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Quantitative single-cell-based modeling reveals predictable response of growing tumor spheroids on external mechanical stress

Computational model simulations show that the response of growing cell populations on mechanical stress follows the same functional relationship and is predictable over different cell lines and growth conditions despite the response curves look largely different. We develop a hybrid model strategy in which each individual cell is represented by coarse-grained individual units calibrated with a high resolution mathematical cell model and parameterized by measurable biophysical and cell-biological parameters. Cell cycle progression in our model is controlled by volumetric strain, the latter being derived from a bio-mechanical relation between applied pressure and cell compressibility. After parameter calibration from experiments with mouse colon carcinoma cells growing against the resistance of an elastic alginate capsule, the model adequately predicts the growth curve in i) soft and rigid capsules, ii) in different experimental conditions where the mechanical stress is generated by osmosis via a high molecular weight dextran solution, and, after calibration of one model parameter in absence of applied stress, iii) for other cell types with different growth kinetics. The findings suggest that the response of cell growth and division on mechanical stress might be generic, robust and predictable. Finally, we give examples of how these biophysical agent-based models progress towards virtual experiments and virtual organ simulations at histological level.

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