BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: MacLean, Adam

eRA COMMONS USER NAME (credential, e.g., agency login): ALMACLEAN

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
University of Edinburgh, Edinburgh	BS	09/2005	06/2009	Mathematical Physics
Imperial College London, London	MS	09/2009	09/2010	Bioinformatics and Theoretical Systems Biology
Imperial College London, London	PHD	01/2011	01/2014	Systems Biology

A. Personal Statement

My training in mathematical and computational systems biology provides me with a broad background to develop high-impact tools and models to gain new insight into cancer. My particular areas of expertise include methods for the analysis of high-dimensional genomic data, mathematical models of cell fate decisions that lead to tumorigenesis or that impact cancer progression, and methods for parameter inference of biological systems. I have a rigorous training background in the physical and mathematical sciences (B.S.), as well as in the investigation of biological systems in light of their underlying mathematical and physical principles (M.S. and Ph.D.), in order to gain insight into their structure, function, and dynamics. My current research agenda includes the development of computational and mathematical models to elucidate the complex and noisy dynamics occurring on cellular and tissue levels, driven by transitions between multiple cellular states, and the subcellular molecular regulatory networks that control them. I will also parameterize these models via statistical inference in light publicly available datasets and data that will be generated in the labs of collaborators. I currently supervise two PhD students and have a track record of leading large interdisciplinary research projects that require excellent communication between mathematical, biological, statistical, and computer scientists, as well as keen appreciation of project structure and time management.

As can be seen below in my “Contributions to Science”, I have contributed several papers on modelling and analysis of cancer, the analysis and interpretation of high-dimensional, multiscale biological data, as well as on predictive modelling of cellular differentiation or reprogramming, and methods for parameter inference in systems biology.

B. Positions and Honors

Positions and Employment

2014 - 2015	Postdoctoral Research Associate, University of Oxford, Mathematical Institute, Oxford
2015 - 2016	Postdoctoral Research Associate, Imperial College London, Department of Life Sciences, London
2016 – 2018	Postdoctoral Scholar, University of California, Irvine, Department of Mathematics, Irvine, CA
2019 –	Assistant Professor of Quantitative and Computational Biology, Dept of Biological Sciences, University of Southern California, Los Angeles, CA

Other Experience and Professional Memberships

2005 - 2010	Student Member, Institute of Physics

Honors

2011	MIT-Imperial Initiative on International Collaboration, MIT/Imperial College London
2016	CPH Biosciences Travel Award, Copenhagen Bioscience

C. Contribution to Science

1. Analysis of high-dimensional multiscale single-cell data. I have recently developed methods in collaboration with the Nie Lab and others to interrogate high-throughput single-cell data and reveal new function and mechanisms associated with cell states, cell state transitions, and the intricate regulation involved with both of these. This includes a particularly novel method we recently presented on predicting the signalling relationships between single cells using specific ligand-receptor-target gene expression data. These analyses are especially relevant for cells actively transitioning through multiple states (as is the case during reprogramming), which may be rare, transient, or intermediate states, and thus hard to identify by traditional means.

    a. Jin S, MacLean AL, Peng T, Nie Q. scEpath: Energy landscape-based inference of transition probabilities and cellular trajectories from single-cell transcriptomic data. Bioinformatics. 2018; PubMed. PMID: 29415263
    b. MacLean AL, Hong T, Nie Q. Exploring intermediate cell states through the lens of single cells. Curr Opin Sys Biol. 2018; 9;31-42. doi:10.1016/j.coisb.2018.02.009.
    c. Wang S, MacLean AL, Nie Q. SoptSC: Similarity matrix optimization for clustering, lineage, and signalling inference. BioRxiv; submitted. 2018 May 12. https://doi.org/10.1101/168922.

2. The dynamical state transitions and stability of cellular differentiation. Cell state stability is a crucial biological concept; I have developed computational methods that allow us to characterize particular properties (e.g. existence and extent) of stem cell states. Investigation of models of cancer or stem cell fate led me to identify how cell state transitions are made, e.g. from a stem to a differentiated cell, or from epithelial to mesenchymal identity. These methods also inform us of the stability of the states associated with each model. I have also developed methods to study the existence and stability of (transient) cell states globally (i.e. in large parameter spaces). These provide crucial information about the dynamics of a particular biological system and offer great potential to generate insight into systems biology models by providing means to compare them and reject those that are not compatible with the experimental data.

    a. Peng T, Liu L, MacLean AL, Wong CW, Zhao W, Nie Q. A mathematical model of mechano-transduction reveals how mechanical memory regulates mesenchymal stem cell fate decisions. BMC Syst Biol. 2017; 11(1):55. PubMed PMID: 28511648; PubMed Central PMCID: PMC5434622.
    b. Guo Y, Nie Q, MacLean AL, Li Y, Lei J, Li S. Multiscale Modeling of Inflammation-Induced Tumorigenesis Reveals Competing Oncogenic and Oncoprotective Roles for Inflammation. Cancer Research. 2017; 77(22):6429-6441. PubMed PMID: 28951462.
    c. MacLean AL, Kirk PD, Stumpf MP. Cellular population dynamics control the robustness of the stem cell niche. Biol Open. 2015; 4(11):1420-6. PubMed PMID: 26453624; PubMed Central PMCID: PMC4728354.

d. Kirk P, Rolando DMY, MacLean AL, Stumpf MPH. Conditional random matrix ensembles and the stability of dynamical systems. New journal of physics. 2015; 17(8):083025.

3. Quantitative and qualitative parameter inference of spatiotemporal biological systems. My research pursues discovery and insight into the biological mechanisms that underpin homeostatic and pathological systems. Thus success relies on our ability to test model predictions with experimental data. I have developed new methods for parameter inference and model selection that enable us to test and (in)validate specific model predictions given complex datasets. These vary from the quantitative, e.g. the in vivo dynamics of hematopoietic stem/progenitor cell populations during malaria infection and the spatial dynamics of branching organogenesis, to qualitative predictions, such as the therapeutic goal of the eradication of leukemia cells from the bone marrow. In addition I have contributed novel parameter-free methods for inference in cases when the resolution of data is low. In each of these cases theoretical modeling predictions have been tested against data, leading to insight that could not have been gained by either the theoretical or the experimental knowledge alone.

   a. Lambert B*, MacLean AL*, Fletcher AG, Coombes AN, Little MH, Byrne HM. Bayesian inference of agent-based models: a tool for studying kidney branching morphogenesis. J Math Biol. 2018; doi.org/10.1101/096032.
   b. Vainieri ML, Blagborough AM, MacLean AL, Haltalli ML, Ruivo N, Fletcher HA, Stumpf MP, Sinden RE, Celso CL. Systematic tracking of altered haematopoiesis during sporozoite-mediated malaria development reveals multiple response points. Open Biol. 2016. 6(6) PubMed PMID: 27335321; PubMed Central PMCID: PMC4929935.
   c. MacLean AL, Rosen Z, Byrne HM, Harrington HA. Parameter-free methods distinguish Wnt pathway models and guide design of experiments. Proc Natl Acad Sci U S A. 2015; 112(9):2652-7. PubMed PMID: 25730853; PubMed Central PMCID: PMC4352827.
   d. MacLean AL, Lo Celso C, Stumpf MP. Population dynamics of normal and leukaemia stem cells in the haematopoietic stem cell niche show distinct regimes where leukaemia will be controlled. J R Soc Interface. 2013; 10(81):20120968. PubMed PMID: 23349436; PubMed Central PMCID: PMC3627104.

4. Ecological interactions between hematopoietic and cancer stem cells determine leukemia prognosis. A particular application of the complex dynamical models that I have developed has been the study of leukemia progression and competition with bone marrow stem cell niches. This work has yielded several startling predictions, including 1) that maintaining a population of hematopoietic stem cells may be a better strategy against leukemia than direct killing of cancer cells; 2) that competition within stem cell niches drives the disease and that this ought to be specifically targeted during therapy; and 3) that within regions of coexistence (of healthy and malignant stem cells), the outcome is acutely and non-intuitively sensitive to the feedback present from progeny on to the stem cells.

   a. MacLean AL, Lo Celso C, Stumpf MP. Concise Review: Stem Cell Population Biology: Insights from Hematopoiesis. Stem Cells. 2017 Jan;35(1):80-88. PubMed PMID: 27671750.
   b. Crowell HL, MacLean AL, Stumpf MP. Feedback mechanisms control coexistence in a stem cell model of acute myeloid leukaemia. J Theor Biol. 2016 Jul 21;401:43-53. PubMed PMID: 27130539; PubMed Central PMCID: PMC4880151.
   c. MacLean AL, Filippi S, Stumpf MP. The ecology in the hematopoietic stem cell niche determines the clinical outcome in chronic myeloid leukemia. Proc Natl Acad Sci U S A. 2014 Mar 11;111(10):3883-8. PubMed PMID: 24567385; PubMed Central PMCID: PMC3956166.
   d. MacLean AL, Lo Celso C, Stumpf MP. Population dynamics of normal and leukaemia stem cells in the haematopoietic stem cell niche show distinct regimes where leukaemia will be controlled. J R Soc Interface. 2013 Apr 6;10(81):20120968. PubMed PMID: 23349436; PubMed Central PMCID: PMC3627104.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/adam.maclean.1/bibliography/51862899/public

D. Additional Information: Research Support and/or Scholastic Performance

Completed Research Support

PhD Studentship, BBSRC
Stumpf, MPH (PI)
01/01/11-01/01/14
Dynamics and stability of stem cell lineage hierarchies
Role: GR