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The "Go-or-Grow" hypothesis in glioma growth: mathematical modeling and analysis

Gliomas are very aggressive brain tumors, in which tumor cells gain the ability to penetrate the surrounding normal tissue. The invasion mechanisms of this type of tumor are not yet fully understood. Our work is motivated by the migration/proliferation dichotomy ("Go-or-Grow" hypothesis), *i.e.* the antagonistic migratory and proliferating cellular behaviors in a cell population, which may play a central role in these tumors [3].

In a first part, we present results obtained by using a lattice-gas cellular automaton and show the influence of the Go-or-Grow mechanism on the dynamics of glioma growth, which we qualitatively compare to *in vitro* data [5].

In a second part, we formulate continuum models to investigate the influence of quiescence phases on the dynamics of a population of glioma cells. We propose a "Go-or-Rest" model and describe cell migration as a velocity-jump process including resting phases. We derive the corresponding macroscopic model and show that anomalous diffusion arises from the switch between motile and quiescent phases. In particular, sub- and super-diffusion regimes can be observed and are governed by a parameter describing intrinsic migratory properties of cells [2]. We show that our results are in excellent agreement with *in vitro* data of glioma tumor expansion [1] when the switch to quiescence is regulated by the cell density. We furthermore show how this density-regulation allows for the the formation of immotile aggregates in the context of the Turing instability. We use a combination of numerical and analytical techniques to characterize the development of spatio-temporal instabilities and traveling wave solutions generated by our model. We demonstrate that the density-dependent Go-or-Grow mechanism can produce complex dynamics similar to those associated with tumor heterogeneity and invasion.

References

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