MULTISCALE CELL AND TISSUE MECHANICS IN TISSUE MORPHOGENESIS WITH SUBCELLULAR ELEMENT MODELING

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Introduction

How do tissues and organs build themselves? Modeling morphogenetic processes to answer this question is hard. In fact, continuum mechanics deals poorly with non-linear, large deformations caused by individual cells migrating or proliferating. But, discrete Potts models that naturally deal with cellular events fail to capture the underlying multiscale mechanics. We present an enhanced version of the subcellular element modeling (eSEM) framework to tackle this problem. SEM models tissue mechanics by describing cells as ensembles of particles whose interactions are governed by empirically defined potentials. Here, we chose a potential that preserves single-cell rheology to demonstrate how eSEM offers multiscale mechanics in cell proliferation.

Methods

In eSEM, we model cells with Np particles subjected to the overdamped Langevin: $\boldsymbol{\eta \dot{r}_{ijk} = \xi_{ijk} + F(r_{ijk})}$. Where $\boldsymbol{r_{ijk}}$ is the position of the i-th particle of type j in cell k, $\boldsymbol{\eta}$ is the cell viscosity, $\boldsymbol{\xi_{ijk}}$ is a noise term, and $\boldsymbol{F(r_{ijk})}$ is the net force of all pairwise interactions at $\boldsymbol{r_{ijk}}$. For $\boldsymbol{F}(.)$, we used Morse-like potentials to model adhesion and volume exclusion[1].

By invoking spherical packing, the parameters of these potentials can be linked with values of cell stiffness and viscosity as measured in rheology experiments[2]. Additionally, we modelled the active control of the nuclear intracellular position using spring-like forces that tie the nucleus with the cell's centroid.

To perform simulations, we updated SEM++, a user library[1] for the molecular dynamics solver LAMMPS [3]. We used Ovito[4] for visualization and analysis.

Results

To verify our potential scalability, we simulated a creep experiment in which a cell formed by Np = [250, 10k] particles was stretched to 2.5% strain along the Z-axis in the absence/presence of a larger nuclear particle (Fig. 1). We performed simulations using cells equilibrated in five different initial conditions to account for stochastic effects. As expected, there was a degree of variability around each condition, but no statistically significant differences were observed. Together, these results suggest that whatever the chosen modelling resolution, the particle ensemble will simulate single cell rheology

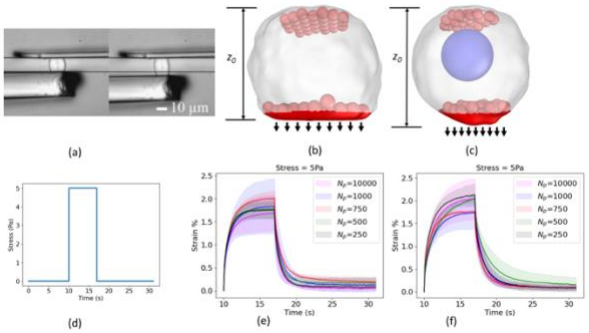

Figure 1: Cell creep simulations varying particle number (Np. Example particles in red, grey envelope), type (blue nucleus), and orientation (variance).

In other words, in eSEM cells act as mechanically-sound agents that can be imbued with biologically relevant activity. For example, we simulated three rounds of cell division and demonstrated how eSEM provides descriptions of multi-scale mechanics (Fig. 2).

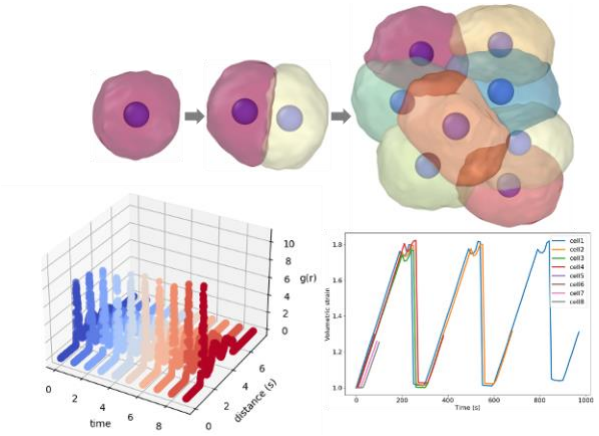

Figure 2: eSEM modelling of cell division (top) showing particle- (bottom left, radial density function) and cell-level mechanics (bottom right) for eight resulting cells.

Discussions

For eSEM to model morphogenesis, we will work on better modeling (potentials) and computing (GPU).

References

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2. Desprat et al, Biophys J, 2224-2233 (2005)
3. Thompson et al, Comp Phys Comm 271 (2022)
4. Stukowski et al, Mod Sim Mater Sci Eng 18 (2010)

Acknowledgements

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