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Modeling the mechanical behavior of cell aggregates and their invasion of mesothelial linings.

The transmigration across the mesothelial lining is a fundamental step in the process of cancer invasion and formation of metastasis. We reproduce in vitro trans-mesothelial migration of ovarian cancer cells, through a mathematical model that integrates: (a) an Extended Cellular Potts Model (CPM), that captures mechanisms of cellular adhesion, shape constraints, motion in response to chemo-attractants and degradation of extracellular matrix (ECM); (b) a continuous model for the diffusion and uptake of chemo-attractants, and for the release of matrix metalloproteinases (MMPs). Simulations are in good agreement with biological experiments (provided by N. Lo Buono and A. Funaro, Laboratory of Immunogenetics of the Molinette Hospital in Turin), showing that the overall process is strongly regulated by the activity of matrix metalloproteinases (MMPs) and by the interplay of adhesive properties between cells. In particular in the case of cellular aggregates the process is more destructive.
Indeed the ability of cells to form aggregates is fundamental in many biological processes and it seems promising to study spheroid mechanical behavior, because the response of soft biological tissues may serve as a parameter in the diagnosis of tumor metastatic potential. We study the mechanical behavior of multicellular aggregates, treated as porous materials, composed of cells and filled with water, to derive an elasto-visco-plastic model. The cellular constituent is responsible for the elastic and the plastic behavior (due to the rearrangement of adhesive bonds between cells). On the other hand, the liquid constituent is responsible of the viscous-like response during deformation. The model is used to describe the uni-axial homogeneous compression both when a constant load is applied and when a fixed deformation is imposed and subsequently released. Results are compared with the dynamics observed in mechanical experiments found in literature.

References

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