Plug & Perfuse

A Vitroscope–CONDUCTink Collaboration for Scalable Organoid Perfusion

Title: *Intraluminal Perfusion of Vascularized Human Brain Organoids*

Authors: Paone, L.[1]; Jernström, S.[2]; Galie, P.[1]; Dyer T.H.[2]; Kriesi, C.[2]; Sjöman, H.[2]
Affiliations: [1]CONDUCTink Inc., NJ, US; [2]Vitroscope AS, NO

Our Purpose

Vitroscope (Norway) and CONDUCTink (USA) have joined forces to address one of the most persistent limitations of organoid research: functional access to vascular networks. While vascularized organoids have transformed the way researchers model disease and tissue development, the field still lacks a practical and scalable method to perfuse these networks, limiting both the delivery of oxygen and nutrients and maturation.

By integrating Vitroscope's precision-controlled perfusion technology with CONDUCTink's bioactive, tunable hydrogels, we have developed the first scalable system capable of controlled intraluminal flow through vascularized organoids, without damaging the tissue or relying on cells external to the organoid.

This technology is consistent with recent regulatory shifts toward human-relevant *in vitro* systems (FDA Modernization Act 2.0, NIH prioritization of human-based technologies, UK government efforts to phase out animal models) and directly addresses the need for scalable, non-animal, human-relevant models. Our joint goal is to create a **platform that advances organoid culture to the point that renders animal models obsolete for drug discovery and disease modeling**.

The Challenge

Despite major advances in organoid development, current culture systems rely on the use of rockers or perfusion chambers to provide exchange of nutrients only over the surface of the organoids. Although this strategy facilitates a level of oxygen and nutrient transport up to a few hundred microns, the lack of bulk perfusion limits tissue growth and maturation. Additionally, in vascularized organoids, the lack of intraluminal perfusion limits the study of physiologically relevant drug distribution, effectiveness, and toxicity. Unlocking the potential of vascularized organoids requires functional perfusion under controlled conditions and with real-time readouts.

The Perfusiv™ Platform

The Vitroscope–CONDUCTink platform, Perfusiv™, introduces two capabilities not previously available in a single system:

1. **Bulk interstitial flow** through organoids
2. **Intraluminal perfusion** through organoid vasculature

Key Components

Bioactive Hydrogel Architecture (CONDUCTink)
3D-printed tunable biomaterials to anchor organoids and promote self-assembly of vascular networks, enabling consistent loading and orientation for perfusion.

CONDUCTink's Biomaterial Toolbox

- Synthetic & naturally derived biopolymer hydrogels
- Bioactive peptide portfolio
- Compatible with 3D-printing

Precision Perfusion & Environmental Control (Vitroscope)
Vitroscope's vitro.alive system delivers

- Programmable flow (1-1000 µL/min),
- Digitally controlled temperature and gas mixture,
- Longitudinal live imaging,
- Automated data logging, and
- Cloud-based visualization tools.

Real-Time Vascular Readouts
Integrated optics and cloud-based analysis enable fluorescent tracer tracking to confirm functional connectivity, flow dynamics, and enables long-term monitoring of vascular integrity, transport, and barrier behavior.

Proof of Concept: Flow Through Human Brain Organoid Vasculature

Using human stem cell–derived vascularized brain organoids (CD31+ endothelial labeling), the team demonstrated that perfusion can be **successfully initiated and maintained across an intact organoid vascular network**.

Experimental Highlights:

- Organoids embedded in CONDUCTink-printed hydrogel structures fitted with Vitroscope's chamber system. (*Figure 1 & 2a*)
- Perfusion media was circulated for 7 days at 37 °C / 5% CO_2.
- 2.1 µm green fluorescent beads entered and traveled through the vascular lumen, visualized by live fluorescence microscopy. (*Figure 2b*)
- Flow remained stable without leakage or tissue disruption.
- Post-clearing imaging confirmed bead localization strictly within CD31+ vessels. (*Figure 2c*)

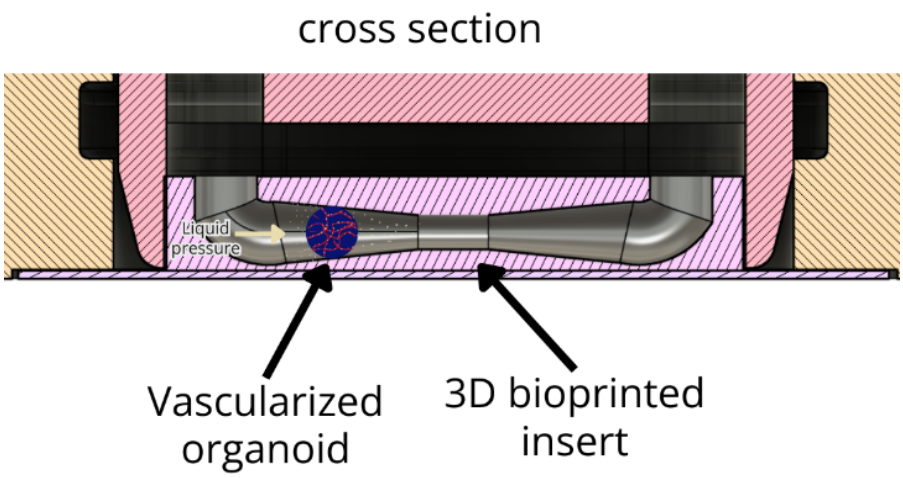

Figure 1. Cross section view of organoids embedded in CONDUCTInk bioprint within a chamber of Vitroscope.

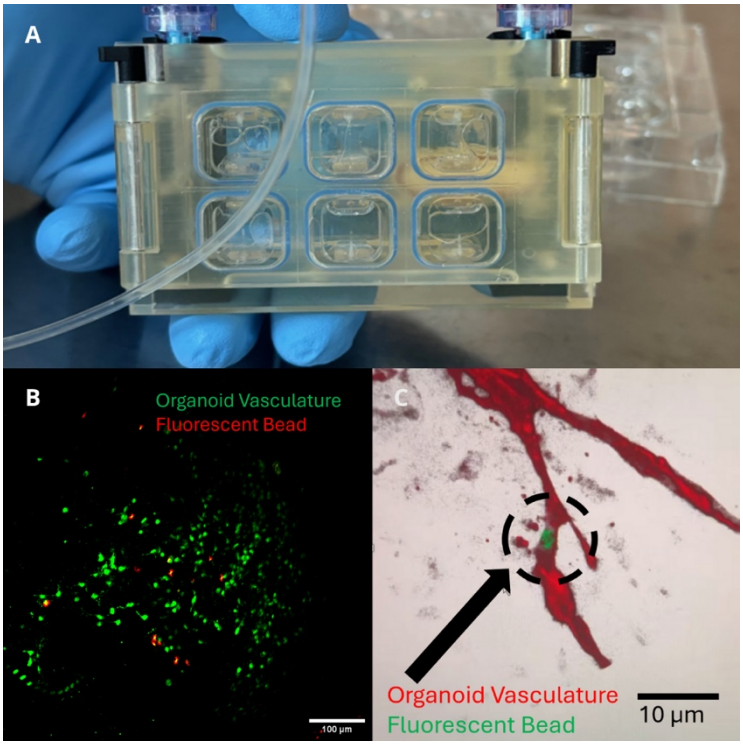

Figure 2. A) Photograph of Perfusiv™ within a 6-well Vitroscope perfusion chamber, including a close-up of an organoid loaded into a CONDUCTink hydrogel. B) Confocal stack showing fluorescent beads along CD31-positive cells within the organoid following perfusion with the beads. Scale = 100 µm. C) High magnification image of fluorescent bead within CD31-positive vasculature in cleared organoid. Scale = 10 µm. A video recording of fluorescent beads exiting a vascularized organoid can also be accessed via this link (https://www.vitroscope.no/organoid_perfusion_video).

This proof-of-concept establishes the first functional demonstration that vascularized organoids can be perfused at scale in a controlled, reproducible manner, a key step toward advancing organoids as microphysiological systems.

Discussion

The Perfusiv™ platform's ability to access organoid vasculature not only advances physiological relevance of organoid models but also creates new experimental avenues, including:

- **Organoid Maturation:** Intraluminal flow exerts biochemical and biomechanical stimuli that are important to drive tissue maturation.
- **Exosome and Aging Studies:** Continuous perfusion allows sampling of secreted vesicles and biomarkers over time.
- **Drug Transport & BBB Models:** The platform facilitates quantitative assessment of compound permeability and toxicity across human-relevant vasculature.

Applicability is not limited to vascularized organoids. Bulk perfusion of avascular organoids can also be used to study how interstitial flow affects gene expression of vascular markers.

Collaboration Roles

- **CONDUCTink:** Design and fabrication of 3D-printed structures in Vitroscope's perfusion chambers, including hydrogel topology and peptide anchors chosen by the end user.

- **Vitroscope:** Development of perfusion hardware, imaging systems, and data acquisition software for real-time analysis.

Both parties share intellectual property on the **gasket-based sealing mechanism** (US Patent 63/869,346), which enables leak-free sealing between soft biomaterials and rigid flow chambers.

Conclusion

Perfusiv™ represents a next-generation research platform for vascularized organoids that moves beyond surface perfusion and enables true physiological flow dynamics. By providing both bulk and intraluminal perfusion, the system expands what researchers can measure, model, and manipulate in human-relevant systems.

Perfusiv™ is designed to be modular, scalable, and ready for integration into laboratories developing microphysiological systems. It sets the stage for a new generation of human-based research tools, enabling organoids that function **not just as miniature tissues, but as miniature organs**.

Our next focus is benchmarking Perfusiv™ against current culturing systems to quantify the improvement in ADME toxicity testing provided by this technology.

Vitroscope X CONDUCTink

References

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2. Paone L. S. et al. *A 3D-Printed Blood–Brain Barrier Model with Tunable Topology and Cell–Matrix Interactions.* Biofabrication 16 (2023).
3. Paone L. S. et al. *Effects of Drag-Reducing Polymers on Hemodynamics and Whole Blood–Endothelial Interactions in 3D-Printed Vascular Topologies.* ACS Appl. Mater. Interfaces 16, 14457–14466 (2024).

For collaboration opportunities involving vascularized organoids or custom perfusion workflows, please reach out:

contact@vitroscope.com
www.vitroscope.com

contact@conduct-ink.com
www.conduct-ink.com/