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Mini Review

Emergence of Data-Driven Microfluidics

Takasaki Yumi*

Department of Material Science, Tsinghua University, China

ABSTRACT

Microfluidic devices currently rely on researchers to select the initial operating conditions empirically, then monitor and modify parameters throughout studies to achieve and maintain stable conditions that produce repeatable data. Multiple factors can cause inconsistent experimental conditions in polydimethylsiloxane-based microfluidic devices, including fabrication flaws, clogging, bubble formation, chemical impurities, or long-term effects like temperature and pressure fluctuations, surface fouling, and substrate deformation. Because of the adsorption of hydrophobic small molecules, these differences can alter chemical synthesis by changing solution concentrations or biological analyses. In this section, we discuss new research on the application of machine intelligence in microfluidic chips in conjunction with optical microscopy. This method has been used to forecast droplet size and stability, as well as to assess droplet chemical composition and fluid characteristics, as well as to monitor and correct flow rates and droplet sizes to avoid undesirable consequences such as bubble formation. Multiple inputs are converted into low-dimensional feature representations (codes) using autoencoders, which can then be processed and decoded to reconstruct the inputs.

Keywords: Microfluidic; Emergence; autoencoder; isopropanol

INTRODUCTION

These techniques are primarily used in unsupervised machine-learning models, which do not require labelled data. Khor employed an eight-dimensional code to learn the geometry of droplets in a concentrated emulsion and used it to forecast whether the droplets will shatter or stabilise using a deep convolutional autoencoder. Drop skewness, elongation, throat size, and surface curvature were identified as four of the eight dimensions in the code, and these characteristics were shown to have a substantial impact in determining emulsion stability. Meanwhile, Dressler looked into using machine learning to control volumetric flow rates in a microfluidic channel [1]. The researchers used a deep Q-Network, which is a deep neural network that uses end-to-end reinforcement learning, as well as a model-free episodic control, which is based on hippocampal learning and memory. Reinforcement learning is a method of training algorithms that uses a cumulative reward scheme. The scientists used a range of 0.5–10 mL/min to train their models by altering the flow rates of the dispersed and continuous phases of a double laminar flow and a water-in-oil emulsion at random.

The algorithms were able to monitor the volumetric flow rates using an optical microscope. A scalar reward was assigned to each iteration based on the current and intended interface location or droplet. The algorithms adjusted the flow rates of each phase in 0.5-mL/min increments based on the phase's size. The two models were able to learn appropriate flow rates and locate an interface at any point in a double laminar flow while controlling the sizes of water-in-oil droplets in this way. Two human testers were trained to execute the identical tasks as the algorithms, and their results were compared. The deep Q-Network improved its performance algorithmically up to human level in the control of interface placement over 27 hours. Meanwhile, the model-free episodic control reached peak performance after just 2 hours, stabilising at 90% of human performance. Both systems exhibited constant above-human performance in droplet size control, but the model-free episodic control did so in a matter of minutes, whilst the deep Q-Network required 20 hours of training [2]. The network design was found to play a substantial effect in the performance of each activity, implying that alternative models should be implemented and tested to determine the most suited to tackle a problem. Convolutional neural networks use a combination of convolutional and pooling layers to turn inputs into stacks of feature maps, allowing for powerful image identification. In a microfluidic device, Hadikhani used a deep convolutional neural network to forecast the volumetric flow rate and concentrations of each component in water/isopropanol droplets.

The network was trained on photos of droplets at various flow rates and water/isopropanol concentrations, allowing it to distinguish morphological characteristics related with flow rate

***Correspondence to**: Takasaki Yumi, Department of Material Science, Tsinghua University, China, E-mail:-yumitak@gmail.com

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and isopropanol dilution. The authors speculated that this method may be used to evaluate the chemical compositions of various mixtures in droplet microreactors, as well as to forecast other fluid properties like surface tension and viscosity, which are significant in the production of a range of microparticles. Fluid property prediction has also been explored from a different angle. Using the dimensionless capillary and Reynolds numbers of the two phases as inputs, Mahdi and Daoud51 proved that a deep neural network can predict droplet sizes in a water-in-oil emulsion. These figures are related to the flow rate, microchannel diameter, and fluid parameters including viscosity and surface tension. These findings show that using a mix of optical monitoring and neural networks, it may be possible to infer numerous fluid parameters in microfluidic chips. We've talked about how machine learning can be used to forecast or correct parameters during microfluidic device operation [3]. Furthermore, ideal device designs that give tailored behaviours can be predicted. In the field of flow sculpting, this concept has recently been shown. Flow sculpting is a technique for using fluid inertia to shape the cross-section of flows within microfluidic channels. It has applications in the production of nanomaterials and microfluidic manipulation, such as the creation of microfibers and microstructures with variable tridimensional geometries and the selective transit of microparticle-laden flows around cells or particles. When the size of pharmacologically active molecules is reduced to the nanoscale, they have improved bioavailability, which is a benefit of nano-sized dosage forms in pharmaceutics.

DIFFERENT TYPES OF FABRICATION TECHNIQUES

Target ability

The design of microfluidic reactors is examined in light of the attention that nano-sized dosage forms have generated. The system consists of both "soft" vesicular systems (like liposomes) that are dynamically in equilibrium after preparation and "hard" organic nanoparticles that are kinetically stable after preparation (such as micelles, polymer-based liposomes, and polymerases). The rate of animal exchange must be taken into account in order to accurately classify "hard" nanoparticles as "frozen" core micelles.

In recent years, pharmacological research apparatus has been built using microfluidic technologies. Using organ-on-a-chip technology, for instance, to examine chemical reactions, to synthesise micro-simplifications, to research the mechanics of drug-device combination goods. These tools offer a number of benefits that make them desirable technological platforms for generating particles with carefully regulated size distributions and examining the creation of nanomaterials by integrating various measurement systems into the microreactor. Despite its potential, few research have thoroughly examined the microfluidic techniques for making organic nanomaterials. We will also discuss the advantages of microfluidic technology for researching and comprehending the production of nanomaterials. The use of microdevices in nanomaterial study and manipulation is then discussed, with examples of how microfluidic devices might be useful tools for examining nanomaterial synthesis [4]. Additionally discussed is the biological activity of nanoparticles produced using microfluidic technology.

Moulding

The expansion of microfluidics in recent years has largely been fueled by the creation of novel materials for microfluidic chips. Microfluidic chips and multiple readily available materials for the manufacture have been stimulated by the search for various methods to integrate microfluidics with biological cell research, as demonstrated in. Because of its ongoing development, microfluidics has become a crucial enabler technology in biological research. Glass and silicon were used to create the first microfluidic devices. Due to their exceptional inertness, strength, and thermo-conductivity, these materials are suitable for solvent-based methods and high-speed capillary electrophoresis. Because they are gas-tight, these microchannels cannot support long-term cell culture. After silicon and glass, several silicon-based elastomers—in particular, polydimethylsiloxane (PDMS)—became the primary components for microfluidic chips. PDMS is a gas-permeable polymer that is perfect for creating integrated valves, as shown by numerous landmark demonstrations in cell-related Microfluidics. PDMS is the most frequently used material for frames despite hydrogels becoming more and more popular because of its great optical and mechanical capabilities, low cost, and flexibility. For the integrated hydrogel designs, in-situ scaffolding channels. To satisfy the various requirements of culture-related microfluidic devices, novel PDMS device implementations are continually being researched [5]. The material's adaptability has been one of its strongest selling points. One essential component is integrated pneumatic valves. Over a million pneumatic valves per square cm made up the highest integration density in PDMS. Additionally, programmable PDMS valve arrays were used to create composite materials. Researchers have developed cell-filled microfibers with pneumatic valves that identify the contents of each fibre segment using this technology, which is backed by laminar flow manufacturing. A perfect example of this is the work of Ingber and colleagues, who used a flexible hybrid membrane constructed of PDMS as the framework for a delicate device to mimic the function of the lung.

A porous PDMS thin membrane coated with cell-filled hydrogel, used to replicate the lung interface, was used by the scientists to separate the device's two chambers. They connected the membrane to adaptable PDMS chambers at both ends, enabling pneumatic stretching of the membrane. Because of this, the device may be able to restore lung function. The Jiang group's effort on creating a hybrid bio-membrane framework into a one in terms of material, technique, and the main applications of the devices is another significant accomplishment. A comparison of the various materials that can be used to create microfluidic platforms. Adapted from the sources in the literature. Cost-effectiveness of the substrate Elastomer

Fused Deposition Moulding

Plastic Hydrogel Paper Excellent Mechanical Strength Excellent Fabrication, Process Excellent Poor Sterilization Ease. Toxicity Outstanding Surface Functionalization Transparency minimal auto fluorescence Outstanding Excellent Poor Microchannel Width: 1 m, 100 nm, 1 m, and 1 m Fluorescence that varies Outstanding Negative Cell culture development is Excellent Bioelectronics and biosensors: X 10 (2022) 100106 structure with three dimensions. When a load was applied, the hybrid membrane rolled back to form a tube-like structure mimicking a blood vessel after the researchers placed a cell-filled hydrogel layer to a pre-stretched PDMS membrane. Fused deposition modelling is the most popular extrusion-based 3D printing technique (FDM). Using a nozzle, extrusion-based technologies print several two-dimensional layers on top of one another. In fused deposition modelling, the materials are melted

in the nozzle and then extruded into the layer, where they connect and cool. After the initial patent expired, other companies created and enhanced the method, leading to a practical process and a wide range of improvements. The biocompatible thermoplastics that can be employed with this strategy include ABS, PLA, polycarbonate, polyamide, and polystyrene, to name just a few. Nanocomposites and reinforced polymer composites are examples of composite materials. In addition to the usual materials, these ones can be used. Additionally, objects comprised of multiple materials, such as a sacrifice, can be printed using the FDM. a substance (Figure 1). It is suitable for a range of applications because of its low cost, small footprint, speed, and simpler fabrication process. Additionally, because the filament sizes for microfluidic channels are very large, 3D printed parts are vulnerable to leakage. The three-dimensional printed ability structures are impenetrable depending on the material, extrusion conditions, channel design, and fluid used on that channel. Although it can only be used with low melting point thermoplastic polymers, has a limited resolution, and cannot be controlled for surface roughness, among other drawbacks, FDM has gained popularity in comparison to competing 3D printing technologies like stereo lithography [6].

Stereo lithography

Layers are built on top of layers using the classic, quick, and revolutionary technique known as stereo lithography. It works well for swiftly producing very fine features. It uses a pool of resin that has been polymerized using a controlled light source to create each layer. Although some resins can be created with longer wavelengths, stereo lithography primarily utilises UV light. The photo-initiators utilised in this dependency on the polymerization wavelength are intercalated by adding a liquid resin to the polymer molecules. The two most popular ways to expose the photopolymer to light are stereo lithography equipment (SLA) and digital light processing (DLP) [7]. SLA devices use a concentrated lamp (light emitting diodes) laser with a scanning Galvano mirror for applications to cure spots on the vat's surface. This technique is used by many commercial printers. For custom-built 3D printers, a DLP projector is a more popular option. "Free Surface" and "Constrained Surface" combinations are the two types of layering. The most common stereo lithography setup at the moment is "Constrained Surface." The bath must be the same height as the structure in the "Free Surface" configuration. In proof-of-concept

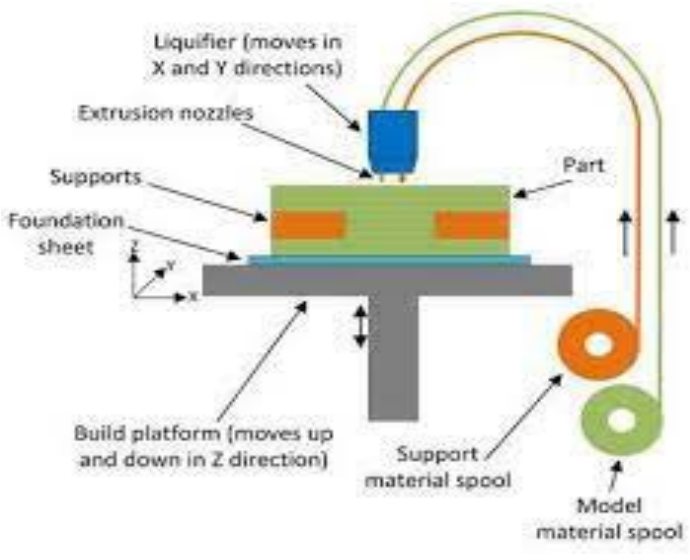

Figure 1: Schematic of fused-deposition modelling (FDM) process.

microfluidics demonstrations, SL printers have been used to print micromixers, cell sorting apparatuses, contrast synthesisers, and micro-needles [8].

CONCLUSION

The current developments, current difficulties, and future directions at the nexus of biomedical engineering and microfluidics are surveyed. The developments in microfluidics for biomedical engineering, including its use in bioassays, bio-fabrication, and drug delivery, put the spotlight on the fundamental concepts and emerging research directions in the discipline. To determine whether novel microfluidic techniques for clinical research offer valuable capabilities, they should be compared to more established techniques. New real-world applications, ranging from the use of cutting-edge industrial procedures to specialised medicines and diagnostics for med-tech, will be made possible by the emerging breakthroughs in microfluidics. Despite tremendous advancements in microfluidics, there are still many obstacles to overcome before such frameworks can be fully and effectively integrated into applications like routine clinical diagnosis. To accomplish this, the systems must be adaptable, user-friendly, and durable. The development of clinical diagnoses and testing, such as bioassays for patient clinical indices, point-of-care testing, home testing, and the regeneration of organs on human-on-chip systems, would also be on the future roadmap for microfluidics-based platforms. Additionally, combining various technologies makes microfluidics better and allows it to develop further in the biological and medical domains. It remains a significant challenge to strengthen multidisciplinary research between microfluidics and end users. As a result, the biomedical sector has seen significant technological advancements on a clinical scale.

Declaration of Interest

The authors have no conflicts of interest to declare.

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