Towards Personalized Computer Simulation of Breast Cancer Treatment: A Multi-scale Pharmacokinetic and Pharmacodynamic Model Informed by Multi-type Patient Data

MONDAY, October 8, 2018 at 4:30 PM
Eckhart 133, 5734 S. University Avenue
Refreshments before the seminar at 4:00PM in Jones 111

ABSTRACT

Mathematical modelling and simulation have emerged as a potentially powerful, time- and cost effective approach to personalised cancer treatment. In order to predict the effect of a therapeutic regimen for an individual patient, it is necessary to initialize and to parametrize the model so to mirror exactly this patient’s tumor. I will present a comprehensive approach to model and simulate a breast tumor treated by two different chemotherapies in combination and not. In the multiscale model we represent individual tumor and normal cells, with their cell cycle and others intracellular processes (depending on key molecular characteristics), the formation of blood vessels and their disruption, extracellular processes, as the diffusion of oxygen, drugs and important molecules (including VEGF which modulates vascular dynamics). The model is informed by data estimated from routinely acquired measurements of the patient’s tumor, including histopathology, imaging, and molecular profiling. We implemented a computer system which simulates a cross-section of the tumor under a 12 weeks therapy regimen. We show how the model is able to reproduce patients from a clinical trial, both responders and not. We show by scenario simulation, that other drug regimens might have led to a different outcome. Approximate Bayesian Computation (ABC) is used to estimate some of the parameters. have strong theoretical guarantees that significantly improve the computational lower bounds of classical optimization algorithms.