Rapid and facile light-based approach to generate complex hydrogel structures for organ-on-a-chip models

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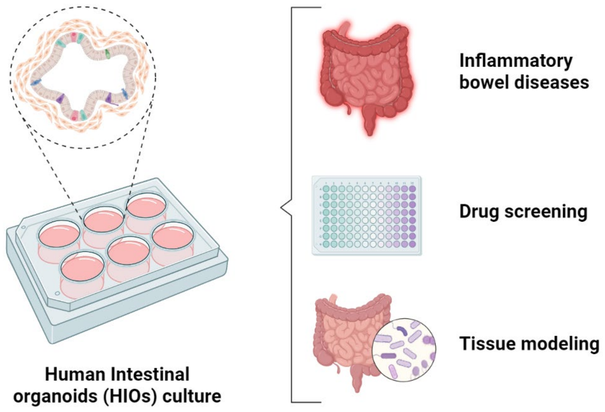
Motivation

Human intestinal organoids (HIOs) represent an excellent tissue source for intestinal diseases and tissue modeling:



HIOs derivation in three-dimensional matrices **without perfusion can restrict their development and functionality**, resulting in closed architectures with reduced growth and homeostasis.

Fabrication of current perfusable gut-on-a-chip platforms based on hydrogels:

- Involve painstaking, time-consuming, and laser-based equipment-intensive methodologies.
- Are limited to natural, biological matrices (e.g., Matrigel).

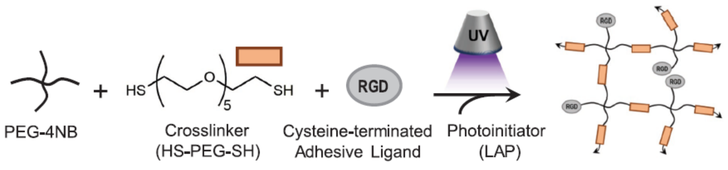
Our approach

We propose a rapid and facile light-based approach to generate complex hydrogel structures to use in gut-on-a-chip models:

- ✓ **Reduction of preparation times** from several hours to seconds.
- ✓ **Simple instrumentation.**
- ✓ Ability to use **synthetic hydrogels** over natural matrices: flexibility and lowers regulatory burdens.

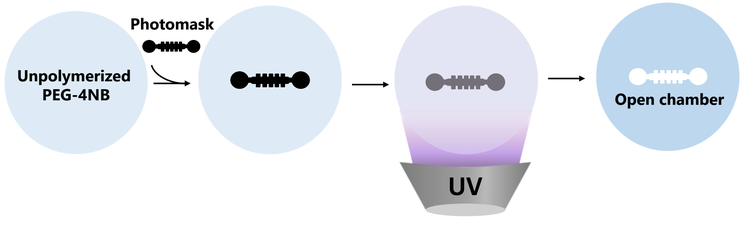
Methodology

Synthetic hydrogel photopolymerization mechanism:



Hunckler, M. D., Adv. Healthcare Mater. 2019, 8, 1900371.

Photopatterning of PEG-4NB hydrogels for the fabrication of perfusable mini-gut structures using UV light and a photomask:



Photopatterning of **complex structures in synthetic hydrogels**, including perfusable channels for cell culture and media perfusion, in **less than 1 second**

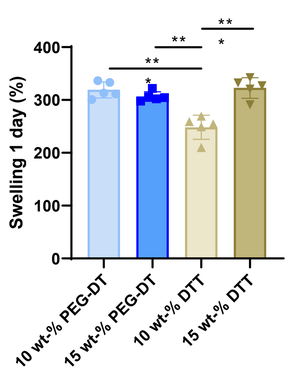
Photopatterning hydrogels with controlled swelling and high shape fidelity

The big challenge: control hydrogel swelling

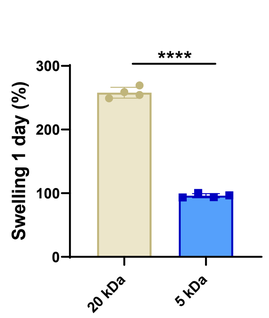
Swelling is a key parameter to maintain high shape fidelity in the hydrogel features.

Different parameters were analyzed: crosslinker agent, polymer concentration (wt-%) and molecular weight (MW), and temperature.

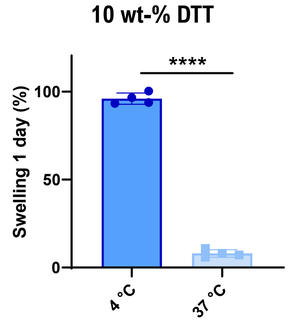
Crosslinker and wt-%



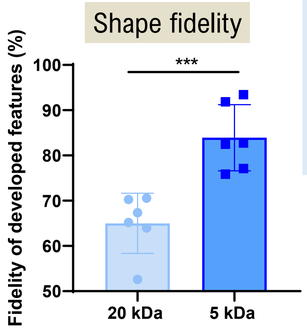
PEG-4NB MW



Temperature

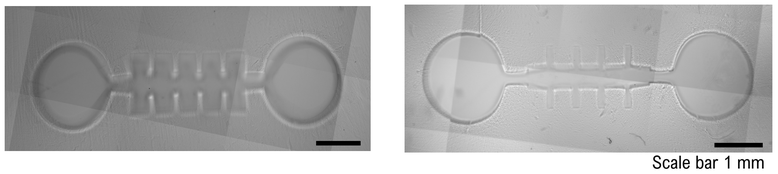


Shape fidelity



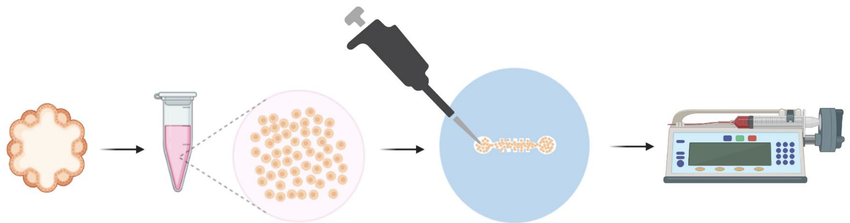
Our hydrogel formulation provides a **reduced swelling (8±2%)**, which leads to **high shape fidelity (83±8%)** of photopatterned features with different geometries.

Different photomask designs can be used to create complex geometries.



Scale bar 1 mm

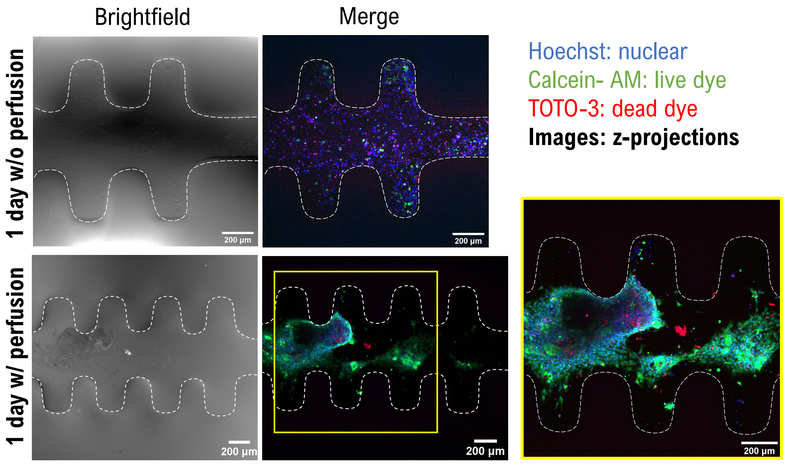
Seeding HIOs in our gut-on-a-chip

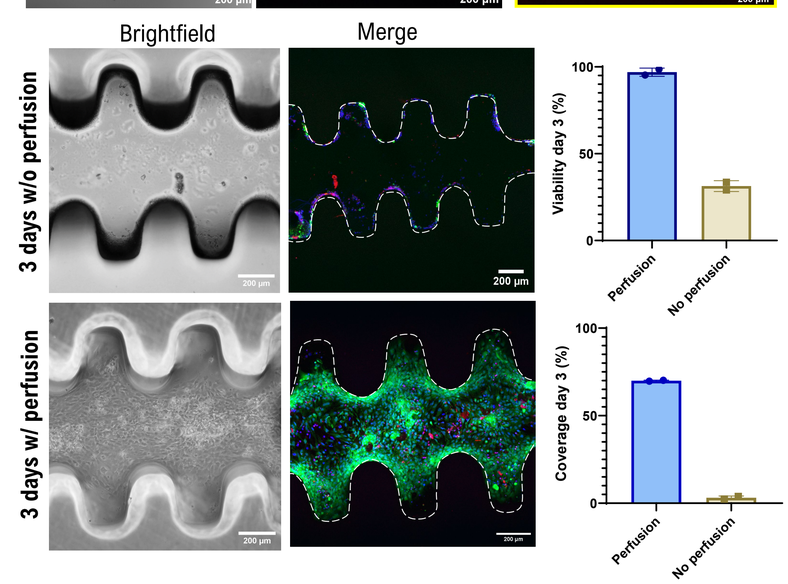


Single cells of HIOs at day 28 were used for seeding in the devices (5-10x10^6 cells/mL).

Culturing single cells of HIOs in our gut-on-a-chip

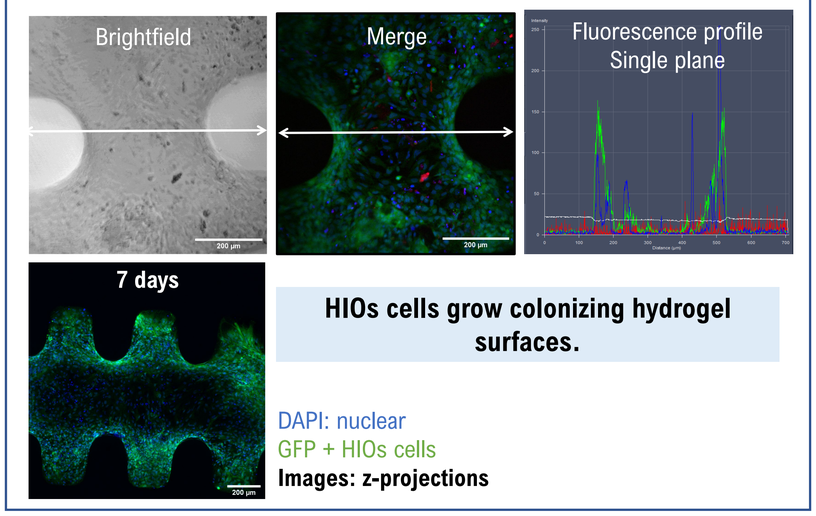
Media perfusion is essential for cell survival over time





Media perfusion improves cell viability and device % surface coverage over time.

Gut-on-a-chip devices allow long-term culture of HIOs



HIOs cells grow colonizing hydrogel surfaces.

Conclusions

- These preliminary results demonstrated that our gut-on-a-chip systems are suitable and accessible platforms for the development of relevant intestinal organoids as well as long-term culture systems.
- Further experiments will focus on the evaluation of cell types distribution and intestinal functional studies.

Acknowledgements

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