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Towards a reproducible intervertebral disc model – a bioprintable nucleus pulposus-like material

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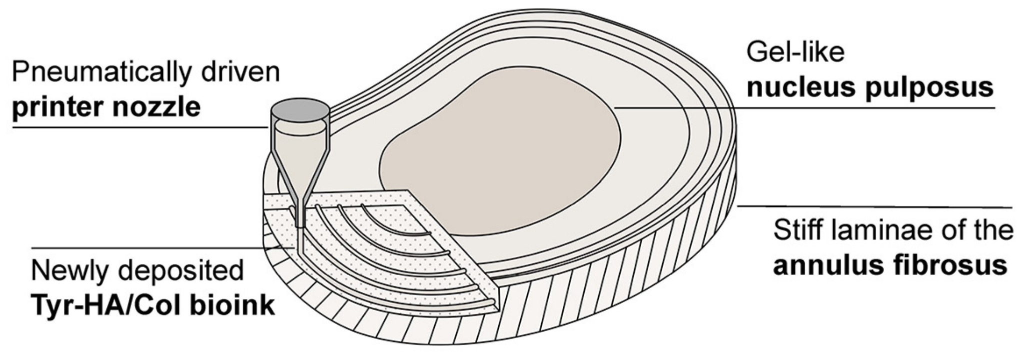
Introduction

- Disk degeneration is a major source of pain and disability, and a significant financial burden on healthcare providers worldwide[1].
- Treatments are limited due to the lack of a suitable model reproducing the disk composition, organization, and mechanical properties[2-4].

Design

- A bioink based on a tyramine derivative of hyaluronic acid (Tyr-HA) and unmodified type I collagen (Col) was developed to mimic the nucleus pulposus in the core of the intervertebral disc.
- Enzymatic (HRP/H_2O_2) and light crosslinking were utilized stepwise to modify the printability and final strength of the material.
- Various compositions of the bioink were evaluated rheologically.



Results

- Varying the concentration of HRP and H_2O_2 allows tuning of gelation time (Figure 1) and stiffness (Figure 2).
- Gels with 30 mg/ml of Tyr-HA and 20 mg/ml of Col were successfully prepared and tested across a range of strains (Figure 3).
- Light crosslinking can double the modulus of the material, stiffening the final structure and improving its mechanical properties (Figure 4).
- When exposed to high shear conditions, the Tyr-HA/Col bioink exhibits a fluid-like behavior, which facilitates extrusion through a printer nozzle (Figure 5).

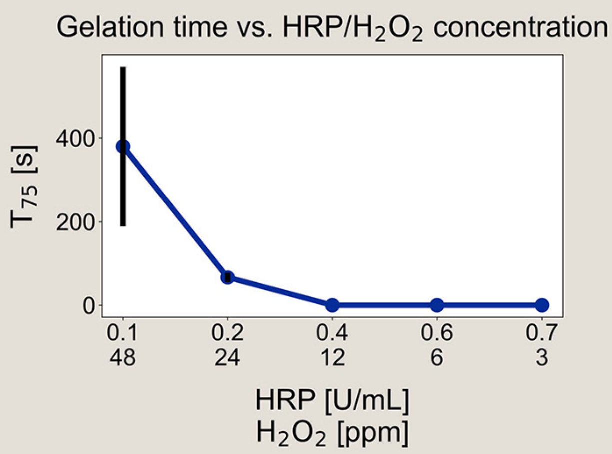


Figure 1: Gelation time decreases with an increase in HRP concentration. At 0.4 U/ml of HRP, the material formed a gel faster than it could be set-up for testing on the rheometer. Black error bars represent the standard deviation.

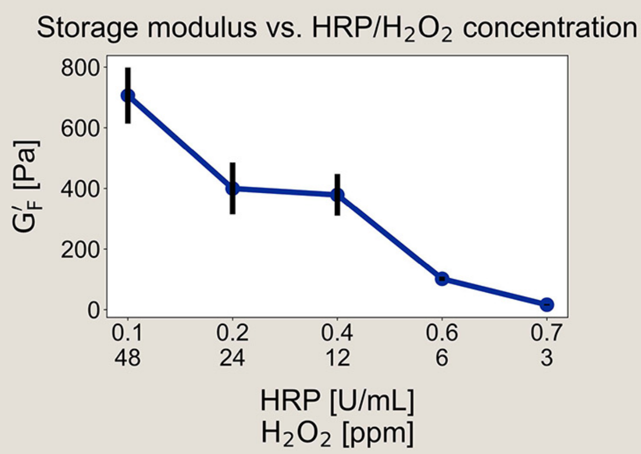


Figure 2: Storage modulus of the gel can be adjusted by varying the H_2O_2 concentration. With an increase in H_2O_2, the degree of crosslinking between Tyr-HA chains is higher. Black error bars represent the standard deviation.

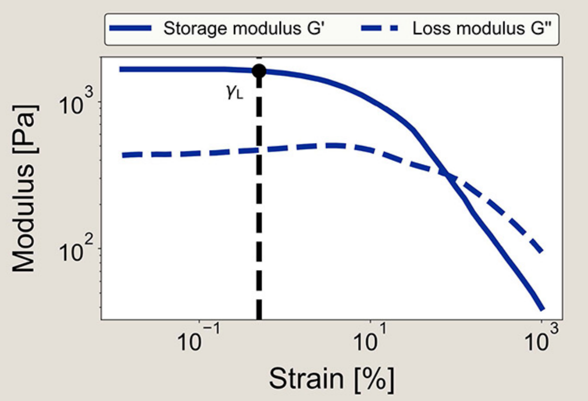


Figure 3: An amplitude sweep of the Tyr-HA/Col gel reveals the end of the linear viscoelastic region at a strain of 0.5%.

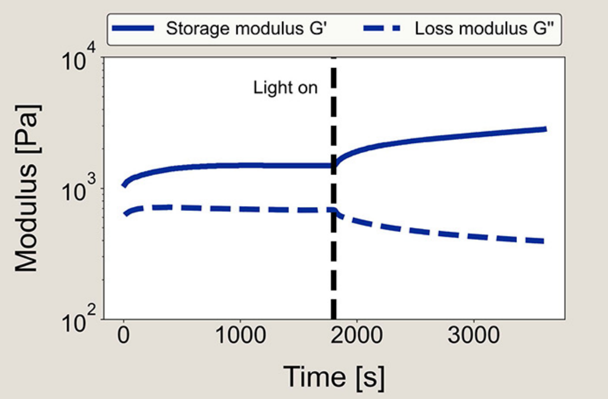


Figure 4: Shining green light on the gel at the half-point of a time sweep results in a rapid rise of storage modulus, doubling that achieved by enzymatic crosslinking alone in the first half of the test.

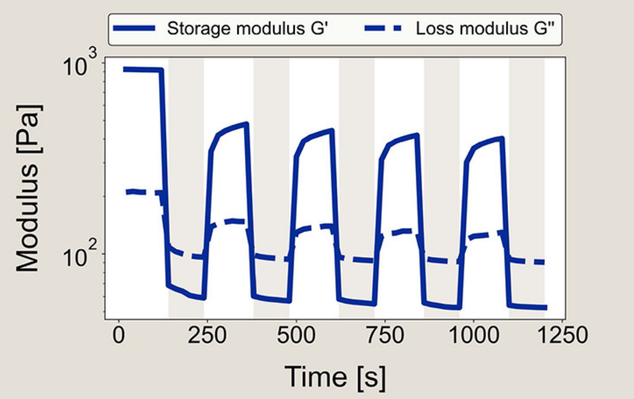


Figure 5: During high shear, the bioink exhibits a more fluid-like behavior. After the shear is removed, it once again behaves like a gel. Shaded areas represent intervals of high shear stress.

Conclusion

A versatile Tyr-HA/Col bioink system based on modified matrix components is presented. Due to its double-crosslinking mechanism, the material properties can be tuned both prior to and after printing, ensuring the material is extrudable following enzymatic crosslinking, retains its shape after deposition, and can be further stiffened with light crosslinking.

Acknowledgements

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References

1. Hartvigsen, J. et al. Lancet 391, 2356–2367 (2018)
2. Whatley, B. R. et al. Mater Sci Eng: C 32, 61–77 (2012)
3. Daly, C. et al. BioMed Res Int 2016, 1–14 (2016)
4. Yang, Q. et al. Orthop Surg 8, 11–18 (2016)

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