MODELING AND SIMULATION OF TISSUE GROWTH CAUSED BY CELL PROLIFERATION DURING MORPHOGENESIS

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Introduction

Biological tissues have a variety of characteristic shapes corresponding to their functions. The tissue shapes are formed through various cell behaviors during morphogenesis, such as hypertrophy and proliferation. In this process, multicellular dynamics is spatiotemporally regulated by the mechanical and biochemical environments [1]. However, the effect of changing environment on individual tissue shapes is difficult to investigate through *in vivo* experiments. In this study, to clarify the regulation mechanism of tissue shape by the stage-dependent mechanical environment, we developed a model that can simulate tissue growth caused by cell proliferation during morphogenesis.

Methods

To simulate tissue growth during morphogenesis, it is necessary to consider spatiotemporally heterogeneous cell activities regulated by the stage-dependent mechanical and biochemical environments. Therefore, we employed the material point method (MPM) [2], in which the physical domain is discretized by material points and the displacement field is calculated on background grid nodes based on continuum mechanics. To describe multicellular dynamics, we regarded a material point as a single cell. Tissues composed of numerous cells were modeled as a hyperelastic material following the compressible Neo-Hookean model. To express tissue growth caused by cell proliferation, we constructed a cell proliferation model by combining the unidirectional growth and split of material points (Fig. 1).

Results

Based on the cell proliferation model, we simulated the growth of spherical tissue with the surface of the lower half fixed. The tissue was composed of regularly distributed 6.6×10^4 cells. Young's modulus and Poisson's ratio of the tissue were set as E = 1.0 kPa and ν = 0.4, respectively. The composing cells proliferated with random planes of division at random timings. Figure 2 shows the resulting volume of each cell in the growing tissue. The cell volume became spatially heterogeneous due to the randomness of proliferation. Because of the constraint, relatively large cells (red cells in Fig. 2) were observed in the upper half of the tissue. These results suggest that cellular mechanical behaviors depend on the constraint condition and their own activities.

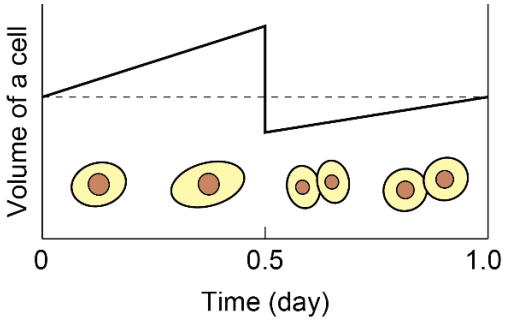

Figure 1: Concept of the cell proliferation model. A material point grows unidirectionally and splits into two material points.

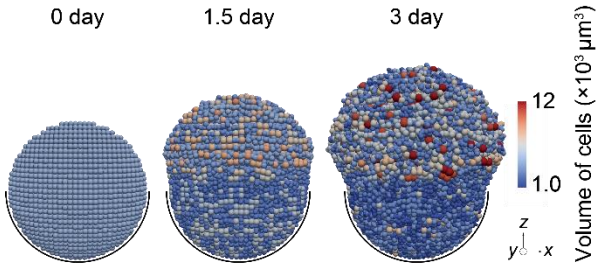

Figure 2: Multicellular tissue growth caused by cell proliferation.

Discussion

In this study, we developed the cell proliferation model that can simulate tissue growth caused by spatially heterogeneous cell activities during morphogenesis. By extending this model through the consideration of cell activities depending on the spatiotemporal mechanical and biochemical environment, it will be possible to simulate the formation of characteristic tissue shapes, such as femurs with femoral heads. Therefore, the proposed model will contribute to understanding the mechanism of tissue morphogenesis.

References

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2. Bardenhagen and Kober, CMES, 5, 6:477-495, 2004.

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