Project title: Spatial game-theoretical models of cancer treatment

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Proposal: The "war on cancer" introduced by Nixon in 1971 shaped the objective of cancer treatments to attempt maximal cancer cell death at all costs. Naturally, the outcome of this language was the implementation of the maximum tolerable dose paradigm. In metastatic castrate resistant prostate cancer, abiraterone is given at a daily maximal dose until treatment failure, adding only 3.9 months of survival versus placebo. This treatment failure is caused by evolution of resistance to abiraterone, similar to evolution of resistance in pests when pest control is introduced. Unfortunately, incorporating techniques that attempt to delay or prevent this evolution of resistance have only recently entered the clinical setting.

Here we will model the abiraterone therapy as a Stackelberg game with an oncologist as a leader and cancer as the follower, while the underlying evolutionary dynamics of metastatic castrate resistant prostate cancer will be described as a spatial evolutionary game. We will compare the results of the standard treatments with treatments with other objectives, such as keeping the tumors small but not trying to remove cancer completely (known also as evolutionary enlightened or adaptive therapies), which we believe can lead to a longer patient's lifespan. Using the data available from clinical trials at the Moffitt Cancer Center, we will subsequently design a treatment regimen which will be adjusted depending on the physiological state of a patient.

Requirements candidate: Highly motivated student with good English communication skills and proactive and resolute attitude, with a master degree in (applied) mathematics or computer science (preferably game theory, optimal control or optimization) and experience with Matlab and/or Java programming. This research will be carried out within a collaboration with the Moffitt Cancer Center in Tampa, Florida, US, and, therefore, the PhD candidate might be required to spend few months there, especially when dealing with the clinical data.

Keywords: Dynamic noncooperative game theory, evolutionary game theory, metastatic castrate-resistant prostate cancer, Stackelberg games, competitive release, model validation using clinical data

Top 5 selected publications:

1. L. You, J.S. Brown, F. Thuijsman, J.J. Cunningham, R.A. Gatenby, J. Zhang, and K. Staňková, "Spatial vs. non-spatial eco-evolutionary dynamics in a tumor growth model", in *Journal of Theoretical Biology*, 2017, https://doi.org/10.1016/j.jtbi.2017.08.022
2. P. Uyttendaele, F. Thuijsman, P. Collins, R. Peeters, G. Schoenmakers, R. Westra, "Evolutionary games and periodic fitness", in *Dynamic Games and Applications*, vol. 2, pp. 335-345, 2012

3. M. Abrudan, L You, K. Staňková, and F. Thuijsman, “A game theoretical approach to microbial coexistence”,in *Advances in Dynamic and Evolutionary Games: Theory, Applications, and Numerical Methods,* Springer, pp. 267-282, 2016.
4. K. Staňková, J.A.J. Metz, and J. Johansson, "The adaptive dynamics of life histories: From fitness-returns to selection gradients and Pontryagin's maximum principle", in *Journal of Mathematical Biology*, vol. 72, no. 4, pp. 1125-52, 2016
5. J.S. Brown and K. Staňková, “Game theory as a conceptual framework for managing insect pests”, in *Current Opinion on Insect Science*, vol. 21, pp. 26-32, 2017