

Dominik Jenz Otto

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Highlights

Funding: K99/R00 Pathway to Independence Award (NIGMS, NIH), 2025–present; the R00 phase, up to three years of funding, activates at the hiring US institution upon appointment.

Research focus: Probabilistic machine learning for single-cell and spatial genomics: cell-state distributions learned from millions of cells, with the uncertainty of every estimate (Mellon, Kompot, 2for1separator, AnnZarro).

Publications: first author in *Nature Methods* (Mellon, 2024), co-first author in *Genome Biology* (CUT&Tag2for1, 2022) and *European Urology* (ProstaTrend, 2020); Kompot under review at *Cell Systems*; co-author in *Nature Biotechnology*, *Nature Communications*, and *Cell Reports*.

Education and Training

Postdoctoral Fellow *Fred Hutchinson Cancer Center*

Seattle, WA 2021 – present

- **Cell-state distributions and transitions.** Developed Mellon, which estimates how densely cells populate each state as a Gaussian process that scales to millions of cells, distinguishing stable from transient states and locating fate commitment; applied to human hematopoiesis (*Nature Methods*, 2024; first author).
- **Comparison of phenotypic manifolds.** Developed Kompot, which compares conditions cell by cell across the continuum of cell states, without clusters, by Gaussian-process differential abundance and expression with posterior uncertainty; applied to aging bone marrow (under review at *Cell Systems*; first author).
- **Chromatin signal deconvolution.** Developed 2for1separator, which separates active and repressive chromatin signals profiled together by CUT&Tag2for1, using massively parallel variational inference; with the Henikoff laboratory (*Genome Biology*, 2022; co-first author).

PhD Informatics *Universität Leipzig*

Leipzig, Germany 2016 – 2021

- Research carried out at the *Fraunhofer Institute for Cell Therapy and Immunology IZI*.
- Bioinformatics, statistics and Bayesian inference on large data sets
- Gene-expression marker discovery for Prostate Cancer
- Dissertation: *Computational Gene Expression Deconvolution*, Universität Leipzig (submitted Nov. 2020, defended July 2021).

MSc Mathematics *Freie Universität Berlin*

Berlin, Germany 2013 – 2015

- Specialization in partial and ordinary differential equations.
- Master's thesis on the determining nodes of regulatory networks, correcting a theorem on which feedback loops must be broken to control a network.

Internship *Max Delbrück Center for Molecular Medicine*

Berlin, Germany 2014 – 2014

- Computational modeling of NF- κ B signaling dynamics from time-resolved mass spectrometry data with ordinary differential equations (with Jana Wolf)

Internship *Cesmec Group a company of Bureau Veritas*

Santiago, Chile 2012 – 2012

- Statistics and process optimization

BSc Mathematics *Freie Universität Berlin*

Berlin, Germany 2009 – 2013

- Specialization in topology. Theoretical and experimental physics as a minor.
- Bachelor's thesis in topology on isotopies of closed loops.

Awards, Grants, and Fellowships

NIGMS, NIH *K99/R00 Pathway to Independence Award*

2025–present

Mechanistic Inference of Tissue Dynamics from Multimodal Single-Cell Data (1K99GM159044). Mentors: Manu Setty (primary), Erick Matsen, and Cyrus Ghajar. K99 mentored phase 2025–2027, including a no-cost extension through September 2027; R00 independent phase, up to three years of funding, activates at the hiring US institution upon appointment to a tenure-track (or equivalent) position.

CCEH Leadership and Management Skills Course

Competitive selection 2024

SPAC Travel Award Scholarship

Travel support 2024

TDS IRC Annual Retreat *IAB Favorite (Poster)*

Research award 2023

Publications

Lead-author publications

- [1] **D. J. Otto**⁺, S. Baasri, and M. Setty⁺, *AnnZarro: scalable, interactive exploration of cell-by-cell and gene-by-gene relationships in single-cell data*, **bioRxiv**, Oct. 2026, DOI: [10.64898/2026.10.10.758158](https://doi.org/10.64898/2026.10.10.758158).
- [2] **D. J. Otto**, E. Arriaga-Gomez, E. Thieme, R. Yang, S. C. Lee⁺, and M. Setty⁺, *Comparing phenotypic manifolds with Kompot: Cluster-free differential expression at single-cell resolution*, **bioRxiv**, June 2025, under review at Cell Systems, DOI: [10.1101/2025.06.03.657769](https://doi.org/10.1101/2025.06.03.657769).
- [3] **D. J. Otto**, C. Jordan, B. Dury, C. Dien, and M. Setty, *Quantifying cell-state densities in single-cell phenotypic landscapes using Mellon*, **Nature Methods**, July 2024, DOI: [10.1038/s41592-024-02302-w](https://doi.org/10.1038/s41592-024-02302-w).
- [4] D. H. Janssens*, **D. J. Otto***, M. P. Meers, M. Setty, K. Ahmad, and S. Henikoff, *CUT&Tag2for1: a modified method for simultaneous profiling of the accessible and silenced regulome in single cells*, **Genome Biology**, Mar. 2022, DOI: [10.1186/s13059-022-02642-w](https://doi.org/10.1186/s13059-022-02642-w).
- [5] M. Kreuz*, **D. J. Otto***, S. Fuessel*, C. Blumert, C. Bertram, S. Bartsch, D. Loeffler, S.-H. Puppel, M. Rade, T. Buschmann, S. Christ, K. Erdmann, M. Friedrich, M. Froehner, M. H. Muders, S. Schreiber, M. Specht, M. I. Toma, F. Benigni, M. Freschi, G. Gandaglia, A. Briganti, G. B. Baretton, M. Loeffler, J. Hackermüller, K. Reiche, M. Wirth, and F. Horn, *ProstaTrend—A Multivariable Prognostic RNA Expression Score for Aggressive Prostate Cancer*, **European Urology**, Sept. 2020, DOI: [10.1016/j.eururo.2020.06.001](https://doi.org/10.1016/j.eururo.2020.06.001).

Other publications

- [6] C. Mills, Y. Huang*, C. M. Lee*, C. Finkbeiner, R. K. Lex, **D. J. Otto**, R. Yang, H. West-Foyle, D. Jones, A. Long, S. Minot, E. Nguyen, P. Itagi, S. Schuster, A. Elz, L. Schroeder, N. Futran, E. Marchiano, R. Ferrandino, R. A. Risques, G. Ha, A. Bandhlish, B. Barber, M. Setty⁺, and S. Beronja⁺, *Dysregulation of epithelial differentiation architecture underlies field cancerization in head and neck cancer*, **bioRxiv**, Oct. 2026, under review at Nature, DOI: [10.64898/2026.10.12.757511](https://doi.org/10.64898/2026.10.12.757511).
- [7] C. Finkbeiner, **D. J. Otto**, and M. Setty, *Echo characterizes the desynchronization of gene expression and chromatin accessibility during cell-state transitions*, **bioRxiv**, May 2026, DOI: [10.64898/2026.05.20.726634](https://doi.org/10.64898/2026.05.20.726634).
- [8] D. H. Janssens, C. A. Codomo, **D. J. Otto**, L. Silberstein, K. Ahmad, and S. Henikoff, *Sequential RNA polymerase II activation drives human hematopoiesis*, **Cell Reports**, Jan. 2026, DOI: [10.1016/j.celrep.2025.116802](https://doi.org/10.1016/j.celrep.2025.116802).
- [9] C. Jordan, **D. J. Otto**, J. Greene, S. Henikoff, and M. Setty, *Detecting lineage-specific regulatory activity and stemness retention in single-cell multiomics of human hematopoiesis*, **Blood**, Supplement 1, vol. 146, Nov. 2025, DOI: [10.1182/blood-2025-6119](https://doi.org/10.1182/blood-2025-6119) (conference abstract).
- [10] D. Kirkey, D. H. Janssens, M. Hines, S. Shin, G. Hawkins, M. Blankenfeld, N. Panahi, I. Lira, T. Hylkema, L. Robinson, B. Liu, R. Ries, J. Peplinski, L. Wallace, C. Nourigat, L. Perkins, L. Pardo, M. Makatsa, M. R. Loken, **D. J. Otto**, K. Ikegami, B. Hadland, B. de Angelis, C. Quintarelli, S. Furlan, K. Tarlock, S. Henikoff, B. Huang, F. Locatelli, W. Li, and S. Meshinchi, *Multi-omics analysis reveals CLEC2A is a leukemia-restricted CART target in KMT2A-rearranged Acute Myeloid Leukemia*, **Research Square**, Oct. 2025 (preprint, under review), DOI: [10.21203/rs.3.rs-7768680/v1](https://doi.org/10.21203/rs.3.rs-7768680/v1).
- [11] T. Bencomo, C. Morningstar, H. J. Rodriguez Chevez, **D. J. Otto**, M. Smith, E. Newell, M. Setty, and P. Nghiem, *Spatial transcriptomics analysis of Merkel cell carcinoma reveals novel immune cell subsets and hypoxia as correlates of immunotherapy response*, **Journal of Investigative Dermatology**, vol. 145, no. 8, p. S219, Aug. 2025 (conference abstract), DOI: [10.1016/j.jid.2025.06.1542](https://doi.org/10.1016/j.jid.2025.06.1542).
- [12] M. D. Luecken, S. Gigante, D. B. Burkhardt, R. Cannoodt, D. C. Strobl, N. S. Markov, L. Zappia, G. Palla, W. Lewis, D. Dimitrov, M. E. Vinyard, D. S. Magruder, M. F. Mueller, A. Andersson, E. Dann, Q. Qin, **D. J. Otto**, M. Klein, O. B. Botvinnik, L. Deconinck, K. Waldrant, S. N. Yasa, A. Szałata, A. Benz, Z. Li, Open Problems Jamboree Members, J. M. Bloom, A. O. Pisco, J. Saez-Rodriguez, D. Wulsin, L. Pinello, Y. Saeys, F. J. Theis, and S. Krishnaswamy, *Defining and benchmarking open problems in single-cell analysis*, **Nature Biotechnology**, July 2025, DOI: [10.1038/s41587-025-02694-w](https://doi.org/10.1038/s41587-025-02694-w).
- [13] D. H. Janssens, M. Duran, **D. J. Otto**, W. Wu, Y. Xu, D. Kirkey, C. G. Mullighan, J. S. Yi, S. Meshinchi, J. F. Sarthy, K. Ahmad, and S. Henikoff, *MLL oncoprotein levels influence leukemia lineage identities*, **Nature Communications**, Oct. 2024, DOI: [10.1038/s41467-024-53399-8](https://doi.org/10.1038/s41467-024-53399-8).
- [14] B. S. White, A. de Reyniès, A. M. Newman, et al., Tumor Deconvolution DREAM Challenge consortium (**D. J. Otto**, consortium

- member), J. Saez-Rodriguez, L. M. Heiser, J. Guinney, and A. J. Gentles, *Community assessment of methods to deconvolve cellular composition from bulk gene expression*, **Nature Communications**, Aug. 2024, DOI: [10.1038/s41467-024-50618-0](https://doi.org/10.1038/s41467-024-50618-0).
- [15] M. Rade, M. Kreuz, A. Borkowetz, U. Sommer, C. Blumert, S. Füssel, C. Bertram, D. Löffler, **D. J. Otto**, L. A. Wöller, C. Schimmelpfennig, U. Köhl, A.-C. Gottschling, P. Hönscheid, G. B. Baretton, M. Wirth, C. Thomas, F. Horn, and K. Reiche, *A reliable transcriptomic risk-score applicable to formalin-fixed paraffin-embedded biopsies improves outcome prediction in localized prostate cancer*, **Molecular Medicine**, Feb. 2024, DOI: [10.1186/s10020-024-00789-9](https://doi.org/10.1186/s10020-024-00789-9).
- [16] C. Schimmelpfennig, M. Rade, S. Füssel, D. Löffler, C. Blumert, C. Bertram, A. Borkowetz, **D. J. Otto**, S.-H. Puppel, P. Hönscheid, U. Sommer, G. B. Baretton, U. Köhl, M. Wirth, C. Thomas, F. Horn, M. Kreuz, and K. Reiche, *Characterization and evaluation of gene fusions as a measure of genetic instability and disease prognosis in prostate cancer*, **BMC Cancer**, June 2023, DOI: [10.1186/s12885-023-11019-6](https://doi.org/10.1186/s12885-023-11019-6).
- [17] **D. J. Otto**, *Computational Gene Expression Deconvolution*, **Doctoral dissertation, Universität Leipzig**, Aug. 2021, URN: [urn:nbn:de:bsz:15-qucosa2-757637](https://nbn-resolving.org/urn:nbn:de:bsz:15-qucosa2-757637).
- [18] M. Bauer, S. Zürner, M. Kreuz, **D. J. Otto**, G. Popp, and U.-D. Braumann, *Histological grading of the prostate carcinoma using deep learning: an unsupervised approach*, in **Medical Imaging 2021: Digital Pathology**, **SPIE**, Feb. 2021, DOI: [10.1117/12.2581043](https://doi.org/10.1117/12.2581043).

*equal contribution, ⁺co-corresponding authors

Software

- **Mellon**: cell-state density estimation; integrated into Palantir. Lead developer. DOI: [10.5281/zenodo.7328898](https://doi.org/10.5281/zenodo.7328898).
- **Kompot**: cluster-free comparison of conditions across cell states; scverse ecosystem package. Lead developer. DOI: [10.5281/zenodo.17281114](https://doi.org/10.5281/zenodo.17281114).
- **Palantir**: cell-fate probabilities along differentiation trajectories; scverse ecosystem package. Co-maintainer; integrated Mellon.
- **2for1separator**: deconvolution of active and repressive chromatin signals in CUT&Tag2for1 data. Lead developer. DOI: [10.5281/zenodo.5498376](https://doi.org/10.5281/zenodo.5498376).
- **kdpeak**: genomic peak calling by kernel density estimation. Lead developer, with M. Setty. DOI: [10.5281/zenodo.8200403](https://doi.org/10.5281/zenodo.8200403).
- **AnnZarro**: browser viewer for kernels and similarity matrices in AnnData. Lead developer. DOI: [10.5281/zenodo.23222216](https://doi.org/10.5281/zenodo.23222216).
- **agent_sandbox**: kernel-enforced sandboxing for AI coding agents on shared HPC clusters; the operator controls which files and credentials agents reach, and Slurm jobs they submit stay sandboxed. Developer; 27 releases, Homebrew, MIT license.
- **Nexus**: orchestration of teams of coding agents from GitHub issues, with independent re-checks of results and every result and decision documented. Developer; public, documented, MIT license.

Talks & Conference Presentations

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| BCB 2026: Bertinoro Computational Biology Meeting | Bertinoro, Italy Sep 2026 |
| Spatial context as a statistic on the phenotypic manifold: cluster-free differential analysis of liver metastases spatial transcriptomics (invited talk) | |
| GAIN26 Annual Conference (German Academic International Network) | San Francisco, USA Aug 2026 |
| Co-host and moderator, GAIN26 Science Slam (invited) | |
| Center for Metastasis Research eXcellence (MET-X), Fred Hutch | Seattle, USA Jul 2026 |
| Characterizing liver metastasis from spatial sequencing data (talk) | |
| CSHL Cell Modeling in Space and Time | Cold Spring Harbor, USA Jun 2026 |
| Continuous representations and label-free differential analysis of single-cell data (poster and flash talk) | |
| TDS IRC Annual Retreat, Fred Hutchinson Cancer Center | Seattle, USA Jun 2026 |
| Panelist, “Bridging Research and Clinical Uses of AI at Fred Hutch” (panel discussion) | |
| HHMI Janelia Research Campus | Ashburn, USA Jan 2026 |
| Computational Tissue Dynamics (talk) | |
| CSHL Single Cell Analyses | Cold Spring Harbor, USA Nov 2025 |
| Label-Free Differential Analysis of Single-Cell Data (poster and flash talk) | |
| ISSCR Seattle Symposium (International Society for Stem Cell Research) | Seattle, USA Oct 2025 |
| Continuous representations and label-free differential analysis of single-cell data (talk) | |

Florian Wimmers Group, University of Tuebingen

Comparing single-cell datasets with Kompot (seminar)

Tuebingen, Germany Jul 2025**CHC Seminar, Helmholtz Munich**

Continuous tissue representations from single-cell data (invited talk)

Munich, Germany Jul 2025**Systems Biology of Single Cells, UC Irvine**

Cell-differentiation dynamics inference using cell-state-density functions (poster)

Irvine, USA Mar 2025**BCB 2024: Bertinoro Computational Biology Meeting**

Cell-differentiation dynamics inference using cell-state-density functions (invited talk)

Bertinoro, Italy 2024**scverse Community Meeting**

Quantifying cell-state density with Mellon (talk)

Online May 2024**Center for Metastasis Research eXcellence (MET-X), Fred Hutch**

Density landscapes of single-cell phenotypic manifolds (talk)

Seattle, USA May 2024**Seattle Cancer Biology Postdoctoral Symposium**

Quantifying cell-state density with Mellon (talk)

Seattle, USA May 2024**Deep Learning Affinity Group, Fred Hutch**

Quantifying cell-state densities with Mellon and inferring dynamics (seminar)

Seattle, USA Apr 2024**Dana Pe'er Lab, Memorial Sloan Kettering**

Quantifying cell-state density with Mellon (seminar)

New York, USA Mar 2024**CSHL Systems Biology: Global Regulation of Gene Expression**

Quantifying cell-state densities in single-cell phenotypic landscapes using Mellon (poster)

Cold Spring Harbor, USA Mar 2024**Center for Metastasis Research eXcellence (MET-X), Fred Hutch**

Applications of cell-state density (talk)

Seattle, USA Jul 2023**Memorial Sloan Kettering**

Mellon: continuous cell-state density estimation (invited talk)

New York, USA Mar 2023**NeurIPS Workshop on Learning Meaningful Representations of Life (LMRL)**

Characterization of rare transitory cell states with Mellon (poster)

Virtual Dec 2022**Machine Learning in Computational Biology (MLCB)**

Continuous cell-state density inference and applications (poster)

New Orleans, USA Nov 2022**Single Cell Genomics (SCG)**

Characterization of rare transitory cell states with Mellon (poster)

Utrecht, Netherlands Oct 2022**NeurIPS Workshop on Learning Meaningful Representations of Life (LMRL)**

Simultaneous CUT&Tag profiling of the accessible and silenced regulome in single cells (talk)

Virtual Dec 2021**Machine Learning in Computational Biology (MLCB)**

Simultaneous CUT&Tag profiling of accessible and silenced regulome in single cells (talk)

Virtual Nov 2021

Teaching Experience

MCB 536 Introduction to Computational Biology [University of Washington](#)**Seattle, WA** 2025

- Two lectures on scRNA-seq analysis (Winter 2025) for first-year graduate students in the Molecular & Cellular Biology program.

Workshop Leader [Seattle Area Single Cell \(SASC\) User Group](#)**Seattle, WA** 2025

- Led an introductory workshop on single-cell analysis in Python

Undergraduate Mentorship [Fred Hutchinson Cancer Center](#)**Seattle, WA** 2023 – 2025

- Mentored Brennan Dury (Univ. of Washington, CS major), whose work on computational methods culminated in coauthorship on the Mellon *Nature Methods* paper.
- Mentored Siddharth Baasri (Univ. of Washington, CS major), co-author of the AnnZarro preprint (bioRxiv, 2026).

Undergraduate Mentorship [Fraunhofer Institute for Cell Therapy and Immunology IZI](#)**Leipzig, Germany** 2021

- Mentored undergraduates in principles of RNA-seq data analysis and statistical methods for medical research
- Assisting in the implementation of novel computational analysis tools

- Led two weekly tutorial sections of about 20 students each; graded homework and examinations.
- Computer-Oriented Mathematics I and II (numerical methods, error analysis, interpolation, ODE integration; with R. Kornhuber and F. Noé) and Logic and Discrete Mathematics (with K. Wolter), WS 13/14 to SS 15.

Patents

Novel RNA-biomarkers for diagnosis of prostate cancer WO2024052258A1

2022

Co-inventor. Universität Leipzig and Fraunhofer-Gesellschaft. Priority Sep. 2022; PCT filed Sep. 2023, published Mar. 2024; national and regional applications filed (EP, US, CN, JP, KR, AU).

Multi-gene expression assay for prostate carcinoma WO2021213981A1

2020

Co-inventor. Universität Leipzig and Fraunhofer-Gesellschaft. Priority EP20170321.2, Apr. 2020; PCT published Oct. 2021; pending in Europe (EP4139489A1, under examination) and the US (US20230265522A1). Basis of the ProstaTrend score.

Academic, Professional, and Public Service

Seminar series: Co-chair, MET-X (Center for Metastasis Research eXcellence) Seminar Series, Fred Hutch (2025–2026): bi-weekly seminars; invite external speakers across career stages; chair trainee talks.

Journal review: *Nature Computational Science* (2026), *Bioinformatics* (2024–2026), *BMC Genomic Data* (2026), *Theory in Biosciences* (2026), *Genome Medicine* (2025), *BMC Bioinformatics* (2025), *Discover Oncology* (2025); with senior researchers for *Genome Research*, *Cell Systems*, and *ICML*.

Conference review: MLCB and ACM-BCB (papers); ISSCR 2026 Annual Meeting (abstracts).

Fred Hutch: Reviewer, SPAC Mentoring Awards (McDougall Award for Faculty, Hutchison Award for Non-Faculty), 2025; poster judge, TDS IRC Retreat (2026) and Basic Sciences Division Retreat (2026).

Community: Organizer of bi-monthly Seattle networking events (Stammtisch) for the German Academic International Network (GAIN; Humboldt Foundation, DAAD, DFG), since 2023; co-host and moderator, GAIN26 Science Slam (San Francisco, 2026).

Open science: Maintain the tools under Software with documentation, continuous integration, and user support, and the AI-agent tools under Technical Skills; Open Problems in Single-Cell Analysis Jamboree (2021; *Nature Biotechnology*, 2025).

Leadership training: CCEH Leadership and Management Skills Course for Postdocs (2024, competitive selection); CIMER-based Inclusive Research Mentor Training (2024).

Technical Skills

AI Agents & Safety Infrastructure: Building and operating sandboxed teams of AI agents on HPC clusters (agent_sandbox and Nexus, under Software): since April 2026 they have run more than 4,000 agent tasks and 5,000 cluster jobs for my research, including the liver-metastasis atlas and Kompot.

Language Models & Model Internals: [moral-dials](#), continuous behavioral control for language models: a low-rank weight adjustment that moves a localized behavior with a scalar set at inference time and is bitwise identical to the base model at the neutral setting (PyTorch; demonstrated on a 7B model). Working with the internals of large pretrained transformers, the model class of the sequence-to-function and single-cell foundation models my research builds on, fine-tunes and tests.

Machine Learning & Scientific Computing: Gaussian processes, variational Bayes, diffusion maps, PDE-based dynamics modeling, Bayesian optimization, discrete diffusion models for biological sequence synthesis, language-model steering; JAX, PyTorch, scikit-learn, NumPy, pandas.

Compute: HPC/Slurm, cloud (AWS, GCP), large-scale GPU/TPU training, massively parallelized variational inference.

Programming & Dev: Python, R, JavaScript/TypeScript, Bash/Zsh; API design, package development, continuous integration (GitHub Actions, GitLab CI).

Single-cell & Multi-omics: RNA velocity, lineage tracing, spatial transcriptomics, multimodal integration.

Reproducibility: Version control (Git, GitHub), environment management (micromamba, conda, renv), containerization (Docker, Singularity), reproducible workflows.