Saradha Venkatachalapathy

saradhavpathy@gmail |+41 77 973 39 67
Website | LinkedIn

SUMMARY

I specialize in microscopy, computer vision and genomics and have developed computer vision and machine learning models to interpret causality in highly variable processes.

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 singe 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 varies with tumor progression.

Deconvolving cell variability in cancer

- Developed a 3D in-vitro tissue model to study 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 micorscopy 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, Karren, Anastasiya Belyaeva, **Saradha Venkatachalapathy**, Karthik Damodaran, Abigail Katcoff, Adityanarayanan Radhakrishnan, GV Shivashankar, Caroline Uhler. "Multi-domain translation between single-cell imaging and sequencing data using autoencoders." *N*ature Communications12, no. 1 (2021)
- Dai Yang, Karren, Karthik Damodaran, **Saradha Venkatachalapathy**, Ali C. Soylemezoglu, G. V. Shivashankar, and Caroline Uhler. "Predicting cell lineages using autoencoders and optimal transport." *P*LoS computational biology16, no. 4 (2020): e1007828. [PMID: 32343706]
- **Venkatachalapathy S**, Jokhun DS, and Shivashankar GV. Multivariate analysis reveals activation-primed fibroblast geometric states in engineered 3D tumor microenvironments. *M*ol. 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. *M*ol. 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. *P*roc. 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. *P*roc. 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 TNFα*A*-induced genome response. *P*roc. 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. *B*iophys.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 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.