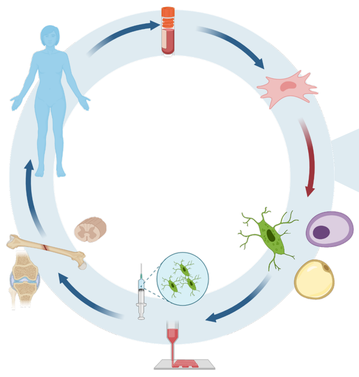
Engineering Material-Mediated Bioelectric Cues for Stem Cell Response

Kaiwen Zhang, Chayla Reeves, Luke Martino, ***Amy Gelmi****
RMIT University, Melbourne VIC, Australia
** amy.gelmi@rmit.edu.au*



- External physical stimulation offers a precise and tailorable approach to manipulating the cellular response.[1]
- Stem cells can be 'primed' for the desired phenotype with an *in vitro* treatment, enabling a wide range of stem cell therapies to be delivered from a single cell culture platform.

Elucidating the Transient Response of Stem Cells

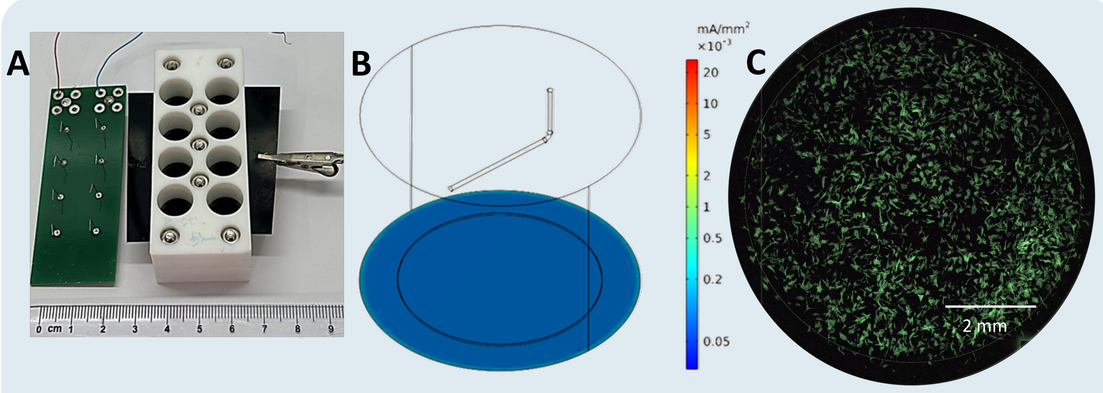


Figure 1: (A) Custom stimulation devices for conductive materials (pictured: polypyrrole), (B) field simulation, (C) actin stained hMSCs, (D) injected current, (E) mineralisation quantification after 14 days culture, 5 days applied stimulation.

0.08 µC (1Hz) demonstrated to enhance osteogenesis and 0.4 to 1.5 µC (1Hz) inhibits osteogenesis. [2]

Standardised stimulation protocol to apply the same charge in the same pulse timeframe enables comparison between different conductive materials, both result in osteogenesis.

Charge injection is key – but how does it trigger cellular response?

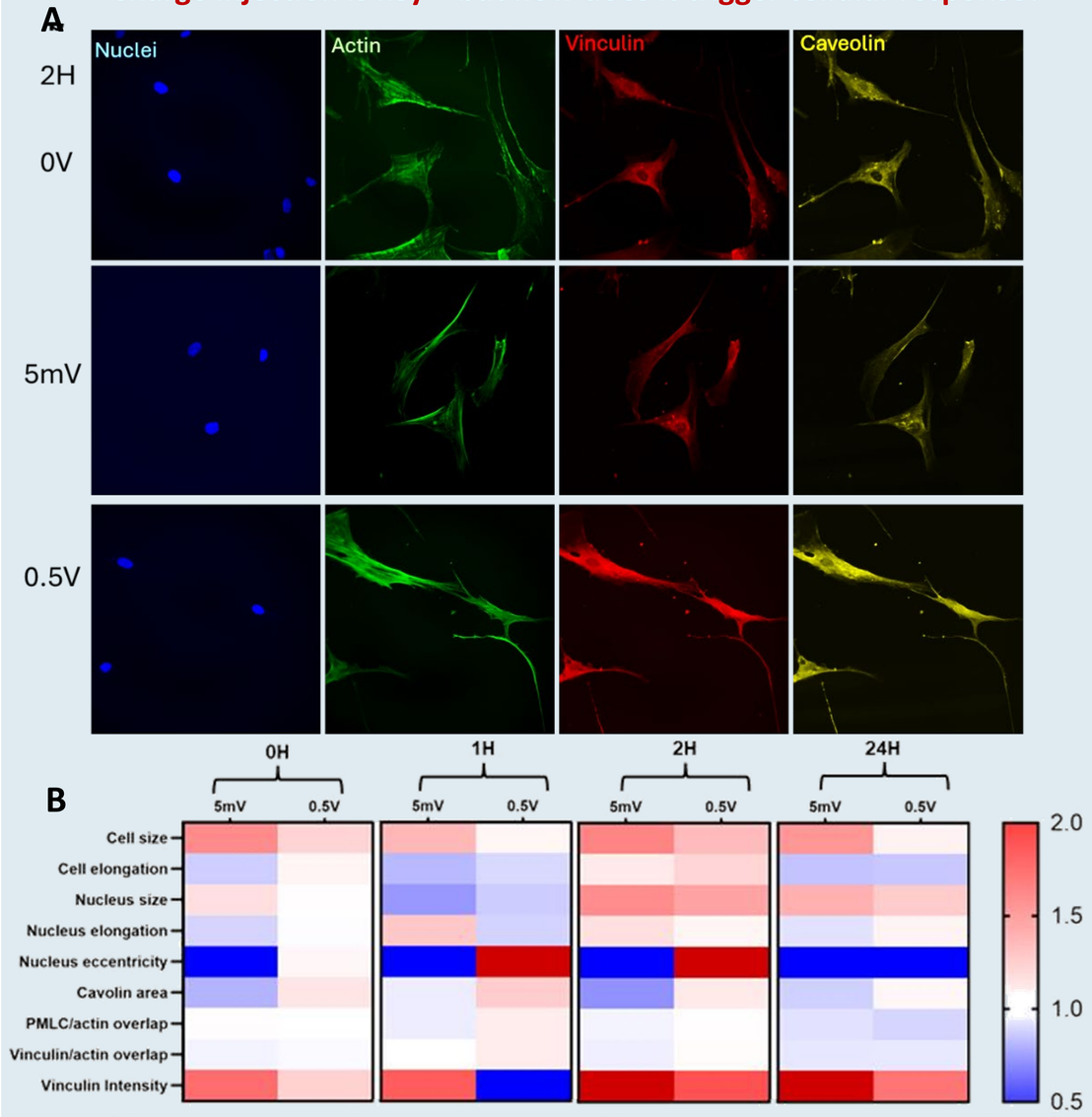
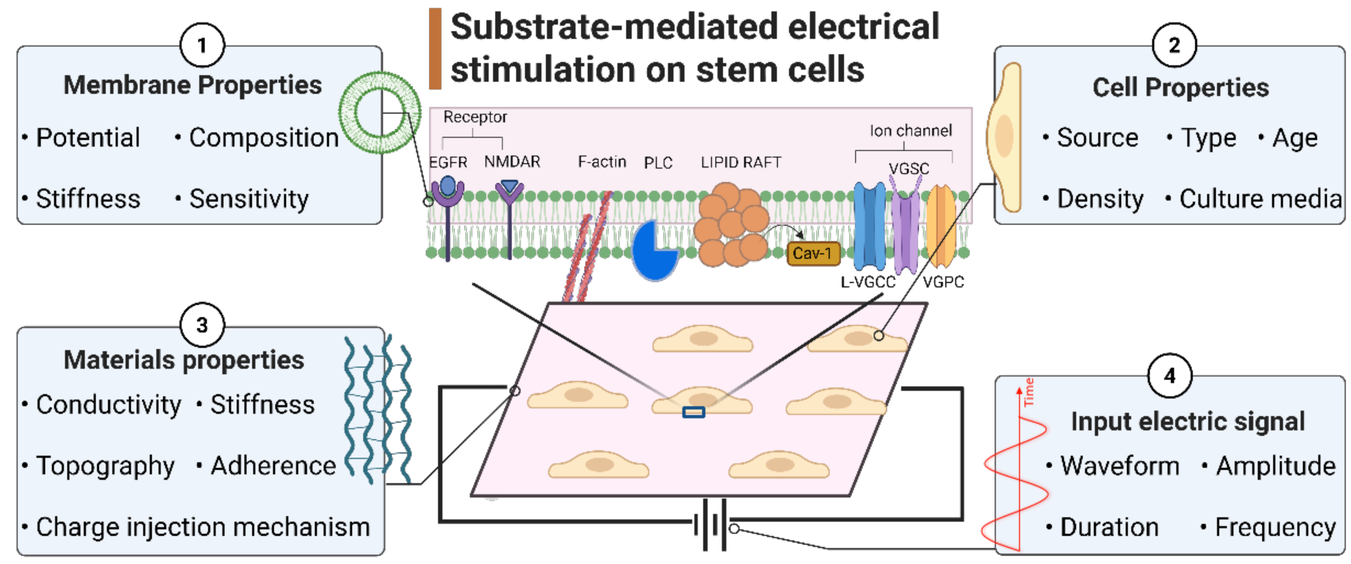


Figure 2: (A) Representative images of hMSCs 2h post-stimulation. (B) Time point high content image analysis of hMSCs post-stimulation, normalised to the unstimulated controls.

Electrical Stimulation Modulates Mechanically Sensitive Components

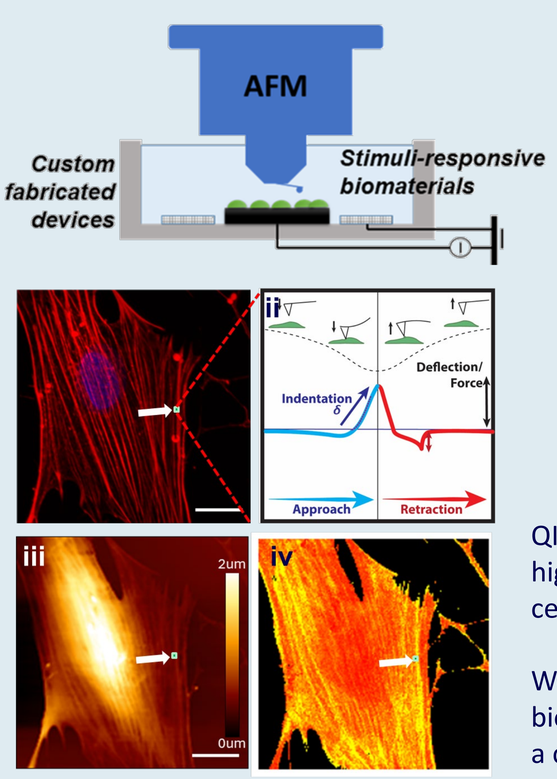
K. Zhang, et al, "*The Bionic Interface: Considering the Material Mediated Electrical Stimulation of Stem Cells*." Advanced Materials, 2025

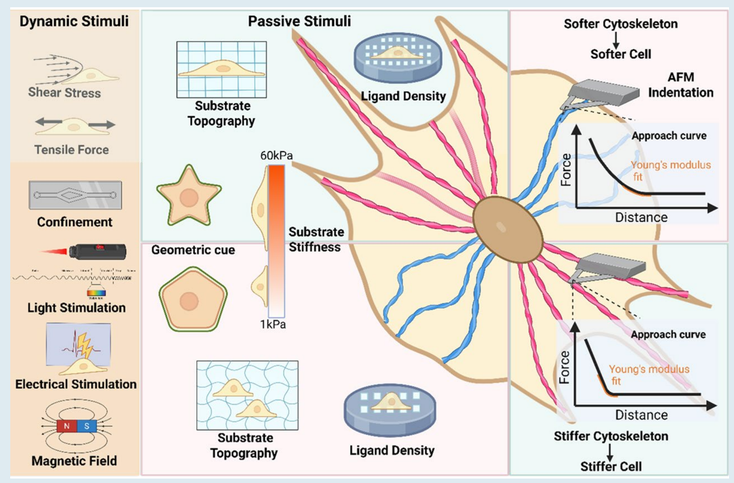


Conductive materials deliver electrical charge, directing stem cell differentiation in the absence of exogenous biochemical triggers down several phenotype pathways (osteogenic, neurogenic, smooth muscle, and chondrogenic).[2-5] Here we investigate the underlying mechanisms in human mesenchymal stem cells (hMSCs) triggered by electrical stimulation.

How stem cells transduce the electrical signal into a biological one is still unclear.
Does the nature of the conductive material play a role?
Can we modulate electrical signals for different cell outcomes?

Bio-AFM: Live Cell Analysis to Track Biomechanical Changes





QI-mode AFM enables fast indentation scanning, resulting in high resolution stiffness maps with negligible disruption to live cells.

We simultaneously stimulate and scan the hMSCs to quantify biomechanical response to an applied electrical stimulation via a conductive biomaterial.

Applied electrical stimulation induces a 'stiffening' response from the hMSCs, which persists and further develops post-stimulation.

BioAFM enables tracking of the cytoskeletal rearrangement, with no need for stains or fixation.

K. Zhang, et al, "*At the Pointy End of Mechanobiology: AFM for Transient Biomechanical Analysis*." Advanced Healthcare Materials, 2025

K. Zhang, et al, "*Live Quantitative Characterization for Stem Cell Biomechanics.*" Advanced Materials Interfaces, 2025

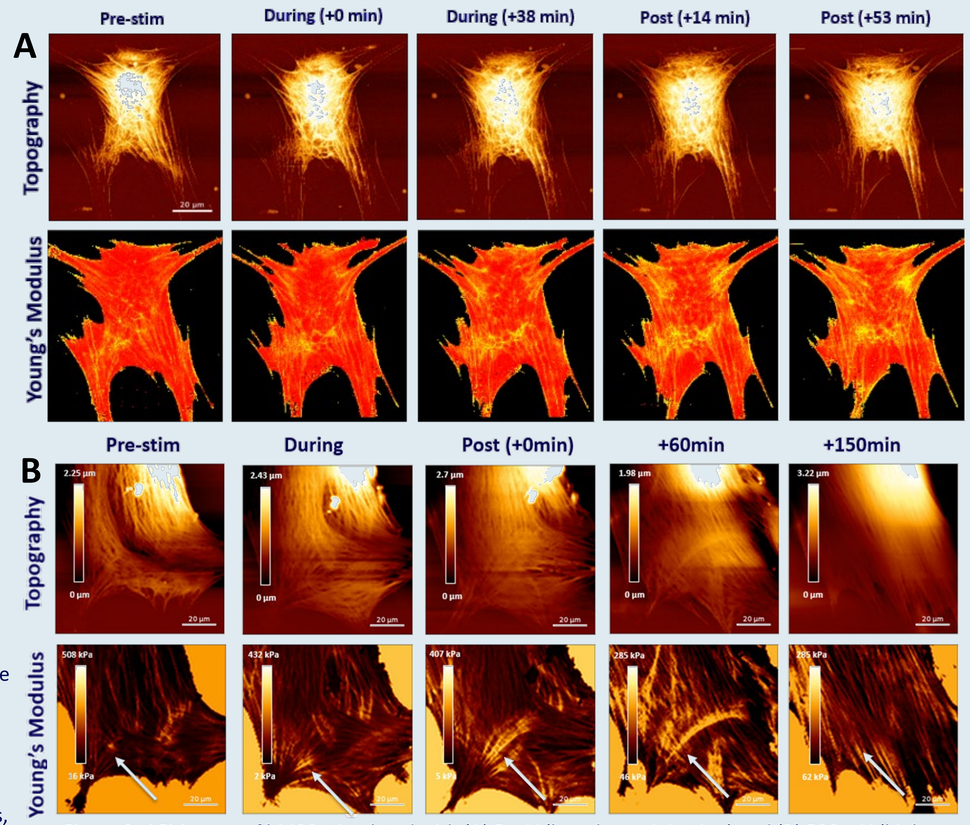
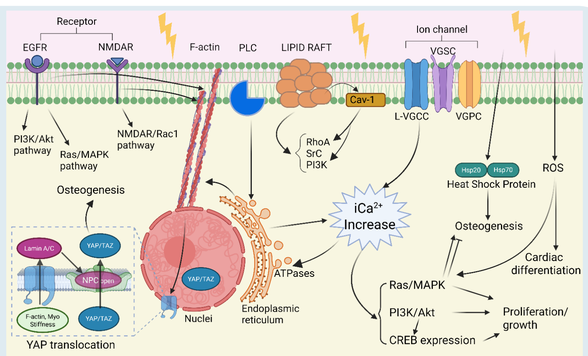


Figure 3: AFM scans of hMSC stimulated with (A) 5 mV (low charge injection) and (B) 500 mV (high charge injection), pulsed at 1 Hz for 1h.

Stem cell fate is known to be directed via mechanical cues - electrical stimulation can in turn be tuned to trigger different mechanotransduction response in hMSCs.

Further *omics* analysis will help elucidate immediate and downstream pathway activations.



References

[1] Gelmi, A., et al. (2021). Advanced Healthcare Materials, 10; [2] Balikov, D. A., et al. Nanoscale 2016, 8 (28); [3] Björninen, M., et al. Ann. Biomed Eng 2017, 45 (4); [4] Kwon, H. J., et al. Scientific reports 2016, 6; [5] Zhou, J., et al. Frontiers of Mat. Sci. 2016, 10 (3)

Acknowledgements

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