Potential Supervisors

Mark Coles

Mark recently move to the Kennedy Institute of Rheumatology at the University of Oxford (summer 2017) from the University of York where he was appointed Professor of Immunology in 2016. His group focuses on the interface between experimental and computational immunology developing both software tools and simulations to address key challenges in immunology and translate these to human medicine. He has five computational modelling students to completion and currently supervisor 3 PhD students focused on computational/mathematical immunology. Funding for software development has come from NC3Rs and the Wellcome Trust. He has a long-term interest in development robust open source software to support systems biology based approaches and applying outcomes to patient care. He co-founded Simomics, a software company developing evidence based virtual disease labs to accelerate, de-risk and reduce the use of animals in therapeutic discovery and development.

Software Tools Developed:

Opensource software tools:

1. SPARTAN: www.york.ac.uk/computational-immunology/software/spartan/

Successful integration of computer simulation with wet-lab research requires the relationship between simulation and the real-world system to be established. Spartan, described in our paper in PLoS Computational Biology, is a package of statistical techniques specifically designed to understand this relationship and provide novel biological insight. These techniques help reveal the influence that pathways and components have on simulation behaviour, offering valuable biological insight into aspects of the system under study.
Spartan is open source, implemented within the R statistical environment, and freely available from both the Comprehensive R Archive Network (CRAN) and on this page below. Use of the package is demonstrated via the tutorial published in the R Journal. Key references:

K. Alden, M. Read, J. Timmis, P.S. Andrews, H. Veiga-Fernandes, M.C. Coles SPARTAN: A Comprehensive Tool for Understanding Uncertainty in Simulations of Biological Systems.. PLoS Comput Biol 9(2): e1002916. doi:10.1371/journal.pcbi.1002916. 2013

K.Alden, M.Read, P.S.Andrews, J.Timmis, M.C.Coles. Applying spartan to Understand Parameter Uncertainty in Simulations. R Journal. 2014

K.Alden, P.S. Andrews, H. Veiga-Fernandes, J. Timmis, M.C. Coles. Utilising a Simulation Platform to Understand the Effect of Domain Model Assumptions. Natural Computing. doi: 10.1007/s11047-014-9428-7. 2014

K.Alden, J. Timmis, M.C. Coles. Easing Parameter Sensitivity Analysis of Netlogo Simulations using Spartan. Proceedings of the 14th International Conference on the Synthesis and Simulation of Living Systems. MIT Press. doi: 10.7551/978-0-262-32621-6-ch100. 2014

K.Alden, J.Timmis, P.S.Andrews, H.Veiga-Fernandes, M.C.Coles. I Extending and Applying Spartan to Perform Temporal Sensitivity Analyses for Predicting Changes in Influential Biological Pathways in Computational Models. EEE Transactions on Computational Biology and Bioinformatics. vol.PP, no.99. doi: 10.1109/TCBB.2016.2527654. 2016

Industry involvement:
GSK: This software has been used in several GSK CASE PhD studentship projects

2. ASPASIA: www.york.ac.uk/computational-immunology/software/aspasia/

Calibrating computational models of biological systems, assigning parameter values to ensure the model reflects behaviours observed biologically, can greatly impact the strength of hypotheses the model generates. A calibrated model provides baseline behaviour upon which sensitivity analysis techniques can be used to analyse potential pathways impacting model response. Where a behaviour depends on an intervention, model responses may be dependent on conditions at the point when the intervention is applied, complicating the calibration process and making it difficult to assess the extent to which an alteration in behaviour can be attributed to the intervention alone. Where a model is specified in Systems Biology Markup Language (SBML), there is a key deficiency in tools for solving models dependent on interventions. ASPASIA, a cross-platform, open-source (GPLv2 license) Java toolkit, addresses this problem. ASPASIA can generate and modify models using SBML solver output as an initial parameter set, allowing interventions to be applied once a steady state has been reached. Additionally, multiple SBML models can be generated where a subset of parameter values are perturbed using local and global sensitivity analysis techniques, revealing the model's sensitivity to the intervention.

Evans S, Alden K, Cucurull-Sanchez L, Larminie C, Coles MC, Kullberg MC, Timmis J. ASPASIA: A toolkit for evaluating the effects of biological interventions on SBML model behaviour. PLoS Comput Biol. 2017 Feb 3;13(2):e1005351

Industry involvement:
GSK: This software has been used in several GSK CASE PhD studentship projects

3. ARTOO: www.york.ac.uk/computational-immunology/software/artoo/

A tool to enable the construction of logical arguments to support our simulations. This tool enables you to build and manipulate a graphical structure consisting of text-containing nodes and arrows that represents your argument. Specifically, it uses the syntax of the Goal Structuring Notation. Structures can be saved to file and exported as PNG images.

Alden K, Andrews PS, Polack FA, Veiga-Fernandes H, Coles MC, Timmis J. Using argument notation to engineer biological simulations with increased confidence. J R Soc Interface. 2015 Mar 6;12(104):20141059. doi: 10.1098/rsif.2014.1059.

Information on a commercialised version of the software (ArtooPro)
www.simomics.com/artoopro.html

Industry involvement

GSK: This software has been used in several GSK CASE PhD studentship projects
This commercial software is used by both bio-pharamceutical, chemical companies and personal care companies.

Opensource Published Computational Biology models:
Artimmis: www.york.ac.uk/computational-immunology/software/artimmus/
Agent based simulation of a mouse model (EAE) of multiple sclerosis

Read, M, Andrews PS, Timmis J, Williams RB, Sheng H, Coles M, Kumar V, Determining Disease Intervention Strategies Using Spatially Resolved Simulations, PLOS ONE, 2013, DOI:10.1371/journal.pone.0080506

PPSim: https://www.york.ac.uk/computational-immunology/software/ppsim/
Adopting an agent-based modelling approach, we have developed a simulator that captures the development of lymphoid organs in the gut: Peyer's Patches. With this tool, we have shown that we can create cell behaviour that is statistically similar to that observed in cell culture systems and have generated testable biological hypotheses concerning the cellular interactions leading to the development of these organs: necessary for triggering adaptive immune responses.

Patel, N. Harker, L. Moreira-Santos, M. Ferreira, K. Alden, J. Timmis, K. Foster, A. Garefalaki, P. Pachnis, P. Andrews, H. Enomoto, J. Milbrandt, V. Pachnis, Coles MC, D. Kioussis, H. Veiga-Fernandes, Differential RET Signaling Pathways Drive Development of the Enteric Lymphoid and Nervous Systems. Science Signalling 5, no. 235, 2012.

Alden k, Timmis j, Andrews PS, Veiga-Fernandes H, Coles M, Pairing experimentation and computational modelling to understand the role of tissue inducer cells in the development of lymphoid organs. Frontiers in Immunology. Vol 3. DOI:10.3389/fimmu.2012.00172, 2012.

Involvement of DTC Students

Oxford SABS: 2 Current students:
Liam Brown: Co-supervisor with Eamonn Gaffney
Joanneke Jansen: Co-supervisor with Eamonn Gaffney and Holm Uhlig

Oxford Non-SABS: 2 current students
University of York: 1 current student
University of York: 18 completed

Industrial links (Software/Modelling)

GlaxoSmithKline Pharmaceuticals
GlaxoSmithKline Vaccines
Roche
Simomics
Unilever