




Jan Skotheim

Associate Professor of Biology and, by courtesy, of Chemical and Systems Biology

 NIH Biosketch available Online

 Curriculum Vitae available Online

CONTACT INFORMATION

• Administrative Contact

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Bio

BIO

My interdisciplinary research group draws on diverse scientific cultures to develop a creative, rigorous and quantitative approach to the fundamental question of how growth drives cell division. Our diverse backgrounds include mathematics, physics, engineering, biochemistry, genetics, and cell, molecular, and systems biology. This reflects my interdisciplinary training (BS Mathematics; BS Physics - MIT 1999; PhD Applied Mathematics - Cambridge 2004; Postdoctoral training Genetics, Cell, and Systems Biology - Rockefeller)

ACADEMIC APPOINTMENTS

- Associate Professor, Biology
- Associate Professor (By courtesy), Chemical and Systems Biology
- Member, Bio-X
- Member, Stanford Cancer Institute

ADMINISTRATIVE APPOINTMENTS

- Faculty member, F1000, (2018- present)
- Standing Member, NIH CSRS study section, (2017- present)
- Co-Organizer of 9th, 10th, and 11th Meetings, Salk Institute Cell Cycle Meeting, La Jolla, CA, (2015- present)
- Scientific Advisory Committee Member, 16th International Conference on Systems Biology (ICSB 2015), Singapore, (2015- present)
- Design Team, University Long Range Planning Natural World Design Team, (2018-2019)

HONORS AND AWARDS

- Postdoctoral Fellowship (F32), NIH (2006-2008)
- Career Award at the Scientific Interface, Burroughs Wellcome Fund (2008)
- Recipient, Hellman Faculty Scholar Award (2009)
- Recipient, NSF Career Award (2011)
- Named David Huntington Dean's Faculty Scholar, David Huntington Dean's (2012)

- HHMI, Gates Foundation & Simons Foundation Faculty Scholar Award, HHMI (2016)
- Trends in Cell Biology, Young and Trending, Trends in Cell Biology (2016)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Scientific Advisory Committee, American Society for Cell Biology (2009 - present)
- Scientific Advisory Committee, Genetics Society of America (2009 - present)
- Scientific Advisory Committee, Lake Tahoe Cell Size Control Meeting, Truckee, CA (2017 - present)
- Scientific Advisory Committee, European International Cell Cycle meeting, Trieste, Italy (2017 - present)
- Scientific Advisory Committee, EMBO Cell Size and Growth Meeting, Rehovot, Israel (2017 - present)
- Member of the Advisory Board, Molecular Systems Biology (2017 - present)
- Scientific Advisory Board, Billiontoone, Inc (2018 - present)

PROFESSIONAL EDUCATION

- PhD, University of Cambridge , Applied Mathematics (2004)
- CASM Pt III, University of Cambridge , Applied Mathematics (2001)
- BS, MIT , Mathematics (1999)
- BS, MIT , Physics (1999)

LINKS

- Lab web site: <http://skotheimlab.com/>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

My laboratory's goal is to understand how cell growth triggers cell division. Linking growth to division is important because it allows cells to maintain a specific size range to best perform their physiological functions. Today, thanks to decades of research, we have an extensive, likely nearly complete parts-list of key regulatory proteins. Deletion, inhibition, or over-expression of these proteins often results in changes to cell size. However, the underlying molecular mechanisms for how growth triggers division are not understood. How do the regulatory proteins work together to produce a biochemical activity reflecting cell size or growth? Since we now have most of the parts, the next step to solving this fundamental question is to better understand how they work together.

My laboratory recently made a breakthrough discovery in understanding how growth triggers division in budding yeast. While it was expected that growth would act to increase the activities of the cyclin-dependent kinases (Cdk) known to promote cell division, this is not the case. Rather, we found that cell growth acts in the opposite manner. Cell growth triggers division by diluting a protein that inhibits cell division. We recently discovered an analogous mechanism operating in human cells.

Our discovery of a mechanism linking cell growth to cell division in budding yeast opens many avenues of research, three of which we are currently pursuing:

1. Cell size control results from the dilution of the cell cycle inhibitor Whi5 because its synthesis is independent of cell size. In contrast, most proteins are produced in proportion to cell size. We identified the set of proteins whose expression is largely independent of cell size. We now aim to determine the molecular mechanism(s) through which this occurs and identify the biological processes impacted.
2. We are addressing how gene expression depends on cell size in human cells. We are working with the Chan Zuckerberg Biohub Cell Atlas Project to establish a workflow so that all their single cell sequencing experiments will include data on cell size. This will allow us to examine cell size dependency of gene expression across an unprecedented number of human cell types.

3. Our work in yeast led us to the hypothesis that cell growth could trigger division in human cells by diluting a cell cycle inhibitor. We can apply our quantitative single-cell imaging approach because CRISPR-based genome editing allows us to tag cell cycle regulators with fluorescent proteins at their endogenous loci. We are now measuring and manipulating concentration dynamics in live cells to determine how cell growth impacts key regulators of division.

Our work has fundamental implications for understanding how the most basic aspect of cell morphology, cell size, is controlled. In the next 5 years, we aim to determine how growth triggers division in human cells, which has the potential to revolutionize our understanding of how cell division is regulated in both natural developmental contexts and in disease. Over the 5-10 year time horizon, we intend to pursue both developmental and medical directions.

Teaching

COURSES

2019-20

- Principles of Cell Cycle Control: BIO 171, BIO 271, CSB 271 (Aut)

2018-19

- Principles of Cell Cycle Control: BIO 171, BIO 271, CSB 271 (Aut)

2017-18

- Principles of Cell Cycle Control: BIO 171, BIO 271, CSB 271 (Aut)

2016-17

- Principles of Cell Cycle Control: BIO 171, BIO 271, CSB 271 (Aut)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Andrea Chaikovsky, Vivian Chen, Ray Futia, Eirini Tsekitsidou, Mike Van

Postdoctoral Faculty Sponsor

Michael Lanz, Matthew Swaffer, Shicong Xie, Evgeny Zatulovskiy, Shuyuan Zhang

Doctoral Dissertation Advisor (AC)

Daniel Berenson, Cecelia Brown, Benjamin Topacio

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biology (School of Humanities and Sciences) (Phd Program)
- Biophysics (Phd Program)
- Chemical and Systems Biology (Phd Program)

Publications

PUBLICATIONS

- **Constitutive expression of a fluorescent protein reports the size of live human cells.** *Molecular biology of the cell*
Berenson, D. F., Zatulovskiy, E., Xie, S., Skotheim, J. M.
2019: mbcE19030171
- **Cyclin D-Cdk4,6 Drives Cell-Cycle Progression via the Retinoblastoma Protein's C-Terminal Helix** *MOLECULAR CELL*
Topacio, B. R., Zatulovskiy, E., Cristea, S., Xie, S., Tambo, C. S., Rubin, S. M., Sage, J., Koivomagi, M., Skotheim, J. M.
2019; 74 (4): 758-+

- **Reversible Disruption of Specific Transcription Factor-DNA Interactions Using CRISPR/Cas9** *MOLECULAR CELL*
Shariati, S., Dominguez, A., Xie, S., Wernig, M., Qi, L. S., Skotheim, J. M.
2019; 74 (3): 622-+
- **Cell cycle, cell division, cell death** *MOLECULAR BIOLOGY OF THE CELL*
Maddox, A., Skotheim, J. M.
2019; 30 (6): 732
- **Cell cycle, cell division, cell death.** *Molecular biology of the cell*
Maddox, A. S., Skotheim, J. M.
2019; 30 (6): 732
- **Chromatin-associated RNA sequencing (ChAR-seq) maps genome-wide RNA-to-DNA contacts** *ELIFE*
Bell, J. C., Jukam, D., Teran, N. A., Risca, V. I., Smith, O. K., Johnson, W. L., Skotheim, J. M., Greenleaf, W., Straight, A. F.
2018; 7
- **A Precise Cdk Activity Threshold Determines Passage through the Restriction Point.** *Molecular cell*
Schwarz, C., Johnson, A., Kõivomägi, M., Zatulovskiy, E., Kravitz, C. J., Doncic, A., Skotheim, J. M.
2018; 69 (2): 253–64.e5
- **Form and function of topologically associating genomic domains in budding yeast** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Eser, U., Chandler-Brown, D., Ay, F., Straight, A. F., Duang, Z., Noble, W. S., Skotheim, J. M.
2017; 114 (15): E3061-E3070
- **Spatial and temporal signal processing and decision making by MAPK pathways.** *journal of cell biology*
Atay, O., Skotheim, J. M.
2017; 216 (2): 317-330
- **The Adder Phenomenon Emerges from Independent Control of Pre- and Post-Start Phases of the Budding Yeast Cell Cycle.** *Current biology : CB*
Chandler-Brown, D., Schmoller, K. M., Winetraub, Y., Skotheim, J. M.
2017
- **Zygotic Genome Activation in Vertebrates.** *Developmental cell*
Jukam, D., Shariati, S. A., Skotheim, J. M.
2017; 42 (4): 316–32
- **Switch-like Transitions Insulate Network Motifs to Modularize Biological Networks.** *Cell systems*
Atay, O., Doncic, A., Skotheim, J. M.
2016; 3 (2): 121-132
- **Dissecting direct reprogramming from fibroblast to neuron using single-cell RNA-seq** *NATURE*
Treutlein, B., Lee, Q. Y., Camp, J. G., Mall, M., Koh, W., Shariati, S. A., Sim, S., Neff, N. F., Skotheim, J. M., Wernig, M., Quake, S. R.
2016; 534 (7607): 391-?
- **The Yeast Cyclin-Dependent Kinase Routes Carbon Fluxes to Fuel Cell Cycle Progression** *MOLECULAR CELL*
Ewald, J. C., Kuehne, A., Zamboni, N., Skotheim, J. M.
2016; 62 (4): 532-545
- **Punctuated evolution and transitional hybrid network in an ancestral cell cycle of fungi** *ELIFE*
Medina, E. M., Turner, J. J., Gordan, R., Skotheim, J. M., Buchler, N. E.
2016; 5
- **Cell-Size Control** *COLD SPRING HARBOR PERSPECTIVES IN BIOLOGY*
Amodeo, A. A., Skotheim, J. M.
2016; 8 (4)
- **The Biosynthetic Basis of Cell Size Control.** *Trends in cell biology*
Schmoller, K. M., Skotheim, J. M.
2015; 25 (12): 793-802

- **Mitosis is swell.** *journal of cell biology*
Zatulovskiy, E., Skotheim, J. M.
2015; 211 (4): 733-735
- **Dilution of the cell cycle inhibitor Whi5 controls budding-yeast cell size.** *Nature*
Schmoller, K. M., Turner, J. J., Kõivomägi, M., Skotheim, J. M.
2015; 526 (7572): 268-272
- **A genetically encoded Förster resonance energy transfer sensor for monitoring in vivo trehalose-6-phosphate dynamics** *ANALYTICAL BIOCHEMISTRY*
Peroza, E. A., Ewald, J. C., Parakkal, G., Skotheim, J. M., Zamboni, N.
2015; 474: 1-7
- **Compartmentalization of a Bistable Switch Enables Memory to Cross a Feedback-Driven Transition** *CELL*
Doncic, A., Atay, O., Valk, E., Grande, A., Bush, A., Vasen, G., Colman-Lerner, A., Loog, M., Skotheim, J. M.
2015; 160 (6): 1182-1195
- **Histone titration against the genome sets the DNA-to-cytoplasm threshold for the *Xenopus* midblastula transition.** *Proceedings of the National Academy of Sciences of the United States of America*
Amodeo, A. A., Jukam, D., Straight, A. F., Skotheim, J. M.
2015; 112 (10): E1086-95
- **Modularity and predictability in cell signaling and decision making** *MOLECULAR BIOLOGY OF THE CELL*
Atay, O., Skotheim, J. M.
2014; 25 (22): 3445-3450
- **Modularity and predictability in cell signaling and decision making.** *Molecular biology of the cell*
Atay, O., Skotheim, J. M.
2014; 25 (22): 3445-3450
- **Docking interactions: cell-cycle regulation and beyond.** *Current biology*
Kõivomägi, M., Skotheim, J. M.
2014; 24 (14): R647-9
- **Unravelling the Size Sensing Mechanism in Budding Yeast**
Schmoller, K. M., Turner, J. J., Skotheim, J. M.
CELL PRESS.2014: 595A
- **Start and the restriction point.** *Current opinion in cell biology*
Johnson, A., Skotheim, J. M.
2013; 25 (6): 717-723
- **CONSTRAINTS ON THE ADULT-OFFSPRING SIZE RELATIONSHIP IN PROTISTS** *EVOLUTION*
Caval-Holme, F., Payne, J., Skotheim, J. M.
2013; 67 (12): 3537-3544
- **Nuclear Repulsion Enables Division Autonomy in a Single Cytoplasm** *CURRENT BIOLOGY*
Anderson, C. A., Eser, U., Korndorf, T., Borsuk, M. E., Skotheim, J. M., Gladfelter, A. S.
2013; 23 (20): 1999-2010
- **Dead-end phosphorylation of Sic1 by Clb5-Cdk1 within the inhibitory complex controls the G1/S switch**
Venta, R., Doncic, A., Valk, E., Koivomaegi, M., Skotheim, J., Loog, M.
WILEY-BLACKWELL.2013: 195
- **Mutually exclusive phosphorylation events control the decision between mating and cell cycle progression**
Valk, E., Doncic, A., Koivomaegi, M., Venta, R., Iofik, A., Faustova, I., Kivi, R., Siibak, T., Balog, E. M., Rubin, S. M., Skotheim, J., Loog, M.
WILEY-BLACKWELL.2013: 66
- **Control of cell cycle transcription during G1 and S phases** *NATURE REVIEWS MOLECULAR CELL BIOLOGY*
Bertoli, C., Skotheim, J. M., de Bruin, R. A.
2013; 14 (8): 518-528

- **Feedforward regulation ensures stability and rapid reversibility of a cellular state.** *Molecular cell*
Doncic, A., Skotheim, J. M.
2013; 50 (6): 856-868
- **Cell growth and cell cycle control.** *Molecular biology of the cell*
Skotheim, J. M.
2013; 24 (6): 678-?
- **A SHIFT IN THE LONG-TERM MODE OF FORAMINIFERAN SIZE EVOLUTION CAUSED BY THE END-PERMIAN MASS EXTINCTION** *EVOLUTION*
Payne, J. L., Jost, A. B., Wang, S. C., Skotheim, J. M.
2013; 67 (3): 816-827
- **An algorithm to automate yeast segmentation and tracking.** *PloS one*
Doncic, A., Eser, U., Atay, O., Skotheim, J. M.
2013; 8 (3)
- **LATE PALEOZOIC FUSULINOIDEAN GIGANTISM DRIVEN BY ATMOSPHERIC HYPEROXIA** *EVOLUTION*
Payne, J. L., Groves, J. R., Jost, A. B., Thienan Nguyen, T., Moffitt, S. E., Hill, T. M., Skotheim, J. M.
2012; 66 (9): 2929-2939
- **Cell Size Control in Yeast** *CURRENT BIOLOGY*
Turner, J. J., Ewald, J. C., Skotheim, J. M.
2012; 22 (9): R350-R359
- **Evolution of networks and sequences in eukaryotic cell cycle control** *PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B-BIOLOGICAL SCIENCES*
Cross, F. R., Buchler, N. E., Skotheim, J. M.
2011; 366 (1584): 3532-3544
- **Commitment to a Cellular Transition Precedes Genome-wide Transcriptional Change** *MOLECULAR CELL*
Eser, U., Faller-Fettig, M., Johnson, A., Skotheim, J. M.
2011; 43 (4): 515-527
- **Distinct Interactions Select and Maintain a Specific Cell Fate** *MOLECULAR CELL*
Doncic, A., Faller-Fettig, M., Skotheim, J. M.
2011; 43 (4): 528-539
- **Daughter-Specific Transcription Factors Regulate Cell Size Control in Budding Yeast** *PLOS BIOLOGY*
Di Talia, S., Wang, H., Skotheim, J. M., Rosebrock, A. P., Futcher, B., Cross, F. R.
2009; 7 (10)
- **Cell signaling. To divide or not to divide.** *Science*
Skotheim, J. M.
2009; 324 (5926): 476-477
- **Positive feedback of G1 cyclins ensures coherent cell cycle entry** *NATURE*
Skotheim, J. M., Di Talia, S., Siggia, E. D., Cross, F. R.
2008; 454 (7202): 291-U12
- **Settling and swimming of flexible fluid-lubricated foils** *PHYSICAL REVIEW LETTERS*
Argentina, M., Skotheim, J., Mahadevan, L.
2007; 99 (22)
- **The effects of molecular noise and size control on variability in the budding yeast cell cycle** *NATURE*
Di Talia, S., Skotheim, J. M., Bean, J. M., Siggia, E. D., Cross, F. R.
2007; 448 (7156): 947-U12
- **Red blood cells and other nonspherical capsules in shear flow: Oscillatory dynamics and the tank-treading-to-tumbling transition** *PHYSICAL REVIEW LETTERS*

Skotheim, J. M., Secomb, T. W.
2007; 98 (7)

● **Gravitational collapse of colloidal gels** *PHYSICAL REVIEW LETTERS*

Manley, S., Skotheim, J. M., Mahadevan, L., Weitz, D. A.
2005; 94 (21)

● **Physical limits and design principles for plant and fungal movements** *SCIENCE*

Skotheim, J. M., Mahadevan, L.
2005; 308 (5726): 1308-1310

● **How the Venus flytrap snaps** *NATURE*

Forterre, Y., Skotheim, J. M., Dumais, J., Mahadevan, L.
2005; 433 (7024): 421-425

● **Soft elastohydrodynamic contacts** *Phys. Fluids*

J, S. M., L, M.
2005; 17

● **Soft lubrication** *PHYSICAL REVIEW LETTERS*

Skotheim, J. M., Mahadevan, L.
2004; 92 (24)

● **Dynamics of poroelastic filaments** *Proc. R. Soc. London Ser. A*

J, S. M., L, M.
2004; 460: 1995-2020

● **On the instability of a falling film due to localized heating** *J. Fluid Mech.*,

J, S. M., U, T., B, S.
2003; 475: 1-19

● **Evaporatively driven convection in a draining soap film** *Phys. Fluids*,

J, S. M., JWM, B.
2000; S1