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About

I am a doctoral candidate researcher at Harvard University. My research is supervised by Prof. Gad Getz and Prof. Luca Pinello at the Broad Institute of Harvard and MIT as well as Massachusetts General Hospital. I also spent the first two years of my PhD under the guidance of Professor Brian Liau in the Harvard University Department of Chemistry and Chemical Biology.

I am broadly interested in building deep generative models of dynamic biological processes. During my PhD, I've focused on creating new methods to generatively reconstruct dynamic processes (e.g., development, aging) from snapshot measurements of single cells. These models of single-cell data can be used in conjunction with perturbations (e.g., CRISPR, small molecule inhibitors) to profile the gene regulatory networks and mechanistic logic driving cell states in disease.

I am an expert in using python for deep learning (with libraries like PyTorch), CRISPR screen analyses, and single-cell analyses. I also have expertise in chromatin biology, hematopoiesis, cloud computing (e.g., Google Cloud), R, bash, Linux systems, GPU-based computation.

Key words

CRISPR, CRISPR-screens, single-cell, deep learning, epigenomics, scRNA-seq, scATAC-seq, CRISPR-SAR, drug discovery, python, PyTorch, machine learning, neural networks, neural differential equations, dynamical systems

Education

Doctor of Philosophy, Chemistry and Chemical Biology   Spring, 2023
Harvard University (Cambridge, MA)

Bachelor of Arts, Chemistry *with distinction and honors in chemistry*   May 2016
University of Iowa (Iowa City, IA.)

Research experience

NCI F31 NRSA Predoctoral Researcher, Broad Institute of Harvard and MIT, Harvard Medical School, and Massachusetts General Hospital Department of Molecular Pathology, 02/2019 – Present

Research Advisors: **Professor Gad Getz** and **Professor Luca Pinello**

Research Description: Single-cell measurements, when sampled with sufficient depth can capture finely controlled biological transformations between cell states within a single snapshot (i.e., most sc-data). Many methods have proposed solutions to mapping high-dimensional sc-measurements to interpretable, low-dimension manifolds; however, few methods offer insights towards the underlying gene regulatory programs guiding cell state transitions. Using a drift-diffusion framework established by others in the field, I am applying deep-learning based parameterization solutions to study the inherent diffusion underlying cell fate decision making. We are applying this to a multi-omic map of the emergence of multiple myeloma as it progresses from precursor disease stages. These methods and analyses are built around scRNA-seq and scATAC-seq data and integrated with whole-genome sequencing data, all from primary patient bone marrow samples (in collaboration with Dr. Irene Ghobrial, DFCI). We are currently extending these analyses to perturbation-based modeling in combination with CRISPR, drug-induced, and *in silico* perturbations. During this time, I have also contributed to several projects using CRISPR tiling screens wherein perturbations are used to generate functional readouts to gain mechanistic, protein-level insights.

Graduate Research Assistant, Harvard University Department of Chemistry and Chemical Biology, 12/2016 – 02/2019

Research Advisor: **Professor Brian B. Liau**

Research Description: My studies in the Liau Lab focused both on elucidating the biological mechanisms of chromatin regulators as well as adapting and advancing CRISPR-Cas9 technology to investigate such problems. We profiled the interactions between lysine-specific histone demethylase 1 (LSD1) and chemical inhibitors using CRISPR-Cas9

mutagenesis in the context of acute myeloid leukemia (AML). We elucidated drug mechanism of action by disproving the existing notion that LSD1 enzyme activity is required for the propagation of AML. Further, we demonstrate that LSD1 inhibitors function by disrupting an interaction between LSD1 and the transcription factor, GFI1B on chromatin. I additionally discovered that the poorly studied, intrinsically disordered N-terminal region of LSD1 participates in the drug mechanism of action; this finding is currently being studied further in the lab.

Undergraduate Research Assistant, University of Iowa Department of Chemistry, 08/2012-05/2016

Research Advisor: **Professor Hien M. Nguyen**

Research Description: Developed a series of α-fluoromethylated amines via rhodium-catalyzed kinetic

asymmetric transformations of racemic allyic trichloroacetimidates. These fluoromethylated amines are formed in high enantiomeric excess and subsequently functionalized to known, previously difficult to access inhibitors of amino acid decarboxylases required for formation of the neurotransmitter, GABA. This is a validated drug target as GABA is frequently upregulated in various cancers and diseases of the central nervous system.

Snyder Summer Research Scholar, University of Illinois Urbana-Champaign, 05/2014 – 08/2014

Research Advisor: **Professor Paul J. Hergenrother**

Research Description: Generated, in collaboration with a graduate student, Robert Hicklin a library of small, complex molecules that were subsequently screened in phenotypic assays for loss of proliferation effects in various cancers. These molecules were synthesized as part of a novel methodology for rapidly generating complex and diverse libraries suited for high throughput screening drug discovery efforts.

First-author publications and preprints

1. Vinyard, M.E., et al., Deep generative modeling of cell dynamics from single-cell measurements using neural differential equations. *Manuscript in preparation*.

2. Vinyard, M.E., et al., A generalized multi-omic single-cell model of pre-myeloma progression to overt myeloma. *Manuscript in preparation*.

3. Wang, L.[†], Zhang, Q.[†], Qin, Q.[†], Trasanidis, N.[†], **Vinyard, M.E.** [†], *et al.*, (2021) Current progress and potential opportunities to infer single-cell developmental trajectory and cell fate. *Curr Opin in Syst Biol*. ISSN 2452-3100. DOI: 10.1016/j.coisb.2021.03.006.

4. Stein, D.[†], Chen, H.[†], **Vinyard, M.E.**[†], *et al.* (2020) singlecellVR: interactive visualization of single-cell data in virtual reality. *Front Genet*. DOI: 10.1101/2020.07.30.229534.

5. **Vinyard**, **M. E.**, *et al.* (2019) CRISPR-suppressor scanning reveals a nonenzymatic role of LSD1 in AML. *Nat Chem Biol*. DOI: 10.1038/s41589-019-0263-0.

Contributing author publications and preprints

1. Chen, H., Ryu, J., **Vinyard, M.E.**, *et al.* (2023). SIMBA: Single-cell eMBedding Along with features. *Nat Methods*. DOI: 10.1038/s41592-023-01899-8.

2. Chen. Z., Javed, N.M., Moore, M., Wu, J., **Vinyard, M.E.**, *et al.*, (2023). Integrative dissection of gene regulatory elements at base resolution. *Cell Genomics*. DOI: 10.1016/j.xgen.2023.100318.

3. Chen, H., Lareau, C.[†], Andreani, T.[†], **Vinyard, M.E.**[†], *et al.* (2020) Assessment of computational methods for the analysis of single-cell ATAC-seq data. *Genome Biol*. DOI: 10.1186/s13059-019-1854-5.

4. Vedagopuram, S., …, **Vinyard, M.E.**, *et al.* (2023). A molecular glue approach to control the half-life of CRISPR-based technologies. *Submitted.*

5. Lightbody, E., …, **Vinyard, M.E.**, *et al.* (2023). Single-Cell RNA Sequencing of Rare Circulating Tumor Cells in Precursor Myeloma Patients Reveals Molecular Underpinnings of Tumor Cell Circulation. *Manuscript in preparation.*

Teaching experience

1. **CHEM27 – The Organic Chemistry of Life**, Spring 2018
   Teaching Fellow, Harvard University; supervised by Professor Brian. B. Liau
2. **CHEM:27 – The Organic Chemistry of Life**, Spring 2017
   Teaching Fellow, Harvard University; supervised by Professor Brian. B. Liau
3. **CHEM:1120 – Principles of Chemistry II**, Spring 2015
   Teaching Assistant, University of Iowa; supervised by Professor Amy Strathman and Professor Nicole Becker

Selected presentations and posters

1. **Michael E. Vinyard,** Mahshid Rahmat, *et al*. "Generative modeling of stochastic single-cell dynamics with *scDiffEq*." AACR 2023. Orlando, FL. (04/2023).

2. **Michael E. Vinyard,** Ruitong Li, *et al*. "Generative modeling of stochastic single-cell dynamics with *scDiffEq*." Cold Spring Harbor Laboratories Meeting for Probabilistic Genomics 2023. Cold Spring Harbor, NY. (03/2023).

3. **Michael E. Vinyard,** Mahshid Rahmat, *et al*. "In Situ Characterization of Chromatin Landscape in Progression of Smoldering Precursor Stage to Multiple Myeloma." ASH 2022. New Orleans, LA. (12/2022).

4. **Michael E. Vinyard** et al. "CRISPR-Suppressor Scanning reveals non-enzymatic requirements of LSD1 in AML" 2019 Landry Cancer Biology Spring Symposium. Boston, MA. (05/2019).

5. **Michael E. Vinyard** and Brian Liau. "Interrogating the Role of LSD1 in AML through CRISPR-Cas9-Mediated Structure Activity Relationship Mapping" 2018 Harvard Department of Chemistry and Chemical Biology Annual Symposium. Cambridge, MA. (03/2018).

6. **Michael E. Vinyard**. "Undergraduate Research and Graduate School." Honors Lecture Series for Undergraduate Students. (04/2016).

7. **Michael E. Vinyard**. "The Undergraduate Research Experience." Honor Lecture Series for Undergraduate Students. (10/2015).

8. **Michael E. Vinyard** and Hien M. Nguyen. "Rapid Access to α-Fluoromethylated Amino Acids via Rhodium-Catalyzed Amination." American Chemical Society National Organic Symposium, College Park, MD. (06/2015).

9. **Michael E. Vinyard**, Robert W. Hicklin, Evijola Llabani, and Paul J. Hergenrother. "Synthesis of Stereochemically Complex Azide Derivatives of Pleuromutilin." University of Illinois Champaign-Urbana, Summer Poster Symposium. (08/2014).

Honors and distinctions

2020 Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship (F31) – NCI
2020 Bluebonnet Data Fellowship
2016: Elected to Phi Beta Kappa
2015 – 2016, President of the American Chemical Society, University of Iowa Chapter
2015 ACS Division of Organic Chemistry Travel Award
2015 Big Ten Postgraduate Scholarship Recipient
2015 Robert F. Ray Faculty Athletics Representative Award
2015 Russell K. Simms Scholarship – University of Iowa Department of Chemistry
2015 NCAA Postgraduate Scholarship Nominee
2015 NCAA Walter Byers Scholarship Nominee
2014 – 2015, Secretary of the American Chemical Society, University of Iowa Chapter
2014 NASA Iowa Space Grant Consortium Scholarship Award
2014 Snyder Summer Research Fellowship – University of Illinois Champaign-Urbana
2014 Chemistry Alumni Award for Juniors
Captain of the 2012-2013 University of Iowa Men's Swimming & Diving Team
University of Iowa National Scholars Award
University of Iowa Tuition Scholarship
University of Iowa Honors Student (seven consecutive semesters)
Presidential Committee on Athletics Award (five consecutive semesters)
Captain of the 2010-2011 State Champion Carmel High School Men's Swimming & Diving Team

Athletic distinctions

United States Olympic Trials Qualifier
2015 Nile Kinnick Memorial Scholarship Recipient
2011-2015 Member of the Top-10 ranked University of Iowa Men's Swimming & Diving Team
2011-2015 Varsity Letter Winner at the University of Iowa (Men's Swimming)

References

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Additional references available upon request.