Tuning Gellan Gum Hydrogels to Mimic Brain Tissue for Glioblastoma Models

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Background

- Mechanical cues strongly regulate glioblastoma (GBM) cell behaviour.
- Native brain tissue is soft and viscoelastic.
- *In vitro* models must replicate brain-relevant mechanical properties

Aim

- To tune the viscoelastic properties of gellan gum hydrogels to match native brain tissue mechanics for biologically relevant GBM models.

Methods

- Porcine white, grey matter and gellan gum hydrogels characterised by oscillatory shear rheology **(Fig.1)**.
- 1% (w/v) gellan gum hydrogel fabrication by crosslinking via $CaCl_2$ (3.12–200 mM) or DMEM alone.

Results

- Porcine brain tissue: White matter exhibited higher stiffness than grey matter across the tested conditions **(Fig. 2).**
- Storage moduli for native porcine brain tissue were within the range of ~170–220 Pa, confirming the overall softness of the brain microenvironment.
- Gellan gum hydrogels: Storage modulus was highly tuneable via ionic crosslinking with calcium ions **(Fig. 3)** enabling control over gel stiffness.
- High $CaCl_2$ concentrations produced stiff hydrogels (>1 kPa), exceeding native brain tissue mechanics.
- Low $CaCl_2$ concentrations (3.12–6.25 mM) or DMEM crosslinking alone yielded stiffness values closely matching those of brain tissue, producing mechanically relevant substrates **(Fig.4)**.

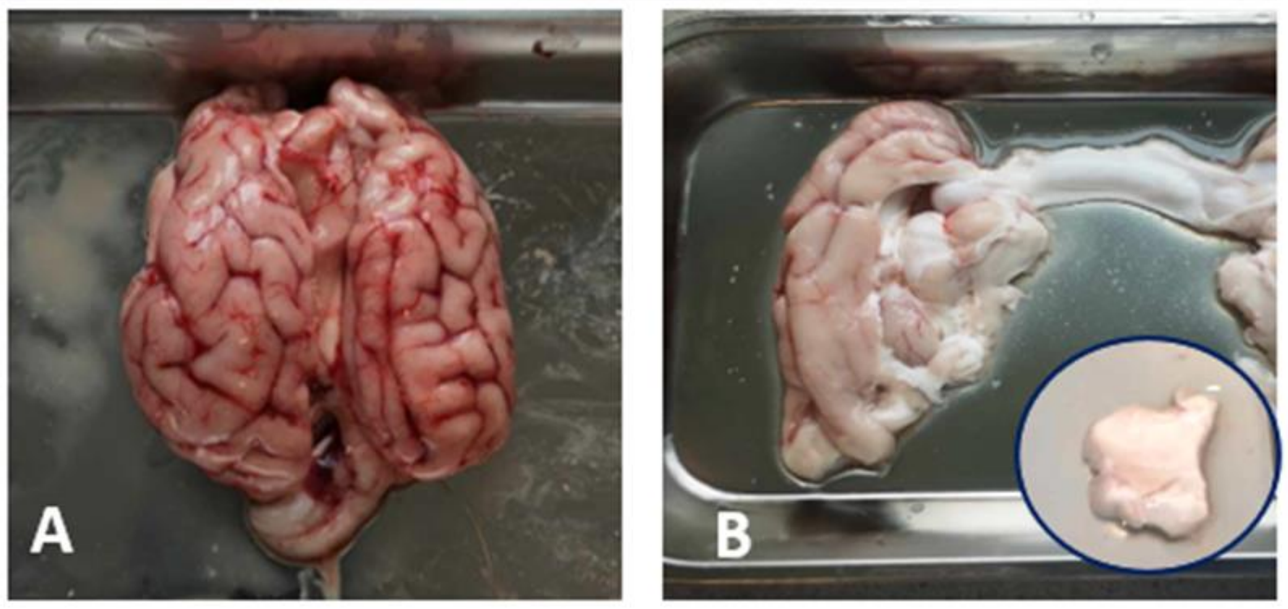


Figure 1. Images of Porcine Brain Before and During Dissection. A) Intact brain as received from local abattoir. B) Pig brain during bilateral dissection and separation of white and grey matter.

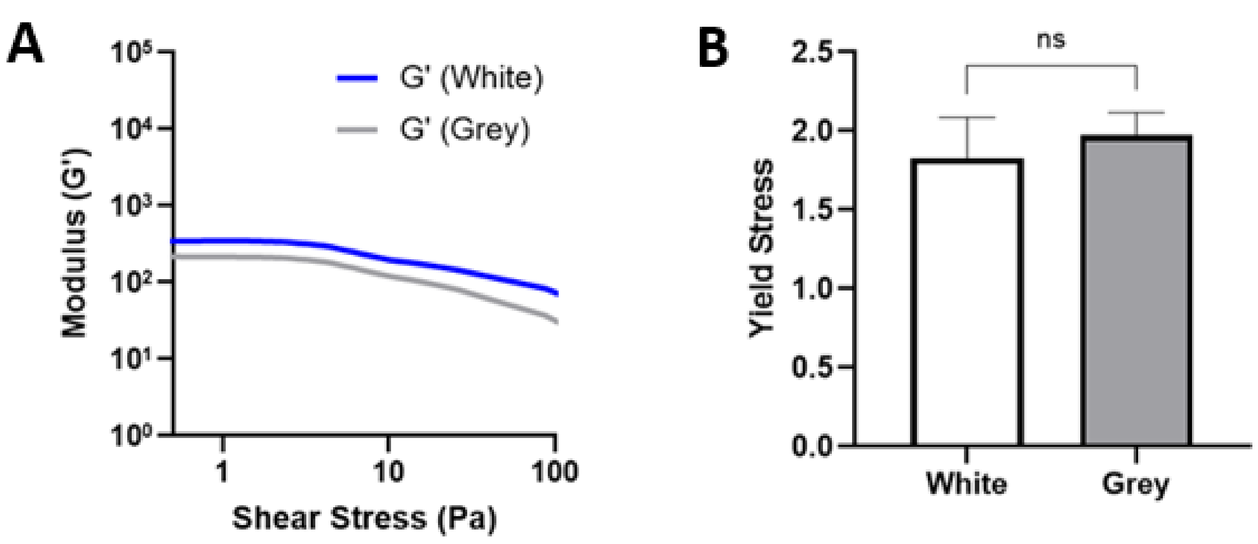


Figure 2. Mechanical Characterisation of Porcine Brain Tissue via Oscillatory Stress Rheology. A) G' values over a range of shear stresses for isolated white and grey brain matter. The amplitude sweep recorded with sample sizes of n=6 for white matter and n=3 for grey matter. B) Bar chart comparing yield stress values derived from stress sweeps. T-test results indicated no significant difference between the two groups (p = 0.40).

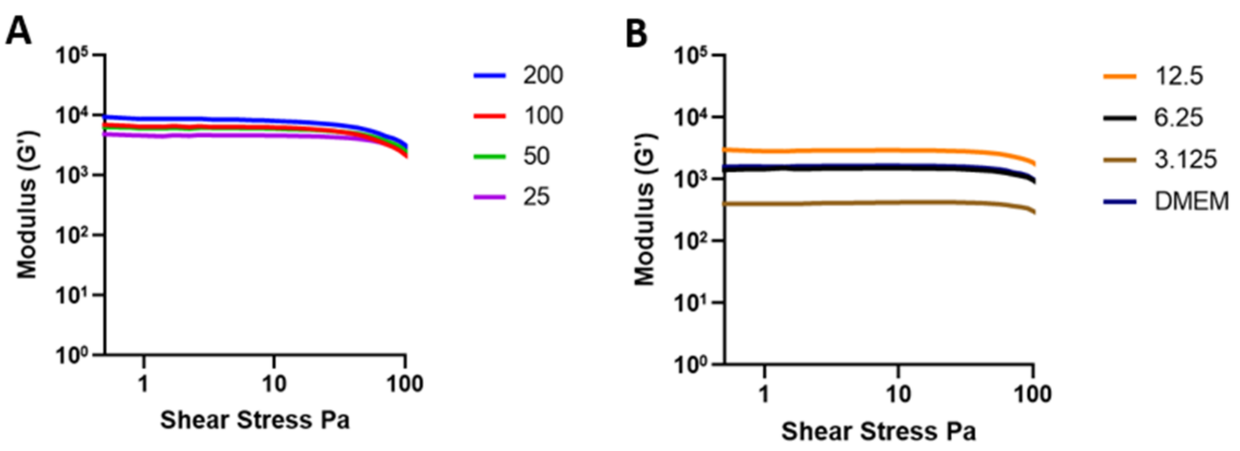


Figure 3. Mechanical Characterisation of 1% Gellan Gum Hydrogels via Oscillatory Stress Test. G' values over a range of shear stresses for hydrogels with different ion concentrations. (A = 200 – 25 mM, B = 12.5 – 3.215 mM including gels crosslinked with DMEM culture media alone (n=3).

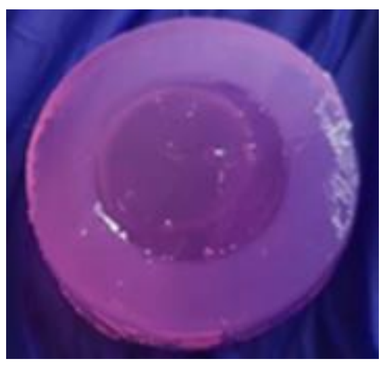


Figure 4. Gellan gum "mini-brain gel" prepared from 1% (w/v) gellan gum and ionically crosslinked using DMEM, demonstrating structural integrity and optical transparency.

Key Findings

- Native porcine brain tissue exhibits distinct mechanical properties, with measurable differences between white and grey matter stiffness.
- The mechanical behaviour of gellan gum hydrogels is highly tuneable through controlled ionic crosslinking, enabling precise adjustment of stiffness.
- Gels crosslinked with low $CaCl_2$ concentrations or DMEM alone most closely replicate brain-relevant mechanics, providing cell-compatible, biologically relevant 3D substrates

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Conclusion: Gellan gum hydrogels provide a mechanically relevant, optically transparent platform for potential use *in vitro* GBM modelling.

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