Saradha Venkatachalapathy

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SUMMARY

PhD graduate specializing in microscopy, computer vision and genomics with extensive experience in developing computer vision and machine learning models to interpret causal relationships in highly variable biological processes. Experienced in 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 - July 2021*
B.Tech Biotechnology (Distinction) , SASTRA University *Jul 2011 - May 2015*

WORK EXPERIENCE

Postdoctoral Fellow, Paul Scherrer Institute *August 2021 - Present*
Visiting Scientist, Paul Scherrer Institute & ETH Zürich *Sep 2020 - July, 2021*
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: Automated Microscopy, Immunohistochemistry, Tissue engineering and 3D Spheroid cultures.
Tools: R, ImageJ, Python, Keras, TensorFlow, QuPath, Git, LaTeX and Inkscape.

SELECTED RESEARCH PROJECTS

Image 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 tissues at single cell resolution

- Performed instance segmentation of dense nuclei from patient tissue biopsies using U-Net based CNN and extracted geometric and textural features of nuclei and cell.
- Identified biologically relevant neighbourhoods using spatial statistical models and clustering.
- Built machine learning models to diagnose early stage breast cancer stages at single cell resolution from patient breast tissue biopsies with 80% accuracy.
- Used dimension reduction to obtain a single cell tumorigenesis score that characterises tumor progression under weak supervision

Deconvolving the contribution of cell mechanics in variability observed in cancer

- Developed a 3D in-vitro organoid tissue model of cancer amenable to high-resolution imaging.
- Implemented a classifier to predict cell shape based on chromatin images 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 micro patterned substrates.
- Established the use of tissue model to assay the treatment efficacy of radiotherapy.

Trajectory inference to map reprogramming of skin cells to stem-like cells

- Established a platform for inducing and tracing partial reprogramming of skin cells (fibroblasts).
- 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 image features.
- Identified sources of low efficiency in large noisy image data which were experimentally validated to accelerate stem cell generation.

PUBLICATIONS

- **Venkatachalapathy, S.***,Tina Pekec*, Michal Grzmil,Roger Schibli, Martin Béhé and Shivashankar GV (2021) Tracing heterogeneous response to radiotherapy using single cell nuclear mechanomorphometrics in 3D engineered skin cancer model (Under Preparation)
- **Venkatachalapathy, S.**, Sreekumar D, Ratna P and Shivashankar GV (2021) Actomyosin contractility as a mechanical checkpoint for cell state transitions. (Under Peer Review)
- **Venkatachalapathy, S.**, Jokhun DS, Andhari M, and Shivashankar GV (2021) Single cell imaging-based chromatin biomarkers for tumor progression. (To appear in Scientific Reports)
- 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. *N*ature 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. *P*LoS 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.*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

TEACHING EXPERIENCE

- Graduate Teaching Assistant *2016-2018*
  Assisted in the instruction and evaluation of 30 students in the Nuclear Mechanics and Genome Regulation module and was an instructor for Mechanobiology Bootcamp.
- Image Analysis workshop *May, 2015*
  Designed and instructed a class on automating image processing task for a class of 30 researchers.
- Supervised and mentored 3 students in the lab towards their undergraduate or masters thesis.

CONFERENCE PARTICIPATION

- 64th Annual Biophysical Society Meeting *San Diego, Feb 2020*
  Selected 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*
  Selected 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*
  Selected Talk: Role of cell geometry and 3D chromatin structure in differential genome regulation"
- The 3rd International Symposium on Mechanobiology *Singapore, Dec 2017*
  Selected 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"

HONORS AND AWARDS

- Best Oral Presentation Award, Genomes and AI: From Packing to Regulation *2019*
- Inspirational Mentorship Award, NUS High School *2017*
- Mechanobiology Institute Graduate Scholarship *2016*
- Dean's Merit list, awarded to the top 10% students in the University *2015*