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Understanding the relationship between cell death and tissue shrinkage via a stochastic agent-based model

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Abstract

Cell death, a process which can occur both naturally and in response to insult, is both a complex and diverse phenomenon. Under some circumstances, dying cells actively contract and cause their neighbors to rearrange and maintain tissue integrity. Under other circumstances, dying cells leave behind gaps, which results in tissue separation. A better understanding of how the cellular scale features of cell death manifest on the population scale has implications ranging from morphogenesis to tumor response to treatment. However, the mechanistic relationship between cell death and population scale shrinkage is not well understood, and computational methods for studying these relationships are not well established. Here we propose a mechanically robust agent-based cell model designed to capture the implications of cell death on the population scale. In our agent-based model, algorithmic rules applied on the cellular level emerge on the population scale where their effects are quantified. To better quantify model uncertainty and parameter interactions, we implement a recently developed technique for conducting a variance-based sensitivity analysis on the stochastic model . From this analysis and subsequent investigation, we find that cellular scale shrinkage has the largest influence of all model parameters tested, and that by adjusting

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