Collaborative Research: Cyber Enabled Online Quality Assurance for Scalable Additive Biomanufacturing (Bio-AM)

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Objective: Design and implement an *in-situ* process monitoring and closed loop control sensor-tissue system for bioprinted constructs

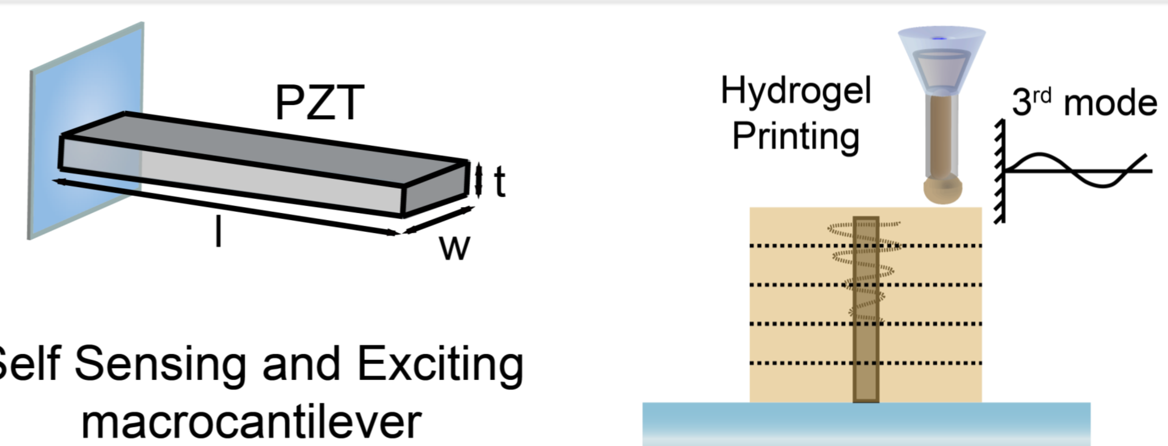
Challenges

- **Lack of understanding** of the process-material interactions (e.g., degree of crosslinking) that govern the quality.
- A need for specialized **in-process sensors** to continuously probe the construct quality in **real time** and correct the process drifts to mitigate defects.
- **New mathematical modeling** approaches are required to represent continuously evolving interlayer bonding of the constructs.

Scientific Impact

- **Fundamental understanding** of the effect of viscoelasticity of the 3D substrate on the cell differentiation and growth process (**mechanotransduction** in 3D substrate).
- **Sensor data modeling** to capture interlayer dynamics.
- **Real-time data closed loop feedback control** for identifying and actuating corrective actions for desired material properties

Millimeter Cantilever Sensor Model



Self Sensing and Exciting macrocantilever

$$f_b^n = \frac{1}{2\pi}\left(\frac{\lambda_n}{L}\right)^2\sqrt{\frac{EI}{\rho_c w t}} \qquad R_e = \frac{\rho\omega w^2}{4\eta}$$

R_e : Reynold's number

f_b^n: n^th bending mode resonant frequency

Γ: Complex hydrodynamic function

- Fluid interaction model used to correlate **phase angle shifts** and **Q-factor to viscoelastic properties**.

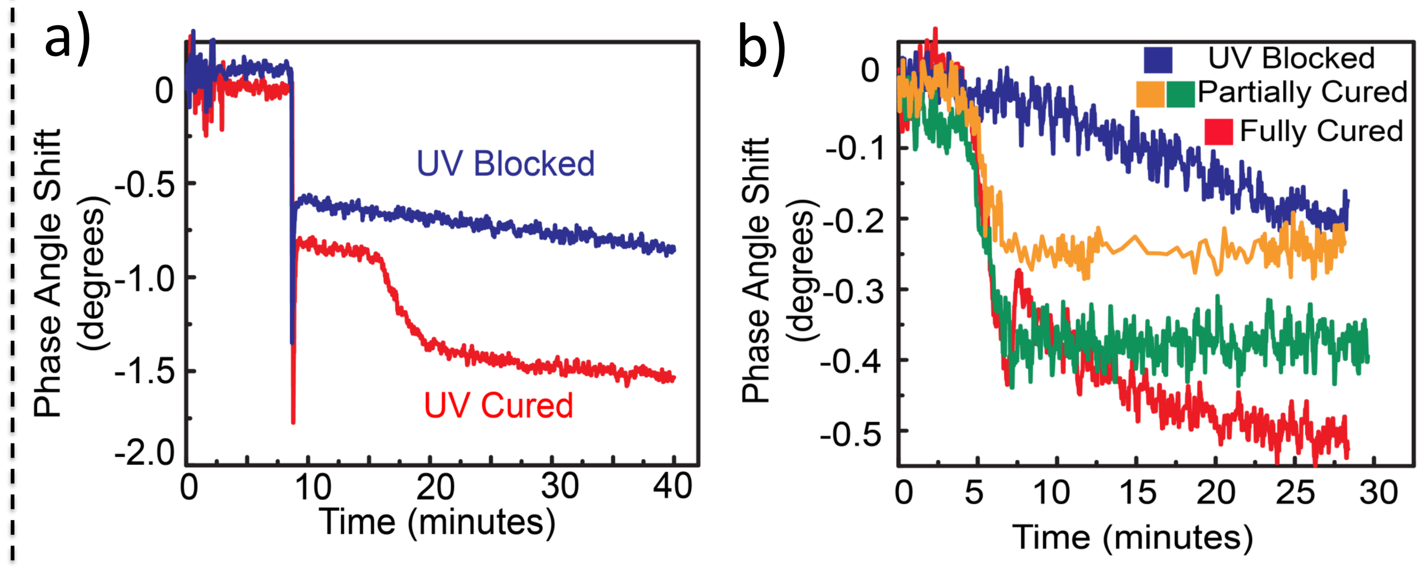
Hydrodynamic loading of the cantilever sensor

$$EI\frac{\partial^4 w(\omega,t)}{\partial x^4} + \mu\frac{\partial^2 w(\omega,t)}{\partial t^2} = F_{drive} + F_{fluid}$$

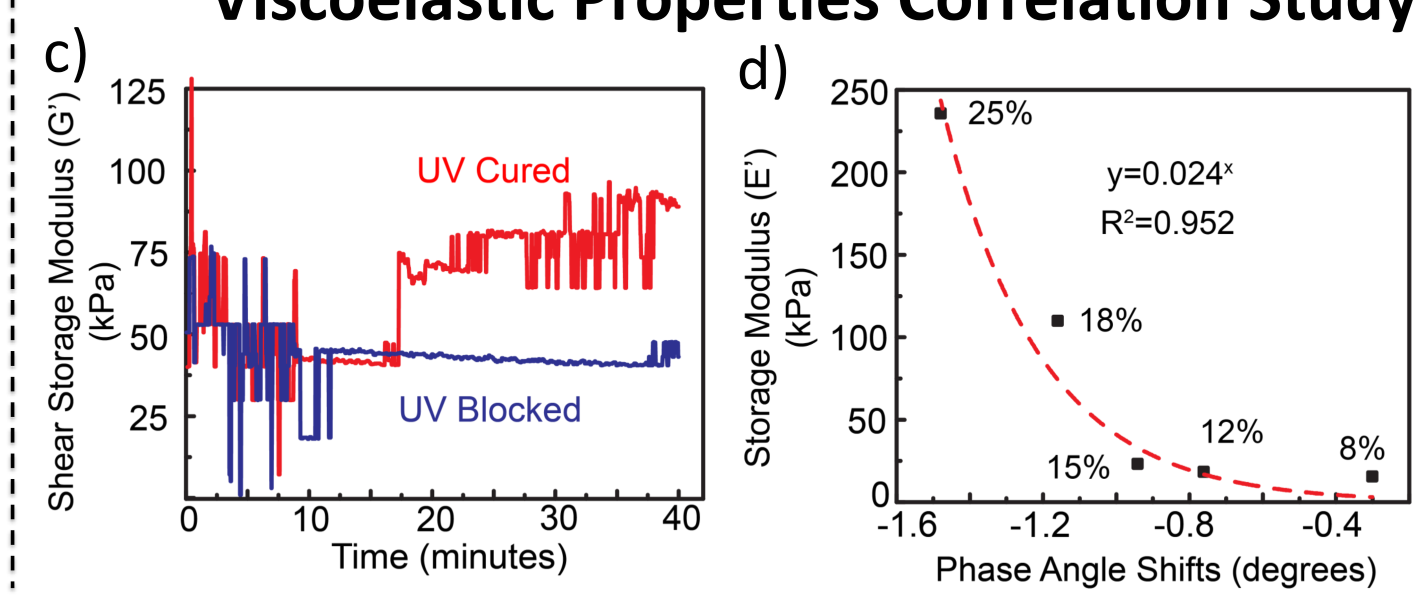
$$F_{fluid} = -i\omega g_1 w(\omega,t) + \omega^2 g_2 w(\omega,t)$$

$$Q = \frac{\frac{4\mu}{\pi\rho_{fluid}b^2} + \Gamma_r}{\Gamma_i + \frac{4\gamma_{internal}}{\pi\rho_{fluid}b^2 L\omega}}$$

Signal Response During Printing



Viscoelastic Properties Correlation Study



Real-time Response

- Phase angle responds to material deposition and UV curing (a).

Closed Loop Feedback Control

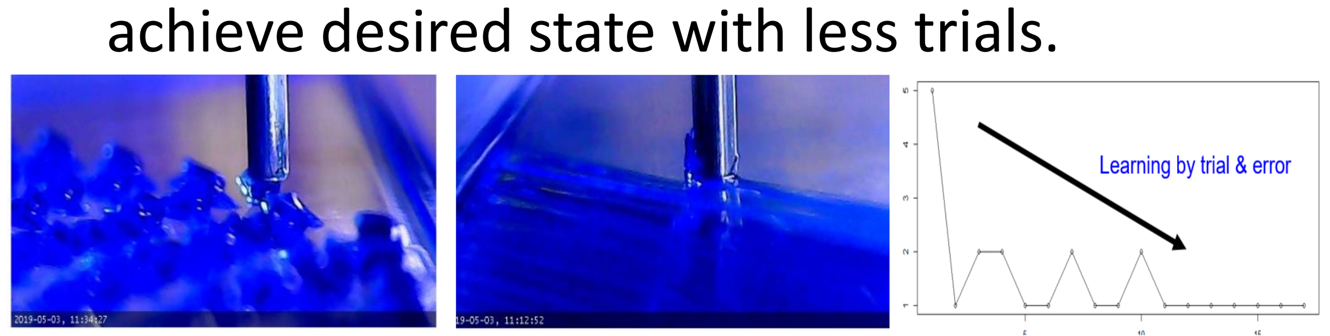
- Rule based closed loop feedback control used to control the degree of polymerization (b).

Signal Change Correlates with Modulus

- Viscoelastic properties derived from sensor value (c); relationship between storage modulus & phase angle shifts of the sensor (d).

Reinforcement Learning (RL) Based Control

- RL learns the sequence of optimal actions to achieve desired state with less trials.



Defect State | Desired State | RL Results

Broader Impact (society)

- Socioeconomic outcomes in public health and organ transplant safety can be realized from the findings of this research.

Broader Impact (education and outreach)

- Provided course materials for five courses in both UG and grad levels.
- Hosted >10 REU students.

Broader Impact (quantify potential impact)

- There are approximately 28,000 organ transplants each year; the waiting list has 120,000 people.
- This research will provide a sustainable solution.

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