Bayesian Optimization for Embedded Ink Writing of Tissue Analogs

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Abstract

Embedded ink writing (EIW) is an emerging bioprinting techniques used to fabricate soft biological structures within a yield-stress support bath. Despite its capabilities of creating complex constructs, the challenge of optimizing diverse factors hampers the further utilization of this 3D bioprinting strategy. This work experimentally summarizes the coupling effects of ink viscosity, support bath rheological properties, and key printing parameters on filament formation. A Bayesian optimization (BO) is used to establish a filament prediction platform, which accurately estimates suitable support bath rheology for alginate-based inks and predict optimal printing parameters for chitosan inks. Two representative eye-relevant tissues are successfully fabricated through the predictions of the platform. The insights lay the foundation for embedded ink writing strategies to guide selected parameters, aiming at the highly efficient reconstruction of human tissues and organs in the future.

Introduction/ Background

During EIW, ink material is printed into 3D structures within a bath, where the surrounding medium provides both omnidirectional mechanical support and a biologically relevant environment. The coupling effects of three key factors, i.e., ink viscosity, support bath rheology, and key printing parameters, lead to the formation of various types of filaments [1, 2]. Nevertheless, only few have well-defined morphology and controllable geometry [3, 4].

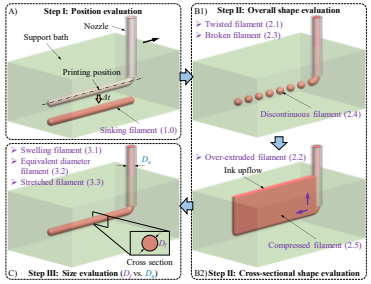

Figure 1. Assessment of printed filaments via the established PSS system.

Identifying optimal conditions is labor-intensive and trial-and-error dependent, making it particularly challenging when working with new bioinks or specific printing constraints [5]. Therefore, predictive platforms are needed to efficiently guide parameter design and enable well-defined filament generation.

Methods/Analysis

Based on the position-shape-size evaluation system published in the previous study [1], these filaments were assessed and categorized, as shown in **Figure 2A**. The collected datasets were further leveraged in the BO to establish a filament prediction platform (**Figure 2B**). To validate its efficiency, this platform designed both a support bath for printing tarsus structures and to select optimal printing parameters for producing sclera structures, as illustrated in **Figure 2C**.

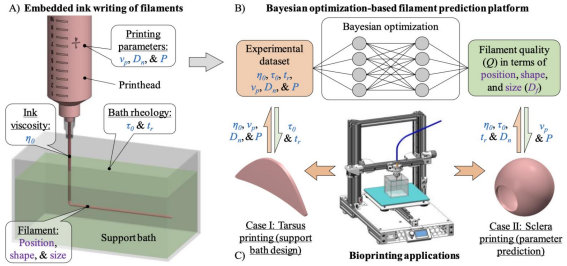

Figure 2. Overarching research plan. **A)** EIW and its three key factors, which collectively affect filament morphology and geometry. **B)** Establishment of a Bayesian optimization-based filament prediction platform. **C)** Efficient design of support bath (Case I) and rapid prediction of printing parameters (Case II) using the platform.

Results

Using the designed support bath and printing parameters, tarsus and sclera structures were biofabricated from alginate-based and chitosan inks, respectively. The tarsus was crosslinked and demonstrated as a biomimetic scaffold for eyelid restoration [6], while the sclera was crosslinked and integrated into a 3D printed orbit model for studying scleral regeneration [7].

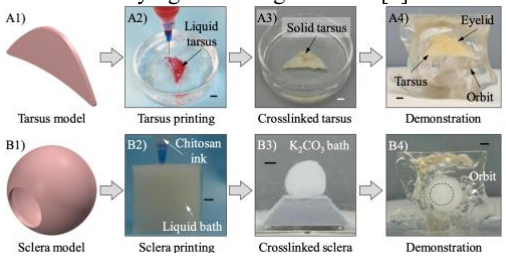

Figure 3. BO-enabled EIW of eye components. **A)** Tarsus model, **B)** Sclera model

Conclusion/ Future Direction

In this work, filament datasets including six input variables and one output variable, were utilized to establish the BO platform, which can accurately predict filament category when the input parameters are identified. This BO platform enabled the efficient design of support bath and printing parameters, which were validated by EIW of tarsus and sclera structures.

While only key rheological properties were considered here, future work will incorporate additional parameters such as flow behavior index, shear moduli, and stress relaxation time to enhance prediction accuracy. The platform will also be expanded beyond hydrophilic ink-bath pairs, and physics-based models will be integrated to upgrade it to a physics-informed BO framework, advancing our understanding of the underlying EIW physics. Furthermore, extending this physics-informed BO framework to microgravity environments, where buoyancy, surface tension, and fluid dynamics behave fundamentally differently, could enable EIW-based biofabrication for space medicine applications.

References

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