Philip Gerlee
Institute of Medicine and Mathematical Sciences, University of Gothenburg
e-mail: philip.gerlee@gu.se
Sven Nelander
Institute of Medicine, University of Gothenburg
e-mail: sven.nelander@gu.se

The impact of phenotypic switching on glioma growth

Tumour growth is contingent on numerous intra-cellular and extra-cellular processes, such as an elevated rate of proliferation, evasion of apoptosis and angiogenesis [1]. Out of these, proliferation has traditionally been singled out as the most important, and has generally been the target of anti-cancer therapies. Recently, there has been a growing interest in the impact of cancer cell *motility*, and this is especially true in the case of glioblastoma, which generally exhibit diffuse morphologies stemming from the high motility of individual glioma cells.

In order to investigate this phenomenon, we propose a 3-dimensional cellular automaton model, which describes the growth of a glioma consisting of up 10^6 cells. In accordance with the *go or grow* hypothesis [2] each cell can be either in a proliferating or motile state. The switching between the states is achieved by means of a two-state Markov chain within each cell, characterised by two parameters p_m, the probability of remaining in the motile state, and p_p the corresponding parameter for proliferation. Simulating the cellular automaton and by sweeping the parameter space of the phenotypic switching model we find that the most invasive tumours (i.e. with the highest growth rate) occur at $(p_m, p_p) \approx (0.9, 0.9)$, i.e. they are characterised by both proliferative and motile behaviour, and by a high degree of phenotypic persistence. We also find that for each $p_p \in [0, 1]$ there is a $p_m \neq 0$ such that the growth rate is maximised.

These observations are in agreement with experimental results, where glioma cell lines with a lower proliferative capacity have been observed to rise to larger tumours when implanted in mice [3]. Further it suggest cancer cell motility as a potential target for therapy.

References

[1] Hanahan, D., Weinberg, R., 2000. *The hallmarks of cancer*. Cell **100**:57–70.
[2] A. Giese, R. Bjerkvig, M.E. Berens and M Westphal, 2003. *Cost of migration: invasion of malignant gliomas and implications for treatment*. Journal of Clinical Oncology **8**:1624–1636.
[3] R. Chen et al. 2010. *A Hierarchy of Self-Renewing Tumor-Initiating Cell Types in Glioblastoma*. Cancer Cell **17**:362–375.