Los Alamos National Laboratory
P.O. Box 1663, MS K710
Los Alamos, NM 87545

Theoretical Division

Dr. Musante and Dr. Shtylla,
QSP group, Pfizer Inc.

Dear Dr. Musante and Dr. Shtylla:

I am writing to apply for the Senior Quantitative Systems Pharmacologist position based at the Boulder Research Unit in the Quantitative Systems Pharmacology (QSP) group at Pfizer Inc. I am currently a postdoctoral research associate with Alan Perelson in the Theoretical Biology and Biophysics group at the Los Alamos National Laboratory. Prior to joining the Theoretical Biology group, I was a junior fellow at the Institut Mittag-Leffler and received my PhD in Applied Mathematics from McGill University where I was supervised by Antony R. Humphries and Morgan Craig. During my doctoral training, I was a summer intern at the QSP group at Pfizer Inc. in 2017 where I contributed to a model of lipoprotein dynamics.

My research uses mathematical models to address problems in physiology and medicine. Broadly speaking, I develop physiologically-based mathematical models to understand disease progression, drug resistance, and optimize treatment scheduling. My doctoral work included using mathematical models to infer a clinically actionable and rational combination therapy schedules in late-stage melanoma that was utilized this model to identify physiological characteristics of solid tumour growth that predict response to dual oncolytic virus therapy. This work has clinical applications and was published in the official journal of the Society for Immunotherapy of Cancer. I also have extensive experience in QSP modelling of the hematopoietic (blood production) system. This work includes establishing equivalences between the most common modelling approaches and a modelling study that suggests using monocytopenia as a warning signal for chemotherapy induced neutropenia may improve clinical outcomes.

I have also developed numerical methods and analytical tools for functional differential equations. These tools allow for more realistic maturation periods to be modelled using the familiar ordinary differential equation framework and thus implemented in common parameter fitting software packages.

As a postdoctoral researcher, I have developed mathematical models to understand the dynamic pathways to resistance against a novel broadly neutralizing HIV-1 antibody, identified the mechanisms by which patients exhibit long-term viral control following a single administration of the broadly neutralizing antibody, and elucidated the immune mechanisms that lead to establishment of the HIV-1 latent reservoir. These projects all involved close collaboration with clinical scientists. Further, we have used our modelling to make testable predictions regarding treatment resistance that may further our understanding of the role of broadly neutralizing antibodies in functional cure of HIV-1.

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My long-term goal is to understand the treatment imposed evolutionary pressures that lead to treatment resistance in solid cancers. Systems-levels experiments probing the complex interactions leading to treatment resistance are currently intractable, so mathematical modelling offers an unparalleled opportunity to understand the physiological mechanisms underlying drug resistance. Drawing upon this understanding, I aim to leverage my work to permit the repurposing and optimization of existing therapeutics through rational treatment scheduling to ultimately improve clinical outcomes.

To achieve these goals, I look forward to closely collaborating with experimentalists and clinicians. Effective collaboration is not limited critically evaluating my mathematical results in the biological context. More importantly, it is crucial to accurately translate these results into language that permits effective communication with experimentalists. My ability to do so has been recognized by poster presentation awards for mathematical modelling studies at non-mathematical conferences as well as publication of my work in clinical journals. As these collaborations are essential to fully realizing the capabilities of mathematical models, I am particularly excited by the collaborative nature of research at Pfizer. Following our conversations regarding this position, I believe the Boulder research unit is a very exciting and unique environment to pursue my goals of improving patient outcomes in oncology.

My work has been nationally and internationally recognized. I was awarded a junior fellowship for the semester in Mathematical Biology at the Mittag-Leffler Institute in Stockholm as well as doctoral and postdoctoral fellowships from the Natural Science and Engineering Research Council of Canada. I have enclosed my CV and can arrange for references to contact you. Thank you for your consideration.

Sincerely,

Tyler Cassidy

Postdoctoral Research Associate

Theoretical Biology and Biophysics

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