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Current Research Interests

- Modeling cell polarization, motility, cell division, and development. Models of cell signaling and organization.

- Using modeling to elucidate the design principles responsible for multicellular processes such as embryonic development and central nervous system repair.

- Mathematical methods for analysis of pattern-forming systems: developing new techniques for non-linear stability analysis and bifurcations analysis in complex and potentially large regulatory systems.

Education

- Ph.D. Mathematics, Indiana University Bloomington, 2010.

    - Thesis: A 3-D Non-Local Model of the Mammalian Cochlea with Numerical Simulation (with Jacob Rubinstein and Michael Jolly)

- M.A. Mathematics, Indiana University Bloomington (IUB), 2007.

- B.S. Engineering Physics, University of Tennessee (UTK), 2005.

Employment

- University of Melbourne, Lecturer, Department of Mathematics and Statistics, 2014 - Present

- University of California Irvine, Assistant Researcher, Department of Mathematics and the Centre for Complex Biological Systems, 2012 - Present

- University of British Columbia (UBC), Postdoctoral Fellow in Mathematics, 2010-2012

- Rolls Royce Aerospace, Experimental Test Engineer , 2002- 2003

    - Design and implementation of testing methods for aircraft engine components.

Publications

- Huijing Du, Qing Nie, W. R. Holmes*, "The interplay between Wnt mediated expansion and negative regulation of growth promote robust intestinal crypt structure and homeostasis.", PLoS Comput. Biol. (Submitted, Dec. 2015, 20 pages)

- W. R. Holmes, Nabora Soledad Reyes de Mochel, Qixuan Wang, Huijing Du, Michael Chiang, Olivier Cinquin, Ken W.Y. Cho, Qing Nie, "Intracellular noise has a significant, positive role in development of early embryonic structures." Nature Communications (Submitted Dec. 2015, editing for second round of review, 20 pages + 16 page SM)

- W. R. Holmes*, May Anne Mata, Leah Edelstein-Keshet, "Local Perturbation Analysis: A computational tool for biophysical reaction-diffusion models." Biophysical Journal (Publication date - Jan. 2015)

– This article has associated tutorials for implementing this method in both XPPAuto and the MatLab based package MatCont.

- W. R. Holmes, "A practical guide to non-parametric approximate Bayesian computation with improved implementation and error characterization" Journal of Mathematical Psychology (Submitted Sept. 2014, editing for second round of review - 28 pages)

  – This article has freely available code for implementing this method in MatLab.

- W. R. Holmes*, Jennifer S. Trueblood, Andrew Heathcoat, "Asymmetric updating and hysteresis in perceptual decision-making with changing information". PLoS Comput. Biol. (Submitted, Aug. 2014 - 26 pages)

- Alexander Gord[a], W. R. Holmes[a], Xing Dai, Qing Nie, "Computational modeling of epidermal stratification highlights the importance of asymmetric cell division for predictable and robust layer formation". Journal of the Royal Society Interface (Accepted, 2014) ([a] equal contributions)

  – This article has associated code for implementing this new modelling framework in C++ and OpenCL.

- W. R. Holmes, Qing Nie, "Interactions and tradeoffs between cell recruitment, proliferation, and differentiation affect CNS regeneration", Biophysical Journal, 106(7), pp. 1528-1536, 2014

- W. R. Holmes, "An excitable compass guides chemotaxis?", Biophysical Journal, 106(5), pp. 989, 2014

- W. R. Holmes, "A local non-linear stability analysis for detecting pattern formation in reaction diffusion systems", Bulletin of Mathematical Biology, 76(1), pp. 157-283, 2014

- L. Edelstein-Keshet, W. R. Holmes, Mark Zajac, Meghan Dutot, "From simple to detailed models for cell polarization", Philos T Royal Society B, 338, pp. 20130003, 2013

- M. Meta, M. Dudot, L. Edelstein-Keshet, W. R. Holmes[b], "A model for intracellular actin waves explored by nonlinear local perturbation analysis", Journal of Theoretical Biology, 334, pp. 149-161, 2013 ([b] WRH conceived, designed, and supervised this work)

- B. Lin, W. R. Holmes, J. Wang, T. Ueno, A. Harwell, L. Edelstein-Keshet, T. Inoue, and A. Levchenko, "Synthetic graded Rac activation drives cell polarity and locomotion", PNAS, 109(52), E3668-E3677, 2012

- W. R. Holmes, L. Edelstein-Keshet, "A Comparison of Computational Models for Eukaryotic Cell Shape and Motility", PLoS Comput. Biol., 8(12), e1002793, 2012

- W. R. Holmes, A. Carlsson, and L. Edelstein-Keshet, "Regimes of Wave Type Patterning driven by Refractory Actin Feedback: Transition from Static Polarization to Dynamic Wave Behaviour", Phys. Biol., 9(4), 046005, 2012

- W. R. Holmes, B. Lin, A. Levchenko, and L. Edelstein-Keshet, "Modelling cell polarization driven by synthetic spatially graded Rac activation", PloS Comput. Biol., 8(6), e1002366, 2012

- W. R. Holmes, M.S. Jolly, and J. Rubinstein, "Hydro-elastic waves in a cochlear model: Numerical simulations and an analytically reduced model", Confluentes Mathematici, Vol. 3, No. 3 pp. 523-541, 2011.

- Perkins T. A.[a], Holmes W. R.[a], Weltzin J. F., "Multi-species interactions in competitive hierarchies: new methods and empirical test". Journal of Vegetation Science: Vol. 18, No. 5 pp. 685-692, 2007 ([a] equal contributions, nominated for annual editors award)

In Preparation

- W. R. Holmes, Jinseok Park, Andre Levchenko, Leah Edelstein-Keshet, "Modeling polar and oscillatory transitions in melanoma cell morphology".

    - A second companion manuscript to this is also in preparation.

- Qixuan Wang, W. R. Holmes, Qing Nie, "Noise mediated plasticity and cell sorting jointly specify gene expression domains in the developing zebrafish hindbrain".

Grants and Awards

- 2015 - NIH (Submitted as Co-PI) - Decoding the self organizing principles of mammalian blastocyst development

- 2015 - NSF (Submitted as Co-PI) - The Impact of Dynamically Changing Information on Decision Processes

- 2014-2018 - NIH #R01GM107264 (Senior Personel, PI's are Qing Nie and Tom Schilling) - Stochastic Dynamics and Noise Control in Patterning Systems (2014-2018) (I devised and wrote components of this proposal.)

- NSF #0913159 (PI) - The effect of spatial heterogeneity on the secretion properties of parotid acinar cells (Matched funds from NZ Ministry of Science, 2009)

- Short Term Visitor (National Institute for Mathematical and Biological Synthesis - NIMBioS, 2011)

- Society of Mathematical Biology Landhi Travel Grant (2011)

- William B Wilcox Mathematics Award (via Indiana University Mathematics Department 2009)

Related Experience and Activities

- Actively helped supervise 2 PhD, 1 MSc, and 1 Undergraduate student in the Keshet group at UBC, and 1 PhD student in the Nie group at UCI.

- Participated in advising and troubleshooting on projects with 2 PDFs, including numerical simulations related to 2D motility.

- International Graduate Training Center (IGTC) Graduate Summer School in Mathematical Biology (UBC) student participant, Summer 2008

- MSRI Climate Change Summer School (MSRI) student participant , Summer 2008

- Summer Research Experience for Undergraduates (REU) Program Participant - UTK, Summer 2004

    - Kinetic Monte Carlo methods for diffusion of defects in crystalline structures.

- Undergraduate in Biology and Math (UBM) Program Research Participant - UTK, 2003-2005

    - Quantification of competitive hierarchies in ecological communities. Designed and ran greenhouse experiments and developed a hierarchical modelling framework.

Teaching Experience

- Infinite Series and Basic Linear Algebra (Math 2J, UC Irvine, Fall 2012, 100 Students)

- PIMS Mathematical Cell Biology Graduate Summer Course, Invited lecturer (University of British Columbia (UBC), 2012, 5 lectures - 2 hours each)

- Integral Calculus with Applications to Life Sciences (UBC, Math 103, 110 students, 2010 and 2011)

- Math Subject Graduate Record Examination (GRE) Prep Course (Indiana University (IUB), 10 students)

- Advanced calculus refresher for incoming graduate students (IUB, 20 students, summer short course)

- Algebra / Pre-Calculus (M025, IUB, 30 students, twice)

- Introduction to Algebra (J010, IUB, 30 students, Groups Program Course for first generation college students from underprivileged backgrounds)

Service

- Lecturer, Systems Biology Short Course (at UC Irvine, 2014)

- Co-supervised summer research experience for a local high school student (2013)

- Volunteer, MathCounts mathematics program for middle school students (2013)

- Volunteer, Euclid high school mathematics competition (Canada, 2012)

- Co-organizer Frontiers in Biophysics (2011) conference at UBC (participation throughout the pacific northwest). Funding secured through the Pacific Institute for the Mathematical Sciences (PIMS) and Mathematics of Information Technology and Complex Systems (MITACS).

- Reviewed for - Biophysical Journal, Discrete and Continuous Dynamical Systems B, PLoS Computational Biology, Molecular Biology of the Cell (MBoC), PLoS One, New Journal of Physics, Journal of Mathematical Biology, Nonlinearity, Journal of Theoretical Biology

Invited Seminars

- **Design principles and control of biological organization**, University of Minnesota (Cellular biophysics seminar, Genetics Cell and Developmental Biology Department), (2015)

- **A unifying mechanism for spontaneous, stimulus induced, and dynamic cell polarity**, University of Utah (Mathematical Biology Seminar), (2014)

- **From cell polarity to embryogenesis**, North Carolina State (Applied Math Seminar), (2014)

- **Topics in Mathematical Cell Biology: Cell polarity, embryogenesis, and central nervous system regeneration**, University of Kentucky (Colloquium), (2013)

- **Asymptotic analysis of models of spontaneous, induced, and dynamic polarity establishment**, Ohio State (Applied Mathematics Seminar), (2013)

- **Response thresholds and noise sensitivity in polarizing cells**, University of California at Irvine (Applied Mathematics Seminar), (2012)

- **Regulatory control of response thresholds during chemotactic polarization**, University of Victoria (Mathematical Biology Seminar), (2012).

- **A local analysis of symmetry breaking with applications to HeLa cell polarization: theory and experiment**, University of Tennessee Knoxville and the National Institute for Mathematical and Biological Synthesis (NIMBioS) (NIMBioS short term visitor and Departmental Colloquium), (2011)

- **New methods for detecting symmetry breaking in cell polarization**, John Innes Centre, Norwich UK, (2011) .

- **The role of the cochlear aspect ratio in hearing: simulation, asymptotics, and experiment**, University of British Columbia (PIMS Seminar), (2009).

- **Modelling the hydro-elastic properties of the cochlea**, University of Auckland (Applied Mathematics Seminar), (2009).

Other Presentations

- **Asymmetries in the distribution of gene expression noise direct spatial organization in the developing mammalian embryo**, Australia New Zealand Industrial and Applied Mathematics meeting, (2015)

- **Dynamic decision making: integration and adapting to new informational**, Australasian Mathematical Psychology Society Meeting, (2015)

- **Static to dynamic wave transitions in cells**, Australian Mathematical Society Annual Meeting, (2014)

- **Regulation of Dynamic Motility: Waves, Polarity, and Links to Cell Invasiveness**, Mathematics of the Cell: Integrating Genes, Biochemistry and Mechanics (Banff - BIRS, 2014)

- **Actin Nucleation Waves in Motile Cells**, SIAM Conference on Nonlinear waves and coherent structures (Cambridge, 2014)

- **Regulation of the First Embryonic Developmental Decision**, SIAM Life Sciences (Charlotte, 2014)

- **Accumulator models of decision-making under changing information**, Society for Mathematical Society Annual Meeting (Quebec City, 2014)

- **Spatio-temporal Regulation of Early Blastocyst Development**, Mathematics at the Frontier of Developmental Biology (PIMS Workshop, Vancouver 2014)

- **Design principles and control in biological systems**, Biomedical Engineering Seminar (University of California Irvine, 2014)

- **Dynamics of central nervous system regeneration**, Biophysical Society Annual Meeting (San Francisco, 2014)

- **Heterogeneity of spatial regulation mitigates tradeoffs between short and long time repair responses in the adult central nervous system**, Q-Bio Conference (Santa Fe, 2013)

- **Spatio-temporal regulation of developmental processes**, AMS Western Sectional Meeting (University of Colorado Boulder, 2013)

- **Population and distribution of cell states defined by a gene regulatory network**, Center for Complex Biological Systems Retreat (Los Angeles, 2013)

- **A multi-scale approach to spatially distributed regulatory networks**, SIAM Life Sciences Meeting (2012)

- **Mechanisms for biochemical sensitivity control in spatially distributed cellular systems**, Society of Mathematical Biology Annual Meeting (2012)

- **Foundations of spatio-temporal pattern formation with applications to cell biology and ecology**, University of Tennessee Knoxville (Undergraduate Colloquium), (2011).

- **A mathematical basis for cell polarization**, International Congress on Industrial and Applied Mathematics, (2011)

- **Cochlear dynamics: dispersion and the uncertainty principle**, SIAM Great Lakes Conference: Modelling and Numerical PDEs in Mathematical Biology, (2010).

- **Mixed method computations in cochlear dynamics**, Society for Industrial and Applied Mathematics (SIAM) Meeting on Dynamical Systems - Snowbird, (2009).

- **Cochlear dynamics**, PIMS Seminar, University of British Columbia, (2008).

- **Competition and invasion, a multispecies view**, Coalition for National Science Funding Annual Meeting at the request of the Math Association of America (MAA), (Washington, 2005) .

- **Monte Carlo vs molecular dynamics in 2D crystalline defect diffusion**, American Physics Society (APS) Annual Meeting, (2004).

Poster Presentations

- **Spatio-temporal control of early blastocyst development** , National Centers for Systems Biology Meeting (NIH - Bethesda, 2013) - Poster

- **Roles of chemotaxis, differentiation and quiescence of progenitor cells in adult CNS repair**, Systems Biology of Stem Cells (UC Irvine, 2013) - Poster

- **Tradeoff arise between conflicting goals of directed motility and differentiation in lineage restricted progenitor populations**, Center for Complex Biological Systems Retreat (Los Angeles, 2013) - Poster

- **Interactions between actin and its effectors yields both polarized and dynamic phenotypes**, American Society for Cell Biology (ASCB) Annual Meeting (2012) - Poster

- **Cytoskeletal waves driven by the interaction of a conservative wave generator with refractory actin feedback**, Biophysical Society Annual Meeting, (2012) - Poster

- **Autonomous symmetry breaking in cell polarization: combined theory and experiment**, Ohio State (Mathematical Biology Institute): Young Researchers Conference, (2011) - Poster.

- **A model for HeLa cell polarization with matching experiments**, Mathematical Biology of the Cell: Cytoskeleton and Motility (Banff International Research Station, 2011) - Poster.

- **A local analysis of symmetry breaking with applications to cell motility**, European Conference on Mathematical and Theoretical Biology, (2011) - Poster.

- **Autonomous symmetry breaking in cell polarization: combined theory and experiment**, Biophysical Society Annual Meeting, (2011) - Poster.

- **Lotka Volterra parameter estimation applied to a micro-organism community**, Joint Math Meetings, (2005) - Poster.

Programming Languages and Software Packages

- Fortran, Matlab

- Auto, Matcont (Numerical continuation software)

Society Memberships

- Society of Mathematical Biology (SMB)

- Biophysical Society

- Society for Industrial and Applied Mathematics (SIAM)

- American Society for Cell Biology (ASCB)