Review

Applications of Hydrogels in Microfluidic Devices

Jasper Fiscus[1] and Kian Hageman[1]

[1] Department of Biomedical Engineering, University of Iowa, Iowa City, Iowa, United States

Abstract

Hydrogels have emerged as a versatile biomaterial for integration into microfluidic devices, as not only is there high biocompatibility, but they also have tunable mechanical properties giving them the ability to mimic native extracellular matrices (ECM) for biology and biomedical microfluidic applications. In these systems, hydrogels are widely used to support two-dimensional and three-dimensional cell cultures models, enabling controlled studies of cellular interactions under physiological flow conditions. Additionally, hydrogel based microfluidic platforms are applied in drug screenings and delivery studies, where the porous structure allows for diffusive transport releasing therapeutics (chemotherapies). Stimuli-responsive hydrogels further expand uses acting as passive valves, sensors, and actuators responding to stimuli whether it be chemical, thermal, or mechanical without needing external power. This integration of hydrogels into microdevices has advanced the understanding physiologically relevant in vitro models, improving experimental throughput, control over microenvironments, positioning hydrogels to be essential in tissue engineering, disease models, and research.

1 | Introduction

The use of hydrogels in microfluidic devices has become increasingly popular in the past 15+ years. This can be tracked by the number of research papers being published each year, rising from over 4000 in 2017 to 6500+ papers in 2021, and the number grows each year [18]. Hydrogels are water-rich polymer networks created by cross-linking polymer chains into 3D networks that can absorb large amounts of water relative to their size. Hydrogels can be made of natural materials like collagen or gelatin, synthetic polymers like PEG, or semi-synthetic polymer blends like GelMA[18]. The material, percentage of cross-linkage, other chemical additives, and the method of fabrication of the hydrogels determine end hydrogel material properties such as biocompatibility, water porosity, stimuli sensitivity, mechanical strength, degradability, and more[18],[4],[30].

1.1 | The significance of Hydrogels for Microfluidic Applications

The significance of hydrogels in the microfluidic world cannot be understated. Most importantly, their material properties and ability to tune properties allow them to closely mimic the biochemical and biostructure micro-environments for cell cultures. Being able to transport nutrients, biochemical signals, electrical response, and more. Hydrogels can be formed in constructed in many ways, allowing researchers to produce bioengineered micro-environments or other flow channels that allow for chemical or biological environmental interactions. Their ability to act as valves, sensors, and actuators is imperative for cell culturing and drug response research and devices[35],[52],[32],[34].

1.2 | A Brief History of Hydrogels in Microfluidic Applications

A brief history of hydrogels in microfluidic devices is in order. The first published use of hydrogels for biological applications was in 1960. Published in Nature magazine, O. Wichterle and D. Lim introduced a hydrogel based on glycolmethacrylate that, when cross-linked and loaded with water was able to mimic native tissue behavior, establishing hydrogels as a viable biomaterial for biological and medical applications[45]. Most research conducted between 1960 into the late 90s focused on wound dressings and drug delivery [18]. During the late 1990s through the 2000s microfluidic devices made their appearance and quickly became a pivotal research tool in labs all around the world[12].

In 2007, Yibo Ling and his team from Massachusetts Institute of Technology (MIT) in Cambridge MA, published a research paper using cell-laden microfluidic channels made out of hydrogels to study cell culture response[26]. From 2007 and onward, improvements to the microenvironment created by hydrogels in microfluidic devices grew. Today's research includes organ-on-a-chip, cell culture, engineered micro-environments, and much more[22].See Figure 1 for a more visual representation of history.

1.3 | Defining Hydrogel Applications in Microfluidic Devices and Scope

Microfluidic devices are patterned fluid flow channels and mechanisms that typically

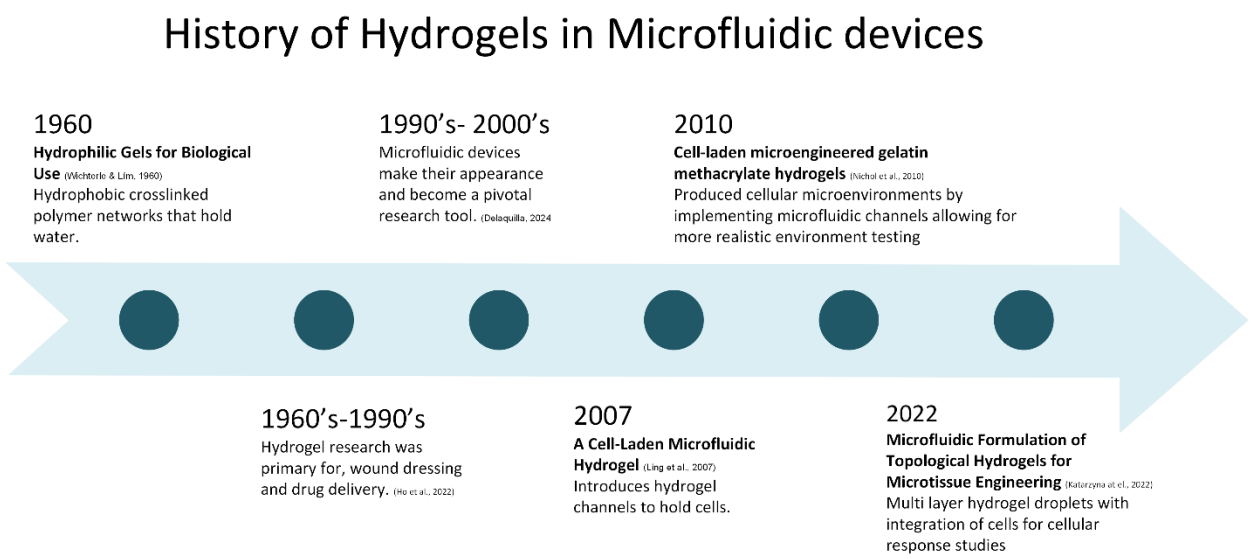


Figure 1: History of hydrogels in microfluidic devices. From the first biological use of hydrogels in 1960 to todays advanced multi-layer hydrogel droplets and lab-on-a-chip applications.

process small amounts of fluid from nanoliter to milliliter volume scales [28]. The exact size of a particular device and what constitutes a device requires a more granular definition. For the purposes of this paper, the application of hydrogel in microfluidic devices is defined into two parts. First, the device must use or create hydrogels, whether it be to supply vital fluids, biochemical signals, create a chemical reaction, or serve as a boundary layer for its mechanical properties. A hydrogel must be used as a part, a subsystem within, as the device itself, or created by the device. Secondly, the device must have micro-sized fluid flow. In the form of channels, perfusion, or other movement mechanisms.

2 | Current State of the Field

2.1. | Fabrication Methods of Hydrogels

There are many different methods of creating hydrogels for any particular application need, however, there are some common approaches shared by many. Hydrogel fabrication typically includes one of the following: molds, droplets, fibrous spinning, and 3 Dimensional (3D) bioprinting.

Molds are the most common method of fabrication. Typically created with polydimethylsiloxane (PDMS) using photolithography and soft lithography, device negatives are produced and reused. Other materials like glass, acrylic, silicone, and other materials are used to create models. Depending on the mold material, it can be fabricated with traditional additive or subtractive manufacturing processes. Additionally, with the ever-evolving and improving field of 3D printing, is has become popular to create hydrogel models in 3D printers. 3D printing molds are particularly popular for larger scale microfluidic devices, where the resolution of the printer plays a minimal role in the device's functionality[48],[9],[52],[36].

Hydrogel Droplets are formed in many ways, but one particularly popular way is to use

an oil slipstream around an outlet tube, pushing hydrogel through the tube, which produces droplets. These droplets can be layered to form hydrogel capsules. These droplets can be used to study individual cell responses, to chemical reaction batches, and drug delivery systems[51],[46],[47].

Fibrous spinning occurs in a similar fashion to droplet formation. In one study done in Switzerland, out of the Swiss Federal Laboratories for Materials Science and Technology, researchers used glass tubes with a primary and secondary inlet ports. Then, they placed up to three sequentially. In order to keep the glass aligned, they were placed in PDMA and attached together with LEGO plates to create a multi-layer strand of hydrogel that can be assembled into more complex structures [44].

3D Bioprinting is relatively new in the hydrogel production realm. With an explosion of papers around 3D Bioprinting being published in 2015[38],[17]. 3D bioprinters are primarily custom built or modified with the few off-the-rack solutions like 3D-Bioplotter from Desktop Health costing $100,000+ range[27]. Bioprinters allow researchers to create complex 3D flow for cell culture and organ-on-a-chip research. Some custom-made 3D bioprinters feed 3 or more materials at once. A study done at Rowan University printed a device onto a glass slide, printing semi-stable cell-laden GelMA solution, GelMA itself, and PEGDA plastic as a substrate support system. Creating a 3D flow cell culture model that would otherwise be impossible or extremely impractical to producing using traditional methods[34].

2.2 | Applications of hydrogels in Microfluidic Devices Categorization

After reviewing the current and past literature around hydrogel applications in microfluidic devices, there seem to be four distinct application categories for current research in the field. These are 2D fluid flow cell culture, 3D fluid flow cell culture, drug delivery, and sensors[31].

The differentiation between 2D and 3D flow is significantly important due to the complexity of the devices. In 2D flow, fluid either moves through a channel or over a plane. As a test of 2D fluid flow, if the device can be fully explained by a single “top-down” view of the device, it is 2D. If the device has lateral and transverse fluid flow, then it is 3D flow. If the device requires multiple parallel planner cuts to visualize and understand the fluid flow it is considered 3D[2],[14]. See table one and figure two for more detailed and visual information about the differences between 2D and 3D flow cell cultures.

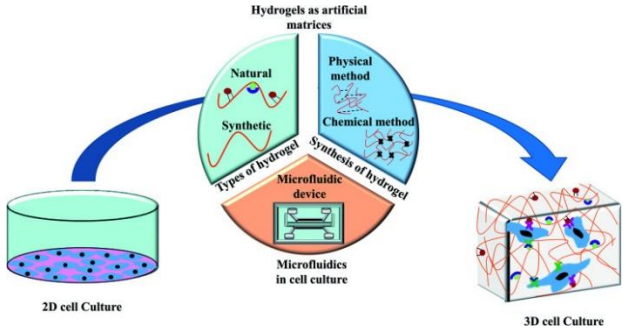


Figure 2: Pulled from an article reviewing 2D and 3D hydrogel cell cultures, it better illustrates a 2D cell culture and 3D cell culture[2].

Table 1: Comparison between two- and three-dimensional flow in microfluidic devices containing hydrogels[14].

Feature/function	In 2D	In 3D	Ref.
Tissue-specific architecture	Poor	Rich	[220]
Cell morphology	Flat, extended	Round, contracted	[17,221]
Interactions	Limited	Multiple	[38]
Cell motility	Fast, free	Slow, restricted	[6]
Cell adhesion	Weak	Strong	[222]
Cell growth	Directional	In all directions	[6,223]
Cell proliferation	High	Low	[5,6]
Apoptosis	Induced	Tissue-like	[223,224]
Intracellular stiffness	An order-of-magnitude higher in 3D		[4]
Cell polarization	Partly	Full	[6]
extracellular matrix remodeling	Absent or poor	Present	[5]
Fluid perfusion	1D	3D	[170]
Signaling and diffusion	Asymmetric	Nearly symmetric	[225]
Metabolic rate	High	Low	[223]
Cell survival when exposed to cytotoxic agents	Low	High	[226]

2.3 | 2D Fluid Flow Cell Cultures

Most microfluidic cell cultures incorporate 2D flow fields due to ease of manipulating planar flow, despite culturing in 3D hydrogel matrices[49].

A team of researchers from the University of University of Wisconsin-Madison led by Virumbrales-Muñoz, developed a hydrogel based microfluidic platform to model the tumor microenvironment using glioblastoma cells under controlled flow (see Figure 2). The device incorporates PEG-encapsulated hydrogels to support the cancer cells 3D cell architecture, which can't be achieved on conventional substrates like Petri dishes. Perfusion channels allow for control of nutrients and chemotherapies, enabling diffusion-limited mass transport mimicking in vivo tumor conditions. Cell viability was seen over several days, especially in regions exposed to steeper gradients. Providing a platform to capture key biochemical and mechanical cues of tumor microenvironment, enabling studies on tumor behavior and screening therapeutic responses that are no accessible with traditional 2D cultures (Virumbrales-Muñoz et al., 2019).

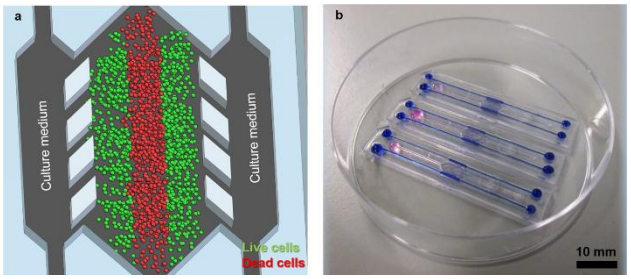


Figure 3: a. Top down view of perfusion channel on both sides, with hydrogel matrix for mimicking TME in the center. b. Full view of microfluidic array[41].

A group out of Harvard Medical School worked around a limitation of traditional PDMS devices creating a hydrogel-coated channel for cardiomyocyte culture (see Figure 4). Conventional PDMS channels are stiff and hydrophobic, preventing cellular adhesion. To overcome this a photocrosslinkable hydrogel precursor composed of gelatin or tropoelastin coated the inner channel, then subsequently cured, permanently bonding the hydrogel to the PDMS surface to create a suitable surface for cardiomyocyte culturing. Exhibiting improved attachment and coordinated contraction, allowing the system to mimic native cardiac function for drug response studies for Lab-on-a-chip applications[3].

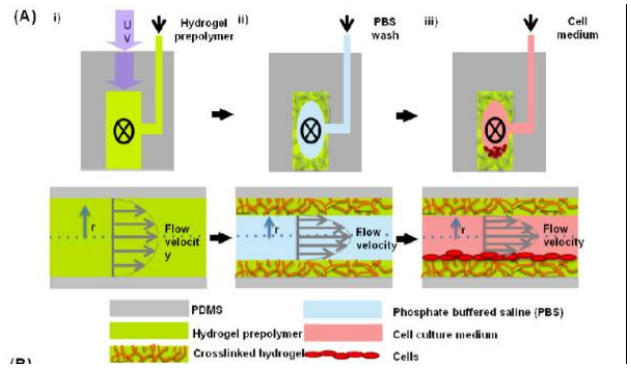


Figure 4: a. Schematic of hydrogel coating of PDMS microchannel via prepolymer injection, UV crosslinking, PBS wash, and cell seeding under 2D flow[3].

Researchers from Boston University created a technique for the fabrication of embedded microfluidic channels utilizing molded gelatin hydrogels as a sacrificial element. To create the arrays, gelatin structures were patterned to then be surrounded by a secondary hydrogel, then the gelatin structures were removed creating a perfusable microchannel. This enabled rapid manufacturing of these hydrogel-based architectures without a harsh processing environment, creating an early foundation for hydrogel integration into microfluidic systems[15].

The last 2D flow cell culture article is from the University of Washington in Seattle, looking at in vitro microfluidic vessel models to study the assembly of von Willebrand factor (VWF) under controlled shear conditions. They used a microchannel coated in endothelial cells to recreate 2D flow fields, providing visualization of VWF fiber and web formation under pathological shear stresses. Having controllable flow rates and shear profiles, allowed the authors to capture the mechanism of thrombus formation unobtainable in typical 2D culture systems[52].

2.4 | 3D Fluid Flow Cell Cultures

While 2D microfluidic flow systems have had extensive review of cellular behavior under controlled conditions, but they are inherently limited in their ability to replicate native 3D extracellular environments. To address this researchers have developed fabrication methods using hydrogel for bioprinting to simulate complex flow patterns and multicellular organization[6].

One approach described by researchers at Harvard uses sacrificial templating to form perusable vascular network in hydrogels. The enabled lumen reconstruction and immunofluorescence imaging of the resulting vasculature; however, fabrication fell short resulting in workflow like 2D flow arrays due to reliance on planar soft lithography and sacrificial elements. Consequently, making a slow throughput than 3D hydrogel systems.

The U-IMPACT (see Figure 5), developed at Rowan University, used injection-molding as an alternative route to create a 3D microfluidic device, to support 3D co culture systems. The device enables modeling of biological processes like angiogenesis and vascularized spheroid formation, highlighting the feasibility of hydrogels in organ-on-a-chip applications, using a mold-based fabrication approach for 3D geometries[23].

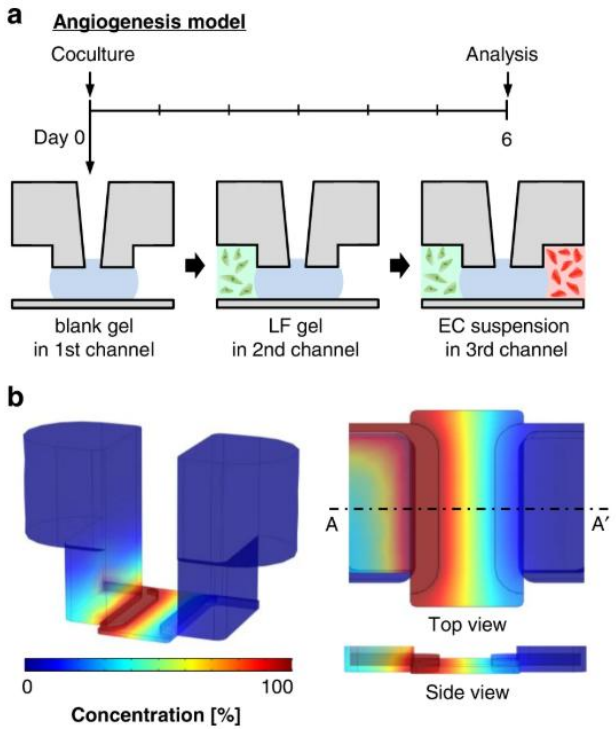


Figure 5: a. Loading of hydrogels for angiogenesis coculture model b. Simulated concentration contour of diffusive transport and gradient formation across hydrogel channels[23].

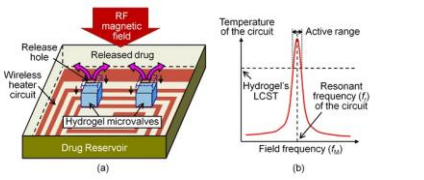
Similarly, at Seoul National University introduced a rail-based open microfluidic fabrication strategy that alters capillary pressure defined by channel geometry and surface properties to pattern hydrogels within predefined regions. With

just a pipette, aspiration is done to remove excess material while keeping retained materials to designated channels, resulting in 100 parallel channels. While this method simplifies patterning of hydrogels, it remains sensitive to manufacturing tolerances, highlighting the[32].

2.5 | Drug Delivery

Most drug delivery found was concentrated in microfluidically derived hydrogel droplets/spheres. However, other devices are out there[42],[47],[35].

A group from the University of British Columbia, led by Rahimi, created an implantable hydrogel-based microfluidic drug delivery system (see Figure 6). The devices use thermo-reactive hydrogel microvalves utilizing wireless radio frequency (RF) actuation. The thermos-reactive hydrogel is surrounded by embedded planar inductive copper coils and a resonant LC circuit that, when placed over a drug reservoir, creates an on-demand drug delivery system. The group demonstrates reliable valve operation with a narrow frequency range around 2 MHz, creating a 20 °C change in temperature. This system does not rely on an on-board power supply, showing the effectiveness of wirelessly controlled device integrated hydrogel actuators and their ability to deliver drugs in a controlled manner[35].



(a) Drug delivery device with frequency-controlled wireless hydrogel microvalves. (b) Working principle of the device

Figure 6: RF magnetic field activated microvalves releasing drugs[35].

Hydrogel microdroplets are used for drug delivery throughout the gastrointestinal (GI) track, a classically difficult environment to work in with hydrogels due to their poor mechanical properties and harsh pH, temperature, residence times, heat levels, and more throughout the GI track[7].

Hydrogels designed to release in the stomach often utilize buoyant hollow carriers to ensure the hydrogels stay within the stomach. Cheng Zhao's group used the "Cheerios effect," where floating objects, in this case hydrogels, are drawn towards the edge of the fluid's container walls. Developing hollow microbubbles within the hydrogel droplet structure to adhere to the stomach wall. The group used a microfluidic electrospray platform that utilizes coaxial two-phase flow with an electrostatic field to produce hollow particles with precise control, creating gas-trapped liquid spheres that were then placed into hydrogel droplets[50].

In the Large intestine with a much higher pH than the stomach, Bahman Homayun's group out of the University of Alberta used a microfluidic flow focusing devices created with cylindrical glass capillaries to create therapeutic drug laced hydrogel filaments that where then turned into hydrogel droplets/spheres to create pH responsive drug delivery that would open in the large intestine[24].

A more recent study out of Tsinghua University in Beijing used magnetic core-shell hydrogels to create magnetic thermosensitive hydrogel droplets for on-demand drug delivery. Looking to tackle malignant tumor cells, they used droplet microfluidic principles to create hydrogel droplets with embedded iron oxide (Fe_3O_4) in the shell and therapeutic cancer drugs in the center. When exposed to an alternating magnetic field, the iron generates heat, releasing the drugs. Heating also enables

hyperthermia effects that can aid in selectively damaging cancer cells[8].

2.6 | Sensors

Sensor applications of hydrogels in microfluidic devices range from pH sensors, point-of-use disease and contamination sensing, health care monitoring, and other biosensing applications[34].

The first sensor article is from Donghua University in China, where the team integrated a microfluidic device to create a pH-sensing optical response hydrogel with robust mechanical properties. The team used water-in-oil hydrogel droplets with silica nanoparticles that assemble into photonic crystal beads. These beads created structural color shifts corresponding to pH levels with responsive times under 30 seconds. The droplets were dried on a chip, eliminating the need and risks associated with moving hydrogels[39].

Researchers at the University of Utah in Salt Lake City developed a microfluidic device with patterned hydrogel channels and microarrays to create a point-of-use drinking water contaminants sensor. The device measures the electrical resistance of the hydrogel that is affected by the contamination of the water running through the device[24].

A paper out of the University of Texas showed that hydrogel-immobilized enzymes can detect analytes such as glucose and galactose in real time. Enzymes are stuck into the hydrogels' own cross-linking capabilities, allowing for the targets to penetrate the hydrogel and activate the enzymes by creating a change in detectable products. Researchers were able to create multi-channel chips that allow for multiple tests to be run simultaneously[16].

3. | Evaluation of The Current Knowledge Base

3.1 | Current Limitations of the Field

We believe the two largest limitations of hydrogels in microfluidic devices is the fabrication and maintenance difficulties that drive up the overall cost of the field.

The fabrication of hydrogels is the largest limitation currently. We are able to recreate relatively accurate biochemical or biophysical models for organ-on-a-chip, but the combination of both in the same device is insufficient at the moment, coupled with the resolution issues that come along with 3D bioprinting, and you have a very big limitation. Producing hydrogels from molds does not allow for finite control of your special structures, and often, having a higher resolution than 3D bioprinting comes with the cost of making the mold. 3D bioprinting is fabrication intensive and suffers from limited scalability and reproducibility[9][33].

Secondly, the cost of equipment and maintaining laboratories and facilities to support hydrogel microfluidic research is tremendous. Significant capital investment in infrastructure is needed, requiring cleanrooms depending on the application and sterile laboratory environments. Cleanroom construction ranges from $200 to $1,000 per square foot, with recurring maintenance costs[1]. Maintaining cell culture environments further requires $25,000 to $100,000 in equipment like autoclaves and incubators to ensure sterility and environmental control[13]. Beyond infrastructure, hydrogels are delicate introducing a recurring economic burden, as hydrogel cost is dominated not by raw material cost but process inefficiencies, handling losses, and frequent material replacement,

significantly increasing overall device replacement[37].

It is important to note the scalability problem with hydrogels in microfluidic devices. Almost all devices discussed and researched for this review are linearly scalable. For example, if you are looking at drug delivery applications, most were hydrogel droplet formations. The only way to start mass-producing them is to simply add more throughput devices. If you want twice the output numbers, you need twice the devices to create droplets. However, at the moment, we believe that this isn't the biggest issue for the field; it does limit the research capabilities, but for scalability, there isn't a lot of the field that needs to be scaled. Most of these devices are designed for research purposes.

3.2 | Future Directions and Gaps in Current Work

Hydrogels have emerged as a cornerstone material in microfluidic device research due to their tuneability, biocompatibility, and mimicry of the biological environment. We are hoping that, in the coming years, more research will be conducted in order to further develop the complexity of organoid-on-a-chip and multi-organ-on-a-chip devices. Creating more physiologically relevant models, high precision patient-specific geometries and models, studies on the complex behavior of drug delivery within complex channel flow, hemodynamically relevant cell cultures, and more. The versatility of hydrogels, we believe, can support these advancements[18],[26].

Going along with the creation of more complex models, it would be great to see more off-the-shelf options for 3D bioprinters with a reduction of cost, a big ask, we know. The extremely limiting cost of these devices, as well as creating simple cell cultures with these complex fluid flows, severely limits the amount of research being conducted. The integration of these 3D bioprinters allows for precise spatial control over the hydrogel formation and thus cellular organization[17],[38].

In addition to organ modeling, sensing applications are increasingly being integrated into hydrogel-based microfluidic platforms. Hydrogels can serve as responsive matrices in biosensors, changing volume, conductivity, or optical properties in response to pH, glucose, or other analytes. Advances in hydrogel functionalization, combined with microfluidic architectures, allow the creation of highly sensitive and miniaturized sensors capable of real-time monitoring of biological or environmental parameters. These devices hold promises for wearable diagnostics, point-of-care testing, and continuous monitoring of disease markers, with hydrogel responsiveness providing a direct transduction mechanism for sensor readouts [24],[16].

Overall, the future of hydrogels in microfluidic device applications lies in interdisciplinary integration, combining materials science, microfabrication, cell biology, and engineering. Continued innovation in hydrogel chemistry, microfluidic control, and sensing technologies will enable the creation of biologically relevant and miniaturized platforms that revolutionize how we study human physiology, disease, and therapeutics.

References

1. *(2025) How much does a cleanroom cost? A simple guide*. Allied Cleanrooms.
2. Akther, F., Little, P., Li, Z., Nguyen, N., & Ta, H. T. (2020). Hydrogels as artificial matrices for cell seeding in microfluidic devices. RSC Advances, 10(71), 43682–43703.
3. Annabi N, Selimović Š, Acevedo Cox JP, Ribas J, Afshar Bakooshli M, Heintze D, Weiss AS, Cropek D, Khademhosseini A. (2013). Hydrogel-coated microfluidic channels for cardiomyocyte culture. Lab Chip. 13(18):3569-77.
4. Aye, S. S. S., Fang, Z., Wu, M. C. L., Lim, K. S., & Ju, L. A. (2025). Integrating microfluidics, hydrogels, and 3D bioprinting for personalized vessel-on-a-chip platforms. Biomaterials Science, 13(5), 1131–1160.
5. Bae, C. Y., Son, J., Kim, H., & Park, J. (2017). Demonstration of interposed modular hydrogel sheet for multicellular analysis in a microfluidic assembly platform.
6. Bhusal, A., Dogan, E., Nieto, D., Shaegh, S. A. M., Cecen, B., & Miri, A. K. (2022). 3D bioprinted hydrogel microfluidic devices for parallel drug screening. ACS Applied Bio Materials, 5(9), 4480–4492.
7. Cai, L., Li, N., Zhang, Y., Gu, H., & Zhu, Y. (2022). Microfluidics-derived microcarrier systems for oral delivery. Biomedical Technology, 1, 30–38.
8. Chen, Z., Song, S., Ma, J., Da Ling, S., Wang, Y. D., Kong, T. T., & Xu, J. H. (2021). Fabrication of magnetic core/shell hydrogels via microfluidics for controlled drug delivery. Chemical Engineering Science, 248, 117216.
9. Ching, T., Vasudevan, J., Chang, S., Tan, H. Y., Ranganath, A. S., Lim, C. T., Fernandez, J. G., Ng, J. J., Toh, Y., & Hashimoto, M. (2022). Biomimetic vasculatures by 3D‐Printed porous molds. Small, 18(39), e2203426.
10. Clancy, A., Chen, D., Bruns, J., Nadella, J., Stealey, S., Zhang, Y., Timperman, A., & Zustiak, S. P. (2022). Hydrogel-based microfluidic device with multiplexed 3D in vitro cell culture. Scientific Reports, 12(1), 17781.
11. Cosson, S., & Lutolf, M. P. (2014). Hydrogel microfluidics for the patterning of pluripotent stem cells. Scientific Reports, 4(1), 4462.
12. Delaquilla, A. (2024, September 24). The history of microfluidics - Elveflow. Elveflow.
13. Excedr. (2025). *How much does cell culture equipment cost?*
14. Geckil, H., Xu, F., Zhang, X., Moon, S., & Demirci, U. (2010). Engineering hydrogels as extracellular matrix mimics. Nanomedicine, 5(3), 469–484.
15. Golden, A. P., & Tien, J. (2007). Fabrication of microfluidic hydrogels using molded gelatin as a sacrificial element. Lab on a Chip, 7(6), 720.
16. Heo, J., & Crooks, R. M. (2005). Microfluidic biosensor based on an array of hydrogel-entrapped enzymes. Analytical Chemistry, 77(21), 6843–6851.
17. Hinton, T. J., Jallerat, Q., Palchesko, R. N., Park, J. H., Grodzicki, M. S., Shue, H., Ramadan, M. H., Hudson, A. R., & Feinberg, A. W. (2015). Three-dimensional printing of complex biological structures by freeform reversible embedding of suspended hydrogels. Science Advances, 1(9), e1500758.
18. Ho, T.-C., Chang, C.-C., Chan, H.-P., Chung, T.-W., Shu, C.-W., Chuang, K.-P., Duh, T.-H., Yang, M.-H., & Tyan, Y.-C. (2022). Hydrogels: Properties and applications in biomedicine. Molecules.
19. Huang, J., Li, Z., Hu, Q., Chen, G., Ren, Y., Wu, X., & Ren, J. (2018). Bioinspired anti-digestive hydrogels selected by a simulated gut microfluidic chip for closing gastrointestinal fistula. iScience, 8, 40–48.
20. Katarzyna O. Rojek, Monika Ćwiklinska, Julia Kuczak, & Jan Guzowsk. (2022, September 15). Microfluidic formulation of topological hydrogels for microtissue engineering. Chemical Reviews, 122(22), 16839–16909.

21. Kim, D., & Beebe, D. J. (2006). Hydrogel-based reconfigurable components for microfluidic devices. Lab on a Chip, 7(2), 193–198.
22. Kinstlinger, I. S., Calderon, G. A., Royse, M. K., Means, A. K., Grigoryan, B., & Miller, J. S. (2021). Perfusion and endothelialization of engineered tissues with patterned vascular networks. Nature Protocols, 16(6), 3089–3113.
23. Lee, SR., Kim, Y., Kim, S. et al. (2022) U-IMPACT: a universal 3D microfluidic cell culture platform. Microsyst Nanoeng 8, 126.
24. Leu, H., Farhoudi, N., Reiche, C. F., Körner, J., Mohanty, S., Solzbacher, F., & Magda, J. (2018). Low-cost microfluidic sensors with smart hydrogel patterned arrays using electronic resistive channel sensing for readout. Gels, 4(4), 84.
25. Li, W., Liu, D., Zhang, H., Correia, A., Mäkilä, E., Salonen, J., Hirvonen, J., & Santos, H. A. (2016). Microfluidic assembly of a nano-in-micro dual drug delivery platform composed of halloysite nanotubes and a pH-responsive polymer for colon cancer therapy. Acta Biomaterialia, 48, 238–246.
26. Ling, Y., Rubin, J., Deng, Y., Huang, C., Demirci, U., Karp, J. M., & Khademhosseini, A. (2007). A cell-laden microfluidic hydrogel. Lab on a Chip, 7(6), 756
27. Listek, V., & Listek, V. (2024, November 27). Meet Xell, xolo's budget-friendly bioprinter for labs. 3DPrint.com | Additive Manufacturing Business.
28. Microfluidic Devices | Microfluidic Chips Manufacturer | UFluidix. (2023, April 8). uFluidix.
29. Nichol, J. W., Koshy, S. T., Bae, H., Hwang, C. M., Yamanlar, S., & Khademhosseini, A. (2010). Cell-laden microengineered gelatin methacrylate hydrogels. Biomaterials, 31(21), 5536–5544.
30. Nie, J., Gao, Q., Wang, Y., Zeng, J., Zhao, H., Sun, Y., Shen, J., Ramezani, H., Fu, Z., Liu, Z., Xiang, M., Fu, J., Zhao, P., Chen, W., & He, Y. (2018). Vessel‐on‐a‐chip with Hydrogel‐based Microfluidics. Small, 14(45), e1802368.
31. O'Brien, M., Spirrison, A. N., Halim, M. S. A., Li, Y., Neild, A., Gemrich, C., Nosrati, R., Solorio, L., & Gong, M. M. (2025). Open microfluidic cell culture in hydrogels enabled by 3D-Printed molds. Bioengineering, 12(2), 102.
32. Park, D., Lee, J., Lee, Y., Son, K., Choi, J. W., Jeang, W. J., Choi, H., Hwang, Y., Kim, H., & Jeon, N. L. (2021). Aspiration-mediated hydrogel micropatterning using rail-based open microfluidic devices for high-throughput 3D cell culture. Scientific Reports, 11(1), 19986.
33. Polacheck, W. J., Kutys, M. L., Tefft, J. B., & Chen, C. S. (2019). Microfabricated blood vessels for modeling the vascular transport barrier. Nature Protocols, 14(5), 1425–1454.
34. Pourmostafa, A., Bhusal, A., Menon, N. H., Li, Z., Basuray, S., & Miri, A. K. (2024). Integrating conductive electrodes into hydrogel-based microfluidic chips for real-time monitoring of cell response. Frontiers in Bioengineering and Biotechnology, 12, 1421592.
35. Rahimi, S., Sarraf, E. H., Wong, G. K., & Takahata, K. (2010). Implantable drug delivery device using frequency-controlled wireless hydrogel microvalves. Biomedical Microdevices, 13(2), 267–277.
36. Shen, C., Li, Y., Wang, Y., & Meng, Q. (2019). Non-swelling hydrogel-based microfluidic chips. Lab on a Chip, 19(23), 3962–3973.
37. *Sorour, M. H., Tewfik, S. R., Abulnour, A. G., Shaalan, H. F., Hani, H. A., & Al-Bazedi, G. A. (2020, February 27). Development and assessment of adsorptive hydrogel: Process Engineering and economic considerations - sorour - 2020 - engineering reports - wiley online library. Wiley.*
38. Stanton, M. M., Samitier, J., & Sánchez, S. (2015). Bioprinting of 3D hydrogels. Lab on a Chip, 15(15), 3111–3115.
39. Sun, Y., Zhang, Y., Liu, J., & Nie, F. (2016). Integrated microfluidic device for the

spherical hydrogel pH sensor fabrication. RSC Advances, 6(14), 11204–11210.
40. Tejavibulya, N., Colburn, D. A., Marcogliese, F. A., Yang, K., Guo, V., Chowdhury, S., Stojanovic, M. N., & Sia, S. K. (2019). Hydrogel microfilaments toward intradermal health monitoring. iScience, 21, 328–340.
41. Virumbrales-Muñoz, M., Ayuso, J. M., Lacueva, A., Randelovic, T., Livingston, M. K., Beebe, D. J., Oliván, S., Pereboom, D., Doblare, M., Fernández, L., & Ochoa, I. (2019). Enabling cell recovery from 3D cell culture microfluidic devices for tumour microenvironment biomarker profiling. Scientific Reports, 9(1), 6199.
42. Wang, J., Chen, Z., Mauk, M., Hong, K., Li, M., Yang, S., & Bau, H. H. (2005). Self-Actuated, Thermo-Responsive hydrogel valves for lab on a chip. Biomedical Microdevices, 7(4), 313–322.
43. Watanabe, T., Motohiro, I., & Ono, T. (2019). Microfluidic formation of hydrogel microcapsules with a single aqueous core by spontaneous cross-linking in aqueous two-phase system droplets. Langmuir, 35(6), 2358–2367.
44. Wei, K., Wang, W., Giovannini, G., Sharma, K., Rossi, R. M., & Boesel, L. F. (2025). A plug-and-play microfluidic device for hydrogel fiber spinning. Lab on a Chip, 25(6), 1575–1585.
45. Wichterle, O., & Lím, D. (1960). Hydrophilic gels for biological use. Nature, 185(4706), 117–118.
46. Yang, M., Shi, Y., Wang, F., Zhang, X., Shao, J., Yang, F., Sun, H., Zhang, C., Zhou, Z., Huang, J., Lv, P., Yung, P. S., Cheng, J., Huang, H., & Wang, J. (2025). Hydrogel Microspheres as versatile platforms for biomedical research: design, properties, and applications. MedComm, 6(10), e70423.
47. Yang, J., Zhu, Y., Wang, F., Deng, L., Xu, X., & Cui, W. (2020). Microfluidic liposomes-anchored microgels as extended delivery platform for treatment of osteoarthritis. Chemical Engineering Journal, 400, 126004.
48. Yi, B., Li, T., Yang, B., Chen, S., Zhao, J., Zhao, P., Zhang, K., Wang, Y., Wang, Z., & Bian, L. (2024). Surface hydrophobization of hydrogels via interface dynamics-induced network reconfiguration. Nature Communications, 15(1), 239.
49. Young, E. W. K., & Beebe, D. J. (2010, February 1). Fundamentals of microfluidic cell culture in controlled microenvironments. Chemical Society Reviews.
50. Zhao, C., Cai, L., Nie, M., Shang, L., Wang, Y., & Zhao, Y. (2021). Cheerios effect inspired microbubbles as suspended and adhered oral delivery systems. Advanced Science, 8(7), 2004184.
51. Zhao, D., Qian, L., Yang, Q., Li, X., Ye, C., Shi, T., & Wang, Y. (2024). Microfluidic synthesis of stimuli-responsive hydrogel particles. Applied Materials Today, 42, 102571.
52. Zheng, Y., Chen, J., & López, J. A. (2015). Flow-driven assembly of VWF fibres and webs in in vitro microvessels. Nature Communications, 6(1), 7858.