1106-92-2178 **James Greene*** (jmgreene@math.umd.edu), Department of Mathematics, University of Maryland, College Park, MD 20742. *The Cell-Cycle and Drug Resistance: A Spatial Mechanism.*

Resistance to chemotherapy is a major cause of the failure cancer treatment. Our current understanding of drug resistance is that tumor heterogeneity and complex genetic and epigenetic changes contribute to the development of multi-drug resistance. Tumor heterogeneity accounts both for genetic variation, as well as non-constant tumor microenvironments. Indeed, experimental evidence suggests that different spatial configurations of cells affect drug sensitivity in a genetically homogenous population. The work presented here is focused on understanding this phenomenon.

As chemotherapeutic agents primarily target proliferating cells, spatial resistance is mediated by the variation of observed cell-cycle lengths. We first propose a continuous time Markov chain model utilizing intrinsic distributions governing the time spent in the cell-cycle. We use probabilistic techniques to derive a system of integro-differential equations, which when compared with experimental data provided by collaborators at the NIH, permit the use of optimization techniques to calculate parameter values. Furthermore, recent work uses individual-based models with explicit spatial dependencies to produce the observed cell-cycle distributions, as well as the variation in treatment efficacy based on geometry. (Received September 16, 2014)