Closed-Loop Control and Spatiotemporal Tracking of Hydrogel Extrusion and Cell Morphology

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Extrusion-based bioprinting is inherently challenged by the non-Newtonian and often time-dependent nature of hydrogel bioinks, which compromises flow stability, reproducibility, and control over the mechanical cues experienced by encapsulated cells [1]. Here, we design, build, and validate a closed-loop extrusion platform able to quantitatively track hydrogel flow dynamics and cell morphology from in-needle transport to post-extrusion deposition. The system combines a dual-syringe architecture, flow-rate and pressure-drop sensing, and adaptive proportional–integral–derivative (PID) control to regulate extrusion in real time under both stress- and deformation-controlled conditions, thereby overcoming key limitations of conventional open-loop pneumatic dispensing.

The platform was first validated using water and glycerol as Newtonian reference fluids and then applied to self-healing gelatin–oxidized laminarin hydrogels, with and without embedded cells. In addition, the setup was shown to operate as a capillary rheometer for non-Newtonian fluids, including correction of entrance and exit effects and assessment of wall-slip contributions. These measurements were complemented by torsional rheometry, computational fluid dynamics (CFD), and micro-particle image velocimetry (μPIV), enabling direct comparison between rheological constitutive behavior, predicted velocity fields, and experimentally resolved in-channel flow profiles.

Closed-loop operation markedly improved flow-rate accuracy relative to open-loop extrusion, particularly for hydrogels. Velocity-profile measurements confirmed parabolic flow for Newtonian liquids and plug-like flow for hydrogels, in agreement with their yield-stress character. The framework also provided access to the spatiotemporal mechanical history experienced by cells during extrusion, enabling correlation between in-needle hydrodynamics, post-extrusion filament stretching, and cellular morphological evolution.

Overall, this work establishes a reproducible methodology for real-time hydrogel extrusion control and characterization, with direct implications for improving structural fidelity, process standardization, and biological performance in extrusion bioprinting.

Keywords:

Hydrogel extrusion, bioprinting, closed-loop control, capillary rheometry, micro-PIV

References:

[1] P. Wei, C. Cipriani, C.-M. Hsieh, K. Kamani, S. Rogers, and E. Pentzer, "Go with the flow: Rheological requirements for direct ink write printability," *J. Appl. Phys.* , vol. 134, no. 10, p. 100701, Sep. 2023, doi: 10.1063/5.0155896.

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