Development of a Correlative AFM and MALDI-MSI Platform to Map Spatial Mechanobiological Remodeling of the Hippocampal ECM

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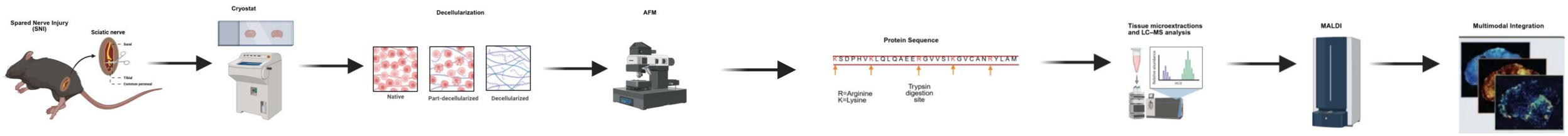
Background & Objective

- Context: **Hippocampal extracellular matrix (ECM)** = A biophysical niche regulating neuro-immune signaling.
- Gap: How **ECM mechanobiological remodeling** stabilizes chronic neuropathic pain remains undefined.
- Objective: Establish a novel correlative platform (AFM + MALDI-MSI) to decode ECM spatial mechanics & molecular signatures.

The Correlative Platform



Q1: How to Preserve ECM Integrity During Decellularization?

Strategies for ECM Decellularization

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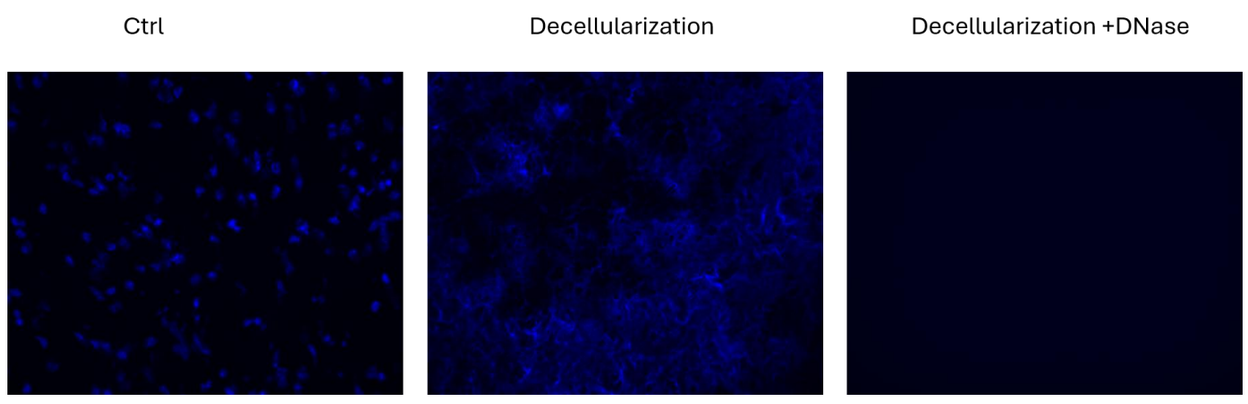
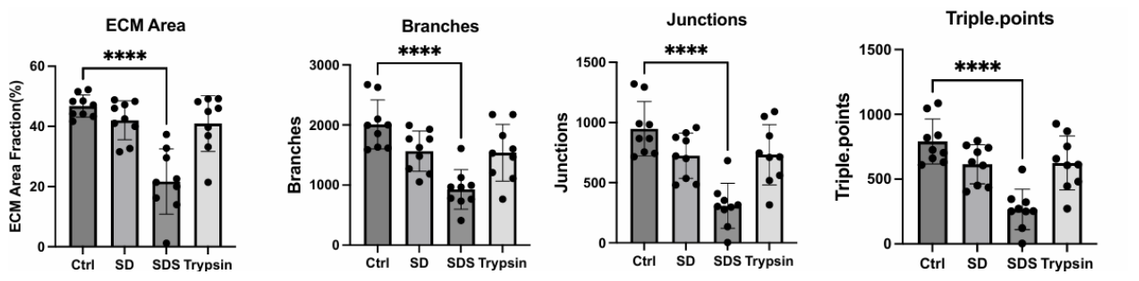
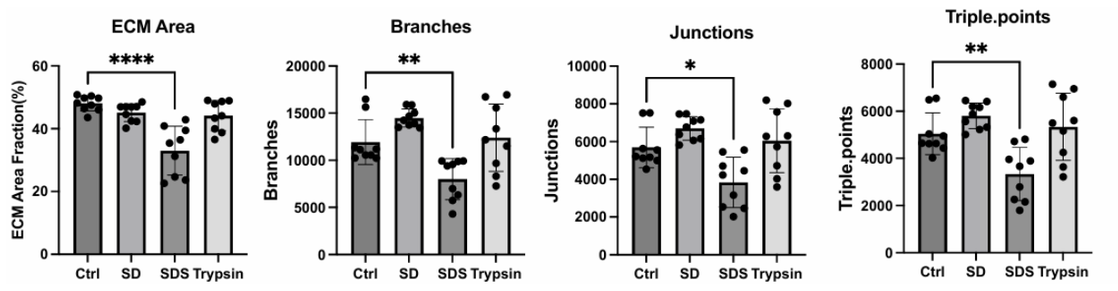
Method	Type	How decellularization is achieved
Sodium deoxycholate (SD)	Ionic detergent	Disrupts cell membranes and releases cellular contents
Sodium dodecyl sulfate (SDS)	Strong ionic detergent	Solubilizes membranes and denatures proteins for efficient cell removal
Trypsin	Proteolytic enzyme	Cleaves cell-adhesion proteins to detach cells
Triton X-100	Non-ionic detergent	Mildly permeabilizes membranes



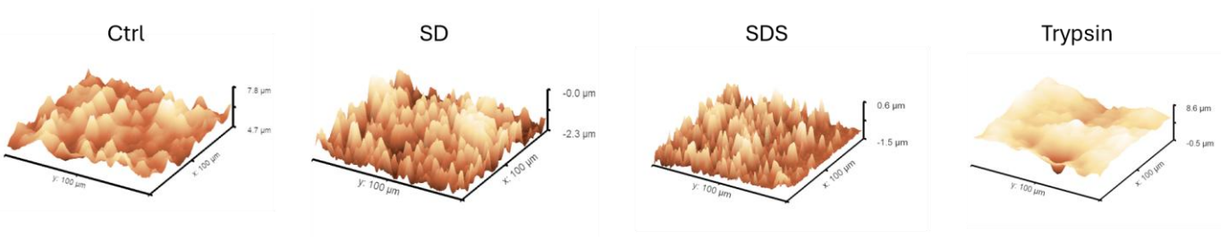
Atto 488 NHS-the overall protein distribution and abundance

Direct Red 8-labels fibrillar collagen

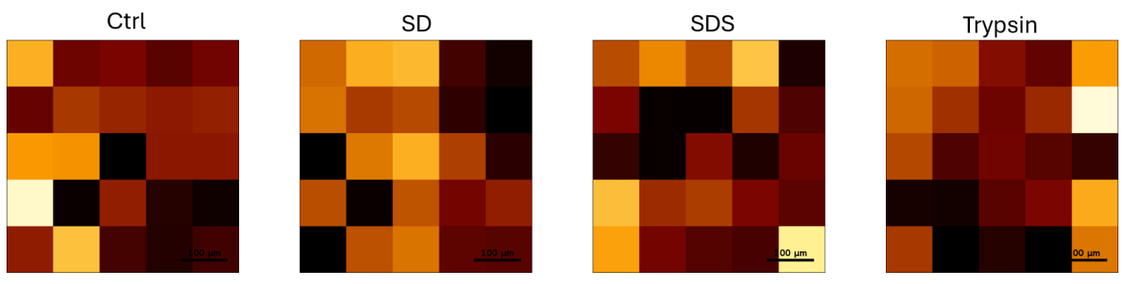




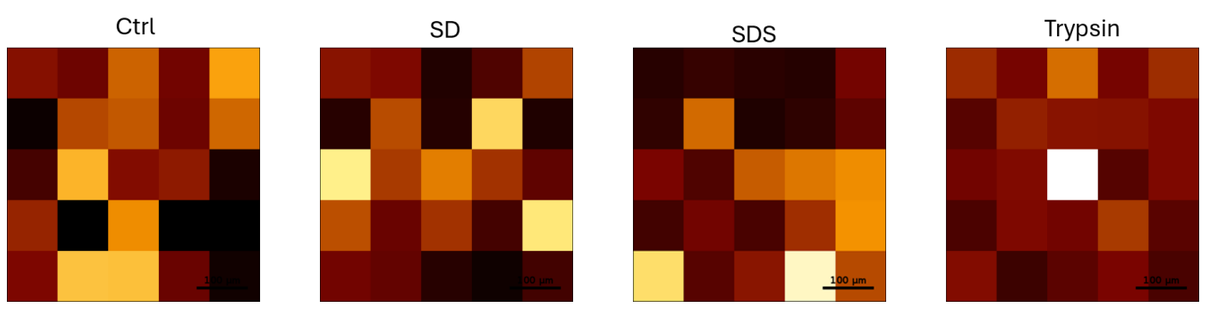
Hippocampus Roughness

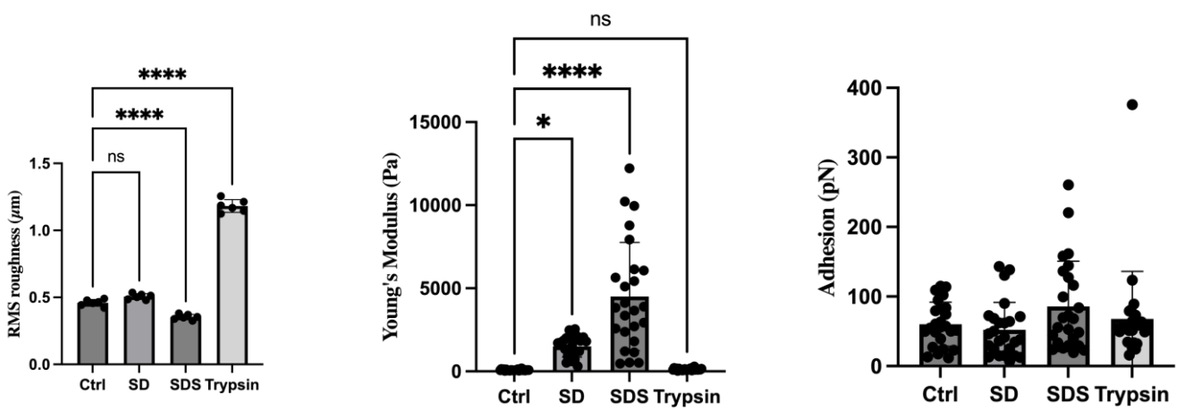


Hippocampus Stiffness



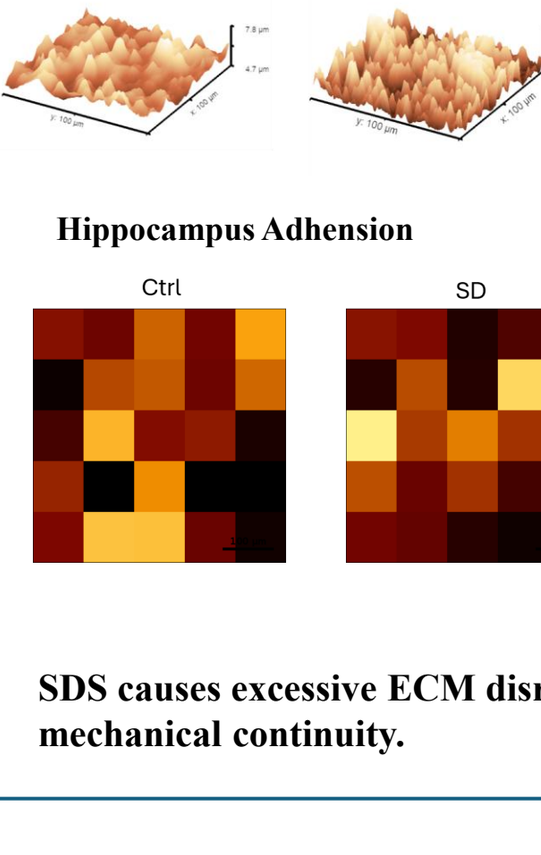
Hippocampus Adhension

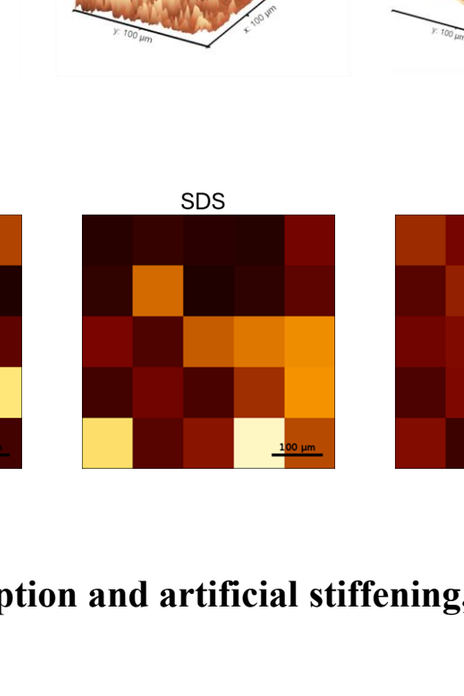


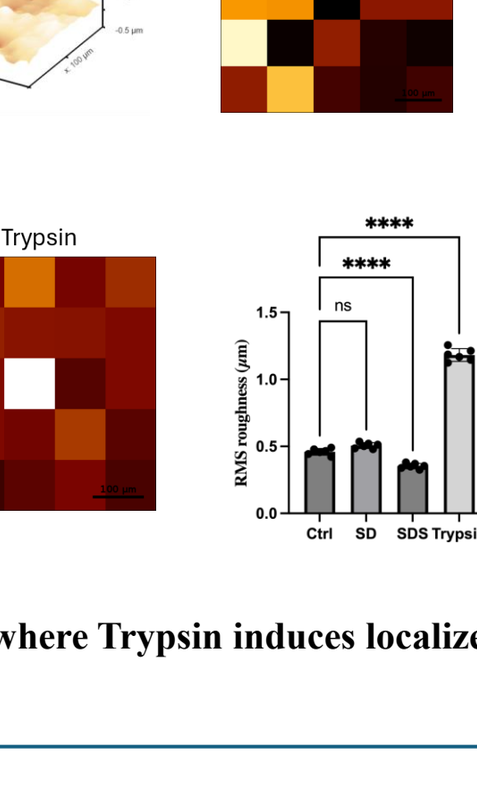


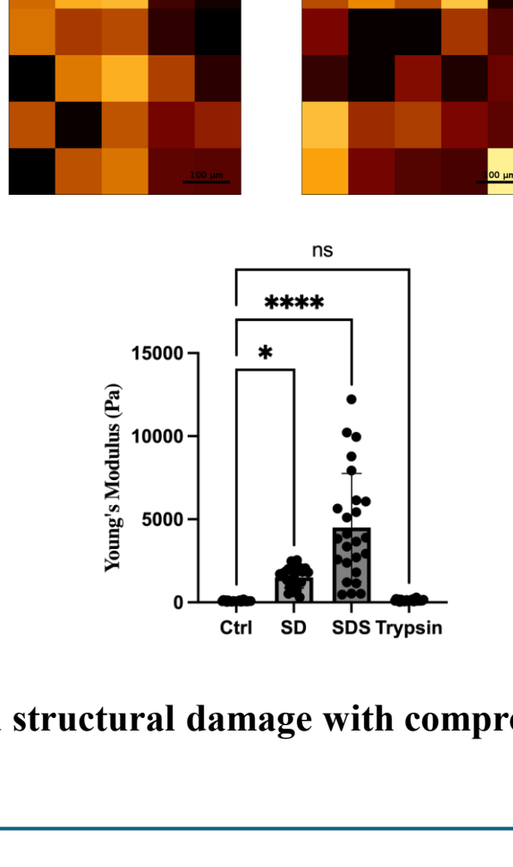
SDS causes excessive ECM disruption and artificial stiffening, where Trypsin induces localized structural damage with compromised mechanical continuity.

Q2: How to Maximize ECM Ionization Efficiency in MALDI-MSI?









Tajerian *et al., Mol Psychiatry* (2018)

Applying our workflow, we demonstrated that the targeted decrease in ECM protein expression correlates with reduced hippocampal stiffness following tibia fracture.

Summary of Current Work

Platform Established: AFM and MALDI-MSI workflows successfully integrated for consecutive hippocampal sections.

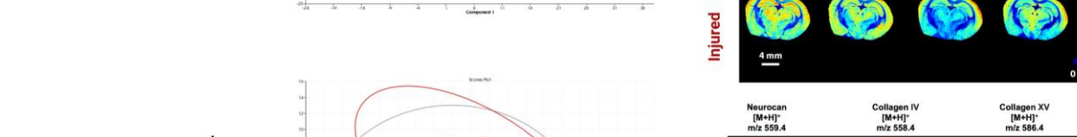
Method Optimized: Decellularization preserves true ECM mechanics; tailored digestion maximizes MALDI-MSI signal

Model Validation: Demonstrated that targeted decreases in ECM protein expression correlate with reduced hippocampal stiffness following tibia fracture.

Future Directions

Disease Application: Map ECM mechano-molecular remodeling in a neuropathic pain model.

Bioinformatic Integration: Pixel-level co-registration of mechanical and biochemical signatures.



We invite you to view our lab website!

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