Cell culture facilitated by elastic interaction

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細胞集団の成長ダイナミクスにおいてはしばしば細胞と細胞外基質の力学的相互作用が重要な役割を果たす。その古典的な例としてコラーゲンゲル上の繊維芽細胞の自己組織化現象がある。繊維芽細胞はゲル培地に異方的な収縮力を及ぼすことでコラーゲン繊維を整列させ、その方向に沿って細胞は移動、成長して行く。ここでは細胞を弾性双極子とみなした離散モデル、及びこれを粗視化した連続体モデルを用いて、細胞凝集における弾性相互作用と異方的拡散の役割を検証する。

A classic experimental model of tissue morphogenesis is the self-organization of fibroblast cells in a collagen gel [1]. Traction forces exerted by the cells induce reorientation of collagen fibers in the extracellular matrix (ECM), which facilitates cooperative motion and growth of fibroblasts. Here I present a minimal model of fibroblast culture, focusing on long-range elastic interaction between anisotropic force dipoles [2], anisotropic diffusion along the tensile direction [3] and migration induced by strain gradients [4]. The model is formulated in two dimensions, with both discrete and coarse-grained pictures for cell distribution.

In the model, the deformation of ECM is determined by minimizing the harmonic elastic energy $F = \int d^2r \left[\frac{K}{2}E_{ii}^2 + \mu\left(E_{ij} - \frac{1}{2}E_{kk}\delta_{ij}\right)^2 - (\partial_i P_{ij})u_j\right]$, where $E_{ij} = \frac{1}{2}(\partial_i u_j + \partial_j u_i)$ is the strain tensor and $f_i = \partial_j P_{ij}$ is the force field created by the cell, with P_{ij} the force dipole tensor. In the discrete picture, P_{ij} is given as $P_{ij}(\boldsymbol{r}) = \sum_a Q_{ij}(\boldsymbol{r}^a)\delta(\boldsymbol{r} - \boldsymbol{r}^{(a)})$, where $\boldsymbol{r}^{(a)}$ is the position of the a-th cell and $Q_{ij} = Q_0\delta_{ij} + Q_1 E_{ij} + Q_2 E_{kk}\delta_{ij}$ represents the orientation of cells. Each cell moves by anisotropic diffusion with a diffusion coefficient proportional to Q_{ij}. In the coarse-grained picture, P_{ij} is the product of Q_{ij} and the cell concentration $c = c(\boldsymbol{r})$, which is convected by velocity $v_i = V_1\partial_j E_{ij} + V_2\partial_i E_{jj}$. We compare simulation results with the two pictures and experimentally observed patterns of cell aggregation. The role of the coupling between strain and orientational order of collagen fibers is also discussed.

References

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