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Undergraduate Abstract

Model of Mesenchymal Stem Cells Migration in Tissue Engineered Scaffolds for Articular Cartilage Repair

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Intro (50-250)

Osteoarthritis is a degenerative disease that damages articular cartilage in the joints, afflicting more than 528 million people worldwide (World Health Organization). The prevalence of this disease has led biomedical engineers to pursue the development of artificial tissue scaffolds which could be used to replace damaged cartilage and restore normal joint function. One challenge is to get cells (chondrocytes) into the artificial tissue scaffold in order to support and maintain long-term tissue health. Recent strategies to encourage cell migration and differentiation in scaffolds include seeding the cells directly in the scaffold, changing the physical and chemical makeup of the materials to incite mesenchymal stem cell (MSC) differentiation, and promoting chemical pathways to support cell migration through chemotaxis. In this study a mathematical model is developed to characterize the migration of MCSs from their source in subchondral bone marrow into an engineered articular cartilage scaffold. Cell migration is programmed in MATLAB, to explore a variety of different cases. The research is being performed in collaboration with biomedical engineers in Ireland.

Word Count: 168

Materials and Methods (50 to 250)

Three models are presented. The first is a 2D model showing cell migration beginning at the origin. Movement of 10,000 individual cells are simulated using iterative loops in MATLAB (2023b), with each cell taking 500 steps in random directions. In the next model, 50 cells start from random positions along the y axis, representing MSC migration from a confined boundary in the bone to the engineered tissue. In addition, drift was added in the y-direction. This drift in the code has the potential to represent data from various factors affecting cell migration, including chemical signals, pore size within the articular cartilage, cell morphology as it differentiates, or an engineered scaffold used in conjunction with other methods to repair a cartilage defect. (Xiaorong Fu, et al., 2019, R.J. McCoy et al., 2011, Joyce et al., 2023.). The last model in this study expands to a 3D cartesian coordinate system, with the cells starting from a random position on the XY plane and drifting upwards through four zones. The zonal representation models cell movement through the subchondral bone, an osteoarticular middle layer, and finally into the engineered scaffold. Each of these zones has its own rate of drift in the z-direction.

(0.5 units/step, 0.05 units/step, 0.005 units/step, 0.05 units/step), respective of the zone. The code calculates the distribution of the ending position of the cells, and outputs how many cells made it in each zone.

Word Count: 235

Results, Conclusions, Discussions (50 to 350)

Fig. 1A shows unrestricted cell migration by random walk in two dimensions. After tracking all cells to their final location, a histogram is created to show the distribution of distances traveled from the origin (Fig. 1B). The red circle indicates the average final position from the origin. This model represents fully stochastic cell movement, without consideration of any external factors. The second 2D model begins from a bounded random location on the horizontal line and shows the influence of drift and random movement on cell migration (Fig. 1C). The red line indicates the final average position of 50 cells with 500 steps each due to drift. The distribution of final cell locations from the x axis was calculated (Fig. 1D). The model was expanded to simulate movement in three dimensions (Fig. 2), in which 10,000 cells migrate through four semi-transparent planes. As shown, the cells move at different rates of drift respective to the particular zone the cell occupies. The code calculates how many cells are in each zone after 1,000 steps (Zone 1: 0; Zone 2: 8,174; Zone 3: 1,709; Zone 4: 117).

This approach not only has theoretical applications, but also relates to the research conducted in multi-layered Collogen Scaffolds for osteochondral defects (Levingstone et al., 2015). This study demonstrated that the layers all have different rates of diffusion and differentiation, which led to the development of the zonal strategy used above. In addition to diffusion, other physical characteristics of the material can play a large role in stem cell migration. As McCoy et al. demonstrated, flow rate and pore size greatly influence cell morphology, and subsequently the differentiation and migration of stem cells (McCoy et al., 2011). While these are not modeled in the present work, they are an element of ongoing research and discussion. Overall, the models presented in this project have the potential to be integrated with cell migration experiments and studies to develop new engineered tissues for articular cartilage. Combining mathematical modeling and experimental research may accelerate the development of artificial tissues to treat osteoarthritis and other diseases and injuries requiring articular cartilage replacement.

Word Count: 355

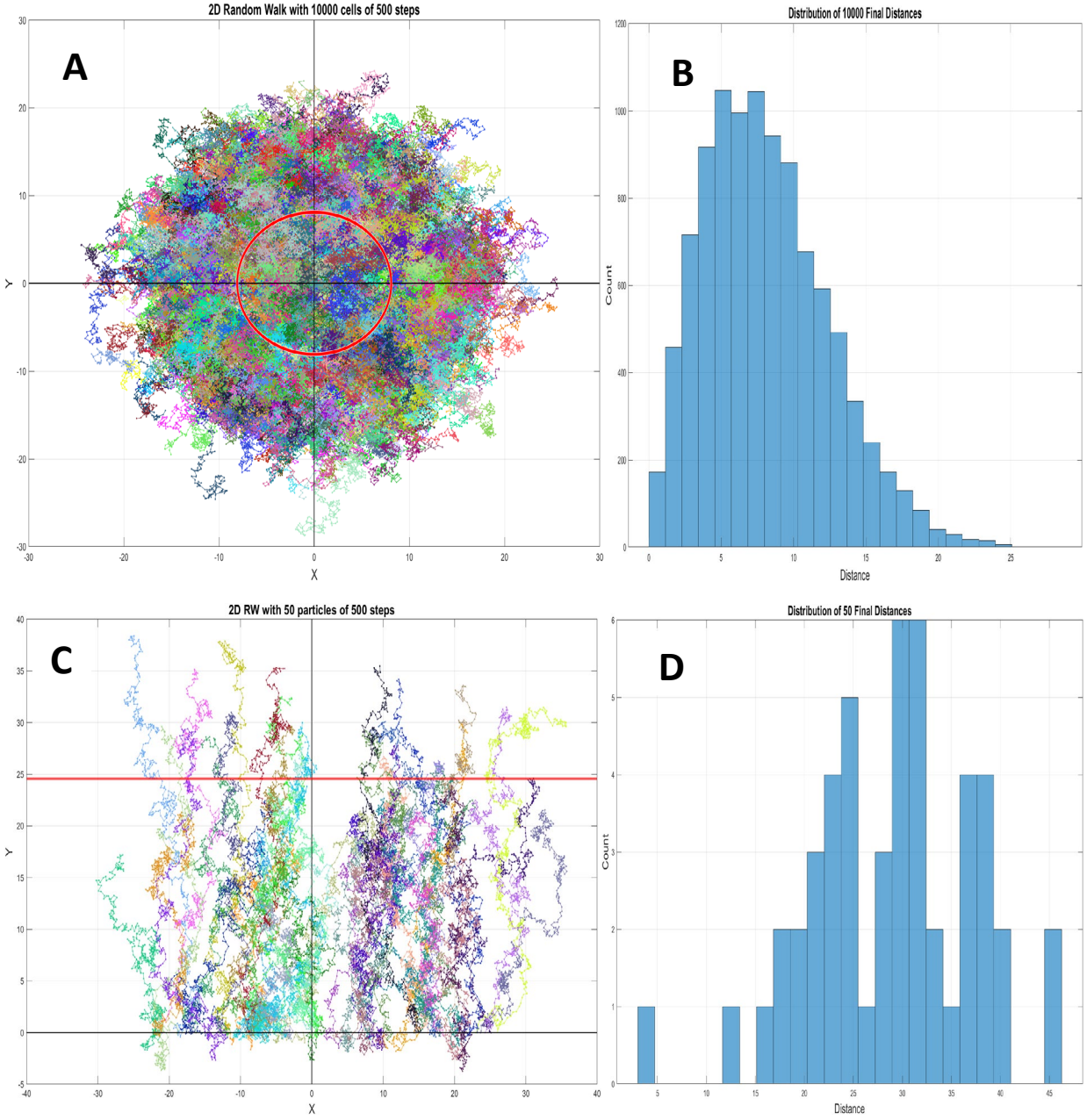

Figure 1: 2D cell migration models with a starting point at the A) origin and C) y=0 axis. Histogram of mean distances from the origin B) and the D) the x-axis.

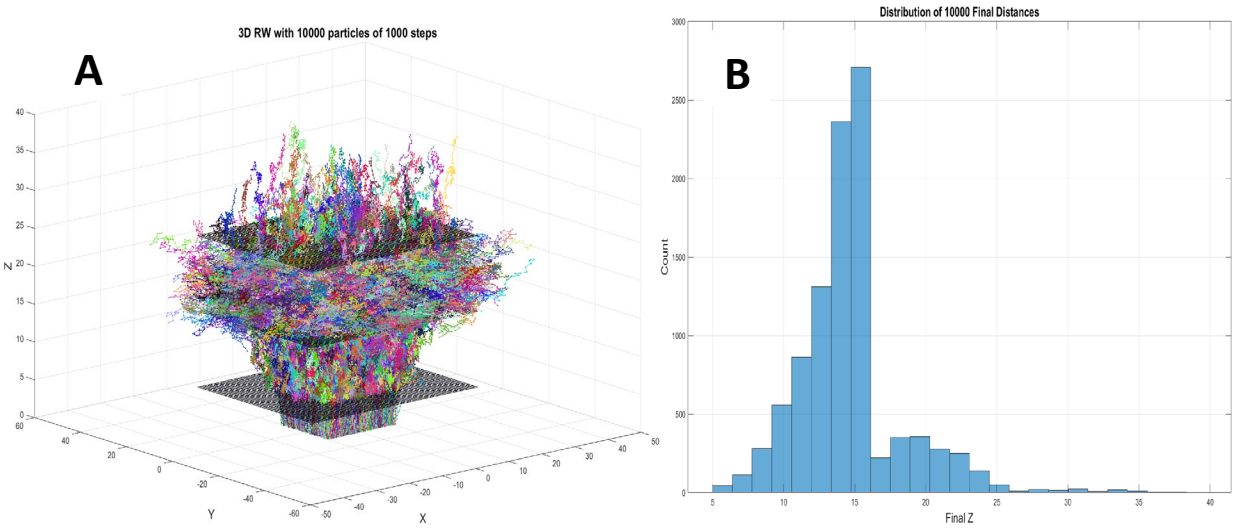

Figure 2: 3D cell migration model shows migration from the A) bone, through the subchondral layer and the articular cartilage, and into the engineered scaffold. The Histogram B) represents the 3D cell migration model.