Supragel Assembly of HA-PAAm Microgels via UV-Crosslinking Using a Low-Cost LEGO® 3D Printer

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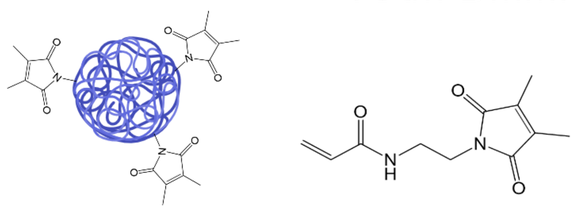
INTRODUCTION

Hyaluronic acid (HA) is widely used in tissue engineering due to its excellent biocompatibility and support for cell viability [1]. However, its low viscosity limits its suitability for extrusion-based 3D bioprinting. To address this, we convert HA into **microgels** and combine it with **acrylamide-based (AAm)** microgels to formulate a **biphasic particle-based ink**. This approach enables tunable viscosity while preserving cell-friendly characteristics. AAm microgels offer **improved printability** and **cost-efficiency**, making them a complementary component to HA.

Both microgel types are **chemically modified for intra- and inter-particle crosslinking**. UV-triggered [2+2] cycloaddition between **DMMIAAm groups** and a **PEG-based crosslinker** enables scaffold stabilization. Incorporation of **dynamic thiol–ester bonds** into the crosslinker allows for controlled degradation and stress relaxation—key features for tissue remodeling and regeneration [2,3].
To ensure precision during printing, we developed a **modular 3D printer built from LEGO Technic bricks**, based on and extended from the open-source platform by Moukachar et al. [4]. The system uses **custom nozzles** fabricated via projection microstereolithography (PμSL), designed to interface seamlessly with the LEGO system. We introduce **three novel nozzle geometries**, each optimizing flow control and **minimizing clogging** during microgel extrusion [5].

MATERIAL DESIGN

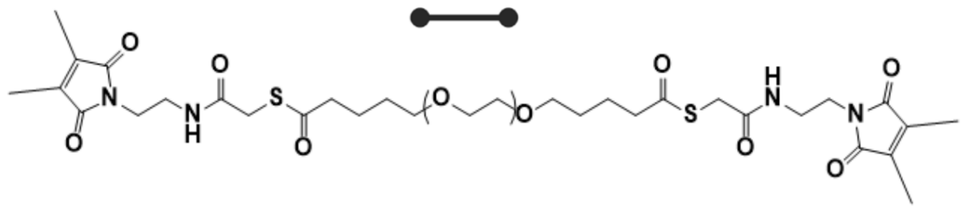
AAm-DMMI



DMMI-functionalized AAm provides:
- Cost-effectiveness
- Easy handling
- Easy modifications
- (DMMI) Free group ready for the inter-particle crosslinking [**2+2 cycloaddition**]

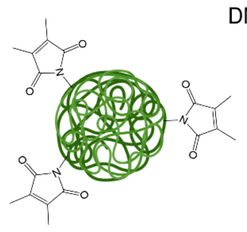
Volumetric ratio:

Functional PEG-based crosslinker

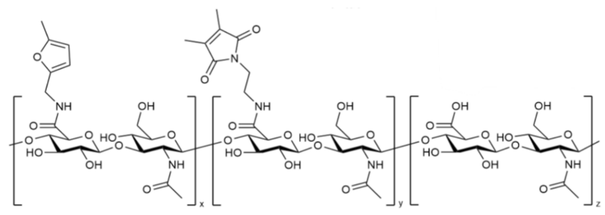


- Inter-particle crosslinking **[2+2] cycloaddition**
- Dynamic thiol-ester bonds – controlled degradation properties

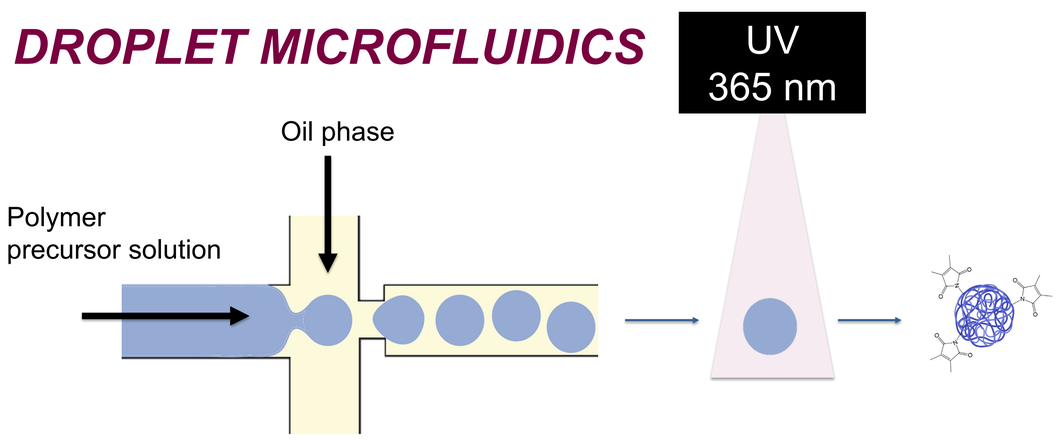
HA-mFU-DMMI



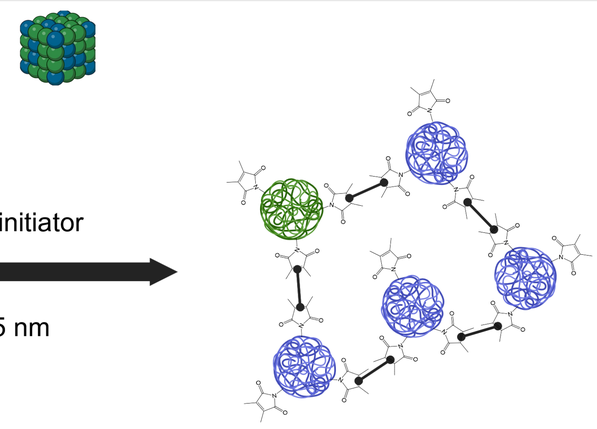
DMMI-mFU-bifunctional HA provides:
- Unparalleled **biocompatibility**
- (mFU) Intra-particle crosslinking [**thiol-ene click reaction**]
- (DMMI) Free group ready for the inter-particle crosslinking [**2+2 cycloaddition**]



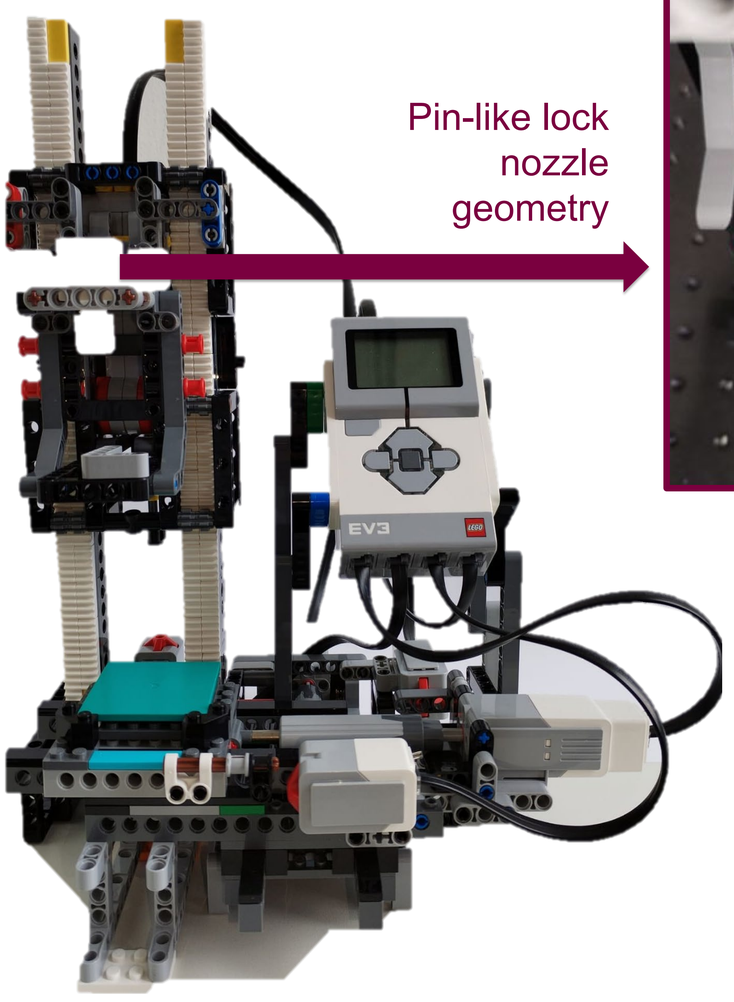
DROPLET MICROFLUIDICS

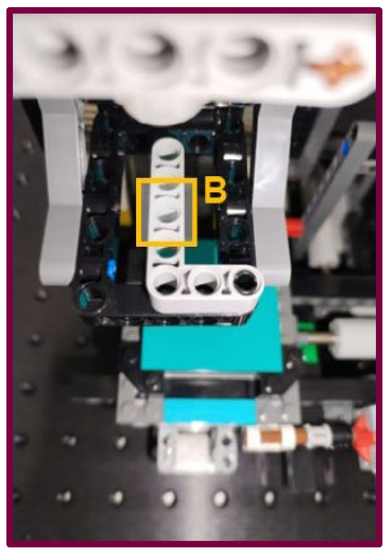


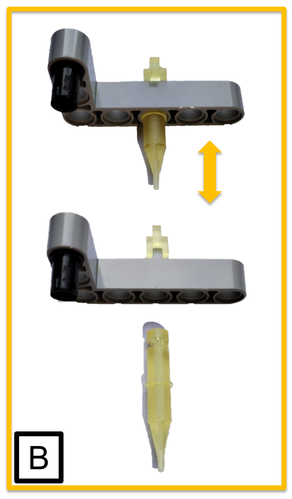
Inter-particle crosslinking



LEGO® 3D Printer





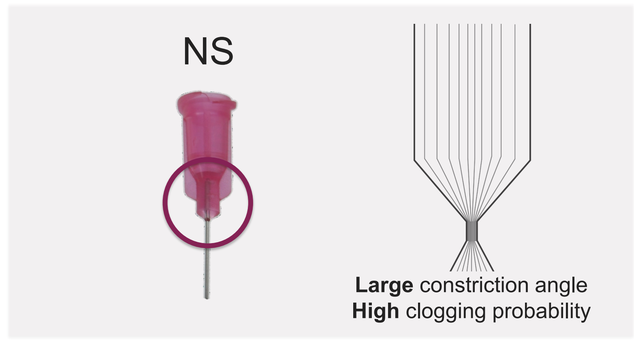


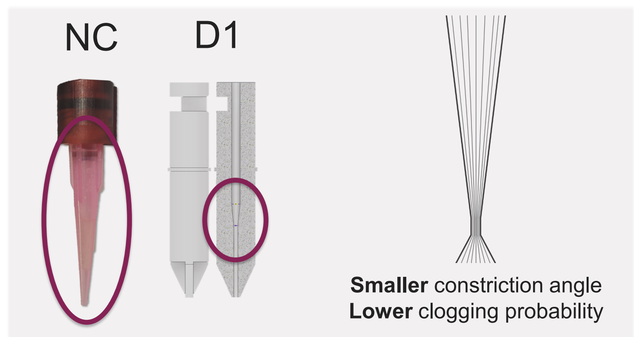
Nozzle Development

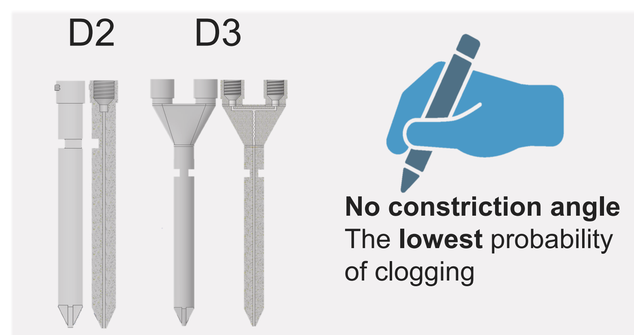
There is a great influence of the constriction angle on clogging by bridging in the confined flow of particles. To deal with this physical phenomenon, we developed multiple nozzles with the aim of having the lowest possible constriction angle.

Commercial nozzles:
- **NS** – large constriction angle
- **NC** – smaller constriction angle

Custom-made nozzles:
- **D1** –significantly smaller constriction angle
- **D2** –almost no constriction angle
- **D3** –double-inlet nozzle
  - foreseen for printing of bi-phasic inks







CONCLUSION

We successfully developed a **bi-phasic microgel ink** system combining mFU- and DMMI-functionalized hyaluronic acid and DMMIAAm-functionalized acrylamide microgels, enabling **tunable rheological** properties and **UV-induced interparticle crosslinking**. A **modular LEGO-based 3D printer** with **custom-designed**, PμSL-fabricated nozzles offers precise extrusion capabilities.

To address clogging caused by particle bridging during confined flow, we investigated the effect of **nozzle constriction angle**. Our findings highlight the **critical role of geometry in flow stability**, and we designed **multiple nozzle variants** with minimized constriction angles to **reduce clogging risk** and ensure consistent microgel extrusion.
While scaffold microstructure imaging and degradability **testing are ongoing**, this platform demonstrates strong potential for customizable, biocompatible 3D printing in tissue engineering. **Future work** will focus on integrating thermo-responsive microgels (e.g., PNIPAAm) to enhance scaffold functionality and cell responsiveness

[1] T. Heida, et al. Polymers 2020, 12(8), 1760, [2] T. A. Neuendorf, et al. Gels 2022, 8, 117. [3] Konieczynska, M. D., Acc. Chem. Res. 2017, 50(2), 151-160, [4] A. Moukachar, Adv. Mater. Technol. 2023, 8, 2100868 [5] N. Vani, Sacha, Phys. Rev. Research, 2024, 6, 032060, Figures created in Biorender https://BioRender.com