Microvascular channel bioprinter shutoff valve

Product Design Specifications

BME 400 Design

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Function

On any given day, over 100,000 people in the United States are waiting for a life saving organ donation [1], [2]. The need for organs far exceeds the amount of organs donated per year. Because of this, many researchers are looking towards tissue engineering to fill the demand for transplants, as well as tailor them to a patient's specific needs. One of these methods is known as "bioprinting," which is the use of viable cells, biomaterials, or biomolecules in a 3D printer [3].

Within bioprinting there exist several methods, one such is "chaotic printing." Chaotic printing is a bioprinting strategy utilizing a kenics static mixer (KSM) to produce alternating channels of high resolution filament (less than 10 μm in width). These KSMs can be combined with a Continuously Extruded Variable Internal Channeling, or CEVIC, device to extrude these high resolution hydrogels into sheets while maintaining the alternating channel structure of chaotic printing. It should be noted that both the KSM and CEVIC devices are patent-pending [3].

Currently, the CEVIC devices can autonomously print hydrogel sheets of one resolution. If multiple resolutions from multiple KSMs are needed, the inputs must be manually changed. This takes time for the researcher and does not allow for a seamless transition between hydrogel channel resolutions. Therefore, the purpose of this project and the function of the device is to be an automatic valve to seamlessly shut off or switch between KSM outputs, and therefore hydrogel resolutions, ideally programmed so as to not need an operator.

Client requirements

The client has the following requirements:

- The shutoff valve can seamlessly switch between KSM resolutions.
- The shutoff valve can switch the KSM fluid without human intervention.
- The resulting vascular networks must maintain their resolutions (from 10 micrometers at the smallest to 1 millimeter at the largest).
- The resulting vascular networks must maintain their alternating pattern.
- The shutoff valve must limit dead space.
- The shutoff valve must be low shear on the cells passing through.
- The shutoff valve must be sterilizable via UV and autoclave and must withstand the following for 15 minutes:
    - 121°C [4]
    - 15 psi [4]
    - 100% humidity [4]
- The shutoff valve material must be biocompatible.

Design requirements

1. **Physical and Operational Characteristics**
    a. **Performance requirements:** The CEVIC device enables the fabrication of hierarchical, branching channels with continuous gradients in geometry and materials, effectively mimicking natural microvascular networks. Its main advantage is precise structural control, but the microvalve's slow opening (around 9.2 seconds for a 30 degree valve) due to pressure drop and oxide buildup limits rapid, dynamic switching in bioprinting [3]. The syringes must operate at a rate of 1 milliliter per minute and 0.5 bar. The kenics static mixers should be able to mix GelMA and HEC fugitive ink to ultimately form a consistent, cohesive striated composition pattern that can be printed. The KSMs should also be able to maintain a watertight seal when attached to the valve rotary. The valves near the KSMs should be able to shut on/off to allow the appropriate mixture compositions to be printed. The final fluid mixture is then transported to the nozzle output and should be able to extrude between 8 to 512 channels between 10 and 30 micrometers.

Printing can occur via an automated or manual process. In the automated version, pumps operate at a rate of 3.3 millimeters per second. In this setup, LabVIEW controls 2 rotary valves that switch between KSMs to control printing time and overall fluid composition. The automated electric rotary valve should be able to direct fluid to its appropriate KSM. In the manual process, the user must manually operate a stopcock on the valves to maintain hydrogel flow between KSMs without interruption.

b. **Safety:** The valve should be removable for sterilization purposes after each use. The manually operated valves should prioritize ergonomic design to ensure safe clamping and minimize potential injury risks during use. To reduce risk, the design should minimize direct contact with device components. A programmed pause feature can also be incorporated, allowing the user to safely adjust the equipment without concern of automated parts moving. The components should also be able to withstand autoclave temperatures. Proper precautions should be implemented to minimize safety risks in accordance with ISO 14971, 62366.

c. **Accuracy and Reliability:** The system should be able to operate with a high degree of precision and accuracy, given that capillary sizes are small (μm range) the morphology of the printed biomaterial is directly correlated to its function. The hydrogels undergo a sodium alginate and $CaCl_2$ reaction to cure the hydrogel, ensuring its structural integrity and durability.

   A 10 percent error between measured and theoretical channel widths, which stresses the importance of incorporating valve shutoff mechanisms to avoid depositing too much/little bioprint fluid. Additionally, it is critical to expose the hydrogel to $CaCl_2$ while it prints to help improve thickness uniformity and minimize disruptive channel flows.

   Finally, transition lengths between varying channel number regions were around 1 centimeter [3]. However, decreasing the fluid output rate and automating the valve switch could help achieve reduced transition lengths which would enhance the reliability of the hydrogel.

d. **Life in Service:** The device must be able to operate for 5 minutes for each hydrogel sheet. Over time the device should be able to print multiple hydrogels per hour.

e. **Shelf Life:** The shutoff valve is expected to maintain reliable performance for approximately 5 years.

f. **Operating Environment:** Materials must be biocompatible in accordance with ISO 10993 and capable of withstanding operating temperatures up to 70 degrees celcius. Standard laboratory conditions will apply during use, with ambient temperatures maintained between 20 and 25 degrees celsius and relative humidity in the range of 35–50 percent relative humidity, as recommended for controlled laboratory environments [5].

g. **Ergonomics:** Valves should be designed to minimize shear stress on the materials passing through and must allow intuitive manual operation with a controllable flow rate as low as 1 milliliters per minute [3]. The motors controlling the valves should be able to be neatly and compactly integrated within the device to prevent interference with biological samples and to isolate electrical components from user contact.

h. **Size:** The KSMs are about 12 centimeters in height and 1 centimeter in diameter, with channel flow rates ranging from 1 to 1.5 milliliters per minute. It is important to account for physiological dimensions, including artery and capillary diameters, as well as the distance between capillaries and cells in the body. The smallest arteries measure roughly 150 microns in diameter, while the smallest capillaries are approximately 10 microns [3]. A capillary must be within 50 to 70 microns of every cell in the body in order for the cell to have sufficient blood flow. Accordingly, the CEVIK device must be able to print within these dimensional constraints. The current manual valve to select the channel the bioink flows through is 16 centimeters in width and the current automatic valve to select the KSM is 5 centimeters in diameter [3].

i. **Weight:** The shutoff valve, positioned around either the manual or automatic rotary valve, should not exceed 10% of the total system weight. This restriction ensures that the valve remains sufficiently lightweight to operate effectively without compromising the performance of the mechanical components [6].

j. **Materials:** The CEVIK device and KSM are fabricated using clear biocompatible resin. The material selected for the shutoff valve must be chemically compatible with this resin, ensuring that it does not cause degradation or alter its properties. A solution of 3 percent GelMA and 2 percent sodium alginate is usually heated to allow it to flow through the KSMs [3].

k. **Aesthetics, Appearance, and Finish:** The shutoff valve should integrate seamlessly with CEVIK machine and any relevant connected components without causing excessive wear or interfering with functionality.

2. **Production Characteristics**

a. **Quantity:** The client requires only 1 to 2 units. For testing purposes, 5 units will be produced to support the testing requirements. The testing protocol will involve repeating experiments with the same prototype across multiple runs to ensure reliable and statistically meaningful results.

b. **Target Product Costs:** The total budget is $500, with a target cost of $15 per unit. Most expenses are expected to arise from 3D printing materials, with some additional electronic components purchased separately. The actual production cost for 5 units, estimated at $75, is projected to remain well below the allocated budget.

3. **Miscellaneous**

a. **Standards and Specifications:** Production and testing will follow established standards to ensure accuracy, safety, and regulatory compliance. The protocols and reference materials described below define the requirements for fabrication, measurement, and validation of the prototypes. Fluidic resistance measurements follow standard protocols using pressure steps (5 and 10 milibar) with controlled flow intervals (30 seconds), employing ISO-calibrated instrumentation such as the Druck DPI520 pressure controller and Sartorius MC1 LP620P scale, ensuring traceability and compliance with ISO 9001 and ISO/IEC 17025. EN-ISO 10993-1:2009/AC:2010 (Class I Biocompatibility) is referenced for guaranteeing biocompatibility and safety for direct or indirect biological contact, which is critical for cell culture applications and potential medical device use.

b. **Customer:** The client prefers that the valve be programmable to run for different combinations KSM, thereby reducing operator time and effort.

c. **Patient-related concerns:** This device is not patient contacting, therefore there are no patient-related concerns. This device does not store any patient data. However, this device may come into contact with a cell-seeded bioink. Therefore, the material and finish of the device should be biocompatible, non-toxic and low-shear to prevent unnecessary cell death and cell rupture.

d. **Competition:** There are numerous bioprinting valve techniques that have demonstrated low leakage rates and adaptability for systems operating at resolutions as fine as 10 micrometers. The Continuous Chaotic Bioprinting of Skeletal Muscle-like Constructs produces multi-layered, multi-material filaments with microvascular channels at resolutions down to 10 micrometers, demonstrating strong potential for complex tissue architectures [7]. The chosen material, alginate hydrogels, presents a challenge as it may not be optimal for clinical translation [7]. Configurable 3D Printed Microfluidic Multiport Valves with Axial Compression use stepper motor control for precise, automated switching, with no leakage in static tests and less than 0.5 percent in dynamic use [8]. The testing configuration used 800 micrometers channels, which are relatively large, raising uncertainty about performance at the smaller sizes needed [8]. The

novel on-chip liquid-metal microvalve enables precise directional control of fluid flow, with no leak detected at pressures up to 320 millibar and a leak rate of less than or equal to 0.043 microliters per minutes at 330 millibar [9]. The method does not address sequential layering or branching between K mixers, requiring adaptation for applications involving complex fluid routing [9].

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