Stanford

Alistair Boettiger

Assistant Professor of Developmental Biology

CONTACT INFORMATION

- **Alternate Contact**

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Bio

BIO

Alistair Boettiger is an Assistant Professor in the Department of Developmental Biology at the Stanford University School of Medicine and is a member of Bio-X and the Biophysics Program. As an undergraduate he studied Physics and Molecular Biology at Princeton University, where he had the opportunity to experience lab research under the mentorship of Stas Shvartsman, who introduced him to his abiding interest in quantitative imaging and animal development. He conducted his Ph.D. research under the guidance of Michael Levine at UC Berkeley, where he studied cis-regulatory sequences that modulate the precision and robustness of gene expression (in particular shadow enhancers and paused promoters). As a postdoc in Xiaowei Zhuang's single-molecule imaging group at Harvard University, he studied gene regulation through super-resolution microscopy, multiplexed, error-correcting imaging, and deep sequencing. Dr. Boettiger started his lab at Stanford in 2016.

ACADEMIC APPOINTMENTS

- Assistant Professor, Developmental Biology
- Member, Bio-X

HONORS AND AWARDS

- New Innovator Award, NIH (2018-2023)
- Packard Fellowship, Packard Foundation (2018-2023)
- Beckman Young Investigator, Beckman Foundation (2018-2022)
- Kavli Fellow, NAS/Kavli Frontiers of Science (2018)
- Searle Scholars Award, Chicago Community Trust (2017-2020)
- Career Award at the Scientific Interface (CASI), Burroughs Wellcome Fund (2016-2021)
- Dale F. Frey Award for Breakthrough Scientists, Damon Runyon Cancer Research Foundation (2016-2018)
- Damon Runyon Fellowship Award, Damon Runyon Cancer Research Foundation (2012-2016)
- Graduate Research Fellowship, National Science Foundation (2009-2011)

PROFESSIONAL EDUCATION

- Postdoc, Harvard University , Single-molecule Imaging (2016)

- Ph.D., UC Berkeley , Biophysics (2011)
- A.B., Princeton University , Physics (2007)

LINKS

- Lab website: http://boettigerlab.stanford.edu

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

My research aims to improve our understanding of how cells with the same genome can develop dramatically different behaviors. For example, consider the mechanical abilities of a muscle cell compared to the electrical excitability of a neuron, or the industrious activity of bone building cells in a youthful person compared to an elderly one. Each of these cells, (if taken from the same individual) has an identical genome — and yet each is “reading” a very distinct subset of that genome and consequently carrying out very different behaviors. The choice of what to read and what to hide away is made during development. An increasing body of data suggests this is accomplished by modifying the genome both in the nature of the proteins bound to different sequences and in the spatial organization of those sequences relative to each other. The spatial organization or folding of the genome may be particularly important in complex multicellular organisms, since many of the sequences known to interact based on genetic data are nonetheless substantially separated from each other along the linear genome. By regulating the folding of this linear sequence into a higher order structure, a cell might change which regulatory sequences have access to which genes, and achieve different behavioral states.

So far we have little imaging data on how the genome is folded within a cell on the length scale of individual genes, or whether this folding is regulated in any way relevant to the behavior of the cell. Our limited knowledge stems largely from want of a method that has both the resolution and specificity to visualize such genomic substructure. Conventional fluorescent microscopy has developed excellent tools for coloring specific regions of DNA and particular DNA-associated proteins with uniquely colored dyes — but lacks the resolution to turn these colored blurs into structures. Electron-microscopy has substantially greater resolution but lacks compatibility with specific labeling techniques to tell different gene clusters or different protein types apart. Super-resolution imaging approaches promise to address this balance by allowing the use of fluorescent labels while simultaneously resolving structures on the nano-scale. I have been adapting this approach to uncover the nano-scale structure of chromatin and determine to how this structure changes when bound by different types of nuclear proteins. While individual gene clusters appear as quite diverse structures, there appear to be a few general features, for example, linking structure with the epigenetic state.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Rachel Grant, Devon Harris, Albert Hinman, TzuChiao Hung, Kay Kobak, Naz Koska, Cayla Miller, Kei Yamaya

Postdoctoral Faculty Sponsor

Tonia Hafner

Orals Evaluator

Bo Gu

Doctoral Dissertation Advisor (AC)

Leslie Mateo, Sedona Murphy, Aparna Rajpurkar

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biophysics (Phd Program)
- Developmental Biology (Phd Program)

Publications

PUBLICATIONS

- **Atlas of Subcellular RNA Localization Revealed by APEX-Seq.** *Cell*
  Fazal, F. M., Han, S., Parker, K. R., Kaewsapsak, P., Xu, J., Boettiger, A. N., Chang, H. Y., Ting, A. Y.
  2019

- **Visualizing DNA folding and RNA in embryos at single-cell resolution.** *Nature*
  Mateo, L. J., Murphy, S. E., Hafner, A., Cinquini, I. S., Walker, C. A., Boettiger, A. N.
  2019

- **Super-resolution chromatin tracing reveals domains and cooperative interactions in single cells.** *Science (New York, N.Y.)*
  Bintu, B., Mateo, L. J., Su, J. H., Sinnott-Armstrong, N. A., Parker, M., Kinrot, S., Yamaya, K., Boettiger, A. N., Zhuang, X.
  2018; 362 (6413)

- **In Situ Super-Resolution Imaging of Genomic DNA with OligoSTORM and OligoDNA-PAINT** *SUPER-RESOLUTION MICROSCOPY: METHODS AND PROTOCOLS*
  Beliveau, B. J., Boettiger, A. N., Nir, G., Bintu, B., Yin, P., Zhuang, X., Wu, C., Erfle, H.
  2017; 1663: 231–52

- **Spatial organization shapes the turnover of a bacterial transcriptome** *ELIFE*
  Moffitt, J. R., Pandey, S., Boettiger, A. N., Wang, S., Zhuang, X.
  2016; 5

- **Super-resolution imaging reveals distinct chromatin folding for different epigenetic states** *NATURE*
  Boettiger, A. N., Bintu, B., Moffitt, J. R., Wang, S., Beliveau, B. J., Fudenberg, G., Imakaev, M., Mirny, L. A., Wu, C., Zhuang, X.
  2016; 529 (7586): 418-?

- **Chromatin topology is coupled to Polycomb group protein subnuclear organization.** *Nature communications*
  Wani, A. H., Boettiger, A. N., Schorderet, P., Ergun, A., Münger, C., Sadreyev, R. I., Zhuang, X., Kingston, R. E., Francis, N. J.
  2016; 7: 10291-?

- **Single-molecule super-resolution imaging of chromosomes and in situ haplotype visualization using Oligopaint FISH probes** *NATURE COMMUNICATIONS*
  Beliveau, B. J., Boettiger, A. N., Avendano, M. S., Jungmann, R., Mccole, R. B., Joyce, E. F., Kim-Kiselak, C., Bantignies, F., Fonseka, C. Y., Erceg, J., Hannan, M. A., Hoang, H. G., Colognori, et al
  2015; 6

- **RNA imaging. Spatially resolved, highly multiplexed RNA profiling in single cells.** *Science (New York, N.Y.)*
  Chen, K. H., Boettiger, A. N., Moffitt, J. R., Wang, S., Zhuang, X.
  2015; 348 (6233)

- **Analytic Approaches to Stochastic Gene Expression in Multicellular Systems** *BIOPHYSICAL JOURNAL*
  Boettiger, A. N.
  2013; 105 (12): 2629-2640

- **Rapid Transcription Fosters Coordinate snail Expression in the Drosophila Embryo** *CELL REPORTS*
  Boettiger, A. N., Levine, M.
  2013; 3 (1): 8-15

- **Multiple enhancers ensure precision of gap gene-expression patterns in the Drosophila embryo** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Perry, M. W., Boettiger, A. N., Levine, M.
  2011; 108 (33): 13570-13575

- **Inferring ecological and behavioral drivers of African elephant movement using a linear filtering approach** *ECOLOGY*
  Boettiger, A. N., Wittemyer, G., Starfield, R., Volrath, F., Douglas-Hamilton, I., Getz, W. M.
  2011; 92 (8): 1648-1657

- **Transcriptional Regulation: Effects of Promoter Proximal Pausing on Speed, Synchrony and Reliability** *PLOS COMPUTATIONAL BIOLOGY*
  Boettiger, A. N., Ralph, P. L., Evans, S. N.
  2011; 7 (5)
- **Shadow Enhancers Foster Robustness of Drosophila Gastrulation** *CURRENT BIOLOGY*
  Perry, M. W., Boettiger, A. N., Bothma, J. P., Levine, M.
  2010; 20 (17): 1562-1567
- **Morphogen Gradients: Limits to Signaling or Limits to Measurement?** *CURRENT BIOLOGY*
  Bothma, J. P., Levine, M., Boettiger, A.
  2010; 20 (5): R232-R234
- **Emergent complexity in simple neural systems.** *Communicative & integrative biology*
  Boettiger, A. N., Oster, G.
  2009; 2 (6): 467-470
- **Synchronous and Stochastic Patterns of Gene Activation in the Drosophila Embryo** *SCIENCE*
  Boettiger, A. N., Levine, M.
  2009; 325 (5939): 471-473
- **The neural origins of shell structure and pattern in aquatic mollusks** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Boettiger, A., Ermentrout, B., Oster, G.
  2009; 106 (16): 6837-6842
- **Evolution of insect dorsoventral patterning mechanisms.** *Cold Spring Harbor symposia on quantitative biology*
  Perry, M. W., Cande, J. D., Boettiger, A. N., Levine, M.
  2009; 74: 275-279
- **Nuclear trapping shapes the terminal gradient in the Drosophila embryo** *CURRENT BIOLOGY*
  Coppey, M., Boettiger, A. N., Berezhkovskii, A. M., Shvartsman, S. Y.
  2008; 18 (12): 915-919
- **Modeling the bicoid gradient: Diffusion and reversible nuclear trapping of a stable protein** *DEVELOPMENTAL BIOLOGY*
  Coppey, M., Berezhkovskii, A. M., Kim, Y., Boettiger, A. N., Shvartsman, S. Y.
  2007; 312 (2): 623-630
- **Role of boundary conditions in an experimental model of epithelial wound healing** *AMERICAN JOURNAL OF PHYSIOLOGY-CELL PHYSIOLOGY*
  Nikolic, D. L., Boettiger, A. N., Bar-Sagi, D., Carbeck, J. D., Shvartsman, S. Y.
  2006; 291 (1): C68-C75