A Discrete Element Framework for Modelling Cell and Tissue Behaviour with Application to Modelling Chondrocyte Migration

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ABSTRACT

Continuum based methods have difficulties in handling the complex mechanical behaviour of cells and tissues, which includes large deformations, migration, growth, cell proliferation and death, as well as changes in behaviour due to external factors (e.g. chemical signals). The discrete element method (DEM) is much better suited for modelling such complicated behaviour, but computational efficiency is difficult to achieve due to the large number of particles in the discretisation.

In contrast to the overwhelming majority of agent based models of biological tissues which use a single discrete agent to represent each cell, we propose to represent cells and extra-cellular matrix (ECM) using multiple agents [1]. This increases the simulation resolution, allowing large deformation of individual cells and realistic cell-cell and cell-ECM physical interactions, and a more nuanced control of cell behaviour. The main disadvantage is an increase in the model size.

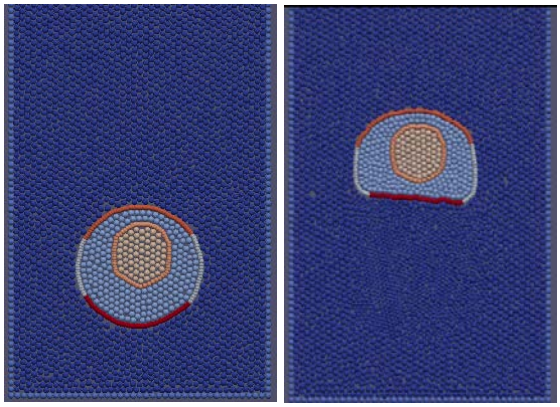

Figure 1. Chondrocyte migration simulation. Initial position (left) and position after 2000 simulation steps (right).

Most mechanical phenomena in cells and tissues take place over relatively long time periods, and therefore can be considered as quasi-static processes. Base on this hypothesis, we have designed efficient solution methods for modelling such phenomena, including a neighbour search algorithm whose computation time scales linearly with the number of particles, efficient algorithms for solution convergence and oscillation damping, as well as an algorithm for handling the stable time step which ensures the numerical stability of the solution. We also created a cell membrane which prevents cell particles seepage [2].

We used the proposed DEM solution methods to model chondrocyte migration under the assumption that the phenomena leading to migration are the secretion of an ECM degrading enzyme on the leading edge and secretion of hyaluronic acid on trailing edge. The simulation results (Figure 1) are able to reproduce the characteristic “bullet shape” of the migrating chondrocyte.

REFERENCES

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