Supramolecular DNA-based hydrogels as tunable scaffolds for cell mechanobiology

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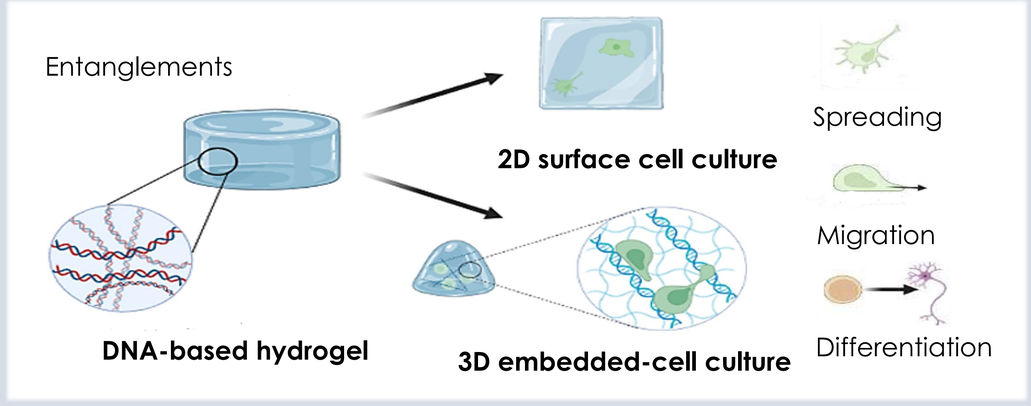
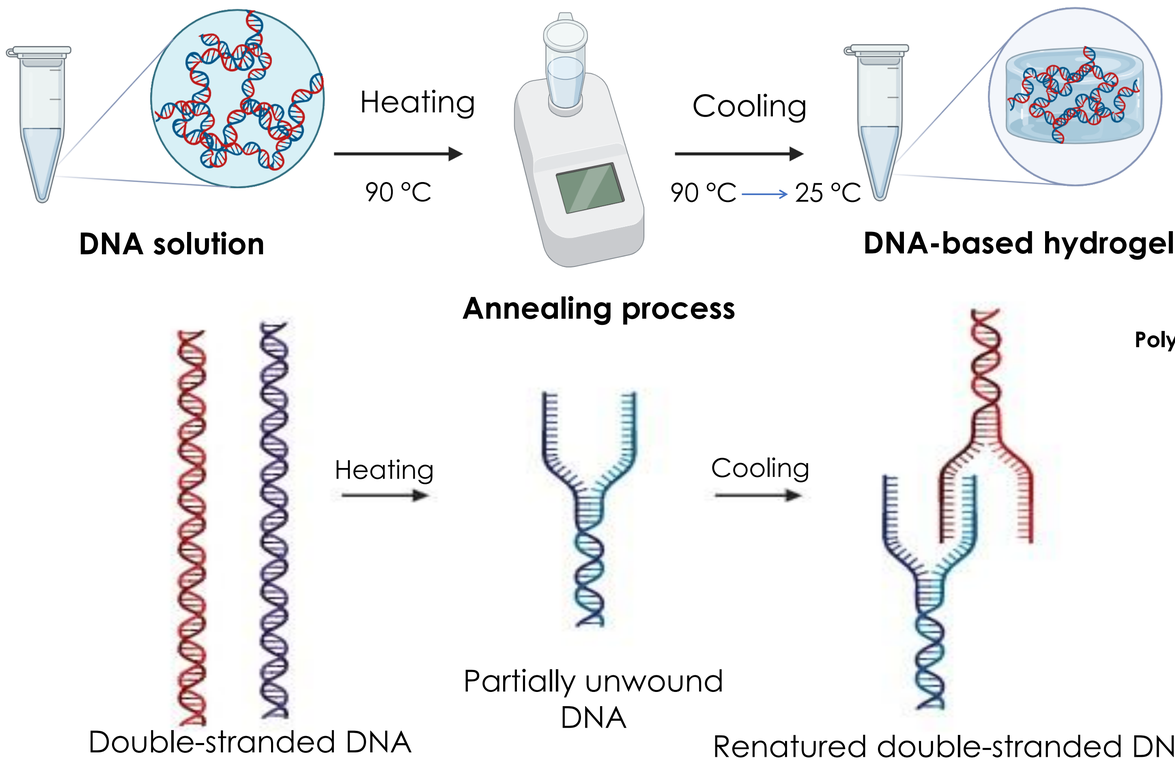
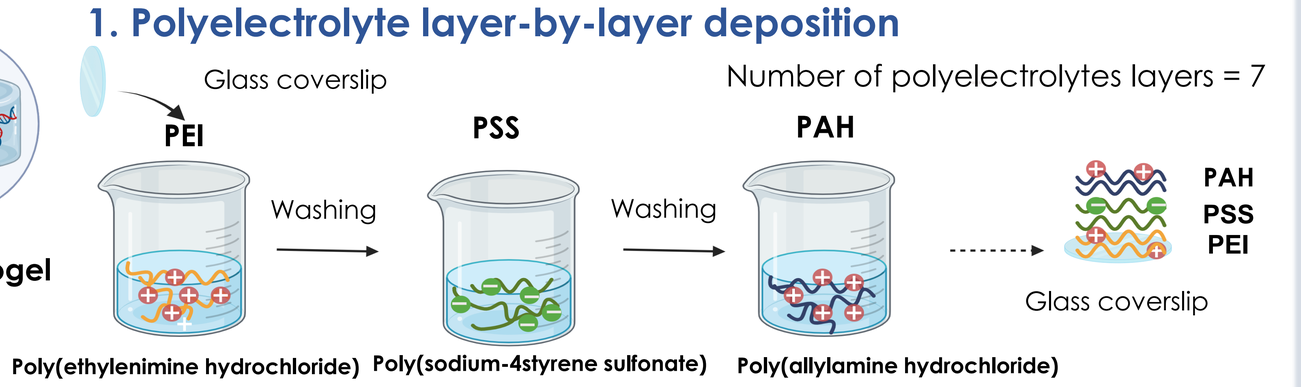
Hydrogels have emerged as promising biomaterials due to their ability to replicate the cellular microenvironment. Among these, DNA-based hydrogels have garnered significant attention because of the intrinsic properties of DNA, including biocompatibility, programmability, and tunable mechanical properties. Here, we propose to use genomic DNA to develop innovative, customizable scaffolds for 2D and 3D cell culture. Using herring DNA of 20,000 base pairs, we formed DNA-based hydrogels of varying stiffnesses. We analyzed their chiroptical properties in solution and gel state. We investigated the stiffness by nanoindentation technique and measured their swelling rate.



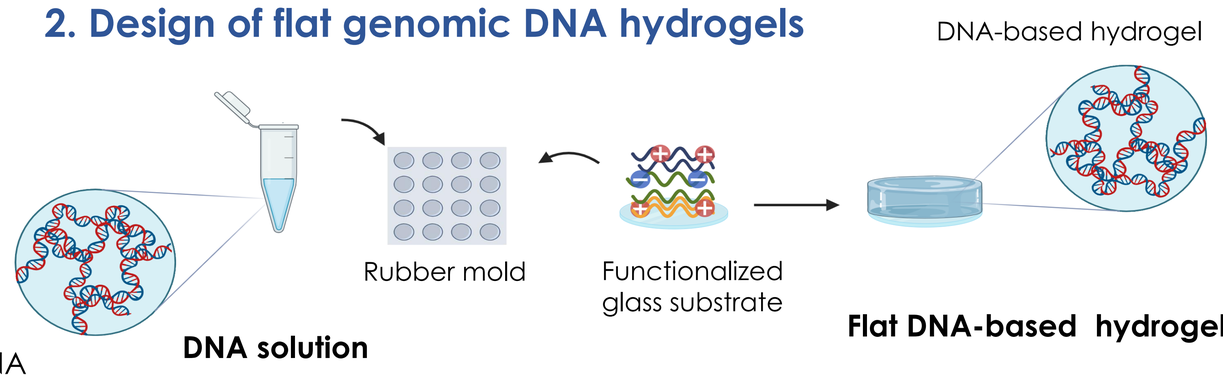
Strategy: design of genomic DNA hydrogels



1. Polyelectrolyte layer-by-layer deposition

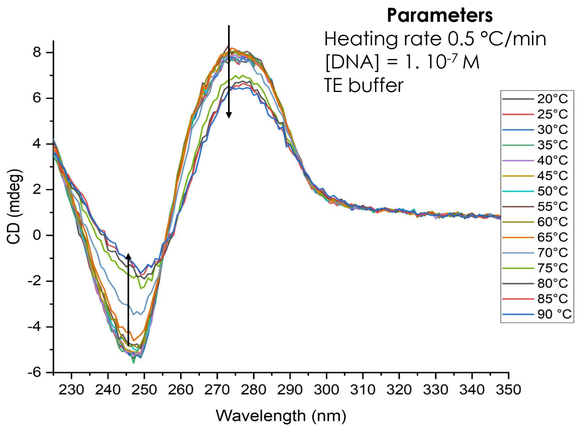


2. Design of flat genomic DNA hydrogels



Chiroptical properties of genomic DNA

In solution

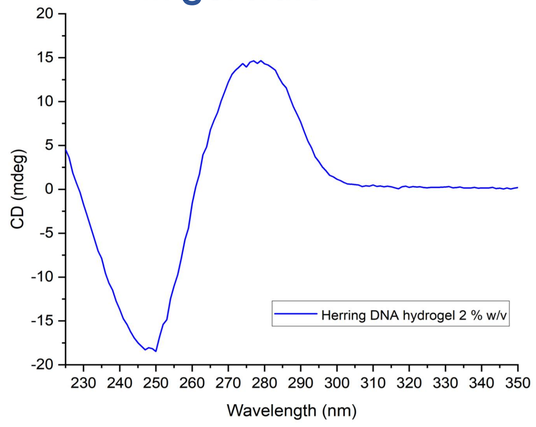


- CD signal of DNA decreases when temperature increases.

Double-strand DNA ⟶ Single-strand DNA

Reduction of excitonic coupling $T_{m\ exp}$ = 65 °C

In gel state

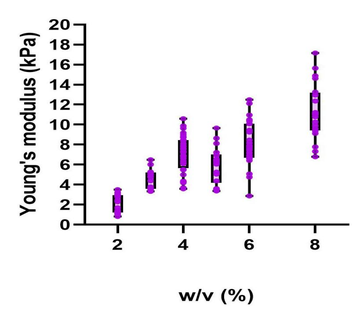


- CD spectrum of genomic DNA is similar in solution and in gel state.

Hydrogels are mainly composed of large portions of double-stranded DNA.

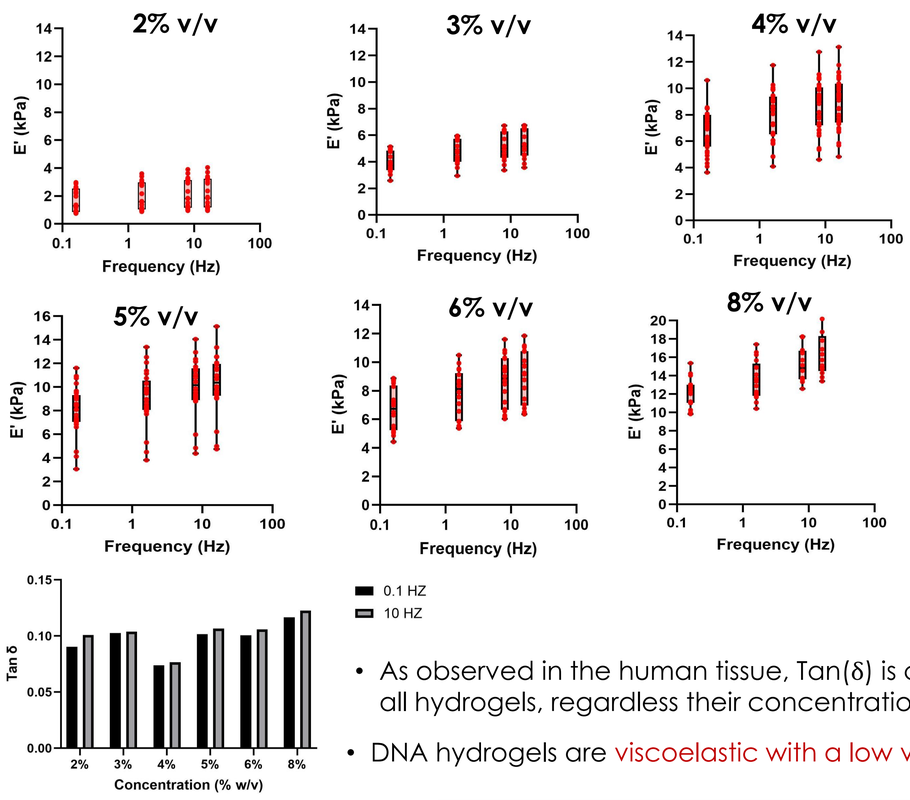
Mechanical properties of genomic DNA hydrogels

1. Elastic properties of DNA hydrogels



- By varying DNA concentration, the stiffness of the herring DNA hydrogels can be modulated from 1.9 ± 0.9 kPa to 11.3 ± 2.8 kPa.

2. Viscoelastic properties of DNA hydrogels



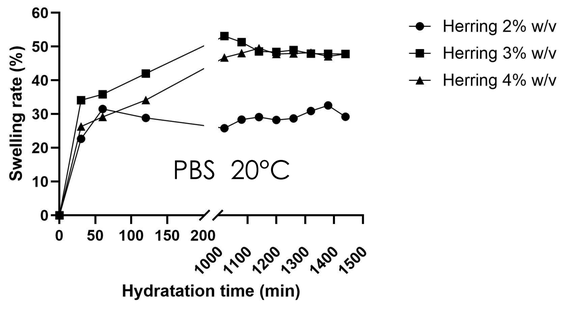
- We observed a stress stiffening regardless the concentration.
- As observed in the human tissue, Tan(δ) is close to 0.1 for all hydrogels, regardless their concentration.
- DNA hydrogels are viscoelastic with a low viscous component.

Swelling analyses of genomic DNA hydrogels

- Concentration effect: The swelling rate of hydrogels at 3% w/v and 4% w/v (≈ 50 %) is higher than for hydrogels at 2% w/v (≈ 30%).
- Swelling kinetics : The hydrogels swell rapidly and the swelling rate reaches a plateau.

$$\text{Swelling rate (\%)} = \frac{m_{wet} - m_{dry}}{m_{dry}}$$

Herring DNA hydrogels



Conclusion

- Herring DNA hydrogels present promising physico-chemical properties and can be used as scaffolds for studying cell migration. By moduling their stiffness, we will investigate the durotaxis mechanism in epithelial cells in 2D and 3D.

Outlooks

- **Morphological characterization:** use scanning electron microscopy to visualize the architecture of DNA hydrogels (eg, porosity size, …).
- **Swelling analysis:** swelling ratio of herring DNA hydrogels (5% w/v, 6% w/v and 8% w/v).
- **Cellular culture:** analysis of cells in DNA-based hydrogels (MDCK epithelial cells, MCF 10A epithelial cells).