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USING THE MOLECULAR CLUTCH MODEL TO UNDERSTAND THE REGULATORY ROLE OF THE EXTRACELLULAR MATRIX'S MECHANICAL AND MICROSTRUCTURAL PROPERTIES ON CELL MIGRATION

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The ineffectiveness of wound healing devices to address chronic or long-lasting wounds is due to our lack of understanding of the ideal three-dimensional (3D) environment for wound healing. This insufficient knowledge is due to limitations in our ability to experimentally isolate complex cellular interactions between the mechanical and microstructural properties of the 3D ECM that regulate wound healing. This study aims to develop a lattice-point-based computational model to understand how the ECM's mechanical and microstructural properties and cell properties interact to modulate cell migration and proliferation.

To simulate 3D cell migration, this computational model uses a modified approach to the lattice point model to simulate ECM migration and replication by using probability-based migration and replication (**Fig. 1**). The mechanical properties, microstructural properties, and cell properties are user-input and incorporated into the extracellular matrix (ECM) and into the three primary mechanisms in the model: 1) the force feedback between the cell and the ECM modeled through the molecular clutch, 2) the ring-shaped contact surface area between the ECM pores, and 3) the availability of ligands on the ECM.

We found that increases in ECM porosity and decreases in ECM pore size (pore diameter) led to an overall increase in average cell migratory rates (cell speeds). These trends are consistent with other investigators and demonstrate the model's ability to simulate some microstructural interactions [1], [2]. Furthermore, we found a biphasic trend (an increasing then decreasing phase), modeled by the Molecular Clutch Model, observed between the ECM's mechanical property of stiffness and cell migration rates. This trend was maintained even when changing various other ECM properties.

Our model for simulating 3D cell migration and replication may be conducive towards supporting claims on the effect of ECM pore size and ECM stiffness on cell migration in the ECM. It also supports that the Molecular Clutch Model can effectively represent the cell-ECM interactions essential for cell migration for softer substrates. These findings will help guide future research areas of interest into 3D cell migration behavior.

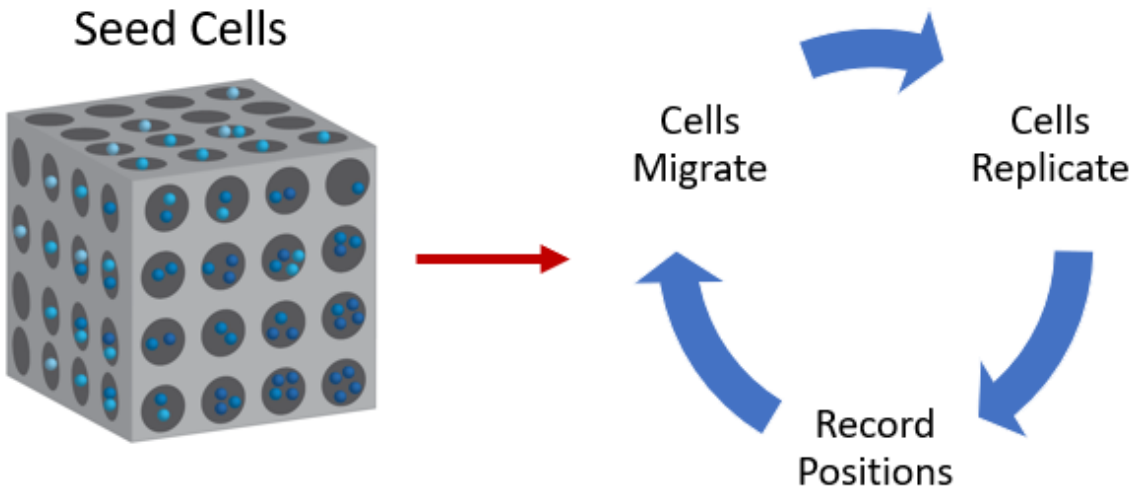

Fig. 1. 3D Cell Simulation. Following cell seeding into the lattice-point ECM structure, cells may perform a cycle of migration, then replication, followed by their positions being recorded. This cycle was repeated for all cells at each time step of the simulation. The positions of the cells were analyzed to derive our results.

References:

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[2] Z. Z. Zhang *et al.*, "Role of scaffold mean pore size in meniscus regeneration," *Acta Biomater.*, vol. 43, pp. 314–326, 2016.