MathSys MSc/PhD Proposal: Structural Identifiability for Organ-on-a-Chip Microfluidics

Supervisors: Adam Noel, Mike Chappell
School of Engineering, University of Warwick; Emails: {adam.noel, m.j.chappell}@warwick.ac.uk

Industrial Partners: Peter Gennemark, David Janzen
AstraZeneca, Sweden

I. Background

The identification of drug targets and therapies relies on accurate models of *in vitro* human physiology, such as what can be achieved with organ-on-a-chip systems; see [1]. These platforms provide a microfluidic environment for long-term (i.e., days) testing of human cells to better understand diseases and study the effects of drug treatment. From time-series observations of chemical concentrations, we can use mathematical tools to infer the underlying physiological system dynamics. These tools include:

- **Structural identifiability** (see [2]).
- **Indistinguishability analysis**.
- **Parameter estimation** (see [3]).
- **Sensitivity analysis**.

A rich set of time-series experimental data has been obtained from an organ-on-a-chip platform where pancreatic cells and liver cells engage in cross-talk signalling for glucose regulation; see [1] and Fig. 1. These data, maintained by our partners at AstraZeneca and curated by a post doc working on a related project, include local measurements of insulin and glucose concentrations over a scale of hours and days. The data are being used to develop understanding and treatment of diabetes.

II. Project Objectives

The MSc project seeks to identify suitable ODE models, such as that proposed in [4], to describe glucose regulation as supported by the existing experimental data. In particular, structural identifiability tools will be used to assess the ability for system parameters to be determined by the available data. Furthermore, new experiments can be proposed and designed to gather any additional data if necessary to satisfy the identifiability requirements. We emphasize that identifiability analysis is a mathematical approach that can still be completed even if the data available is found to be insufficient.

III. Prospective Deliverables

The project deliverables include:

1) Accurate ODE model for glucose regulation.
2) Estimation of the model parameters from experimental data.
3) Based on 1) and 2), proposed design for future experiments.

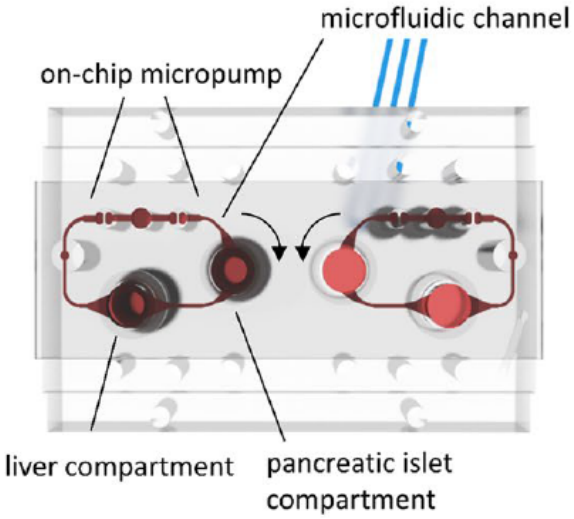

Fig. 1. Organ-on-a-chip platform presented in [1].

IV. Follow-on PhD Project

This project has considerable scope for expansion to a PhD project with the support of our partners at AstraZeneca. In particular, we are interested in stochastic PDE-based models of this and similar systems, in order to account for molecule transport (e.g., flow and diffusion) and the noisiness imposed by low molecule concentrations. Generally, the use of structural identifiability for reaction-diffusion based systems is an exciting open problem with many biomedical applications.

References

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[2] A. F. Villaverde, A. Barreiro, and A. Papachristodoulou, "Structural identifiability of dynamic systems biology models," *PLOS Computational Biology*, vol. 12, no. 10, p. e1005153, Oct. 2016.

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