ten SUS questions in the questionnaire. Scores range from 1 (Strongly disagree) to 5 (Strongly agree). The total score is the sum of scores on the odd questions minus 1, plus the sum of the scores of the even questions when subtracted from five, times 2.5.

1. I think that I would like to use this system frequently	3	5	3	4	3	3	2
2. I found the system unnecessarily complex	2	1	2	3	2	2	3

3. I thought the system was easy to use	5	5	4	4	5	4	3
4. I think that I would need the support of a technical person to be able to use this system	2	2	3	3	2	2	2
5. I found the various functions in this system were well integrated	5	5	4	4	3	3	2
6. I thought there was too much inconsistency in this system	2	1	1	2	3	2	2
7. I would imagine that most people would learn to use this system very quickly	5	5	4	4	5	4	3
8. I found the system very cumbersome to use	1	1	2	3	2	3	2
9. I felt very confident using the system	3	4	4	3	5	3	3
10. I needed to learn a lot of things before I could get going with the system	2	1	2	4	2	2	2
Total SUS score	80	95	72,5	60	75	65	55

In questionnaire data on the topic of understanding (Table 6), it can be seen that users have a clear preference for either the direct actuation mode, or the routing mode, when asked which of the two modes improves the conceptual understanding. Three out of seven users, however, lean towards the opposite option when asked which mode they thought was easiest to control. In general, the interface is perceived as slightly enhancing understanding, regardless of mode A or B.

Table 6. Scores on the questions about understanding. The scale goal from 1 (Strongly disagree) to 7 (Strongly agree), unless otherwise specified between square brackets.

Questions								**Mean**	**S.D.**	**S.E.**
The interface in mode A (direct clicking) helped me to understand the steps in the protocol	7	4	6	6	6	5	5	5.57	0.98	0.37
The interface in mode B (routing) helped me to understand the steps in the protocol	7	4	5	6	6	6	4	5.4	1.13	0.43
A system like this one could be used to increase the conceptual understanding of biology	6	7	4	7	4	6	2	5.1	1.9	0.70
This technology makes it easier to follow the protocol, compared to when doing it in a lab	5	6	5	7	5	5	2	5	1.53	0.58
A system like this one can be used as an addition to regular laboratory education	7	7	6	7	6	6	3	6	1.41	0.53
The hands-on aspect of system helps me to understand biological concepts	5	6	5	7	6	5	1	5	1.91	0.72
The hands-on aspect of system helps me to understand protocol	5	6	5	7	6	5	2	5.14	1.57	0.59
I was aware of the relation between the droplet movements and the steps in the protocol, while using the system	7	4	6	6	7	5	3	5.43	1.51	0.57

When using a scale, which of the two modes improves the conceptual understanding? [1 = Mode A (direct clicking), 7 = Mode B (routing)]	1	6	2	6	2	6	5	4	2.24	0.85
When using a scale, which of the two modes was easier to control? [1 = Mode A (direct clicking), 7 = Mode B (routing)]	7	7	5	7	2	6	2	5.14	2.27	0.86
The live stream was required to understand what happens at each step	7	4	6	7	4	6	4	5.43	1.40	0.53
I enjoyed using the system more than I enjoy regular laboratory work	2	6	4	4	5	3	1	3.57	1.72	0.65
The information on the protocol aids me in controlling the droplet movements	6	7	4	4	5	5	2	4.71	1.60	0.61
To what extent did you make a connection between the droplet movements and the biochemical protocol, while using the system [1 = A little, 7 = A lot]	7	7	6	5	6	6	1	5.43	2.07	0.78

Regarding technical skills, the participants on average found using the system less complex than pipetting (Table 7). Mode B (routing mode) is judged to be slightly more helpful than mode (direct clicking) in executing the protocol. Participants self-reported to have the skills to use the system without great effort. Participants were positive about the visual control system.

Table 7. Scores on the questions about technical skills. The scale goal from 1 (Strongly disagree) to 7 (Strongly agree), unless otherwise specified between square brackets.

Questions								**Mean**	**S.D.**	**S.E.**
Compared to pipetting, this system is... [1= More complex, 7 = Less complex]	4	7	5	7	7	5	4	5.57	1.40	0.53
I had the technical skills to use this system without much effort	6	7	6	4	7	5	4	5.57	1.27	0.48
The visual control system aids the control of droplet movement	7	7	5	6	7	5	5	6	1	0.38
The visual control system is the best solution for moving the droplets	7	7	6	6	7	4	3	5.71	1.60	0.61
The interface in mode A (direct clicking) helped me in executing the protocol successfully	6	6	6	4	7	5	4	5.43	1.13	0.43
The interface in mode B (routing) helped me in executing the protocol successfully	7	6	6	6	6	6	5	6	0.58	0.22

Especially in the scores on questions on implementation, it can be seen there is a chronological decreasing trend in scores between users (Table 8). A majority of participants strongly hoped that remote laboratories are going to be used in education, but they were less positive that remote laboratories will be a part of biology research. In line with this, a majority leans towards the use of a remote laboratory for education purposes, instead of a simulation.

Table 8. Scores on the questions about the implementation in life science education. The scale goal from 1 (Strongly disagree) to 7 (Strongly agree), unless otherwise specified between square brackets.

Questions								**Mean**	**S.D.**	**S.E.**
A remote laboratory implementation like the system I just tested can be a valuable addition to a study like mine	7	7	6	6	4	5	4	5.57	1.27	0.48
I hope remote laboratories are going to be used in education	7	7	7	6	7	5	2	5.86	1.86	0.70
I think remote laboratories are going to be used in education	7	7	6	6	5	5	3	5.57	1.40	0.53
I think remote laboratories will be a part of biology research	7	6	6	4	3	5	2	4.71	1.80	0.68
For education purposes, it makes more sense to use a... [1 = Simulation, 7= Remote laboratory]	7	7	5	5	4	5	3	5.14	1.46	0.55

Regarding the open questions (Table 9), one participant noted the potential of a remote DMF devices to control protocols between different cities. However, most participants not the simplicity, the ease of use and visual aspects such as colours and buttons as features that are enjoyed in the system. Other advantages when integrated in their respective studies were its accuracy, the ability of error correction, the preparation in terms of knowledge before the start of an experiment, and the low cost. The greatest disadvantage of using such a remote DMF system for Biology education, is the lack of hands-on lab skills and physical experience, which are noted to be the most important for students to gain. There was relatively little response to the question what features would be needed in the system, but the availability of a live video stream was mentioned twice.

Table 9. Answers to the open questions. Answers from one participant are literally translated from Dutch to English.

Name the two features you enjoyed most in the system and provide a short explanation why.
Remote control even between different cities, because it can be very useful when working in different institutes simultaneously. Very easy to use, so it is good for students.
Easy and simple to understand and use
It was a simple system, easy to understand. The colours made it more pleasing to use.

The colours for the routing.
The visual aspect, easiness to understand
Visualization of the droplets, clicking
Few buttons, little complex. Intuitive.
When a system like this one would be integrated in your studies, what would be its two biggest advantages?
Easy to use, so students will feel confident sooner. Better to follow a protocol step by step.
It is simple, so it saves time in the already short available time we usually have
It is way more accurate to use specific sizes of droplets and it's easier to use than your own hands.
Mistakes can be easily corrected.
for my studies I don't see a lot of advantages compared to how we already learned it
Knowledge before starting your experiment, gaining skills
Maybe complex devices that normally are too expensive for education be demonstrated via the computer?
When a system like this one would be integrated in your studies, what would be its two biggest DISadvantages?
You do not learn the classic lab techniques. You do not learn about the safety aspects in the lab.
some people won't understand the concept behind it or why you use it
Nothing I can think of
We need to experience the hands-on experiments.
Not having the physical objects and results in front of you.
I don't know
It is less hands-on than using real devices.
Which two features of the system do you imagine to be most needed?
Everything is fine
It leads to less user error and differences between duplicates
The accuracy and the simplicity.
I'm not sure
Live video of results. Maybe to use more than two fluids.
I don't know
Live feed of the actual droplet. More factual explanation.

The final two questions, intended as a control on the simulation and the lack of video stream, were answered with clear trends: a majority felt as if controlling a simulation instead of a live remote laboratory, and a live video stream was thought to be a helpful addition to the interface (Table 10).

Table 10. Answers to the final two questions. The scale is shown between square brackets.

Questions								**Mean**	**S.D.**	**S.E.**
When using the interface, I felt as if I were controlling a... [1 = Simulation, 7 = Live remote laboratory]	4	4	2	6	2	3	1	3.14	1.68	0.63
A live video stream would be helpful to control the system effectively [1= Strongly disagree, 7 = Strongly agree]	7	7	4	6	7	5	7	6.14	1.21	0.46

User remarks

Spoken remarks that were noted down during or after the tests are shown in Table 11. Besides a critique on the question to compare the complexity of the system to that of pipetting, and the hint at suspiciousness regarding the reality of the droplets, two of the comments are an addition to the results of the questionnaire. One participant mentioned that it would be good to have more insight into the process that makes the droplet move, which would benefit the user. Another participant thought about the applicability of a DMF system for education, and concluded that it would be suitable either for high schools or lower level education to do simple protocols, or for high-end research if the DMF system would be developed as a high-throughput device. For university education, however, the participant saw little value for a DMF system, because learning skills to be used in actual laboratories is a key part of university courses, and the laboratory methods currently practiced allow students to perform more complicated experiments than is possible on a DMF device.

Table 11. Spoken remarks by participants

Participant	Remark by participant
1	About the question whether the system is more or less complex when compared to pipetting, the participant remarked, “that depends, whether you pipette one time, or a thousand times”
3	About the interface, the participant remarked “it could also be a computer programme”
6	When discussing the applicability for education, the participant was doubting its usefulness for university Biology students, because these have to learn lab techniques, e.g. micro pipetting. The DMF chip is well applicable for a lower level of education, e.g. high schools, with a focus on reactions, or at a higher level as high-throughput laboratory equipment, but not for university education.
8	The process with which the droplets move, and how it can be applied, is not so clear from the opening movie and interface testing, it would have been better if that was clearer, according to this participant.

Discussion

The main goal of this study was to develop and test a DMF interface for remote control of fluids, focusing on conceptual and practical skills with participants that tested a simulation. At the same time, ideas on the user interface for DMF in general were explored through a session and interviews, although this goal was not to offer an all-inclusive study, but supportive to the primary goal of actual development. Thirdly, through the interviews, and through the experience of developing the system and interface, the study also reflected on the development of DMF within the DIY Bio community.

Effectivity and usability of the interface

First, the results will be discussed, while simultaneously noting implementation details and confounding factors that could have had an effect on them. Hereafter, a short conclusion is given. This is followed by a section on future plans regarding the current setup.

There was a great variance in the effectivity of the droplet moving task, measured as the successful fulfilment. However, the value of this data is low as the effectivity could not be measured correctly, because the simulation was not perfect, and showed bugs such as water bridge formation and diagonal droplet jumping. Supposed water droplets did not always respond as they would do in reality. Especially the aforementioned formation of water bridges between

both inputs was a problematic, as the interface did not provide a way out of that situation. These fluctuations in functionality trouble the interpretation of the success rate, and also blocked the possibility of a reliant quantitative measurement such as time. Therefore, the user test result relied on self-reporting. Alternatives that could have been explored include questions that test the understanding of the protocol, but that would require a more complex and worked out biology part. However, quantitative measurements such as the time till completion and clicks would be optimal, and this might be possible when software malfunctioning or irregularities is prevented. Of course, another question is whether the simulation bears resemblance to the actual reaction of droplets to voltage switching, which can only fully be testing by using an actual device. In majority, the users felt as if controlling a simulation, and while some bought the video story of a connection with a remote laboratory, other participants might have been sceptical of this. Interestingly, they did rate the potential of a remote laboratory for education higher than the potential of simulated laboratories.

The score of the SUS scale is above average but not excellent, as there was a big variance of scores both in total score and in individual usability aspects. The ease of use and learnability were rated highest, whereas participants were in general the least sure that they would like to frequently use the interface in their studies.

Understanding and technical skills

It has to be noted that the polarity of the majority of questions was similarly "suggestive positive", scaling from negative to positive, contrary to the SUS questions, which were reversed in a fifty-fifty manner. This could have affected the ratings of the users. Another ambiguous aspect related to the layout of the user test, and its effect on the interpretation of the questions. The setup was ambiguous in the sense that questions could be interpreted as both relating to the usage of the just tested user interface, as well as relating to the potential of such a DMF system in general, also based on the video footage participants were asked to see before using the interface. This could have led to different interpretations by different users with regard to numerous questions of the questionnaire, which also might have affected their scores.

Another confounding factor to be mentioned is that the Bachelor students participating in the experiment came directly from a confocal microscopy course, where they used a high-end interface. This exposure might have skewed their perception of the interface build in this study.

Taken into account these points, we can observe that users had a clear preference for either the direct control or routing mode, although this was in all likelihood also affected by the software issues mentioned earlier. Regardless of mode, the interface is judged to be slightly enhancing conceptual understanding.

Regarding practical skills, participants self-reported to have the skills to use the system relatively effortlessly. The routing mode was slightly more practical than the direct clicking, but with a minor difference. The visual control system was valued positively by a majority.

An aspect that needs to be considered in discussing all the above is of course the low number of users. Besides other factors affecting the results, the low power results in that we can only speak of trends, exploring the potential of the developed interface as an initiation of a possible research direction, and not conclude anything based on significant results. It would be good to have been able to study with a larger pool of participants, however, regardless of the state of the simulation at a specific time in development, best would be to test an actual functional hardware with a live video stream. Only that way the current simplified DMF chip can be tested to its full potential, as it is not extrapolated that simulation correspond to reality (cf. second interview Ryan Fobel).

In the scores on questions about the implementation in life science education, a decreasing trend was observed. This increasing scepticism of participants over the day towards using the remote DMF interface in education perhaps can be explained by the amount of questions. The time it took to fill in the questionnaire, compared to the introduction movie and the interface testing, at times was at times perhaps a fivefold. In potential subsequent testing, it is therefore advised to shorten the questionnaire, and revise the ratio of questions to action to an acceptable level for the participants. Nonetheless, there was a shared hope that remote laboratories would become a part of biology research. Remote laboratories are valued over simulations for education purposes. This is a result also found in studies comparing the two forms, which found users of remote laboratories were more engaged with the tasks they did (Sauter et al., 2013). Regarding the implementation of this DMF interface in education, one participant remarked that it would be not suited to university education, both in its current form and in general. Its current form is too simple for the experiment in Biology courses at a university level, which require complex laboratory protocols. More developed DMF systems might suit a high-end laboratory, but for university education, the hands-on experience with various laboratory skills such as micropipetting was thought to be of great importance.

The simplicity, the clarity, the accuracy, and the attractiveness were all described as satisfying, because it provides an ease of use that is very intuitive and pleasing. However, it is not seen as a replacement to current Biology education. The question could have be framed as the possibility of this system as an extra opportunity for Biology courses next to the current curriculum, but it appears participants read the integration to be a replacement of current methods. A live video option was judged to be helpful and needed in the interface.

User interface conclusion and future work

In conclusion, the trend in the reactions to the tested interface to control a remote DMF device interface tested was moderately positive with regards to conceptual understanding and professional skills. Students could see the interface being used in education, but did not see the potential of it for their respective Biology studies and study activities. The technical skills were tested most thoroughly in the test, regardless of the occasional software quirks. Over many questions the interface was perceived to enhance understanding of the protocol. But to really test the concept of Ma & Nickerson (2006), the understanding would have to be related to key concepts taught in the courses of the students. A tailor-made experiment for a specific course, similar to the idea of Hossain et al. (2015), would be a valuable starting point for a future study. This would require first the successful execution of an experiment on the DMF device, which is a bottleneck in the current development (cf. Methods, Exploratory interviews).

Thoughts on the software and interface for DMF in general

Through the session, interviews, and the development, multiple facets of a user interface for DMF in general were considered. This was not a main goal of this study, but as it is a current issue in the DMF development that is understudied because of the necessary focus on engineering and hardware optimization, the observation can be of value to DMF researchers and the community around the technology. As a lot has been said about these subjects by many people, the following considerations and scenarios are selected and shaped by my own interpretation of the input (cf. Results session & Analysis of exploratory interviews).

A recurrent theme in conversation on the user interface development is the dependence on secure software control systems to monitor droplet movement. When these layers are in place, interfaces can be build that abstract away from the actual droplet movement, and let users focus on the protocols. Protocols could be saved and retrieved, saving their electrode actuation. Outside of ideal conditions, however, a control system should still be in place to check whether these

voltage switching protocols have the desired effect, for example through impedance sensing or computer vision. When these systems are in place, however, a standards for both software and hardware could allow the sharing of protocols, allowing biology to become truly digital. The combination of DMF and pipetting robots could transform laboratory research, of course if it were to be made available at a price that is affordable to a great number of labs. In the current setting the observation of droplets makes sense because it adds to the hands-on, interactive user experience, which could both provide an awareness of the biological inputs and of the technology, and hence improve both conceptual and technical understanding. When we leave those assumptions for a broader vision, the droplets could also be hidden for the user, as the biologist does not care about the machine, but about the outcome. The only one fighting against this vision was Urs Gaudenz, who propagates the opening up of technology and the mutual understanding between engineers and users as a necessary aspect of good science. For him, to be able to see the droplets move is the most valuable aspect. In this aspect, the interface developed in this study bears the greatest resemblance to his vision. The graphical aspect of the user interface and the availability of intuitive controls was mentioned as almost a necessity. I personally believe that the knowledge from user interface and experience design will find its way to biology labs in the upcoming years, as people have become extremely used to intuitive and graphical user interfaces in a large part of their lives. Although "biocoders" are needed to develop these new interfaces, the actual biologist will probably need less and less programming skills.

Reflection on the open source development

The current study was initially motivated by the hacker mentality present in the DIY Biology scene, a can-do attitude that favours fun, affordability and openness over the tedious research in engineering labs. It is interesting how the DMF technology is a good example of the potential of open source hardware, with the open source DropBot inspiring other groups to make the design, and even make their own designs inspired by it, such as the OpenDrop and digi.bio's hardware. All open source parties appear to have the motivation of delivering a new standard, which others can use and build upon. This can also be seen in the Digi.Bio hardware, where the Nixie power supply and the HV507 chip were chosen inspired by Urs Gaudenz' use of them in the OpenDrop.

Digi.bio is a collaborative project that mostly shares locally, and not open source over the internet, but I chose not to discuss these matters, mainly because my close connection to its members would make my interpretation very subjective, but also because of the reliance of the present study on their prior work. My chosen association with digi.bio also prevented a successful outreach to Auryn, to hear their vision on the open source development.

An open question is whether the development of this technology benefits more from the academic, the corporate, or the outsider environment. Apart from the Wheeler lab, may institutional DMF researchers appear to be academic islands, which may hinders their knowledge transfer. On the other hand, institutionalized research lab do have money and resources to spend and use, which speeds up prototyping significantly, as it opens up the possibility to try out many options. The open source or DIY Biology community is stimulating, it fosters collaboration between users and engineers. I do believe, however, that geographical colocation is in many situations essential to the success of a collaboration. And in that sense the fragmentation of DMF efforts within the DIY Bio community is both a strength and a weakness.

A future perspective on crowdsourcing biology using DMF

To conclude, the following section is a future scenario for next iterations of the current system, to be used as a remote laboratory for web-related citizen science efforts. Potentially, a system with remote access to a digital microfluidic device can be used for the online crowd sourcing of science. The online game Foldit engaged scientist and non-scientist players alike in solving protein

structure prediction problems, providing tools for directly manipulating 3D protein structures, as well as simplified algorithms from a frequently used structure prediction methodology (Cooper et al., 2000). Together, top-ranking players developed an array of successful search strategies, outperforming the outcome of existing computational heuristics. The authors argued that the use of online puzzle games is a powerful way of solving computationally hard scientific problems. EteRNA took this approach one step further by creating what they call a Massive Open Laboratory. In the game players created RNA designs, the top-voted of which were empirically tested in a laboratory, enabling an iterative RNA design process, wherein the community of players gained experience as to make their solution at times at solving RNA structures then available algorithms (Lee et al., 2014). A digital microfluidics integrated online environment has the potential for both enabling the generation of hypotheses by online users, as well as the potential to let the participants test these hypothesis directly in a remote microfluidics device, creating a space for both theory and experiment to be crowdsourced. In both Foldit and EteRNA the successes of human analytical skills and visual analysis compared to algorithms was explained partly by the observation that players could go beyond the conformational search space, and invent new strategies. A digital microfluidics remote laboratory setup could benefit from this "sandbox principle" and offer open-ended research possibilities for users. Of course, many practical issues would have to solved, but following the optimism of DMF developers, DMF chips could be part of an integrated network of automated liquid handling machines, that offer programmability, reproducibility, and remote access. Potentially, the DIY Bio community and the DMF projects therein could have a role in achieving steps towards this hypothetical future perspective of the use of remote DMF devices for crowdsourcing biology.

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