Sean Hackett

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Summary of Qualifications:
- Actively plans and directs long-term strategy, near-term tactics, and day-to-day operations.
- Leverages statistics and programming to tackle challenging scientific problems. Google Scholar
- Excels at communicating with diverse audiences in both written and oral formats.

Skills:. *Analytics:* statistics (GLMs, nonlinear regression, maximum likelihood, model comparison, Bayesian statistics), ML (LASSO, random forest, LDA, LLMs), optimization (linear/quadratic programming, gradient-based MAP estimation). *Programming* R (dplyr, purrr, ggplot2, devtools, Shiny, Connect), Python (pandas, Jupyter, igraph, package development) *Tools* Building and querying databases (SQL, graphQL, BigQuery), Docker, WDL, GCP, CI/CD with GitHub Actions.

Education

Princeton University — Princeton, NJ
Ph.D., Quantitative and Computational Biology — 2015
DOE Office of Science Graduate Fellowship (SCGF)

Cornell University — Ithaca, NY
B.S., Biological Sciences — 2006
Magna Cum Laude with Distinction in Research

Research

Director

Calico Life Sciences LLC — S. San Francisco, CA

- Formed the Discovery Data Science team to balance collaborations on basic science programs with focal support and methods development. — Jan 2023 - Present
- Established data systems to support the key outputs of the Discovery organization: mechanisms and targets.

Assoc Director

- Collaborated with key stakeholders to develop long-term strategies for causal inference and systems biology. — Jan 2021 - Jan 2023

Manager

- Helped reorganize the Computing team to improve impact, collaboration, and accountability. — Feb 2018 - Jan 2021
- Managed 4-6 data scientists, prioritizing high value projects in a problem-rich environment.
- Led initiatives around computational education, results sharing, and de-duplication of efforts.

Data Scientist

- Created a genome-scale mechanistic network connected to known gene-disease associations to support indication prioritization. — Jan 2017 - Present
- Improved approaches for finding causal connections in high-dimensional time series using a combination of parametric modeling and LASSO.
- Developed an automated metabolomics pipeline to streamline data normalization and compound identification.

Postdoctoral Associate

Princeton University, Lewis-Sigler Institute — Princeton, NJ

- Supervisor: John Storey, Director of the Center for Statistics and ML — 2015 - 2017
- Used Latent Dirichlet Allocation with Empirical Bayes priors to identify latent variables affecting sparse high-dimensional data.

Graduate Fellow

Princeton University, Quantitative and Computational Biology — Princeton, NJ

- Adviser: Josh Rabinowitz, Professor of Chemistry and Genomics — 2010 - 2015
- Supervised two systems biology graduate students.
- Developed a scalable algorithm for combining metabolomics, proteomics and fluxes to identify novel allosteric regulators and dissect how metabolite and enzyme concentrations jointly control metabolism.

Selected Publications

• Sean R. Hackett, Majed Mohamed Magzoub, Tobias M Maile, Ngoc Vu, Kevin M Wright, Eugene Melamud, Wilhelm Haas, Fiona E McAllister, Gary A Churchill, Bryson D Bennett. *The Molecular Architecture of Variable Lifespan in Diversity Outbred Mice.* bioRxiv, 2023.

• Kevin G Hicks, Ahmad A Cluntun, Heidi L Schubert, Sean R. Hackett, ..., Jared Rutter. *Protein-metabolite interactomics of carbohydrate metabolism reveal regulation of lactate dehydrogenase.* Science, 379 (6636), 2023.

• Sean R. Hackett, Edward A. Baltz, Marc Coram, Bernd J. Wranik, Griffin Kim, Adam Baker, Minjie Fan, David G. Hendrickson, Marc Brendl, R. Scott McIsaac. *Learning causal networks using inducible transcription factors and transcriptome-wide time series.* Molecular Systems Biology, 16 (3), 2020.

• Sam S. Schoenholz, Sean Hackett, Laura Deming, Eugene Melamud, Navdeep Jaitly, Fiona McAllister, Jonathon O'Brien, George Dahl, Bryson Bennett, Andrew Dai, Daphne Kohler. *Peptide-spectrum matching from weak supervision.* ArXiv.

• Sean R. Hackett, Vito R.T. Zanotelli, Wenxin Xu, Jonathan Goya, Junyoung O. Park, David H. Perlman, Patrick A. Gibney, David Botstein, John D. Storey, and Joshua D. Rabinowitz. *Systems-level analysis of mechanisms regulating yeast metabolic flux.* Science, 345, 2016.

• J Kamphorst, M Nofal, C Commisso, SR Hackett, W Lu, E Grabocka, G Miller, JA Drebin, MG Vander Heiden, D Bar-Sagi, CB Thompson, JD Rabinowitz. *Human pancreatic cancer tumors are nutrient poor and the tumor cells actively scavenge extracellular protein.* Cancer Research, 75, 2015.

• Jeffrey S. Bruenig, Sean R. Hackett, Joshua D. Rabinowitz & Leonid Kruglyak. *Genetic basis of metabolome variation in yeast.* PLoS Genetics, 2013.

• C Commisso., SM Davidson, RG Soydaner-Azeloglu, SJ Parker, JJ Kamphorst, SR Hackett, E Grabocka, M Nofal, JA Drebin, CB Thompson, JD Rabinowitz, CM Metallo, MG Vander Heiden & D Bar-Sagi. *Macropinocytosis of protein is an amino acid supply route in Ras-transformed cells.* Nature, 497, 2013.

Selected Talks

• 2024 Growing Together Conference (Zürich, Switzerland). Invited Talk
Aging as a Data Science Problem

• 2024 Cold Spring Harbor Mechanisms of Aging.
The Molecular Architecture of Variable Lifespan in Diversity Outbred Mice

• 2024 Winter QBio.
The Molecular Architecture of Variable Lifespan in Diversity Outbred Mice

• 2019 MaxQuant Summer School. Plenary Talk
Bootstrapping the Peptide-Spectrum Matching Problem with Deep Learning

• 2019 Cold Spring Harbor Cellular Dynamics and Models.
Expansive perturbation profiling reveals a causal transcriptional network

• 2017 MIT Sloane Sports Analytics Conference. Research Paper Competition finalist.
Mixed Membership Martial Arts: Data-Driven Analysis of Winning Martial Arts Styles

• 2016 Genomic Sciences Program Annual PI Meeting.
Systems-Level Analysis of Mechanisms Controlling Yeast Metabolic Flux

• 2014 Yeast Genetics Meeting. Plenary Talk: Environmental Sensing Networks.
An Integrated 'Omics Approach to Large-Scale Quantitative Analysis of Cellular Metabolic Regulation

• 2013 International Conference on Systems Biology. Parallel Session: Complex Genetic Traits
Genetic Basis of Metabolome Variation in Yeast