Turning Experiments into Objects: The Cognitive Processes Involved in the Design of a Lab-on-a-Chip Device

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Abstract

Background Increasingly, modern engineers are designing miniature devices that integrate complex activities, actions, processes, or operations involving many steps, persons, and equipment; a good example is a microfluidic lab-on-a-chip device. The design of such devices is cognitively demanding and requires the generation of multiple model representations, which are used in an iterative fashion to analyze and improve prototype designs.

Purpose This study addresses two questions: How are various representations and prototypes used in the iterative design and building of a microfluidic lab-on-a-chip device in a systems biology laboratory? In this design process, what cognitive functions did the representations serve?

Design/Method This case study employed mixed methods. We utilized the standard ethnographic methods of participant observation, open-ended interviewing of participants, and artifact collection in an integrated systems biology research lab. Data were analyzed using open and axial coding. We also used cognitive-historical analysis to collect and analyze data from traditional historical sources (publications, grant proposals, laboratory notebooks, and technological artifacts) to recover how the salient representational, methodological, and reasoning practices were developed and used by the researchers.

Results The device design involved complex interactions among mental models, computational models, and building and testing prototypes; tagging and visualizations were used to query and validate the prototypes as well as the computational models; all these were integrated to meet stringent experimental and fabrication constraints. Integration takes place across many different kinds of representations. The building of external representations helped not just to off-load cognitive load but also to add detail and constraints to the mental model.

Conclusions Representational fluency and flexibility are required to manage the complexity of modern bioengineered devices. To support the development of such fluency and flexibility, engineering students must understand the function and the use of such representations, an instructional goal that has implication for new models of learning.

Key words biomedical engineering; distributed cognition; engineering design; problem-based reasoning and learning

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Introduction

This article reports on an extended case study of situated design, or "design in the wild." More specifically, we focus on the role representational systems played in the design and development of a complex bioengineered artifact. Increasingly, engineers are developing microfluidic lab-on-a-chip (LOC) devices, which bring together in a single apparatus, a number of complex scientific activities executed by researchers in biology laboratories. These LOC devices are often developed to improve the accuracy and quality of measurement as well as to increase the number of possible measurements. The design of such devices requires a reasoning process that translates the goals and actions of intentional agents (researchers executing a complex lab routine) into mechanical procedures that can be accomplished by the device. The design must also take into account the constraints presented by the biological material (such as cell damage and contamination risk), the constraints imposed by the process of fabricating the device, and the research questions the device is seeking to address. Thus, the designer's reasoning process is highly complex and requires the generation of multiple external representations that are used in an iterative fashion to analyze and improve prototype designs. Here we have explored and sought to understand this process in a single case study, which chronicles how a bioengineering graduate student solved the problem of collecting the time series data needed to develop a mathematical model of cell signaling.

This targeted investigation is part of a much larger, multiyear study of reasoning, problem solving, and learning in interdisciplinary research laboratories. A major objective of this work is to develop new models for engineering education that are informed by the work and learning practices found in authentic sites of engineering and science (Osbeck, Nersessian, Malone, & Newstetter, 2011). In our translational approach, we investigate, through immersive engagement with real sites of work and learning (*in vivo* sites), the situated, socio-cognitive practices that engineers use to reason and problem-solve day-to-day. We then translate our findings into design principles (Brown, 1992; Brown & Campione, 1994) for classrooms (*in vitro*). This translational approach has been used in the design of an introductory course in engineering problem solving in biomedical engineering (Newstetter, Khalaf, & Xi, 2012; Newstetter, 2005) and of instructional laboratories (Newstetter, Behravesh, Nersessian, & Fasse, 2010). In both cases, the course design phase was preceded by an immersive, ethnographic phase, where we made a deep dive into the ways of working and learning in authentic work settings, seeking to eventually achieve a better fidelity between the classroom and the world of engineering practice.

In the following section, we situate our work in prior relevant studies of design practice and cognition. Research Design sets out our research questions and describes our study design; we trace the emergent, iterative, and parallel representational practices employed by the designer of a microfluidic lab-on-a-chip device, illuminating how representations at each stage served important functions for the researcher as she progressed towards a final design. In Cognitive Design Processes, we step back and examine the possible cognitive mechanisms involved in this process. In particular, we examine how the researcher built a distributed cognitive system through her representational practices. Finally, we extract from this case study implications both for engineering classrooms and for principal investigators who mentor advanced engineering students.

Designing Engineers

Researchers have long had an interest in the process of engineering design – how one moves into a design space, makes progress under conditions of uncertainty and constraint, until, finally, a design solution is reached. Thus, over the years, the design process has been investigated in a variety of ways. Bucciarelli discovered in his ethnographic studies of engineering design firms that design is essentially a social process in which incongruent understandings or "object worlds" among design team members need to be negotiated and aligned in the design process (1988, 1996). Others have conducted think-aloud protocol studies focused on differences between novice and expert designers, studies which have suggested progressive learning pathways towards expert practice (Atman, Chimka, Bursic, & Nachtmann, 1999; Atman et al., 2007; Ball, Ormerod, & Morley, 2003; Cardella, Atman, & Adams, 2006; Purcell & Gero, 1998). In a normative approach to determining good design practices, Mehalik and Schunn (2006) conducted a meta-analysis of 40 empirical studies of design to identify high frequency design elements or stages, one of them being graphical representation. While initially identified by the authors as an essential design activity, in their meta-analysis, graphical representation turned out to be only a moderately frequent element or a Tier 3 activity. A possible explanation for this finding is that only 50% of the articles reviewed described engineering design processes. In another review of the role of design in engineering education, Dym, Agogino, Eris, Frey, and Leifer (2005) discussed sketching and its functioning as another language or representation for exploring alternative solutions, enabling the generation of new ideas, compensating for the constraints of short-term memory, and facilitating problem solving. Further, it has been demonstrated that better design outcomes correlate with the quality and quantity of graphical representations (Song & Agogino 2004; Yang, 2003). These previous studies establish the importance of graphical representation and strongly suggest the need to continue investigating such practices in the wild while also extending the notion of representation beyond sketching to the various representational systems utilized by practicing engineers in the pursuit of design solutions. These studies also strongly suggest the importance of developing such representational capabilities in engineering students. In this study we take an important next step by investigating the situated, multivariate representational systems designed and employed by a graduate student research engineer in pursuit of an optimal design solution.

Research Design

With NSF funding we have been investigating the cognitive and learning practices in interdisciplinary research settings for 12 years. During this time, we have collected ethnographic data in a tissue engineering lab, a neuroengineering lab, a biorobotics lab, and currently two integrative systems biology labs. Our investigations have been designed to answer two larger questions: How do practicing research engineers conduct their work? How does the lab environment continuously support learning? A subset of the first question includes questions specifically focused on representational systems: How and when do engineers use representational systems in their laboratory work? Which systems do they use and how do they decide on those systems? What cognitive functions do these representational systems serve? The study reported here focuses on one researcher in one of the integrated systems biology labs, but the distributed cognitive practices described here are just as prevalent in the other labs we have investigated.

This lab was identified as a research site because of the multidisciplinary approaches the lab uses to investigate signaling in the context of the biochemical environment of the cell, with a focus on oxidation and reduction reactions. To develop this context-based understanding of signaling, the lab develops mathematical models and does wet lab experimentation in parallel, to gain insight into the parameter settings for the models. As this study attests, the lab also engages in engineering design and fabrication when needed.

Given our research focus on situated socio-cognitive practices and learning ecologies, we conducted an extended ethnography employing the standard methods of participant observation, informant interviewing, and artifact collection. We observed researchers as they conducted their work on the bench tops and as they used instruments, devices, and equipment; we attended lab meetings, which were audiotaped to complement the field notes; we sat in on Ph.D. proposals and the weekly journal club. Field notes were collected by two team members of different genders, age, and disciplinary backgrounds (industrial design and public policy), a methodological strategy that afforded the collection of differing but complementary data. We collected and analyzed relevant artifacts including published lab papers and dissertation proposals. Altogether, we collected 52 interviews (fully transcribed) and audiotaped 15 lab meetings and 2 joint meetings with another integrative systems biology lab. We also used unstructured interviewing with the lab members and collaborators outside of the lab. At present 18% of the transcribed interviews are fully coded.

Broadly consistent with the aims of grounded theory, we have been approaching interpretive coding analytically and inductively (Glaser & Strauss, 1967; Strauss & Corbin, 1998) enabling core categories (and eventually theory) to emerge from the data and remain grounded in it, while being guided by our initial research questions. Coding began with weekly collaborative meetings by at least two research group members. A small sample of interviews was analyzed progressively line-by-line from beginning to end, with the aim of providing an initial description for most if not all passages in the interview. A description and code were recorded only when both researchers were in full agreement about its fit and relevance to the passage; initially, there was no attempt to minimize the number of coding categories. Initial codes were presented in our full research group meetings (all members had read the transcripts in advance) and codes were discussed until there was agreement. Descriptions and codes were revisited throughout the process in keeping with new discussion on the text as well as new observations in the laboratories. Axial coding aimed at continuous refinement and verification of the categories and connections between them. Analyzed for conceptual similarities, overlap, and distinction, codes were grouped under superordinate headings, and so forth, until no further reductions could be made. Altogether the team identified 127 codes organized into 16 superordinate categories.

In addition, using cognitive-historical analysis (Nersessian, 1995), we collected and analyzed data from traditional historical sources (publications, grant proposals, laboratory notebooks, and technological artifacts) to recover how the salient representational, methodological, and reasoning practices have been developed and used by the researchers. We sought out the daily and diachronic dimensions of the research by tracing the intersecting trajectories of the human and technological components of the laboratory, conceived as an evolving cognitive-cultural system (Nersessian, 2006) from both historical records and ethnographic data. We combined these data to understand both the nature of cognition and of learning in these settings. This novel combination of methods has enabled us to develop thick descriptions and analytical insights that capture the dynamics of inquiry characteristic of research laboratories. Our own interdisciplinary research group comprises Ph.D. level researchers with expertise in ethnography, qualitative methods, linguistics, psychology, philosophy and history of science, cognitive science, and learning sciences. Student researchers (graduate and undergraduate) have come from programs in cognitive science, intelligent systems, human-centered computing, and public policy. All members of the team received apprenticeship training in ethnography, qualitative methods, and cognitive-historical analysis. The case study reported here was developed and triangulated from several data sources. These include field observations and notes of the design work unfolding on the bench top; informal, unstructured interviews of C10 (a lab member); notes on lab meetings; the Power Point slides used by C10 for her presentations; two posters created by C10 for conferences; two of C10's publications, and her master's thesis that reported on this work.

Designing a Lab-on-a-Chip Device

A central problem in developing mathematical models of cell signaling is the availability of time-series data, which are difficult to collect because signaling events happen very quickly, sometimes within 20 seconds of stimulating the cell. To get an accurate picture of the signaling process, measurements must be made every half a minute to one minute. This frequency of measurement is challenging for a human experimenter, particularly if the measurement samples must be uniform across all the time points. To overcome this problem, Lab C decided to develop a microfluidic lab-on-a-chip device that would automate the stimulation of the cell and the collection of cell samples at different time points. The automation would improve data collection, particularly for early signaling events that occur immediately after stimulation, and signaling events that occur in quick succession; such a device would provide cleaner and richer data for modeling.

Design Problem

The specific problem the lab wanted to investigate using the LOC device was quantifying senescence, or aging, of T cells, which leads to their inability to replicate, particularly those biomarkers that change with age. Since T cells collected from human donors immediately begin to age rapidly, they are only available in extremely limited quantities and can be used for experiments for only a few days. One of the advantages of the microfluidic device is that – compared with bench top methods – it would need only a limited number of cells for an experiment. To investigate senescence with this approach, the T cells need to be stimulated by mixing them well with a reagent which causes different proteins to form in the cells as a result of the signaling process; the cells are then measured at many time points after stimulation, ranging from 20 seconds to 20 minutes. These measurements can be done at both the population level (a certain group of cells) and at the single cell level. Proteins are not measured in the microfluidic device, but separately using sophisticated biological instruments. The device freezes the cells' internal state at different time points by quenching the biochemical reactions in the cell. This freezing is done by lysing the stimulated cells by adding a reagent that breaks open the cells, which creates population samples, and fixing the stimulated cells by adding formalin, which creates single cell samples. The measurement of proteins is then done offline on these samples of cells, whose internal states are frozen at different time points in the signaling process.

Thus, the LOC device needed to automate three processes: (1) stimulating the cells by mixing with a reagent, (2) freezing the cells' internal state by mixing samples with a lysis buffer and fixing the stimulated cells with formalin, and (3) executing these actions at precisely the right moments as defined by the desired time points. In the initial stage of the design, only lysing was considered; fixing was added towards the end of the design.

One of the early design decisions (made before C10 joined the lab) was to have a modular design: one module for the mixing process (roughly) and another for the freezing process. The two modules would be connected by tubing of different lengths, so that the liquid medium containing the stimulated cells in each tube would take different lengths of time to reach the second module, where the biochemical reactions in the cells are then quenched. The varying tube lengths thus function as an analogue for different time points. The final design is shown in Figure 1.

Design Process

The design of the LOC device was developed in collaboration with another lab. In this case study, we report only the design changes and decisions involving one Lab C member (C10), a graduate student in bioengineering whom we followed closely. C10 has an undergraduate background in electrical engineering and, as a result, she joined the lab with a good understanding of design and fabrication of microelectronic chips, the same techniques that are used to create microfluidic devices. The device was created by specifying the structure of the channels through which the liquid containing the cells would flow using CAD software, and then fabricating this channel design using PDMS, a polymer commonly used in microfluidics. The resulting chip has very narrow channels instead of circuits, and the liquid containing the cells is pumped through these channels using a syringe pump.

The device was developed in an iterative and parallel fashion, with different facets of the device being revised repeatedly. A variety of representations were created and used, sometimes in parallel, throughout the design process. In the following description, for the sake of clarity, we outline the evolution of the device using a sequential narrative of different problems. However, it is important to keep in mind that these design problems were never separate, and the device was built and experiments run using it as a whole unit, not as separate modules.

When C10 joined the lab, the research group had already settled on using a herringbone mixer (HBM) design, both for mixing the cells and stimulant in the first module and also for the mixing needed for lysing in the second module. In our first interview with her, C10 noted: "There were several rounds of the device [design]. So the first device for the first module was like this [referring to an image] – and all of these had herringbones – and [naming a member of collaborating lab] designed it – and to be honest, I really don't know why." The herringbone design involved creating grooves similar to fish bones (see Figure 2a) on the top of the channel; the grooves interrupt the flow of the liquids in a way that the two liquids, for example, cells-in-media and the stimulant, folded into each other, thus getting mixed well.

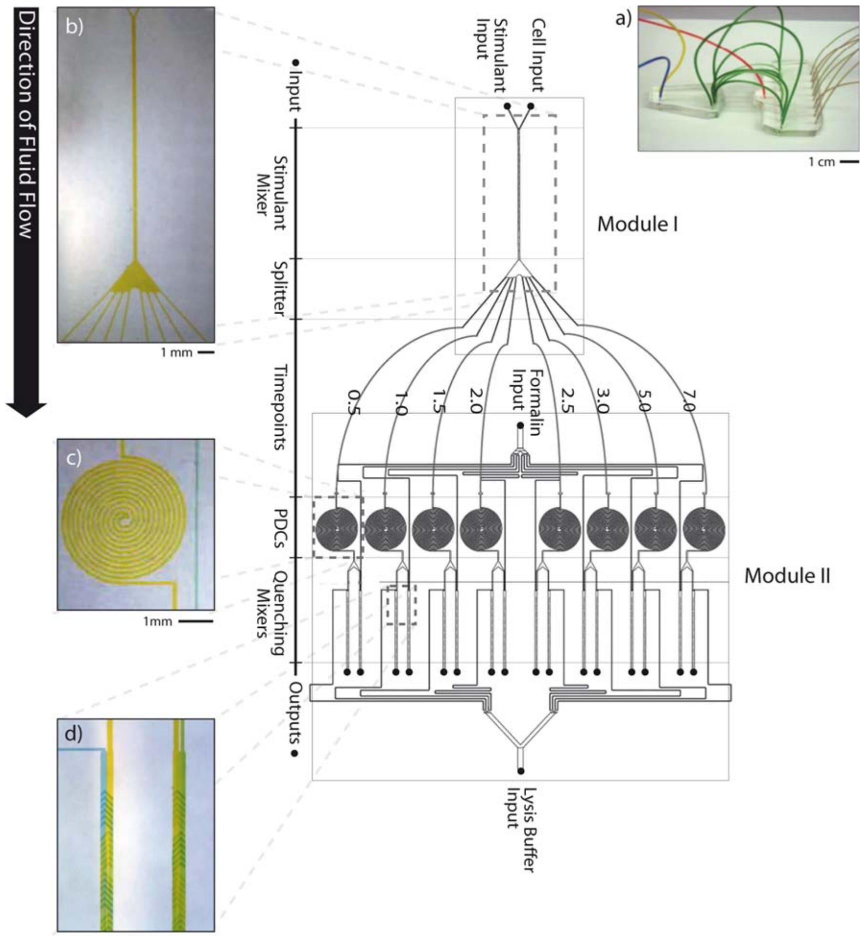

Figure 1 Overview of the LOC device consisting of Modules I and II connected via tubings of varying length. (a) Device set up and running with colored fluids. (b) The stimulation mixing channel (the straight portion) and splitter (distributing the cells into eight tubings). (c) Pressure drop channel. (d) The quenching mixing channels for fixing and lysing operations. All figures reprinted with permission of C10. [Color figure can be viewed in the online issue.]

However, for the design, the flow rate was as important as the mixing:

Another thing that is important in the design is the flow rate . . . because if you use too high a flow rate, then the cells get sheared . . . Imagine I put you in a tunnel and very fast I have liquids going other directions than you do, so you would shear – and the other reason if you go too slow . . . then the time you spent in this region [referring to mixing image on computer] . . . it's big, right?. . .You want the

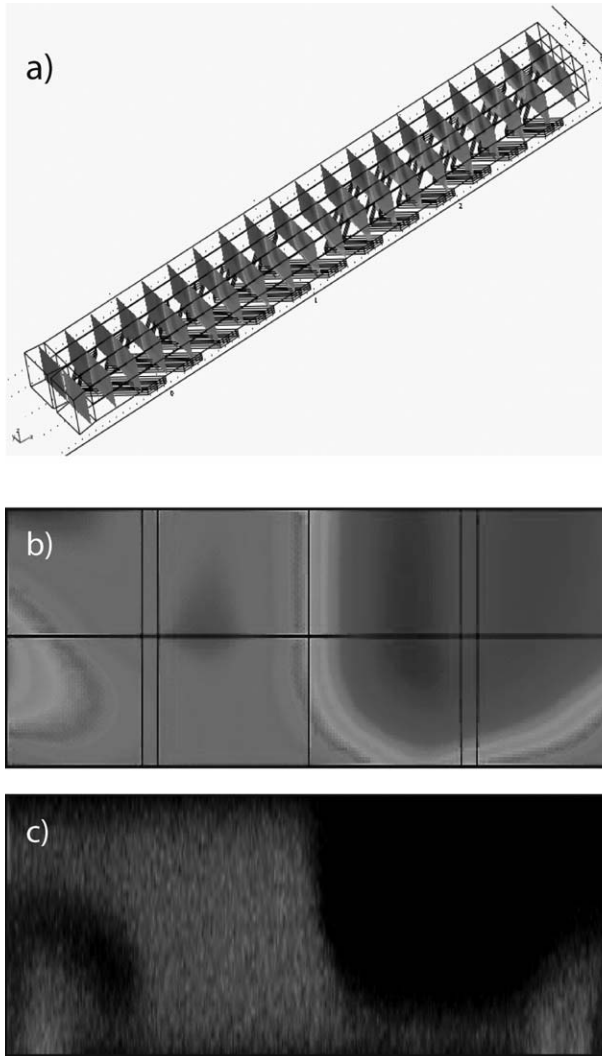

Figure 2 (a) The first cycle of the mixing channel (consisting of six right-bias herringbones followed by six left-bias herringbones) overlaid with cross sections generated by COMSOL. (b) COMSOL model output and (c) experimental results captured using confocal microscopy.

cells to go as fast as possible. In your body, when it encounters that, boom, and that's it – so you want to reproduce this thing. So these were two of the design principles – the volume and the mixing time.

In initial experiments, C10 was part of the investigation into how the geometry of the herringbone structure contributed to mixing, particularly how many cycles would be required to fully mix two liquids of different viscosity or density. Using COMSOL, a finite element analysis software for creating equation-based models of the folding of liquids with different viscosities and densities, C10 compared the model's output with the output of the mixer when using similar liquids, and then adjusted the HBM design and the length of the mixing channel to optimize the mixing. Confocal microscopy was used to qualitatively analyze the mixing throughout the mixing channel (Figure 2c). Using analytical imaging software, C10 could quantify the mixing of the liquids through the channel to verify when the fluids were mixed well enough. These images allowed comparisons between the model output (Figure 2b) and mixer output (Figure 2c). A water and sucrose mixture tagged with dyes was used to examine the effects of viscosity and density mismatch between the two fluids.

From the mixer, the mixed fluids moved to a splitter, which split the flow into the different tubes, the analogues for different time points: "it is completely modular . . . so if you want to look at other types of time points, you change the flow rate or you change the tube size." One problem with using tubing was that to achieve different time points, different lengths and diameters of tubing were used, resulting in pressure drop differences across them. "The smaller tubing will have a lower resistance than the longer tubings and so that the flow rate will go faster there." The different flow rates in each tubing led to an uneven amount of sample volume being collected at their outputs. If the samples were greatly uneven, they could not be used for the experiments. Figure 3 shows the tubing of different lengths, cut and laid out on C10's work surface. The different lengths of tubing provide a physical representation of resistance and flow rate.

To overcome this uneven splitting problem, pressure drop channels (PDCs) were added to the end of the tube outputs located in the second module. The PDCs acted like large resistors that increase the overall resistance of the system so much that they virtually equalized the pressure differences associated with the different tubes. "This is just a way to control . . . to make sure that the liquid would go at the same speed everywhere." C10 created a MATLAB program that mathematically modeled components of the device, allowing her to investigate possible geometries for the PDC by varying its cross-sectional dimensions and length. As she noted, "So, then basically what we could do was like play with the numbers here, like so this was for the first module [pointing to the MATLAB code]. That's the length, that's the height." By comparing its calculated pressure drop with the largest pressure drop calculated for the tubing, she was able to create a PDC that reduced the pressure drop differences in the tubing to within 1%, evening out the fluid outputs.

The PDCs were initially designed as rectilinear channels folded in a zigzag pattern (see Figure 4d) because the PDCs needed to be long and thin but had to fit in the small footprint of the device. The zigzag pattern was thought to be a good way to fit a long, thin channel in the small space of the device: "And the cells, they were turning, and the reason was that, it was to keep space, to not have fifteen millimeters lost." This decision would lead to problems when cells were introduced in the device. Initially, the designs of the device were being tested using only fluids.

Once the fluids were mixing well and the distributions became even across the different tubes, the device was tested using Jurkat cells, analogues to the T cells that were to be used later in the study. The fluids with cells behaved differently from fluids alone in the device. The distribution in the fluid case was fairly even, but in the case of the fluid with cells, the distribution (measured as the number of cells in each output) was highly uneven. It was hypothesized that the problem arose from the splitter design. A COMSOL

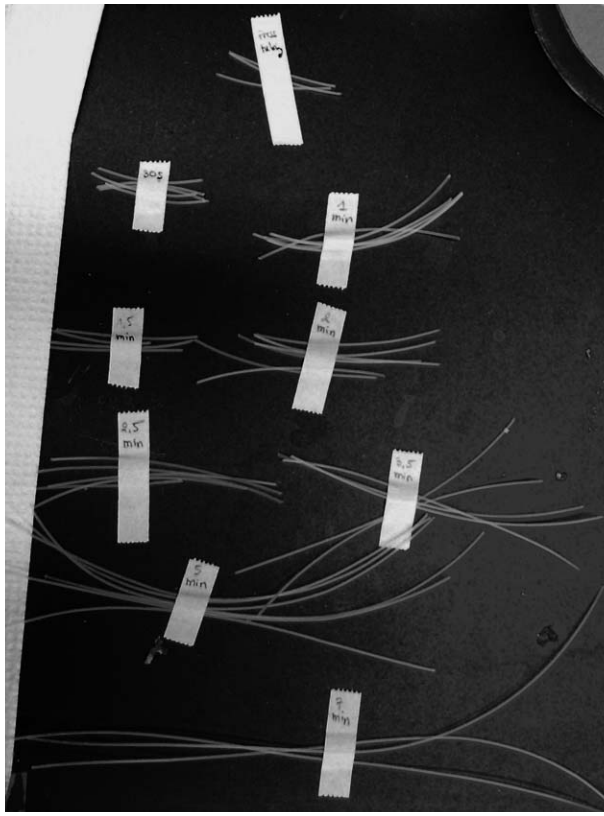

Figure 3 Tubings cut and placed on the table.

simulation visualized the streamlines and fluid velocities within the splitter. Using the simulation and long-exposure photography to capture the flow of cells in the splitter, it was determined that the geometry of the splitter was causing the uneven distribution. The splitter was then redesigned based on a bifurcating structure to create symmetry: "Then we wanted to have it completely symmetric because we thought that because we had ten that the cell distribution was bad." The channels were split three times, producing eight outputs (Figure 5b). The original splitter had ten outputs, but it was based on a somewhat arbitrary decision to make the time points range from 30 seconds to 5 minutes, with time points every 30 seconds. In the redesign, it was decided that eight time points were enough for the senescence study. The output distribution became more symmetrical but remained significantly uneven. Not sure how to fix the problem, C10 generated three different design variations and tested them at the same time (Figure 5c) and settled on a variation that produced the most even cell distribution (Figure 5d).

The use of cells for testing the device also revealed another problem. The cells were getting stressed in the zigzag turns of the PDCs: "That's exactly the story. If you don't have cells, it's almost perfect. You put cells, nothing works anymore." In testing with T cells, it was found that the T cells were larger than Jurkat cells and they tended to get

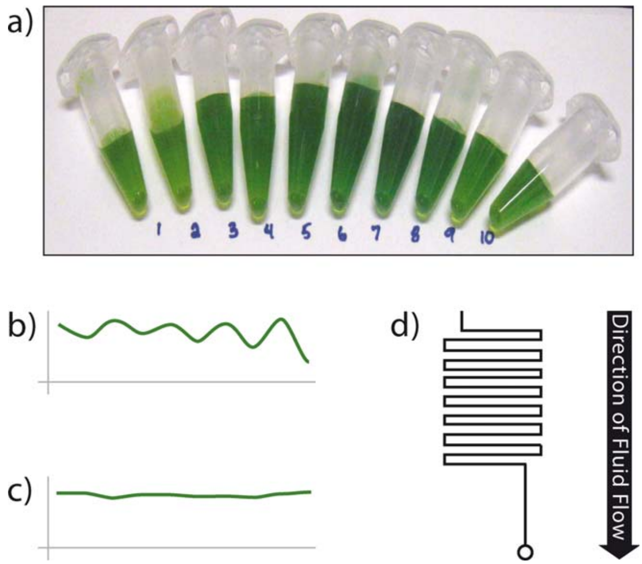

Figure 4 (a) Direct output of the initial splitter without any tubings attached. (b) Output distribution of fluids with various tubing lengths before the first pressure drop channel (PDC) was implemented. (c) Output distribution after the PDC was implemented. (d) Rectilinear zigzag geometry of the PDC. [Color figure can be viewed in the online issue.]

stuck in the PDCs. C10 tried widening the channels to accommodate the larger size of the T cells, which required lengthening them as well to conserve the pressure drop: "The problem is if I make them bigger, they stay in the device longer. Then you are screwed with your mixing time – it's so small." It was also discovered that some of the cells were getting torn and clogging the device. A variety of redesigns were tried (Figure 6a–f), culminating in the spiral model, which emerged during a lab meeting discussing the clogging problem. As C10 recounted, the PDC needed to be redesigned to avoid cell stress and clogging, which led to quite a different design:

> Yeah, the shape, I just changed the shape for the cells not to be stuck on the corners cause they didn't like the corners. And so sometimes they would get lysed cause they would see, on the corners the cells like see more force, because the cells are, liquid turns and so the cells are so, so that more force around them, so that they weren't very happy. So I didn't want like to make them turn ninety degrees too often, so that's why I changed it this way [Figure 5g], so that they only turn once.

Figure 7, a worksheet located on the microfluidics bench top, provides a good representation of how C10 worked with the completed device. This analysis determined where each tubing should be inserted into the device during its operation. It provides an illustration of how she brought together knowledge generated by the MATAB code (the lengths of the tubing and the pressure drops), experimentally determined knowledge about the optimal flow rate for the best distribution, the experimental constraints of the time points,

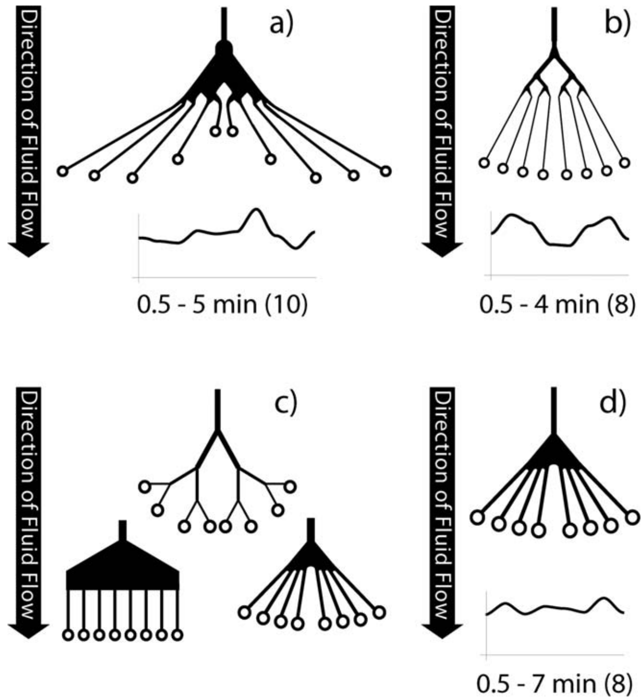

Figure 5 Evolution of splitter design. When (a) was tested with cells, the output distribution was undesirable. A bifurcating design geometry (b) was the first attempt to improve the distribution; output distribution was more symmetrical, but remained significantly uneven. (c) Three tested design variations. (d) The final design.

and knowledge about the design architecture and performance of the device. C10 used this sheet to bring together all these factors to determine the optimal arrangement of the tubing. One interesting feature of this representation is that it shows how C10 still had to carefully tweak the balancing of the pressure differences between the different lengths of tubing, despite the addition of the pressure drop channels to the final device design.

Starting at the top left with 0.5, 1, and 1.5 down to 7 is a list of all of the time points (in minutes) used in the device. The next column to the right maps the lengths of tubing (in centimeters) that correspond to these time points. Notice that the length of the 1-minute time point is longer than the 1.5-minute time point because the diameters of the first two tubes are smaller than the rest, as noted by PE2. The rest of the tubing had the diameter of PE3. The third column contains another set of lengths (in centimeters) that is just slightly different from the second column. Its inscription inside a box perhaps suggests more updated measurements. At the bottom of this column is "@ 38μL/min." which indicates that these are the dimensions that work with a flow rate of 38 microliters per minute, a parameter that is controlled with the microfluidics pump. The last column, on the far right, is a list of the corresponding pressure drops (in Pascals) of the tubing. C10 selected the time points to use and calculated the following numbers using the MATLAB model she created.

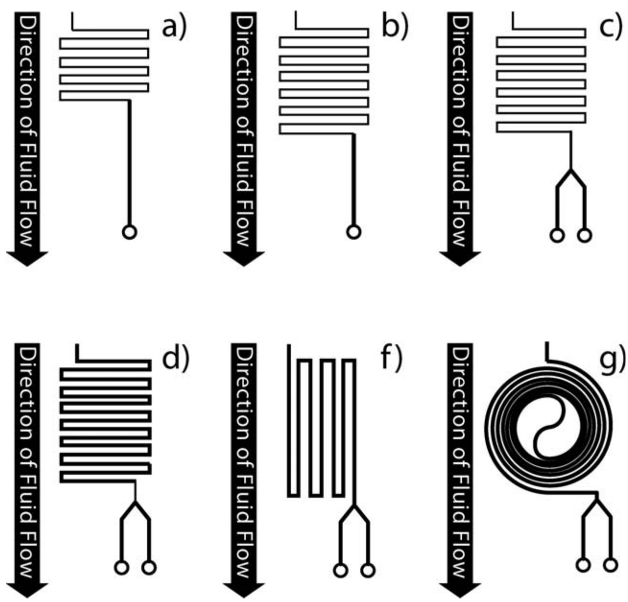

Figure 6 Evolution of pressure drop channel designs (PDCs). (a) Design created to solve the uneven fluid distribution problem, prior to testing with cells. (b) The PDCs are lengthened in response to the first cell trials. (c) Addition of splitter following the PDC after fixing was added. (d) PDCs widened (and subsequently lengthened) to accommodate the T cells. (f) Design attempt to reduce the number of turns the cells experienced because they were being destroyed in the PDCs and clogging the device. (g) Final design; to prevent clogging, the zigzag rectilinear geometry is eliminated.

Below the sketch of the device architecture is a representation of the first module in the device. The time points are mapped to outlets. Notice that they are in a seemingly random order. But just below each of these time points is another line of numbers, which are the pressure drops mapped to each of these time points. And below this on the left, are numbers aligned into two columns and totaled at the bottom. The two columns represent the numbers on the left side of the centerline (actually drawn on the diagram) and on the right side. They have been totaled to see if this arrangement is approximately balanced; the balance helps to even out the output distributions. After the calculation and comparison was done, the order of the tubing was revised; the 0.25 Pa and 0.33 Pa tubes were switched. C10 did not update her calculations on this sheet of paper. Possibly she tried other arrangements and perhaps other methods to find the best order, but we did not capture these processes.

Cognitive Design Processes

The previous section shows that the process of building the device was neither completely top-down (built from an explicit blueprint) nor completely bottom-up (built by trial and error). A complex design such as the microfluidic LOC device cannot be built from a

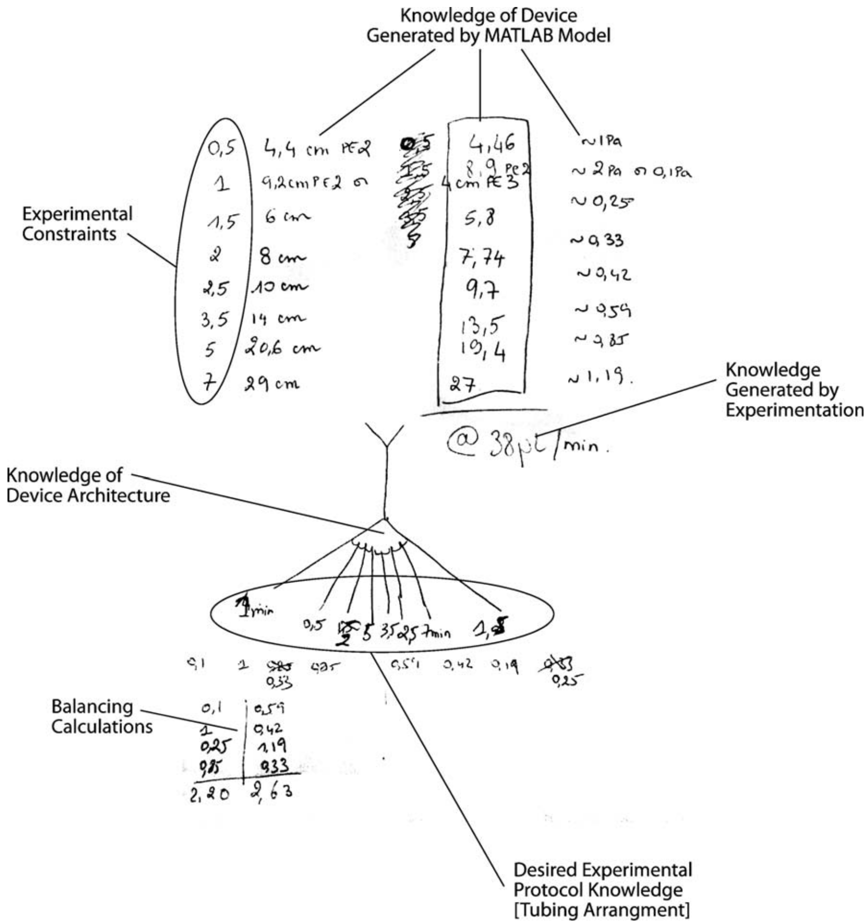

Figure 7 Worksheet located on the microfluidics bench top. Highlighted are the components of knowledge C10 brings together. Clockwise: knowledge generated by the MATAB code (the lengths of the tubing and the pressure drops), experimentally determined knowledge about the optimal flow rate for the best distribution, desired protocol knowledge about tubing, balancing calculations, knowledge about the device design and performance, and the experimental constraints of the time points.

blueprint, since it would require conceiving a priori all possible design constraints, device features, and their interactions. The fully bottom-up approach is similarly not feasible, since it would require building and testing a large number of prototypes to evaluate the different design constraints, device features, and their interactions.

For complex designs, the designing and building processes take a middle path between these two extremes, with some aspects of the design envisioned (usually as rough initial designs) and some aspects tested by building prototypes (mostly to improve the initial designs). As we have seen in the case of the microfluidic design process, however, the process is not completely arbitrary. It involved C10 actively developing an optimal strategy, which we argue, minimizes the cognitive load involved in conceiving of the constraints, features, and interactions, while also minimizing the physical effort and use of resources. In this section, we address the question: What are the cognitive mechanisms that allow this optimization to be achieved?

We will first examine the lab-on-a-chip design case from a process point of view and argue that this optimization is achieved by distributing the cognitive load to the environment, particularly by using external representations. This strategy is best captured by distributed cognition, a theoretical framework in cognitive science that we discuss below. We will then examine the design case from the point of view of the coupling between the external representations and C10's mental modeling processes.

Distributed Cognition

Distributed cognition (DC) is a theoretical framework that describes and analyzes task environments where humans interact with complex machinery, such as airline cockpits, naval ships, and nuclear power plants (Hutchins, 1995a, 1995b). This model of cognition is suited to studying cognitive processes in complex technical and scientific environments, particularly those where external representations are used. The primary unit of analysis in DC is a distributed socio-technical system, which consists of persons working individually or together to accomplish a task and the artifacts or machinery that perform cognitive functions in the process. The people and artifacts are described as agents and nodes of this extended system, respectively. The behavior of the system arises from the interaction between external (artifact) and internal (human) representational structures. Within this framework, understanding how problem solving is achieved requires examining the generation, manipulation, and propagation of the salient representations in the system in accomplishing cognitive work.

A standard example of external representational structures in DC is the use of a speed bug in a cockpit (Hutchins, 1995a). Speed bugs are physical tabs that can be moved over the airspeed indicator to mark a critical setting or settings for a particular flight. When landing an aircraft, pilots have to adjust the speed at which they lose altitude on the basis of the weight of the aircraft for that particular flight. Before the design of the bugs, this calculation was done by pilots using a chart and calculations in memory while landing the aircraft. Once these markers are set between two critical speed values, which are based on the weight of the aircraft for a particular flight, instead of comparing the current airspeed and wing configuration with memorized critical speeds or ones on a chart, pilots simply glance at the dial to see where the speed-indicating needle is in relation to the bug position.

This external representation (i.e., the bug) allows pilots to "read off" the current speed in relation to permissible speeds using perception and to calibrate their actions in response to the perceived speeds. The speed bugs (an external artifact) thus lower pilots' cognitive load at a critical time period by cutting down on calculations and replacing complex cognitive operations with a perceptual operation. The location of the speed bugs also leads to a public structure shared by everyone in the cockpit, which results in the coordination of expectations and actions between the pilots. These two roles of the speed bug – lowering cognitive load and promoting coordination – cannot be understood without considering the human's internal cognitive processes and the artifact as forming a distributed cognitive system.

As with most research contributing to the development of the DC framework thus far, the speed bug case focuses on the human's role in coordinating external representations and does not consider the nature of the human representations in the system. Further, DC analyses typically focus on how external representations are used and not on how they are created. For engineering problem solving, these issues need to be addressed.

First, as we have argued elsewhere (Nersessian, 2008, 2009), our data on how researchers think and reason provide substantial evidence that the mental representations they use in problem solving have a model-like structure. That is, they are organized representations that are customarily referred to as mental models. We have also argued that a range of data on scientific reasoning, mental modeling, mental animation, mental spatial simulation, and embodied mental representation in the cognitive sciences supports the hypothesis that mental models can be manipulated by simulation – what we call "simulative model-based reasoning" (Christensen & Schunn, 2007; Nersessian, 2002, 2008; Trickett & Trafton, 2007). From a DC perspective, simulations are preformed through a coupling between mental models and external representations (Chandrasekharan, 2009; Nersessian, 2009).

Second, Hutchins (1995b) has argued that humans build their cognitive powers by building external environments. However, little attention has been directed to the processes through which people build representational environments, thereby creating distributed cognitive systems. Engineering sciences provide fertile ground for examining these processes because much frontier research involves building the external representational structures that provide the environments through which thinking and reasoning take place. Hollan, Hutchins, and Kirsh – three founders of the DC perspective – have argued for a set of core principles, which includes (1) "people establish and coordinate different types of structure in their environment" and (2) "people off-load cognitive effort to the environment whenever practical" (Hollan, Hutchins, & Kirsh, 2000, p. 181). Focusing on these two principles, our analysis of C10's representational practices establishes how an individual researcher off-loaded the cognitive effort of a design task by creating and coordinating representational structures. In this case, C10 and the representational artifacts she created compose the cognitive system that accomplished the task of designing the microfluidic device.

In the case of designing the microfluidic device, and of sophisticated design tasks in general, the task of mentally envisioning all design constraints and device features and their interactions is cognitively impossible due to its complexity. The alternate solution – generating and testing many variations of prototypes iteratively – is tedious and expensive. Our case shows how a middle path between these approaches is developed, using four strategies that work in combination, all based on the generation of external representations that help transfer cognitive load to the environment.

Simulating External models simulate a large number of possible scenarios and these model scenarios can be used to infer a viable structure for prototypes.

Visualizing Numerous drawings make explicit the designer's mental models of how the device will achieve the design objectives. For analyses of such drawings see Purcell and Gero (1998). The behavior of the prototype can be visualized using imaging techniques and graphical representations of the output of the device.

Tagging Prototypes can be marked to reveal their behavior and properties. Tagging allows the designer to read off visually the relevant behavior and properties and to bypass complex inference processes while evaluating the design. While tagging is commonplace in everyday life, it is a complex problem in biological experimentation because biological tags must meet many experimental constraints.

Interrogating A prototype also serves as a representation because it is possible to make changes to the prototype, and examine the resulting behavior – a process of probing-by-changing. Interrogation helps the designer revise the mental model of the problem and isolate problems.

For such probing-by-changing (interrogation of the device) to be possible, the design needs to be modular so that different variations of device features can be examined in relation to the design constraints. Modularity is often considered part of good design practice, but this is usually recommended from an engineering/manufacturing standpoint (Clark & Baldwin, 2000). From a cognitive standpoint, modularity contributes to the use of the prototype as an external representation, and thus shifts the cognitive load to the environment. A modular prototype can be "probed" by altering different components and using different configurations, and this probing can help the designer to understand the problem better, isolate sub-problems, and sometimes help revise the very way the problem is conceptualized.

The design of the microfluidic device exhibits all these cognitive load-reduction strategies. To understand how and when these strategies help lower cognitive load, we will examine one component of the design process in detail: the design of the herringbones.

Designing the Herringbones

As described above, the herringbone design for quickly and efficiently mixing the fluids was chosen from a set of alternatives before C10 joined the group. Now part of the group, C10 needed to know the relationship between the geometrical features of the herringbone structure and the level of liquid mixing resulting from the fluids passing through a geometrical structure.

One way to make this assessment would be to build many herringbone structures or prototypes, evaluate the mixing for each using some measurement, and then iterate until the optimal mixing is achieved for a specific set of fluids. The iterations would involve changing the geometrical structure, which would require the designer to think about how the mixing would be affected by a particular change. This assessment, in turn, is based on developing a mental model of how the mixing is affected by the current geometry and fluid properties. This iteration process would be cognitively demanding, tedious, and require a high degree of physical effort and resources. Also, the design produced by such a trial-and-error approach would be very specific, suitable only for a given set of liquids or flow rates and not easily varied to suit other conditions.

Instead of such a trial-and-error approach, C10 developed a model using COMSOL, a computational fluid dynamics software which allowed her to capture the pattern of flow for different channel geometries, for different liquids. She compared the results of this model against actual flow patterns in prototype channels, where water and sucrose were used to simulate viscosity. She added a fluorescent tag to the liquids to track the level of mixing. To establish the level of correspondence between the model's output and actual output, she compared confocal microscope images of the flow against the flow patterns generated by the model's visualization.

Once a good correspondence was established, she used the validated model to generate and test different possible geometries. The model geometries that produced the desired mixing most quickly were built and tested. In addition to lowering the number of built prototypes, the COMSOL showed in clear terms the level of mixing achieved and the time taken, and the model's visualizations were used for showing the mixing level in related publications.

The design process made use of the first three externalization strategies, simulating, visualizing and tagging. In combination, these made it cognitively possible for C10 to infer the relation between mixing and geometry and lower the number of prototypes developed. Once validated, the COMSOL model worked as what could be called an "external imagination," which allowed C10 to simulate and visualize many variations and combinations of geometries and liquid properties. The tagging of the liquid in the prototype with the dye allowed her to read off visually the level of mixing instead of inferring it indirectly. The tagging also allowed her to captured the level of mixing using the confocal microscope images, which, in turn, enabled her to make an explicit comparison between this image and the model's output, as well as her own visual impression.

Note, that to vary the herringbone geometry using COMSOL, C10 needed to have a mental representation of the mixing process, and she mentioned thinking of the herringbones as folding the liquids. But her mental model is now coupled (Kirsh, 2010; Nersessian, 2008, 2009) with the computational model's output, which allows the two to work as an integrated system, particularly with the tagged liquids and the resulting visualization. This coupled distributed cognitive system helped C10 arrive at a fine-tuned, adaptable, and optimal design, with minimal prototyping. The coupling between internal and external representations arises from a strategy of actively generating external representations to lower cognitive load. The actual techniques used to externalize processing (modeling, tagging, visualizing, and interrogating) will vary across design situations, but the underlying externalization strategy is the same for other situations.

Simulative Model-Based Reasoning

The analysis presented above focuses on the general design strategy, specifically the process of off-loading cognitive processes to external representations, which is applicable across many types of designs. The DC analysis does not address the cognitive mechanism that helped C10 imagine her particular design problem or how this mechanism is related to the off-loading of cognitive processes to the world. In other words, we have not yet discussed the nature of her mental representations and the cognitive mechanism involved in processing the content, or the way the mechanism integrated the external representations with C10's mental representations. For this we need to bring the notion of simulative model-based reasoning (Nersessian, 2002) into the analysis.

The central problem in the design of the LOC device was translating experimental procedures executed by researchers, in such a way that these procedures were also executed by the device, but more efficiently. The researchers' experimental procedures involved actions, which are dynamic, but the device was static. The dynamic component was replicated in the flow of media through the device, and the effects of the researchers' experimental procedures (mixing and freezing) were recreated by manipulating the flow. Flow was thus the central component of the designer's mental representation.

It is fairly straightforward to imagine mixing being recreated by manipulating flow and freezing being recreated by combining the cell media with lysing and fixing reagents. However, replicating the different time points of measurement using flow required a conceptual shift. C10's use of different lengths of tubing (Figure 3) to recreate lengths of time involved a rather radical representational transformation from time to space, and this transformation drove all later revisions to the device. Instead of waiting a certain amount of time before quenching the reaction – which would be the procedure followed by a human experimenter – the device transformed different time periods into different distances flowed by the liquid. This was a novel transformation of the problem space, and it allowed C10 to conceive the entire design in terms of fluid dynamics. Critically, this unifying mechanism made it easier for the designer to integrate the imagined flow process with the outputs of the external representations.

A mental model is the best way to characterize C10's internal representation of how media flows through the device. Since the flow process involves a combination of both dynamic and static features, imagining it requires integrating simulation and imagery, and a mental model is the cognitive process that supports this integration. Mental modeling allows both dynamic and static features to be manipulated in the mind, and the nature of this manipulation is considered to have correspondences with a built physical model. But the mental model is more abstract than the external built model in the sense that its features need not be, or often cannot be, as specific as those in external built model. In the beginning phase of this design process, C10's mental model was likely quite generic, since the features and the nature of flow were not known. The building of the prototypes, the computational model, the external representations, and the testing using different fluids, gradually added more specificity to the mental model, both in terms of features as well as of the nature of the flow. The building of external representations thus not only off-loads cognitive load but also adds detail to the mental model and constrains it (see also Kirsh, 2010).

A possible way of thinking about the design process would be to consider the prototypes and external representations as instantiations of an existing mental model. However, this description does not capture the design process of the device because of the way the prototypes and the external representations were used to identify and solve problems (such as the splitter design), and also to revise the mental model (to include features of the cell). The case study establishes that there was an interactive process between the internal and external representations and that they were integrated to form a distributed system that performed the reasoning processes. In this case, the final outcome of this simulative model-based reasoning is an object, the LOC, with features that support new experiments.

In this case study, the design of the device involved complex interactions among mental models, computational models (COMSOL, MATLAB), building and testing prototypes, and using tagging and visualizations to query and validate the prototypes and computational models – all the while integrating all these to meet stringent experimental and fabrication constraints. Understanding this outcome requires examining how integration takes place across many representations. We believe that this process of representational use and integration is not just an isolated case of simulative model-based reasoning but rather is emblematic more generally of sophisticated engineering design practice. Striking the middle path between building top-down (following a fully formed blueprint) and building bottom-up requires that the expert engineer find strategies for minimizing the cognitive load and the physical effort and time required. The interplay and interaction between drawings, computational modeling and simulation, and provisional prototypes supports the notion of progression from idea to a fully functional material device. While many researchers, using think-aloud protocols and analysis, have noted the importance of sketches, drawings, and prototypes in advancing a design concept, the complex integration of varied representational systems towards the development of a designed artifact has not been investigated in the wild from a cognitive perspective. This study is a first step towards a better understanding of the important cognitive processes that undergird the sophisticated design of complex interdisciplinary devices. The more we understand the authentic, situated cognitive reasoning and problem-solving practices of expert engineers, the better we can design learning environments that support those practices.

Implications for Engineering Education

Overall, our case study illuminated how a designing engineer distributes reasoning and problem solving over the span of a complex design task and uses simulative model-based reasoning to engage and solve local problems. Drilling down, we excavate three implications of this work for engineering education.

Distributed Cognition as an Antidote to All in the Head

If we consider the situated design practices of C10 as a starting point for thinking about engineering learning, the salience of the distributed cognitive system is most striking. It is not the solo engineer making decisions in his or her head, but the coupling of his or her mind with emergent, iterative, and parallel representations that allows for testing out and settling on solutions in route to a more optimal design solution. By building and manipulating external representations of local problems to be overcome in the design space, the engineer can make inferences not possible without this distribution of cognitive work across the internal and the external representations. Thus, learning to be an engineer fundamentally means learning to embrace the need to develop and use external representations of all kinds – from free-body diagrams to physical prototypes to MATLAB simulations – as essential to the problem solving, generally, and designing, specifically. It is this conception of problem solving and reasoning that we must impart to engineering students.

But as any faculty member knows who has encountered student resistance to drawing diagrams as the prelude to doing the math, this understanding does not come easily to students. We contend that it is not laziness or a desire to plug-and-chug, but rather a failure of students to grasp that the process of diagrammatic representation is central to the actual articulation of the problem and solution, which the mathematics then represents. We conjecture that this failure arises because engineering students harbor naïve conceptions of thinking and learning as being solely in-the-head. To them, few things external are important or essential to problem solving other than mathematics, because they have practiced a math-driven protocol repeatedly in prior schooling. This study of situated design clarifies why we must bring our students to a revised understanding of learning and problem solving, an understanding that appreciates the bootstrapping value of distributing the complexity of cognitive tasks across internal and external representations. Such distribution is the cognitive practice of a skilled engineer, a reason why the free-body or circuit diagram is so emblematic of the engineering habit of mind. Students must understand that external representations and manipulations of the problem are not incidental, that the community practice of leveraging multiple kinds of representations and provisional models fulfills at least three functions: (1) representations allow the engineer to manage complexity and detail that cannot be managed in-the-head alone, (2) they bootstrap new ideas and provide new ways of manipulating these ideas, and (3) they make it possible to run a cognitive process quicker and with greater precision (Kirsh, 2010). A major challenge for engineering faculty is to get students to understand the nature and the power of distributed cognition and simulative model-based reasoning.

Unfortunately, engineering textbooks perpetuate the false notion that the external representations, usually diagrams, are unimportant because these are generally provided to the student, whose task then becomes one of doing the math. More classroom activities must focus attention on diagrammatic representations and computational simulations and their pivotal role in the reasoning and problem-solving process. One way would be giving students several diagrams for them to map back to the problem prompt. Or, students could create a problem prompt from a free-body diagram. Another way would be to give students a constrained design challenge and have them build a MATLAB simulation and manipulate it to find an optimal design solution. We cannot simply assume students understand the value of external representations as cognitive tools; we must intentionally help them understand their value.

Need for Representational Fluency and Flexibility

In engineering classrooms, students should develop a repertoire of representational practices that can be flexibly utilized in problem solving. The more complex the problem, the more onerous the cognitive load, the greater the need to distribute the cognitive tasks to the environment. At such a point, the value of a diverse toolkit of representational strategies can become clear to a student. However, if the classroom task is constrained and relatively simple, the student will feel no need to use or master diverse representational strategies – and their value will not be evident. Unfortunately, the tasks generally posed in engineering classes, perhaps with the exception of the capstone course, rarely require more than one or two representational practices. Students therefore have few opportunities to see how representational chaining or fluid application of different kinds of representations can be foundational to problem solving. From a classroom design standpoint, an instructor could decide on a series of representations students should practice using, and then develop a set of specific complex problems that would benefit from those forms of cognitive distribution. Thus, the learning objective would not focus on the students' mastering content but rather on developing more expert-like representational skills while expanding their existing repertoire. Such pedagogy of course implies moving out of the textbook and into the realm of authentic, real-world problems that are cognitively onerous and need fluency and flexibility in representational practices for solutions.

Envisioning as Supported Through Modeling Fluency and Flexibility

Complex design problems invariably encounter snags or impasses when the immediate problem solution strategy fails. When this happens, the engineer needs to develop a targeted and efficient trouble-shooting strategy. In the case study, such impasses occurred with the mixing and with the uneven splitting. In each case, when the trouble was realized, C10 developed a representational strategy, a kind of cognitive partnering capability (Newstetter, 2005; Osbeck & Nersessian, 2006) that allowed her to "see" into the space in a particularly targeted way that supported the troubleshooting. With the uneven mixing, developing a computational fluid dynamics model of the folding media allowed her to envision the impasse in a way to address the problem. Thus, representational fluency also needs to be understood as a trouble-shooting strategy, which unfortunately is not how engineering students might understand a computational fluid dynamics model.

The reason for this failure is that although engineering students often practice developing mathematical and computational models for class assignments, it is doubtful that they come to understand the envisioning capability afforded by representations when faced with an impasse.

For the most part, such representational practices is about mastering a concept for a test or fulfilling an assignment. Suppose an instructor were to present students with problems like uneven mixing in a device or cells clumping in a tube and then ask them to develop representational approaches for seeing into the space before actually going to the design and manufacturing stage. If we want students to understand the very sophisticated envisioning capabilities offered through flexible representations, they need practice identifying and harnessing such cognitive partners in the context of troubleshooting.

Conclusion

This article reports on a case study of an engineer designing and building a novel lab-on-a-chip; our goal is to highlight the important function that representational fluency and flexibility played in troubleshooting and reaching a design solution. Moreover, we have offered a cognitive lens through which to understand the day-to-day activities of scoping and responding to a real-world design problem. Distributed cognition and simulative model-based reasoning are two particularly significant cognitive theories relevant to unpacking how engineers reason and work. We believe it is very important in designing engineering learning environments to understand engineering as practiced both at the frontiers of science and in industry – especially as traditional lecture modes of delivery are increasingly being called into question. Our work is developing an integrative cognitive-socio-cultural account of such work practices. In this brief analysis, we illuminate the cognitive aspects of research design and problem solving to highlight the distribution of cognition across researchers and representations. If we can better understand how knowledge and skills are deployed in real-world engineering problem solving, we can better identify design principles to assist us in developing educational models that achieve fidelity between the two sites of the classroom and the work place whether it be a lab or industry. This desired fidelity continues to be the goal in our translational approach to educational design.

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