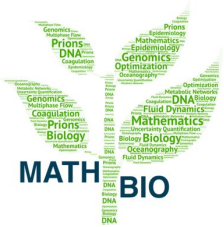
Mathematical Biology Seminar: Wednesday, April 14, 2021
Speaker: Dr. Jill Gallaher, H. Lee Moffitt Cancer Center & Research Institute

Title: Using tumor dynamics to characterize and treat metastatic cancer

Time: 9am
Zoom Link: https://ucmerced.zoom.us/j/98050375649
Passcode: 172069

Abstract: Despite the fact that heterogeneity is a major driver of treatment failure in advanced cancer, treatment strategies often ignore tumor evolutionary dynamics. Adaptive therapy is an evolutionary treatment strategy that exploits competition amongst heterogenous cells and is shown to be effective in pre- clinical models and clinical trials. The aim is to maintain a constant tumor burden by giving a lower dose to a shrinking tumor that selects for resistant cells and a higher dose to a growing tumor that selects for sensitive cells. Additionally, a single cycle of adaptive therapy could be used as a tool to probe tumor dynamics. This may be especially useful for clinical decision-making in the metastatic setting when multiple metastatic lesions contribute to systemic measures of burden but may not be observable through imaging.

Using an off-lattice agent-based model we investigate how spatial competition and heterogeneity affect treatment response. For different tumor compositions we compare outcomes using a continuous application given at the maximum tolerated dose with the intention to cure and an adaptive strategy that incorporates dose-modulation and treatment vacations to sustain control. Drug-sensitive tumors are cured with continuous treatment, but even a few resistant cells will cause eventual recurrence. With the right scheduling algorithm, we can maintain a steady tumor burden with adaptive therapy, as long as there are sufficient sensitive cells to suppress resistant cell outgrowth. Adaptive therapy can also control multiple metastatic lesions, and the dynamics from the first cycle can help characterize several features of the metastatic system. Tumor size, drug sensitivity, and cell turnover affect rates of response and regrowth, while changes in individual metastases gives insight on heterogeneity amongst metastases and can guide treatment. Generally, systems with more intertumor heterogeneity had better success with continuous therapy, while systems with more intratumor heterogeneity responded better to adaptive therapy. Critically, for smarter treatment strategies the underlying heterogeneity and evolutionary response of tumors should be exploited rather than ignored.



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