Shicong (Mimi) Xie, PhD

Postdoctoral Fellow
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RESEARCH INTEREST

I am interested in how cell size is controlled in mammalian tissues *in vivo*: how do cells maintain size homeostasis and how is cell size information conveyed to the cell's signaling machinery? To answer these questions, I use intravital imaging, light sheet microscopy, and computational image analysis to directly observe single cell dynamics in 3D tissues and in the living mouse. By combining live-cell dynamics and quantitative cell size-resolved measurements of transcriptional and proteomic scaling, I seek to understand how cell size affects cell and tissue function.

EDUCATION

Ph.D. **Computational & Systems Biology**
Massachusetts Institute of Technology, Cambridge, MA 2010 - 2016

B.A. Double major: **Physics**, **Applied Mathematics** (Highest honors)
University of California, Berkeley, Berkeley, CA 2006 - 2010

RESEARCH EXPERIENCE

Postdoctoral Research

Stanford University, Stanford, CA 2016 - present
Advisor: Jan Skotheim, Department of Biology

Cell size control in mammalian epithelial tissues

- **G1/S transition controls cell size in mammalian epithelia.** I discovered the G1/S cell cycle transition is cell size-dependent in skin stem cells growing *in vivo* skin and in intestinal stem cells growing in organoid culture. This cell size-dependence of G1/S transition is invariant during fate-specification in the stem cell.
- ***In vivo* single cell imaging of mammalian skin** I adapted and developed imaging methods to allow me to revisit and track single skin stem cells in an intact mouse using two photon microscopy in week-long time courses.
- **Computational image analysis of 4D epithelial dynamics** I developed computational analysis tools to deal with large data volumes (>100Gbs) generated by 4D imaging of tissues. I combining classical machine vision with deep learning neural network-based methods to segment cells in 3-dimensions. I also developed tools to combine

manually tracked cells with semi-automated cell segmentation to follow cell growth and cell cycle progression with single-cell resolution.

Evolution of Retinoblastoma Protein (Rb) C-terminal docking motif

- **Metazoan Rb protein family members have unique helical docking motif.** I used bioinformatics to analyze the evolutionary origin of a C-terminal helical docking motif in mammalian Rb and Rb-related proteins that confers specific binding to Cyclin D/CDK4,6 complexes.

Friedrich Miescher Institute, Basel, Switzerland — Jan - Mar, 2020
Collaborator: Prisca Liberali — (interrupted by COVID-19)

- **Lightsheet imaging of intestinal organoids.** I visited the lab of Dr. Liberali to use lightsheet imaging to study single cell growth in intestinal organoids. I developed computational tools to analyze single cell growth from light sheet datasets.

Graduate Research

Massachusetts Institute of Technology, Cambridge, MA — 2010 - 2016
Advisor: Adam C. Martin, Department of Biology
Thesis committee: Doug Lauffenburger (MIT, Dept. of Biological Engineering), Hazel Sive (MIT, The Whitehead Institute)

Tissue-scale coordination of contractile forces during morphogenesis

- **Investigation of intercellular coordination during collective apical constriction.** I discovered how actomyosin contractions are coordinated to drive tissue folding during *Drosophila* ventral furrow invagination.
- **Computational image analysis of pulsatile actomyosin contractions.** Combining techniques from machine learning, image analysis, and spatial statistics, I developed a computational framework to analyze pulsatile contraction events that drive collective cell constriction.
- **GPCR-signaling buffers actomyosin contractions against cell size heterogeneity.** I uncovered the mechanism by which $G_{\alpha 12/13}$-signaling coordinates apical constrictions the *Drosophila* ventral furrow by buffering actomyosin contractions against cell size-dependent defects.

Undergraduate Research

University of California, Berkeley, Berkeley, CA — 2007 - 2010
Advisor: John Kuriyan, Departments of Molecular & Cell Biology, Chemistry

- Super-resolution imaging of EGFR receptor clustering

HHMI Janelia Research Campus, Ashburn, VA — 2009
Advisor: Harald Hess

- Automation of alignment and focus of the interferometric photoactivatable localization microscope (iPALM)

NASA Ames Research Center, The SETI Institute, Mountain View, CA 2007
Advisor: Friedemann Freund

- Characterization of the electrochemistry of water-rock interfaces for igneous rock under mechanical stress

GRANTS & FELLOWSHIPS

Active Awards

K99/R00 Pathway to Independence Award 2020 - 2025
NIH NIGMS K99GM138712 $951,292

- Title: Determining the molecular mechanism controlling cell size in mammalian epithelia.

Past Awards

F32 Individual Postdoctoral Fellowship 2018 - 2020
NIH NIGMS F32GM129878 $126,484

- Title: Determining how the G1/S cell cycle transition regulates the homeostasis of adult intestinal stem cells

Company of Biologists, Journal of Cell Science Jan - Mar, 2020
Travelling Fellow $3,000

AWARDS

- Regents' and Chancellors' Scholarship, UC Berkeley 2006 - 2010
- Dean's List, UC Berkeley 2006 - 2008
- Phoebe Hearst Scholar 2006 - 2008
- Genzyme Science Scholarship 2006
- Robert Byrd Honors Scholarship 2006
- National Merit Scholar 2006
- Scholastic National Art & Writing Awards, Silver Medal in Creative Writing Portfolio 2006

MENTORING AND TEACHING

Mentor: Stanford ADVANCE Summer Institute (1 student) Summer 2021

- Mentored an incoming international graduate student via informal paper reading discussions on the topics of machine learning and computational biology. I also mentored her through formal scientific presentation for a

journal club as part of a preparatory summer program designed for new graduate students from underrepresented backgrounds.

Mentor: Stanford Raising Interest in Science and Engineering (RISE) Summer Internship Program. (2 students) Summer 2019

- Co-mentored two high school interns through the Stanford RISE Summer Internship Program designed for low-income high school students. I taught them foundational concepts in computer programming in Python and introductory image analysis.

Course: MIT Biological Engineering 20.430, Physical biology. (14 students) Fall 2011

- Helped develop and teach a graduate course in physical biology (20.430), covering topics like statistical mechanics, polymer models, biological motion, cell mechanics. Specifically, I helped develop using Monte Carlo simulations as the unifying computational technique covered in the course.

Workshop: MIT Quantitative Biology Workshop (edX). (40 students) Winter 2012,4

- Developed and taught a minicourse on analyzing biological motion using image analysis in MATLAB and Python/NumPy, using real biological data. This was a part of an on-site workshop series designed to introduce quantitative methods in biology to undergraduates from non-research institutions. Part of this module was adapted for the edX version of this course.

Mentor: MIT Undergraduate Research Apprentice Program. (1 student) Fall 2008.

- Mentored an undergraduate mathematics student to use statistical modeling and Monte Carlo simulations to determine transition points in dynamic biological data.

INVITED TALKS

- **College de France, Center for Interdisciplinary Research in Biology Seminars.** Paris, France. Cell size-dependent G1/S transition controls stem cell size in mammalian epithelia. Oct, 2021
- **4th International Conference on Stem Cells.** Kos, Greece. Cell size-dependent G1/S transition controls stem cell size in epidermal and intestinal stem cells. Oct, 2021
- **Cell Size and Growth seminar series.** Online. G1 sizer coordinates cell size and cell cycle in mammalian stem cells. Apr, 2020
- **Gordon Research Conference, Stochastic Physics in Biology.** Ventura, CA. Interactions Between Contractile Events During Tissue Folding. Oct, 2015
- **Drosophila Research Conference.** San Diego, CA. Coordinating pulsed and ratcheted contractions during Drosophila ventral furrow formation. Mar, 2014

PUBLICATIONS

1. **Xie S** and Skotheim JM (2021). Cell-size control: Chromatin-based titration primes inhibitor dilution. *Current Biology, 31*(19). 1127-1129. [link]

2. **Xie S** and Skotheim JM (2020). A G1 Sizer Coordinates Growth and Division in the Mouse Epidermis. *Current Biology, 30*(5). 916-924. [link]

3. Berenson DF, Zatulovskiy E, **Xie S**, Skotheim JM (2019). Constitutive expression of a fluorescent protein reports the size of live human cells. *Molecular Biology of the Cell, 30*(24), 2985-2995. [link]

4. Shariati SA, Dominguez A, **Xie S**, Wernig M, Qi SL, Skotheim JM (2019). Reversible disruption of specific transcription factor-DNA interactions using CRISPR/Cas9. *Molecular Cell, 74*(3), 622-633. [link]

5. Topacio BR, Zatulovskiy E, Cristea S, **Xie S**, Tambo CS, Rubin SM, Sage J, Kõivomägi M, Skotheim JM (2019). Cyclin D-Cdk4, 6 Drives Cell-Cycle Progression via the Retinoblastoma Protein's C-Terminal Helix. *Molecular Cell, 74*(4), 758-770. [link]

6. **Xie S**, Mason FM, Martin AC (2016). Loss of $G_{\alpha 12/13}$ exacerbates apical area-dependence of actomyosin contractility. *Molecular Biology of the Cell, 27*(22), 3526-3536. [link]

7. Mason FM, **Xie S**, Vasquez CG, Tworoger M, Martin AC (2016). RhoA GTPase inhibition organizes contraction during epithelial morphogenesis. *Journal of Cell Biology, 214*(5), 603-617. [link]

8. **Xie S** and Martin AC (2015). Intracellular signalling and intercellular coupling coordinate heterogeneous contractile events to facilitate tissue folding. *Nature Communications, 6*(1), 1-13. [link]

9. Tikhonova EB, Ethayathulla AS, Su Y, Hariharan P, **Xie S**, Guan L (2015). A transcription blocker isolated from a designed repeat protein combinatorial library by in vivo functional screen. *Scientific Reports, 5*(1), 1-11. [link]

POSTERS

- **Xie S**, de Medeiro GQG, Liberali P, Skotheim JM. Cell size-dependent G1/S transition controls stem cell size in mammalian epithelia. The Salk Institute Cell Cycle Meeting. 2021. Online.
- **Xie S** and Skotheim JM. G1 sizer couples cell cycle and cell growth in epidermal stem cells *in vivo*. Gordon Research Conference on Cell Growth and Proliferation. 2019. Mt. Snow, VT.
- **Xie S**, Mason FM, Martin AC. Loss of $G_{\alpha 12/13}$ exacerbates apical area-dependence of actomyosin contractility. American Society for Cell Biology Meeting. 2016. San Francisco, CA.

- **Xie S** and Martin AC.Twist signaling and intercellular coupling coordinate pulsed and ratcheted apical contractions during tissue folding. American Society for Cell Biology Meeting. 2014. Philadelphia, PA.
- **Xie S** and Martin AC. Coordinating the pulsed and ratcheted contractions in the *Drosophila* ventral furrow. Drosophila Research Conference. 2014 San Diego, CA.
- **Xie S** and Martin AC. Interactions Between Contractile Events During Tissue Folding. Gordon Research Conference on Contractile and Motile Systems. 2013. New London, NH.

MEMBERSHIPS

- The American Society for Cell Biology 2019 - present
- The Biophysical Society 2020 - present
- International Society for Stem Cell Research 2020 - present

OTHER PUBLICATIONS

Poetry

- *Berkeley Poetry Review*, Issue No. 40: "bread also"
- *Berkeley Poetry Review*, Issue No. 41: "this expectant rose"
- *Sinθ magazine*, Issue No. 10: "Moon"