

SUMMARY

I am a Ph.D. student specializing in microscopy, genomics and computer vision. My research focuses on using machine learning models to interpret causal relationships in highly variable biological processes. I have experience leading interdisciplinary projects with pathologists and mathematicians to guide the design of experiments and modeling.

EDUCATION

Ph.D, Mechanobiology | National University of Singapore

Sep 2016 - Present

B.Tech Biotechnology (Distinction) | SASTRA University

Jul 2011 - May 2015

WORK EXPERIENCE

Visiting Researcher | Paul Scherrer Institute & ETH Zürich

Sep 2020 - Present

Consultant, Computer Vision | [Qritive](#)

Sep 2019 - Dec 2019

Research Assistant, National University of Singapore

Sep 2015 - Jul 2016

SKILLS

Statistics: Multivariate Statistics, Linear Algebra, Diffusion maps, Pattern recognition and Machine Learning.

Computer Vision: Segmentation, Feature generation and Particle tracking

Computational Biology: Analysis of bulk and single cell Microarray, RNA-Seq and HiC data.

Experimental Skills: Microscopy, Tissue engineering and mechanical manipulation of cells.

Tools: R, ImageJ, MATLAB, Python, QuPath, Git, LaTeX and Inkscape.

SELECTED RESEARCH PROJECTS

Automated segmentation and feature generator for 3D images

- Built an automatic image processing pipelines for segmentation and feature generation that reduced the processing time by 60%.
- Engineered features for morphology, textural and spatial distribution of objects in images.
- Integrated multi-domain features such as protein expression, RNA seq and image features to enable deduction of functional links.

Digital pathology platform for grading breast cancer stages at single cell resolution

- Performed instance segmentation of single nuclei from patient tissue biopsies using U-Net based CNN and extracted geometric and textural features of nuclei.
- Built machine learning models to diagnose breast cancer stages at single cell resolution from patient breast tissue biopsies with 80% accuracy.
- Developed a single cell tumorigenesis score that characterises tumor progression.
- Identified regions of tissue tension using spatial statistics of nuclear images.

Deconvolving cell variability in cancer

- Developed a 3D in-vitro organoid tissue model for cancer progression amenable to high-resolution imaging.
- Implemented a classifier to predict cell shape with an accuracy of 95% and used the latent feature vectors along with regression models to show that cell shape is coupled to its function.
- Demonstrated a causal relationship between cell shape and activation by cancer cells using multimodal-multivariate analysis.
- Established the use of tissue model to assay the treatment efficacy of radiotherapy.

Trajectory inference to accelerate reprogramming of skin cells to stem cells

- Developed a novel technique to reprogram skin cells to stem cells with high efficiency.
- Performed statistical tests and pathway analysis on RNA seq data to characterize the temporal changes in the transcription profile during reprogramming.

- Modeled trajectories of reprogramming cells using clustering and diffusion models of single cell image features.
- Identified sources of low efficiency in large noisy image data which were experimentally validated to accelerate stem cell generation.

DNA structure informs cellular state

- Identified latent immune cells based on microscopy image based radial DNA distribution within the nucleus and clustering large single cell RNA-Seq dataset.
- Predicted DNA structure from integrating RNA-Seq and ChIP-Seq data and validated the robustness using experiments and HiC data.

Cell shape modulates cellular response to stimuli

- Aligned, analyzed, visualized and interpreted differential gene expression patterns in RNA-Seq and microarray data. Also performed statistical tests and pathway analysis.
- Demonstrated the cell shape can modulate the transcriptional response to compressive load and inflammation.

Identification of dead (Apoptotic) cancer cells in a high-content screen

- Setup preliminary high content screen to characterize cancer cell survival in the presence of various drugs.
- Developed automatic image feature extraction from high content drug screens on cancer cells.
- Deployed multiple machine learning methods for classifying cancer cells as either dead (apoptotic) or live. Achieved identification accuracy of over 90%.

PEER REVIEWED PUBLICATIONS

- Dai Yang, K., Belyaeva, A., **Venkatachalapathy, S.**, Damodaran, K., Katcoff, A., Radhakrishnan, A., Shivashankar GV and Uhler, C. (2021). Multi-domain translation between single-cell imaging and sequencing data using autoencoders. *Nature Communications*, 12(1), 1-10;;[PMID: 33397893]
- Dai Yang, K., Damodaran, K., **Venkatachalapathy, S.**, Soylemezoglu, A. C., Shivashankar, G. V., and Uhler, C. (2020). Predicting cell lineages using autoencoders and optimal transport. *PLoS computational biology*, 16(4), e1007828;[PMID: 32343706]
- **Venkatachalapathy S**, Jokhun DS, and Shivashankar GV. Multivariate analysis reveals activation-primed fibroblast geometric states in engineered 3D tumor microenvironments. *Mol. Biol. Cell.*2020;;mbcE19080420. [PMID:32023167]
- Damodaran K*, **Venkatachalapathy S***, Alisafaei F, Radhakrishnan AV, Sharma Jokhun D, Shenoy VB, and Shivashankar GV. Compressive force induces reversible chromatin condensation and cell geometry dependent transcriptional response. *Mol. Biol. Cell.*2018;;mbcE18040256. [PMID:30256731]
- Roy B, **Venkatachalapathy S**, Ratna P, Wang Y, Jokhun DS, Nagarajan M, and Shivashankar GV. Laterally confined growth of cells induces nuclear reprogramming in the absence of exogenous biochemical factors. *Proc. Natl. Acad. Sci. U.S.A.*2018;. [PMID: 29735717]
- Belyaeva A, **Venkatachalapathy S**, Nagarajan M, Shivashankar GV, and Uhler C. Network analysis identifies chromosome intermingling regions as regulatory hotspots for transcription. *Proc. Natl. Acad. Sci. U.S.A.* 2017;;[PMID:29229825]
- Mitra A, **Venkatachalapathy S**, Ratna P, Wang Y, Jokhun DS, and Shivashankar GV. Cell geometry dictates TNF α -induced genome response. *Proc. Natl. Acad. Sci. U.S.A.*2017;;[PMID:28461498]
- Radhakrishnan AV, Jokhun DS, **Venkatachalapathy S**, and Shivashankar GV. Nuclear Positioning and Its Translational Dynamics Are Regulated by Cell Geometry. *Biophys.J.*2017;112(9):1920-1928;[PMID:28494962]

* indicates equal contribution

Complete List of publications: [Here](#)

CONFERENCE: TALKS AND POSTERS

- 64th Annual Biophysical Society Meeting *San Diego, Feb 2020*
Talk: "Cell Geometry Modulates the Activation of Fibroblasts in 3D Tumor Microenvironment"
- Drug Discovery 2019 – Looking Back To The Future *Liverpool, Nov 2019*
Talk: Invited Speaker: "Mechano-Genomics: from Cell-Fate Decisions to Biomarkers"
- International Conference on Genomes and AI: From Packing to Regulation *Singapore, Oct 2019*
Talk: "Multivariate analysis of fibroblast activation in engineered 3D tumor microenvironments"

- Mechanobiology after 10 Years: The Promise of Mechanomedicine *Singapore, Nov 2018*
Poster: "Heterogeneity in cell geometric states regulate the selective activation of fibroblasts"
- Nuclear Mechanogenomics, EMBO Workshop *Singapore, Apr 2018*
Talk: Role of cell geometry and 3D chromatin structure in differential genome regulation"
- The 3rd International Symposium on Mechanobiology *Singapore, Dec 2017*
Talk: "Role of 3D chromatin architecture in differential genome regulation"
- Mechanobiology of Disease, MBI-BioPhysical Society meeting *Singapore, Sep 2016*
Poster: "Nuclear positioning and its translation dynamics is regulated by cell geometry"

TEACHING AND LEADERSHIP EXPERIENCE

- Graduate Teaching Assistance *2016-2018*
Assisted in the instruction and evaluation of 30 students in the Nuclear Mechanics and Genome Regulation module and was a MATLAB instructor for Mechanobiology Bootcamp.
- Image Analysis for dummies workshop *May, 2015*
Designed and instructed a class on Automating image processing with ImageJ to 30 researchers.
- Supervised and mentored 2 students in the lab for their undergraduate or masters thesis.

HONORS AND AWARDS

- Dean's Merit list given to the top 2-10% students in the University *2015*
- Inspirational Mentorship Award, NUS High School *2017*
- Best Oral Presentation Award, Genomes and AI: From Packing to Regulation *2019*

PAST EXPERIENCES

- Intern, *Biophysics laboratory*, Raman Research Institute (RRI)** *Winter, 2013*
Developed algorithms to identify and track vesicles in axons.
- Medical Intern, *Kanmani Fertility Clinic*, Raju Hospitals** *Summer, 2013*
Performed androgen characterisation, leukocyte culture, karyotyping and follicular study on patient samples.
- Undergraduate researcher, *Chromatin Epigenetics laboratory*, SASTRA University** *2012-2014*
Developed algorithms to identify apoptotic cells with an accuracy of over 90% in a high content screen.