Dr. Sarah E. Jenkins

Computational Genomics & Systems Biology

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August 4, 2026

Dr. Marcus Vance, PI
The Vance Laboratory for Computational Neurobiology
Salk Institute for Biological Studies
10010 N Torrey Pines Rd
La Jolla, CA 92037

Dear Dr. Vance,

I am writing to express my strong interest in a postdoctoral research position in the Vance Laboratory for Computational Neurobiology. Currently a PhD candidate in Genome Sciences at the University of Washington under Dr. Eleanor Wright, my research focuses on developing generative models for integrating single-cell multi-omic datasets. I am eager to apply my computational training to model the spatial-epigenetic regulation of cortical development in your laboratory.

My doctoral work focused on `MultiAlign`, a variational autoencoder (VAE) framework designed to align non-overlapping single-cell RNA-seq and ATAC-seq profiles without joint profiling (*Nature Methods*, 2025). This method successfully resolved transient progenitor cell-states in cortical organoids, demonstrating my ability to develop robust models for heterogeneous genomic data. I have extensive experience processing large-scale sequencing datasets, building deep learning models, and collaborating with experimental biologists to validate computational predictions.

The Vance Lab's pioneering work mapping cell-type distributions in the mammalian neocortex using MERFISH (Vance et al., 2025) highlights the critical importance of spatial architecture in cell-fate decisions. I am highly motivated to extend my work in multi-omic integration to the spatial domain. In your lab, I aim to develop tools that align high-throughput single-cell atlases with spatial transcriptomic scaffolds, unlocking new insights into the microenvironmental signals regulating neocortical lineages.

The attached proposed research plan details my goals of mapping spatial chromatin landscapes and modeling lineage trajectories in the neocortex. I would welcome the opportunity to discuss my application and explore how my computational skills can contribute to the Vance Lab's research. Thank you for your time and consideration.

Sincerely,

Dr. Sarah E. Jenkins
Postdoctoral Applicant
University of Washington

Proposed Research Plan

Candidate: Dr. Sarah E. Jenkins **Target Lab:** The Vance Laboratory

Title: Decoding Spatial Heterogeneity in Neocortical Development via Single-Cell Multi-Omic Integration

1 Introduction & Rationale

The mammalian neocortex is structured into six highly organized layers, arising from a common pool of progenitor cells. While single-cell RNA-seq and ATAC-seq provide high-resolution molecular profiles, they lack spatial context due to tissue dissociation. Conversely, high-resolution spatial transcriptomics (e.g., MERFISH, Stereo-seq) provides spatial coordinates but has limited gene throughput or lacks epigenetic data. To understand the transcriptional networks driving cortical development, we must develop computational methods to project high-dimensional multi-omic features onto spatial coordinates.

2 Specific Aims

I propose two synergetic computational aims to model spatial-epigenetic regulation, designed to leverage the Vance Lab's experimental datasets:

Aim 1: **Robust Spatial-to-Single-Cell Multi-Omic Alignment (Aim 1).** I will develop a spatial-epigenetic mapper (`SpaEM`) utilizing optimal transport and graph neural networks to align dissociated scATAC-seq profiles with spatial transcriptomic templates. By modeling cells as a spatial graph and using accessibility as a prior, `SpaEM` will reconstruct spatial chromatin landscapes at single-cell resolution. I will validate this method using the Vance Lab's published mouse neocortex MERFISH datasets.

Aim 2: **Dynamic Modeling of Lineage Trajectories in Spatial Context (Aim 2).** Using aligned spatial multi-omic maps, I will reconstruct cell lineage trajectories incorporating both differentiation state (pseudotime) and physical migration paths. This analysis will target the ventricular zone (VZ) to subventricular zone (SVZ) boundary, identifying local microenvironmental signals and ligand-receptor interactions triggering progenitor cell-fate decisions.

3 Synergy with the Vance Laboratory

The proposed research directly aligns with the Vance Lab's ongoing investigations. While the Vance Lab excels at generating high-resolution spatial datasets, my computational expertise in generative modeling will provide the necessary tools to extract regulatory mechanisms from them. Collaborating with your wet-lab researchers, I plan to validate our predicted spatial regulators using targeted perturbation assays in organoid slices, establishing a feedback loop between computational modeling and experimental biology.

4 Proposed Project Timeline

Below is the preliminary timeline for the proposed aims and deliverables:

Months 1–6 Develop computational framework for `SpaEM` (Aim 1); validate on public MERFISH datasets.

Months 7–12 Apply `SpaEM` to Vance Lab's spatial datasets; identify regulatory elements at the VZ/SVZ boundary.

Months 13–18 Perform trajectory analysis and model cell-cell communication networks (Aim 2); initiate validation assays.

Months 19–24 Prepare and submit manuscript; package software as open-source; write transition fellowship applications.