Construction and Adaptation of an Open Source Rapid Prototyping Machine for Biomedical Research Purposes - a Multinational Collaborative Development

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ABSTRACT: In this paper we present bioengineering and biomedical research performed with Fab@Home and modifications to the system which improve its performance for these applications. At Cornell University, the Cardiovascular Developmental Bioengineering Laboratory uses the Fab@Home system for tissue engineering research to fabricate replicas of native cardiac valves using hydrogel mixes that include poly-(ethylene glycol) diacrylate (PEG-DA), poly-(ester amide) (PEA), alginate and a commercial photoinitiator. The printed porcine aortic valve demonstrates good shape fidelity and dimensional accuracy compared to medical scans of the valve. CTI has a team working to improve Fab@Home systems for biomedical applications by installing a linear guide with limit switches for deposition tools, attaching a device to align the tip for better deposition with two syringes and making improvements to the software for importing and manipulation of 3D models using high quality open source libraries.

1 INTRODUCTION

The field of tissue engineering develops methods for the treatment of chronic or acute diseases in novel ways via a synergy of biological knowledge and engineering design strategies. Twentieth century medicine was revolutionized by the repair of severe injury to the human body via prosthetic implants. These artificial prosthetics have allowed for substantial improvements to patients’ quality of life, but gaps in our understanding of the human body have limited the efficacy of wholly artificial treatments. Understanding the mechanisms governing recovery of injured tissues is now a major field of research and innovation, and treatments are being developed to engineer or regrow damaged organs rather than replacing them.

In recent years, many researchers have been focusing on utilizing the flexibility of rapid prototyping for computer aided tissue engineering (Sun & Lal, 2002) to plan complex surgeries, to construct tissue scaffolds (Wang et al. 2004, Pham et al. 2008), and to produce custom patient-specific grafts or replacement organs. However, most commercial machines are not suitable for non-industrial and research purposes due to their use of specialized, proprietary processes, and costly materials. Additionally, many commercial systems employ high temperatures, lasers, electron beams, or chemical crosslinkers which are, in general, hostile to biomaterials and living cells.

From this point of view, a viable choice for tissue engineering research is the Fab@Home open source rapid prototyping system (Malone & Lipson 2007). This inexpensive system uses the "robocasting" method of rapid prototyping and can achieve an accuracy of 0.1mm with a wide variety of materials. Unlike the majority of commercially available rapid prototyping systems, Fab@Home can employ multiple materials in the course of fabricating objects, which allows it to produce heterogeneous objects, such as working batteries or circuit boards (Malone & Lipson 2007). This accommodation of various materials also allows it to manipulate living cells and to develop scaffold structures capable of sustaining them (Cohen et al. 2006, Barbanti et al. 2005, Hutmacher et al 2007).

1.1 Biocompatible Fabrication Materials

At Cornell University’s Cardiovascular Developmental Bioengineering Laboratory, a two syringe Fab@Home Model 1 system has been adapted for printing cardiac valve replicas from cytotocompatible hydrogels. The hydrogel mixture was produced by dissolving 10% w/v 8000MW PEG-DA, 0.5% w/v Irgacure 2959 (Ciba Specialty Chemicals, Tarrytown, NJ), and 15% w/v non-medical grade LF10/60 alginate (FMC Biopolymer, Drammen, Norway) in PBS. Addition of alginate increases viscosity of the mixture to control its extrusion during the fabrication process. This mixture is then loaded into one of the two deposition tools.
The second deposition tool is loaded with a solution of 2% LF10/60 alginate and 3% Agarose Type IX-A (Sigma-Aldrich, St. Louis, MO). Agarose Type IX-A solutions have a gelling temperature of $\leq 17^\circ$C and melting temperature of $\leq 60^\circ$C. These temperature characteristics allow the agarose to serve as a washable support for unstable or non-freestanding elements of the valve structure during fabrication.

1.2 Replica Porcine Aortic Valves

Aortic valves were harvested from freshly slaughtered pigs at Shirk Meats (Himrod, NY), rinsed with cold sterile PBS, and preserved in formalin. The GE eXplore CT120 µCT (micro computed tomography) system (General Electric Medical Systems, London, ON) was used to scan the tissue at 100 µm resolution using 80 keV, 32 mA, 220 angles, and 16ms exposure time. The dataset was reconstructed using a modified Feldkamp method and exported to DICOM images using Microview (General Electric Healthcare) v2.2 software. The DICOM image set was analyzed via thresholding and region growing algorithms, and the set was then exported into stereolithography (STL) format. A mold structure was designed to support valve leaflets during the layered manufacturing process and also exported in STL.

For fabrication, a secondary platform was mounted onto the standard z-stage of the Model 1 system. The porcine aortic valve replica and the mold structure were fabricated directly onto this secondary platform using PEG-DA mixture and liquid agar solution at room temperature. The secondary platform was cooled using dry ice to maintain a surface temperature capable of immediately gelling deposited agarose during fab. After printing each layer, a handheld 365 nm UV light was exposed onto the hydrogel to allow crosslinking. The fabricated valve and support mold were then submerged in a water bath and gently heated to 60°C to melt away the agarose mold.

1.3 Findings

Multiple views of the original STL file and fabricated hydrogel valve are shown in Figure 1 for comparison. The printed porcine aortic valve demonstrate good shape fidelity and dimensional accuracy compared to the valves in STL format. Replication of anatomically accurate valves, however, is still incomplete due to the limitation in the Fab@Home Model 1 system. This is mainly due to the extremely high triangle counts and large range of feature sizes in STL file representations of the CT scan data, which can overwhelm the software and create path-planning errors that are detrimental to the quality of the fabricated object. Fabrication thus has been a laborious process that requires an observe to actively correct errors as they occur. It can also be a prolonged process that can take up to 9 hours due to the extremely slow fabrication speeds necessary to achieve fine resolution and detail. Although our preliminary results demonstrate promise in developing living heart valves, further software and hardware improvements are needed to allow the full potential of this technique to be utilized for tissue engineering.

![Figure 1. Fabricated valves in various angles. Top: Imaged valve in STL format. Bottom: Fabricated valve using hydrogel. Left: front view, Middle: top view, Right: isometric view (Bar = 1 cm).](image)

2 SYSTEM IMPROVEMENTS

At CTI, a Brazilian governmental research center, a two-syringe Fab@Home Model 1 system has been modified to enhance its suitability for biomedical and tissue engineering applications. The modifications include hardware and software enhancements which improve system automation, the accuracy of deposition, the ease of incorporating new materials, and which facilitates the use of ultraviolet light-crosslinkable materials.

We have developed an attachment to precisely control the linear movement of the stepper motor shaft that pushes the syringe plungers into the syringes. The linear stepper motors employed in Fab@Home operate by rotating a threaded nut around a threaded shaft, but linear motion of the shaft requires that it be prevented from rotating along with the nut. In the standard Fab@Home design, the threaded shafts are prevented from rotating only by friction between the plunger piston and the syringe barrel. With certain low friction materials, there is insufficient friction, and the piston and shaft will rotate along with the nut, resulting smaller linear motion than desired.

The Linear Guide attachment (Fig. 2) was designed to prevent this unwanted rotation. It is constructed of ABS polymer using a Stratasys FDM Vantage I, one of the commercial rapid prototyping machines available at CTI. We have also attached limit switches to the Linear Guide to make the system detect when material inside the syringe has been depleted, which
enhances system automation by signaling the system to pause for material to be reloaded.

The current Fab@Home software version cannot automatically generate support structures for complex or overhanging parts, but it is possible to design such supports manually using a design software tool, as was performed for the porcine aortic valve models described above. To accelerate the production of objects that incorporate multiple materials or which require a support material in addition to the structural material, the Fab@Home system is designed to control 2 or 3 syringes simultaneously. Figure 3 presents fabrication of a cell phone case using a 2-syringe Fab@Home system, using ordinary toothpaste as support and silicone rubber as the case. Fab@Home employs disposable polyethylene syringe barrels and attachable disposable tips. Because these tips are flexible and manually threaded onto the barrels, the location from which material exits the tips changes relative to the positioning system whenever the syringe or tip is replaced, which reduces the accuracy of fabrication.

To prevent this misalignment, we have developed an attachment to align the two nozzles. This attachment was also built in ABS polymer using a Stratasys FDM Vantage I and is pictured in Figure 3.

Most recently, we have developed a system that automates the exposure of photosensitive materials to ultraviolet (UV) light. UV light emitting diodes (LEDs) are attached to the bottom surface of the syringe tool structure. Figure 4 (left) illustrates the head with UV LEDs attached, and Figure 4 (right) shows the LED control board, which provides software control of a 24VDC, 1A relay suitable for general control purposes. The relay (and thus the LEDs) are controlled via commands sent from the Fab@Home software application to the microcontroller, which in turn sends digital output signals to the relay board.

The CTI group software team has invested effort in increasing the stability and usability of the Fab@Home software. We have added a Log window where all the system messages, including errors and user actions are shown for further consultation. Also, we have developed a new dialog box that greatly simplifies the adjustment of parameters for necessary to employ a new material with the system, reducing the time and quantity of material required to achieve satisfactory performance. This is very beneficial when working with experimental materials which may be time sensitive and costly or difficult to produce. This dialog (Fig. 5) allows users to easily modify parameters while the system is running, while the original method required the use to edit values in an external text file and manually notify the application of the changes.

The STL file format is the standard data exchange format for rapid prototyping, and is used by the
Fab@Home system as well. As is well-known, STL format does not perform well when models are very complex, as a very large number of triangles must be defined, and the chance of topological errors is significant. The original Fab@Home application uses its own STL import code, which lacks the sophistication to detect and correct topological errors. We have modified the software to use the open-source Visualization Toolkit (VTK) library from Kitware to import STL data. VTK allows intelligent merging of STL vertices to reduce topological errors. Also it allows decimation of the number of triangles in an STL mesh without changing its surface details, making possible to import high complex anatomic models without overwhelming the software (Fig. 6).

With the importation of 3D models using VTK library, we have been able to improve the path planning process so that the start angle and rotation angle for each slice can be controlled. This is very important to achieve dense but uniform filling of biological structures that are highly heterogeneous, because sometimes the quality and density of tool paths depends on the raster start angle of the parallel lines. Figure 7 shows that by controlling the initial raster angle it is possible to improve the final quality of the models by allowing small gaps to be filled.

Figure 8 shows several models that were printed using Fab@Home with CTI improvements, including a silicone cell-phone case (center) supported during fabrication with ordinary toothpaste (left), and ceramic parts (right) before furnace sintering (top) and after (cube, bottom).

FIGURE 6. Complex skull model from CTI database a) original model and b) using VTK reduce triangle count by 10%.

FIGURE 7. Toolpaths generated for one layer of a model of a tooth. By controlling the orientation of raster paths, at 15° a narrow gap can be filled (a), while at the default 45° rotation angle the gap will be unfilled (b).

3 CONCLUSIONS AND FURTHER WORK

As can be seen in the tissue engineering research presented, Fab@Home is a very adaptable tool for research applications, but the standard Fab@Home system requires improvements to improve its accuracy, efficiency, and ease of use for biomedical research applications.

Informed by the experience of users such as the Cornell University Cardiovascular Developmental Bioengineering Laboratory, CTI is making hardware and software modifications to the Fab@Home system. The linear guide and tip alignment attachments are making qualitative improvements to the accuracy of deposition with one or two syringes. The addition of limit switches which allow the system to respond automatically to running out of material, and the addition of a software user interface to allow online parameter adjustments save researcher time and valuable materials. By modifying the software to use more sophisticated data import algorithms and allow adjustment of the path orientations, Fab@Home can now work with more accurate biological models and can more accurately fabricate them.

We are in the process of quantifying the effect of these improvements on tissue engineering research, and will continue to work with to improve the Fab@Home system for biomedical (and other) applications.
4 ACKNOWLEDGMENT

The CTI team would like to thank the support of Frederico David Alencar de Sena Pereira who helped make some of the hardware implementations mainly the UV-cure attachment, of Renan Rodrigues dos Santos who started the graphical use interface improvements and, finally, of Renato Archer Information Technology Center for possibiliting the continuous development of this work, FACTI and CNPq by financial support.

5 REFERENCES


