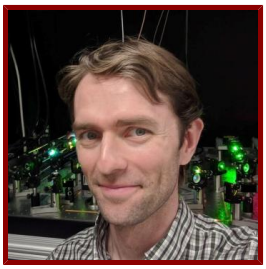
Stanford



Alistair Boettiger

Associate 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

- Associate Professor, Developmental Biology
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)

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

COURSES

2026-27

- Genetics and Developmental Biology Training Camp: DBIO 200, GENE 200 (Aut)
- Responsible Conduct of Research in Genetics and Developmental Biology: DBIO 255 (Spr)

2025-26

- Developmental Biology: DBIO 210 (Spr)
- Genetics and Developmental Biology Training Camp: DBIO 200, GENE 200 (Aut)
- Responsible Conduct of Research in Genetics and Developmental Biology: DBIO 255 (Spr)

2024-25

- Developmental Biology: DBIO 210 (Spr)
- Genetics and Developmental Biology Training Camp: DBIO 200, GENE 200 (Aut)

2023-24

- Developmental Biology: DBIO 210 (Spr)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Cecelia Andrews, Julia Bauman, Eli Costa, Angelika Hirsch, Austin Katzer, Yujin Moon, Saman Tabatabaee, Jordan Valgardson, Chuofan Yu

Postdoctoral Faculty Sponsor

Abrar Aljahani, Ivana Cavka, Derek Le, Jude Lee, Aleena Patel

Doctoral Dissertation Advisor (AC)

Tee Udomlumleart, Tianhong Wang

Doctoral Dissertation Co-Advisor (AC)

Lynette Chan, Simon Gaudin, Achuthan Raja Venkatesh

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biophysics (PhD Program)
- Developmental Biology (PhD Program)

Publications

PUBLICATIONS

- **Multiscale spatial analysis implicates chromosomal metaloops in gene patterning across the Drosophila brain.** *bioRxiv : the preprint server for biology*
  Patel, A. L., Venkatesh, A. R., Borjigin, T., Li, X., Levine, M. S., Boettiger, A. N.
  2026
- **Single-cell 3D genome imaging shows super-enhancer hubs are rare, nonspecific, and neither necessary nor sufficient for transcriptional bursting.** *Cell genomics*
  Le, D. J., Hafner, A., Raja Venkatesh, A., Udomlumleart, T., Gaddam, S., Novacic, A., Wang, K. C., Boettiger, A. N.
  2026: 101331
- **Single-cell chromatin state transitions during epigenetic memory formation.** *Science advances*
  Fujimori, T., Thurm, A. R., Gaudin, S., Rios-Martinez, C., Doughty, B. R., Hinks, M. M., Sinha, J., Le, D., Hafner, A., Greenleaf, W. J., Boettiger, A. N., Bintu, L.
  2026; 12 (30): eaeb0060
- **Promoter strength and position govern promoter competition through transcript-dependent insulation.** *Nature genetics*
  Koska, M., Nagano, M., Swigut, T., Boettiger, A. N., Hansen, A. S., Wysocka, J.
  2026
- **Loop Extrusion Accelerates Long-Range Enhancer-Promoter Searches in Living Embryos.** *bioRxiv : the preprint server for biology*
  Choppakatla, P., Patel, A. L., Borjigin, T., Udomlumleart, T., Hu, J., Gregor, T., Boettiger, A. N., Levine, M. S.
  2026
- **The role of cohesin loading at enhancers in the flux of loop extrusion and long-range transcriptional control.** *bioRxiv : the preprint server for biology*
  Anderson, E. C., Rahmaninejad, H., Aljahani, A., Arnold, E. M., Adachi, A. S., Shah, R., Hansen, K. L., Cavka, I., Boettiger, A. N., Fudenberg, G., Nora, E. P.
  2026

- **Enhancer activation from transposable elements in extrachromosomal DNA.** *Nature cell biology*
  Kraft, K., Murphy, S. E., Jones, M. G., Shi, Q., Bhargava-Shah, A., Luong, C., Hung, K. L., He, B. J., Li, R., Park, S. K., Montgomery, M. T., Weiser, N. E., Wang, et al
  2025
- **Kinetic organization of the genome revealed by ultraresolution multiscale live imaging.** *Science (New York, N.Y.)*
  Lee, J., Chen, L. F., Gaudin, S., Gupta, K., Novacic, A., Spakowitz, A., Boettiger, A. N.
  2025; 389 (6766): eadx2202
- **FAIR sharing of Chromatin Tracing datasets using the newly developed 4DN FISH Omics Format.** *ArXiv*
  Navelkar, R., Cosolo, A., Bintu, B., Cheng, Y., Gardeux, V., Gutnik, S., Fujimori, T., Hafner, A., Jay, A., Jia, B. B., Jussila, A. P., Llimos, G., Lioutas, et al
  2025
- **FAIR sharing of Chromatin Tracing datasets using the newly developed 4DN FISH Omics Format.** *ArXiv*
  Navelkar, R., Cosolo, A., Bintu, B., Cheng, Y., Gardeux, V., Gutnik, S., Fujimori, T., Hafner, A., Jay, A., Jia, B. B., Jussila, A. P., Llimos, G., Lioutas, et al
  2025
- **Promoter strength and position govern promoter competition.** *bioRxiv : the preprint server for biology*
  Koska, M., Swigut, T., Boettiger, A. N., Wysocka, J.
  2025
- **Two unrelated distal genes activated by a shared enhancer benefit from localizing inside the same small topological domain.** *Genes & development*
  Huang, Y., Verstegen, M. J., Tjalsma, S. J., Krijger, P. H., Gupta, K., Park, M., Boettiger, A., de Laat, W.
  2025
- **Long-range regulation of transcription scales with genomic distance in a gene-specific manner.** *Molecular cell*
  Jensen, C. L., Chen, L. F., Swigut, T., Crocker, O. J., Yao, D., Bassik, M. C., Ferrell, J. E., Boettiger, A. N., Wysocka, J.
  2024
- **Enhancer activation from transposable elements in extrachromosomal DNA.** *bioRxiv : the preprint server for biology*
  Kraft, K., Murphy, S. E., Jones, M. G., Shi, Q., Bhargava-Shah, A., Luong, C., Hung, K. L., He, B. J., Li, R., Park, S. K., Weiser, N. E., Luebeck, J., Bafna, et al
  2024
- **Long range regulation of transcription scales with genomic distance in a gene specific manner.** *bioRxiv : the preprint server for biology*
  Jensen, C. L., Chen, L., Swigut, T., Crocker, O. J., Yao, D., Bassik, M. C., Ferrell, J. E., Boettiger, A. N., Wysocka, J.
  2024
- **Super-enhancer interactomes from single cells link clustering and transcription.** *bioRxiv : the preprint server for biology*
  Le, D. J., Hafner, A., Gaddam, S., Wang, K. C., Boettiger, A. N.
  2024
- **Polycomb repression of Hox genes involves spatial feedback but not domain compaction or phase transition.** *Nature genetics*
  Murphy, S. E., Boettiger, A. N.
  2024
- **Harmonizing the Generation and Pre-publication Stewardship of FAIR Image data.** *ArXiv*
  Bialy, N., Alber, F., Andrews, B., Angelo, M., Beliveau, B., Bintu, L., Boettiger, A., Boehm, U., Brown, C. M., Maina, M. B., Chambers, J. J., Cimini, B. A., Eliceiri, et al
  2024
- **Boundary stacking interactions enable cross-TAD enhancer-promoter communication during limb development.** *Nature genetics*
  Hung, T. C., Kingsley, D. M., Boettiger, A. N.
  2024
- **Structural elements facilitate 3D locus topology and regulation of a human disease gene**
  Long, H., Chen, L., Boettiger, A., Wysocka, J.

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- **Single-cell chromatin state transitions during epigenetic memory formation.** *bioRxiv : the preprint server for biology*
  Fujimori, T., Rios-Martinez, C., Thurm, A. R., Hinks, M. M., Doughty, B. R., Sinha, J., Le, D., Hafner, A., Greenleaf, W. J., Boettiger, A. N., Bintu, L.
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- **SnapFISH: a computational pipeline to identify chromatin loops from multiplexed DNA FISH data.** *Nature communications*
  Lee, L., Yu, H., Jia, B. B., Jussila, A., Zhu, C., Chen, J., Xie, L., Hafner, A., Mishra, S., Wang, D. D., Strambio-De-Castillia, C., Boettiger, A., Ren, et al
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- **Leveraging polymer modeling to reconstruct chromatin connectivity from live images.** *Biophysical journal*
  Dutta, S., Ghosh, A., Boettiger, A. N., Spakowitz, A. J.
  2023
- **Spatial and temporal organization of the genome: Current state and future aims of the 4D nucleome project.** *Molecular cell*
  Dekker, J., Alber, F., Aufmkolk, S., Beliveau, B. J., Bruneau, B. G., Belmont, A. S., Bintu, L., Boettiger, A., Calandrelli, R., Disteche, C. M., Gilbert, D. M., Gregor, T., Hansen, et al
  2023
- **Extreme long-range gene regulatory perturbation drives a human craniofacial disorder**
  Long, H., Chen, L., Swigut, T., Boettiger, A., Wysocka, J.
  SPRINGERNATURE.2023: 14
- **Loop stacking organizes genome folding from TADs to chromosomes.** *Molecular cell*
  Hafner, A., Park, M., Berger, S. E., Murphy, S. E., Nora, E. P., Boettiger, A. N.
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- **Structural elements promote architectural stripe formation and facilitate ultra-long-range gene regulation at a human disease locus.** *Molecular cell*
  Chen, L. F., Long, H. K., Park, M., Swigut, T., Boettiger, A. N., Wysocka, J.
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  Chen, L. F., Lee, J., Boettiger, A.
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- **The spatial organization of transcriptional control.** *Nature reviews. Genetics*
  Hafner, A., Boettiger, A.
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- **Polycomb-mediated genome architecture enables long-range spreading of H3K27 methylation.** *Proceedings of the National Academy of Sciences of the United States of America*
  Kraft, K., Yost, K. E., Murphy, S. E., Magg, A., Long, Y., Corces, M. R., Granja, J. M., Wittler, L., Mundlos, S., Cech, T. R., Boettiger, A. N., Chang, H. Y.
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- **Domain stacking enables a limb enhancer to act across multiple TAD boundaries.** *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*
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  2022; 36 Suppl 1
- **A leukemia-protective germline variant mediates chromatin module formation via transcription factor nucleation.** *Nature communications*
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  2022; 13 (1): 2042
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  2021

- **Tracing DNA paths and RNA profiles in cultured cells and tissues with ORCA.** *Nature protocols*
  Mateo, L. J., Sinnott-Armstrong, N., Boettiger, A. N.
  2021

- **Deep learning connects DNA traces to transcription to reveal predictive features beyond enhancer-promoter contact.** *Nature communications*
  Rajpurkar, A. R., Mateo, L. J., Murphy, S. E., Boettiger, A. N.
  2021; 12 (1): 3423

- **Advances in Chromatin Imaging at Kilobase-Scale Resolution.** *Trends in genetics : TIG*
  Boettiger, A., Murphy, S.
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- **Quantitative cytogenetics reveals molecular stoichiometry and longitudinal organization of meiotic chromosome axes and loops.** *PLoS biology*
  Woglar, A. n., Yamaya, K. n., Roelens, B. n., Boettiger, A. n., Köhler, S. n., Villeneuve, A. M.
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- **Atlas of Subcellular RNA Localization Revealed by APEX-Seq.** *Cell*
  Fazal, F. M., Han, S. n., Parker, K. R., Kaewsapsak, P. n., Xu, J. n., 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. n., Cinquini, I. S., Walker, C. A., Boettiger, A. N.
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- **Super-resolution chromatin tracing reveals domains and cooperative interactions in single cells.** *Science (New York, N.Y.)*
  Bintu, B. n., Mateo, L. J., Su, J. H., Sinnott-Armstrong, N. A., Parker, M. n., Kinrot, S. n., Yamaya, K. n., Boettiger, A. N., Zhuang, X. n.
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- **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.
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- **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.
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- **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
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- **Analytic Approaches to Stochastic Gene Expression in Multicellular Systems** *BIOPHYSICAL JOURNAL*
  Boettiger, A. N.
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- **Rapid Transcription Fosters Coordinate snail Expression in the Drosophila Embryo** *CELL REPORTS*
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  2013; 3 (1): 8-15
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  Boettiger, A., Ermentrout, B., Oster, G.
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- **Evolution of insect dorsoventral patterning mechanisms.** *Cold Spring Harbor symposia on quantitative biology*
  Perry, M. W., Cande, J. D., Boettiger, A. N., Levine, M.
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- **Nuclear trapping shapes the terminal gradient in the Drosophila embryo** *CURRENT BIOLOGY*
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  Coppey, M., Berezhkovskii, A. M., Kim, Y., Boettiger, A. N., Shvartsman, S. Y.
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