Computational modelling to study cancer biology and treatments

BACKGROUND
Cancer biology and treatment involves complex, dynamic interactions between cancer cells, the tumour microenvironment, and therapeutic molecules. Quantitative approaches combining mechanistic disease modelling and computational strategies are increasingly leveraged to rationalize pre-clinical and clinical studies, and to establish effective treatment strategies. In this way, mathematical approaches lay the foundation for computational “virtual laboratories” that offer fully controlled, and non-invasive conditions in which we can investigate emergent clinical behaviours and interrogate new therapeutic strategies. As an introduction to such virtual laboratories, this workshop will provide an overview of techniques used in computational oncology, with a focus on in silico clinical trials and agent-based models (ABMs). Virtual (or in silico) clinical trials are useful computational platforms that help distinguish mechanisms of therapeutic successes and failures, stratify patient risk classes based on an individual’s physiology, and optimize drug-specific parameters. In these platforms, in silico patients are generated by drawing from distributions of possible patient characteristics and used to form virtual clinical trials, in which new treatment strategies can be evaluated prior to human trials. Data fitting and optimisation techniques are cornerstones of this computational platform and are used to generate realistic virtual patients and evaluate individualised therapies. ABMs are a computational formalism that describes the way individual agents (e.g. cancer cells) interact through probability distributions based on defined characteristics that have contributed significant insights into cancer biology at the intra-patient tissue level. In oncology, this technique has been applied to model spatial tumour formation, tumour cell heterogeneity, and the dynamics of treatment in the tumour microenvironment. Modelling individual cells as agents allows for direct translation of biological observation into simulation rules and, like virtual clinical trials, the investigation of new hypotheses and treatment strategies.

In particular, this workshop will address:
- the optimization of parameter ranges to generate virtual patients or treatment schedules using a variety of techniques, including simulated annealing, least-squares nonlinear optimisation, gradient-based descent, and genetic algorithms.
- the translation between ABMs and PDEs
- how to code heterogenous tumour environments into an ABM using an open-source software known as PhysiCell

Workshop participants will have the opportunity to see how each of these techniques are applied in computational oncology and learn how to employ them on experimental or generated data in Matlab and in C++. By the end of this workshop, participants will have a comprehensive understanding of computational modelling in oncology, the explicit knowledge for how to design, code, and simulate an agent-based model, and an understanding of how to account for within- and between-patient heterogeneity by deploying in silico clinical trials.

PROGRAM – THURSDAY 13TH OF AUGUST 2020

12:30-13:00    Morgan Craig
Introduction lecture on mathematical oncology, including tumour growth models, cancer resistance modelling, phenotypic switching, and stochastic models

13:00-13:30    Adrianne Jenner
Lecture on computational modelling methods in cancer, with emphasis on in silico clinical trials, optimisation techniques and agent-based models

13:30-13:40    10 minute break

13:40-14:10    Adrianne Jenner
Tutorial on using Matlab to leverage experimental data to generate virtual patients and optimize therapeutic protocols

14:10-15:00    Paul Macklin, Randy Heiland (part 1)
Introduction lecture on the open-source agent-based modelling software PhysiCell and its applications in oncology, followed by the first session tutorial on applications of PhysiCell: exploring PhysiCell-powered nanoHUB apps

15:00-15:15    15 minute break

15:15-16:00    Paul Macklin, Randy Heiland (part 2)
Second session tutorial on PhysiCell: building C++-based codes, reading data into Jupyter, then making a basic XML-based model (e.g. cell swarming, cancer cell proliferation).

16:00-16:10    10 minute break

16:10-16:30    Pantea Poolavand
Lecture on the translation of ABMs to PDEs, case study in oncology
TICKETS
Free registration for the event can be found at:
Make sure to go through the “pre-flight checklist” available on the Eventbrite page and download the appropriate programs and software to run PhysiCell. For the Matlab tutorial, you will need to have Matlab on your computer.

WORKSHOP ORGANISERS AND SPEAKERS
Morgan Craig, Assistant Professor, Université de Montréal/Centre de recherche CHUSJ, Montréal, Canada
Adrienne Jenner, Postdoctoral Fellow, Université de Montréal/Centre de recherche CHUSJ, Montréal, Canada
Paul Macklin, Associate Professor, Indiana University, Bloomington, USA
Randy Heiland, Indiana University, Bloomington, USA
Pantea Poolavand, University of Sydney, Sydney, Australia