Stanford

# Polly Fordyce

Assistant Professor of Genetics and of Bioengineering

Curriculum Vitae available Online

## Bio

### BIO

Polly Fordyce is an Assistant Professor of Genetics and Bioengineering and fellow of the ChEM-H Institute at Stanford, where her laboratory focuses on developing and applying new microfluidic platforms for quantitative, high-throughput biophysics and biochemistry. She graduated from the University of Colorado at Boulder with undergraduate degrees in physics and biology before moving to Stanford University, where she earned a Ph.D. in physics for work with Professor Steve Block developing instrumentation and assays for single-molecule studies of kinesin motor proteins. For her postdoctoral research, she worked with Professor Joe DeRisi to develop a new microfluidic platform for understanding how transcription factors recognize and bind their DNA targets as well as a new technology for bead-based multiplexing. She is the recipient of a number of awards, including an NIH New Innovator Award, an Alfred P. Sloan Foundation Research Fellowship, a McCormick and Gabilan Fellowship, an NIH Pathway to Independence Award (K99/R00), and a Helen Hay Whitney Postdoctoral Fellowship, and was recently named a Chan Zuckerberg Biohub Investigator.

### ACADEMIC APPOINTMENTS

- Assistant Professor, Genetics
- Assistant Professor, Bioengineering
- Member, Bio-X
- Faculty Fellow, Stanford ChEM-H
- Member, Wu Tsai Neurosciences Institute

### HONORS AND AWARDS

- Pathway to Independence Award (K99), NIH (2012-2014)
- Helen Hay Whitney Postdoctoral Fellowship, Helen Hay Whitney Foundation (2008-2011)
- G. J. Lieberman Fellow, Stanford University (2003-2004)
- Graduate Research Fellow, National Science Foundation (2002-2005)

### PROFESSIONAL EDUCATION

- Postdoctoral Fellow, University of California San Francisco , Biophysics (2014)
- Ph.D., Stanford University , Physics (2007)
- B.A., University of Colorado at Boulder , Physics, Biology (2000)

### LINKS

- My Lab Site: http://www.fordycelab.com

# Research & Scholarship

## CURRENT RESEARCH AND SCHOLARLY INTERESTS

The Fordyce Lab is focused on developing new instrumentation and assays for making quantitative, systems-scale biophysical measurements of molecular interactions. Current research in the lab is focused on two main areas: using microfluidic tools we have developed to build ground-up quantitative models of how gene expression is regulated, and developing new tools to transform how scientists explore protein-protein interactions.

Microfluidic studies of transcription factor specificity:

Cutting-edge technologies have identified genomic DNA regulatory elements and revealed the binding preferences for many transcription factors. However, our ability to predict in vivo patterns of transcription factor binding from DNA sequence alone remains poor, and measured in vivo binding often cannot explain gene expression patterns, even for well-studied eukaryotic promoters. Improving our understanding of these processes could have far-reaching impacts for revealing how mutations in regulatory elements cause disease and for designing transcriptional circuits for use in synthetic biology. Using a microfluidic technique we have recently developed for making high-throughput, quantitative measurements of transcription factor binding interactions (MITOMI 2.0), we propose to use a "ground-up" approach to reverse engineer transcriptional regulation by systematically adding in components and observing how they influence steady-state occupancies and binding kinetics.

Spectral encoding for biological multiplexing:

Biological multiplexing allows using very small amounts of samples to test for many different things in parallel. Bead-based multiplexing has many advantages, but poses a central challenge: beads must be encoded in some way. We have recently developed new microfluidic methods to produce beads that are spectrally encoded via the ratiometric incorporation of different lanthanide nanonanophosphors. These materials have unique spectral signatures, meaning that beads can later be imaged to "read" the embedded codes. We have previously demonstrated the ability to make up to 82 distinct codes using three lanthanide species (Europium, Samarium, and Dysprosium). We are currently working on expanding our code space to include up to 1,000 distinct spectral codes by using additional lanthanide species, as well as on functionalizing beads for downstream assays.

# Teaching

## COURSES

**2018-19**

- Microfluidic Device Laboratory: BIOE 301D, GENE 207 (Win)

**2017-18**

- Microfluidic Device Laboratory: BIOE 301D, GENE 207 (Win)

**2016-17**

- Microfluidic Device Laboratory: BIOE 301D (Win)

## STANFORD ADVISEES

**Doctoral Dissertation Reader (AC)**

Kalli Kappel, Surya Murty

**Postdoctoral Faculty Sponsor**

Yinnian Feng, Adam White, Zheng Zuo

**Doctoral Dissertation Advisor (AC)**

Arjun Aditham

**Doctoral (Program)**

Beatriz Atsavapranee, Caitlyn Miller

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Bioengineering (Phd Program)
- Biophysics (Phd Program)
- Genetics (Phd Program)

## Publications

### PUBLICATIONS

- **A Microfluidics-Based Assay for Mapping Connectivity in Highly Proficient Enzymes Reveals Functional Modularity**
  Markin, C. J., Mokhtari, D. A., Sunden, F., Herschlag, D., Fordyce, P. M.
  CELL PRESS.2019: 66A
- **A High-Throughput Platform for Probing Mechanisms of Transcription Factor-DNA Binding**
  Aditham, A., Fordyce, P. M.
  CELL PRESS.2019: 502A
- **Deep Learning Models Explore the Structural Effects of Transcription Factor-DNA Complexes on Binding Specificity**
  Shimko, T. C., Fordyce, P. M.
  CELL PRESS.2019: 503A
- **Bringing Enzymology into the Genomic Era: Developing and Deploying New Tools to Quantitatively Map Functional Connections Throughout an Enzyme**
  Markin, C., Mokhtari, D., Sunden, F., Herschlag, D., Fordyce, P. M.
  CELL PRESS.2019: 23A
- **An open-source software analysis package for Microspheres with Ratiometric Barcode Lanthanide Encoding (MRBLEs).** *PloS one*
  Harink, B., Nguyen, H., Thorn, K., Fordyce, P.
  2019; 14 (3): e0203725
- **Diversification of DNA binding specificities enabled SREBP transcription regulators to expand the repertoire of cellular functions that they govern in fungi.** *PLoS genetics*
  Del Olmo Toledo, V., Puccinelli, R., Fordyce, P. M., Perez, J. C.
  2018; 14 (12): e1007884
- **High-throughput chromatin accessibility profiling at single-cell resolution.** *Nature communications*
  Mezger, A., Klemm, S., Mann, I., Brower, K., Mir, A., Bostick, M., Farmer, A., Fordyce, P., Linnarsson, S., Greenleaf, W.
  2018; 9 (1): 3647
- **Discovering epistatic feature interactions from neural network models of regulatory DNA sequences**
  Greenside, P., Shimko, T., Fordyce, P., Kundaje, A.
  OXFORD UNIV PRESS.2018: 629–37
- **Comprehensive, high-resolution binding energy landscapes reveal context dependencies of transcription factor binding** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Le, D. D., Shimko, T. C., Aditham, A. K., Keys, A. M., Longwell, S. A., Orenstein, Y., Fordyce, P. M.
  2018; 115 (16): E3702–E3711
- **BET-seq: Binding energy topographies revealed by microfluidics and high-throughput sequencing.** *Methods in cell biology*
  Aditham, A. K., Shimko, T. C., Fordyce, P. M.
  2018; 148: 229–50
- **Programmable Microfluidic Synthesis of Over One Thousand Uniquely Identifiable Spectral Codes** *ADVANCED OPTICAL MATERIALS*
  Nguyen, H. Q., Baxter, B. C., Brower, K., Diaz-Botia, C. A., DeRisi, J. L., Fordyce, P. M., Thorn, K. S.
  2017; 5 (3)

- **Multi-step Variable Height Photolithography for Valved Multilayer Microfluidic Devices.** *Journal of visualized experiments : JoVE*
  Brower, K., White, A. K., Fordyce, P. M.
  2017
- **Joker de Bruijn: Sequence Libraries to Cover All k-mers Using Joker Characters**
  Orenstein, Y., Kim, R., Fordyce, P., Berger, B., Sahinalp, S. C.
  SPRINGER-VERLAG BERLIN.2017: 389–90
- **How duplicated transcription regulators can diversify to govern the expression of nonoverlapping sets of genes** *GENES & DEVELOPMENT*
  Perez, J. C., Fordyce, P. M., Lohse, M. B., Hanson-Smith, V., DeRisi, J. L., Johnson, A. D.
  2014; 28 (12): 1272-1277
- **Structure of the transcriptional network controlling white-opaque switching in Candida albicans** *MOLECULAR MICROBIOLOGY*
  Hernday, A. D., Lohse, M. B., Fordyce, P. M., Nobile, C. J., DeRisi, J. L., Johnson, A. D.
  2013; 90 (1): 22-35
- **Microfluidic affinity and ChIP-seq analyses converge on a conserved FOXP2-binding motif in chimp and human, which enables the detection of evolutionarily novel targets** *NUCLEIC ACIDS RESEARCH*
  Nelson, C. S., Fuller, C. K., Fordyce, P. M., Greninger, A. L., Li, H., DeRisi, J. L.
  2013; 41 (12): 5991-6004
- **Identification and characterization of a previously undescribed family of sequence-specific DNA-binding domains** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Lohse, M. B., Hernday, A. D., Fordyce, P. M., Noiman, L., Sorrells, T. R., Hanson-Smith, V., Nobile, C. J., DeRisi, J. L., Johnson, A. D.
  2013; 110 (19): 7660-7665
- **Programmable microfluidic synthesis of spectrally encoded microspheres** *LAB ON A CHIP*
  Gerver, R. E., Gomez-Sjoeberg, R., Baxter, B. C., Thorn, K. S., Fordyce, P. M., Diaz-Botia, C. A., Helms, B. A., DeRisi, J. L.
  2012; 12 (22): 4716-4723
- **Basic leucine zipper transcription factor Hac1 binds DNA in two distinct modes as revealed by microfluidic analyses** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Fordyce, P. M., Pincus, D., Kimmig, P., Nelson, C. S., El-Samad, H., Walter, P., DeRisi, J. L.
  2012; 109 (45): E3084-E3093
- **Systematic characterization of feature dimensions and closing pressures for microfluidic valves produced via photoresist reflow** *LAB ON A CHIP*
  Fordyce, P. M., Diaz-Botia, C. A., DeRisi, J. L., Gomez-Sjoberg, R.
  2012; 12 (21): 4287-4295
- **De novo identification and biophysical characterization of transcription-factor binding sites with microfluidic affinity analysis** *NATURE BIOTECHNOLOGY*
  Fordyce, P. M., Gerber, D., Tran, D., Zheng, J., Li, H., DeRisi, J. L., Quake, S. R.
  2010; 28 (9): 970-976
- **Individual dimers of the mitotic kinesin motor Eg5 step processively and support substantial loads in vitro** *NATURE CELL BIOLOGY*
  Valentine, M. T., Fordyce, P. M., Krzysiak, T. C., Gilbert, S. P., Block, S. M.
  2006; 8 (5): 470-U89
- **Eg5 steps it up!** *CELL DIVISION*
  Valentine, M. T., Fordyce, P. M., Block, S. M.
  2006; 1
- **Simultaneous, coincident optical trapping and single-molecule fluorescence** *NATURE METHODS*
  Lang, M. J., Fordyce, P. M., Engh, A. M., Neuman, K. C., Block, S. M.
  2004; 1 (2): 133-139
- **Stepping and stretching - How kinesin uses internal strain to walk processively** *JOURNAL OF BIOLOGICAL CHEMISTRY*
  Rosenfeld, S. S., Fordyce, P. M., Jefferson, G. M., King, P. H., Block, S. M.
  2003; 278 (20): 18550-18556

- **Combined optical trapping and single-molecule fluorescence.** *Journal of biology*
  Lang, M. J., Fordyce, P. M., Block, S. M.
  2003; 2 (1): 6-?