Viswanadham (Vish) Sridhara

CONTACT

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Current role: Senior Bioinformatics Scientist

Citizenship: USA

Google Scholar | LinkedIn | Github | BitBucket | Blog | DockerHub

PROFILE

I have 15+ years' experience in building bioinformatics pipelines for analyzing data generated from both next-generation sequencing (NGS) and mass-spectrometry technologies. In my last role at Food and Drug Administration (FDA contractor), I built bioinformatics pipelines for single-cell transcriptomics work using cellranger and other R packages (Seurat, Monocle etc). Recently, my focus is on using deep learning neural network and other machine learning models to analyze high-dimensional -omics datasets to infer associations in the data.

I use high-performance computing methods in *nix environment for most of my work. I am well versed in building bioinformatics pipelines using technologies such as Snakemake, docker containerization and cloud computing. I usually program in Python/R/MATLAB and typically use tools built for -omics domain for reproducible research. I'm well versed with R packages and python modules (for data science and machine learning).

Till date, my research work has resulted in ~20 peer-reviewed publications and numerous conference proceedings and poster presentations (google scholar citations: ~720, h-index=13). Most of my work is funded by Army research office (ARO MURI grant), Department of Defense (DoD MURI grant) and National Institutes of Health (NIH research fellowship).

EDUCATION

2003 - 2007

PhD, Electrical and Computer Engineering, ODU, Norfolk, VA
Dissertation (funded by Department of Defense MURI grant): Molecular dynamics simulations to probe effects of ultra-short high-intensity electric pulses on biological suspensions to understand how nano-second pulsed electric fields (nsPEFs) kill cancer cells.

2001 - 2003

MS, Electrical and Computer Engineering, ODU, Norfolk, VA
Thesis: Monte carlo analysis of millimeter-wave GaN Gunn diodes

TECHNICAL SKILLS

Machine learning	Regression, Regularization, Hierarchical Clustering, Discriminant analyses
Programming	Python (including data science and ML modules such as numpy, pandas, scikit-learn, matplotlib, keras), R (tidyverse, ML packages), MATLAB, Perl, C, C++, Fortran, UNIX, MacOS, LaTeX
BioFX Pipeline	Cloud computing, Git, Snakemake, Docker
Engineering	Monte-carlo models [MS Thesis focus], Molecular dynamics simulations for atomic modeling [PHD Disseration focus]
NGS	Bulk RNA-seq: HISAT2, featureCounts, GATK, BWA, Bowtie, Samtools, BEDtools (familiarity with TCGC, ICGC datasets) Single cell RNA-seq: CellRanger, Seurat, Monocle3, fastMNN, SAVER
Mass-spec	Byonic, PEAKS, Proteome Discoverer, OMSSA, MODa (familiarity with CPTAC, Tranche, PRIDE, PeptideAtlas datasets)
Systems Biology	BioCyc, MetaCyc, SAINT
MD Simulations	GROMACS, NAMD, VMD

PROFESSIONAL EXPERIENCE

Jun '19 - Present

Senior Bioinformatics Scientist

Argentys (FDA, universities and hospitals contract work)

Contractor at Food and Drug Administration (Jun' 19 - Aug' 20) CBER HIVE Team

Informatics Projects at FDA

• Helped in building RNA-seq pipeline for automated bulk processing of large-scale genomics datasets (fastp, HISAT2, featureCounts, DESEQ2)

• Built single-cell RNA-seq pipeline for analyzing 10X single cell datasets (CellRanger, SAVER, Seurat/Monocle, fastMNN and other R packages)

Sample Research Projects at FDA

• Characterization of the Immune-Driven Drug Hypersensitivity by Single-Cell RNA Sequencing Technologies

• Identifying Molecular Features of Neural Stem Cells in Varied Differentiation Stages
• Single cell RNA-seq analyses to investigate sub-populations of bone-marrow and adipose derived multipotential stromal cells (MSCs) from 3 donors

Universities and medical centers (current contract)
• NGS analyses of targeted LINE-1 retrotransposons data
• NGS analyses to understand vaccine stability
(took a 5 month break to stay in India between FDA role and current contract)

Apr '16 - May '19   Independent Contractor
Universities, Hospitals and Startups

Independent Consultant / Contractor for MGH, WRI, biofuel startup, Booz Allen Hamilton and ProteinMetrics
• At ProteinMetrics, tested ProteinMetrics suite of tools.
• At Booz Allen Hamilton, helped in automating preprocessing of gene expression data (microarray and RNA-seq) for placental datasets using raw data stored in NCBI's GEO repository (PAT - Placental Atlas Tool).
• At Booz Allen Hamilton, improved analytics of differential expression, gene ontology and pathway analyses of the above preprocessed placental datasets (>20 RNA-seq and >300 microarray datasets).
• At Mass General Hospital, improved primer design for a proof-of-principle assay to capture long genomic regions.
• At biofuel startup, built NGS pipeline and developed new computational methods for downstream analyses.
• At biofuel startup, whole genome sequence (WGS) analyses, including variant analyses, copy number variation and strain specific analyses for biofuel production.
• At biofuel startup, set-up in-house Jbrowse genome browser and Sequenceserver (blast+ web server).
• At WRI, helped analyze diverse mass-spectrometry datasets (global proteomics, phosphoproteomics) of breast cancer tissue samples.
• At WRI (in collaboration with PNNL), integrated proteogenomics data to identify markers in laser capture microdissected breast tumor samples (Preliminary work published in AACR).

Dec '12 - Apr '16   **THE UNIVERSITY OF TEXAS SYSTEM (UT AUSTIN, UTSW MEDICAL CENTER DALLAS)**
Research Engineering/Scientist Associate V Dec '12 - Aug '15
The University of Texas at Austin – CENTER FOR COMPUTATIONAL BIOLOGY AND BIOINFORMATICS
• Army research office MURI grant (multi university, incl. Boston University) to build mathematical models to infer associations in multi-omics data
  a. Novel PTM identification using Unrestricted bioinformatic search of large-scale mass-spectrometry based proteomics data generated for mutiple E. coli growth conditions.
  b. 13C Metabolic flux analyses for the same above mentioned samples using FiatFlux and other software.

• Built machine learning models using LASSO regression to predict bacterial growth conditions from in-silico metabolic fluxes generated from metabolic network based flux balance analyses (FBA) methods.
• Helped multiple labs with proteomics bioinformatics consulting and short-term contracts.
• Taught computational mass-spectrometry in Big Data Summer School organized by CCBB (Center for Computational Biology and Bioinformatics every summer – 4 day course)

Computational Biologist Aug '15 - Apr '16
UT Southwestern Medical Center – PROTEOMICS CORE FACILITY

• Protein identification and quantitation using bioinformatics tools (e.g., OMSSA, MASCOT, Sequest, ProteomeDiscoverer, MaxQuant, SAINT).
• Bioinformatics proteomics consultant work with UT Southwestern investigators.

Jan '12 - Dec '12

Scientific Programmer
Samuel Roberts Noble Foundation

• Helped integrated GenoLogics LIMS system with mass-spec equipment • Built pathway databases using MetaCyc and PathwayTools

Jun '07 - Jan '12

Postdoctoral Fellow
National Center for Biotechnology Information (NCBI)

• NCBI OMSSA (Open Mass Spectrometry Search Algorithm) project:
a. Improved noise filtering routines/filters to accommodate high-resolution mass-spectrometry data.
b. Optimized algorithm for ETD data analysis (ion-types, precursor peak filtering).
c. User support by addition of requested enzymes, modifications, and other iontypes required for quantitative proteomics (iTRAQ, TMT 6-plex etc.).
d. Improved sensitivity by adjusting for mass offsets, precursor charge assignment for low-res data. Presented related mass-spectrometry work in ASMS '08, '09, '10 and '11.

• Integration of sequence data & high-throughput phosphoproteomics data:
a. Developed a new method (proof-of-principle) for PTM annotation on genomes (NCBI RefSeq) by using high-throughput proteomics data (PhosphoSite, PhosphoELM) and domain definitions of protein families within NCBI Conserved Domain Database (CDD).
b. Apart from the large-scale annotation of conserved PTM sites on genomes, this method could facilitate identification of novel evolutionarily conserved posttranslational modifications.

• Developed a prototype for new class of peptide identification search algorithm OMSSA-SIM.
a. Motivation is to remove most of the limitations faced by present generation sequence library search algorithms, for example, exact precursor mass match, unknown PTM's, mutations, different enzymatic cleavage etc.
b. Preliminary work in ASMS 2011 (oral presentation in computational mass-spectrometry).

Summer '06

Student Volunteer

Old Dominion University - Aerospace Engineering

• Helped improve programming drives for a test bogie run on MAGLEV (train using magnetic levitation).

Summer '04   Intern

Siemens Limited. Siemens Vdo Automotive

• Finite element analyses (2D) to improve fuel injection solenoid models using Ansoft software.

Aug '03 - May '07   **OLD DOMINION UNIVERSITY (JOSHI LAB, FRANK REIDY RESEARCH CENTER FOR BIOELECTRICS)**

Graduate Research Assistant Aug '03 - May '07

COMPUTATIONAL RESEARCH LAB - BIOELECTRICS

• DoD MURI grant (multi university, incl. MIT) to model/simulate how nano-second pulsed electric fields (nsPEFs) kill cancer cells

a. Compute intense Molecular Dynamics (MD) simulations to understand multiple nanopore formation in lipid bilayers using advanced high performance computing environment.

b. Microscopic calculation of local lipid membrane permittivities and diffusion coefficients using molecular dynamics simulations.

c. MD simulations to understand effects of sodium (Na) and calcium (Ca) ions in pore formation within the biological suspensions.

Research Assistant V May '04 - Dec '06

FRANK REIDY RESEARCH CENTER FOR BIOELECTRICS

• Time Domain Dielectric Transient Spectroscopy (TDDS) measurements to monitor intrastructural changes in leukaemic cells after nanosecond pulsed electric field application.

SELECTED TALKS

1. Large-scale analysis of PTMs @ UT-Austin, Thermo Fisher Scientific, MD Anderson Cancer Center
2. Using subspectral interval matches to make novel identifications of ETD tandem mass spectra @ ASMS 2011
3. Predicting bacterial growth conditions from bacterial physiology @ Center for Systems and Synthetic Biology, UT-Austin
4. Open Mass Spectrometry Search Algorithm @ George Washington University

PUBLICATIONS

1. Tosi, L., Sridhara, V., Yang, Y., et. al., "Engineered DNA Capture Probes for Massively Multiplexed Cloning of Kilobase-Sized Genome Regions", Nature Biomedical Engineering, 2017;1. pii: 0092. doi: 10.1038/s41551-017-0092. Epub 2017 Jun 26.
2. Caglar, M. U., et. al., "The E. coli molecular phenotype under different growth conditions", Scientific Reports 2017 Apr 18;7:45303. doi: 10.1038/srep45303.

3. Brown, C. W., Sridhara, V., Boutz, D. R., et. al., "Large-scale analysis of post-translational modifications in E. coli under glucoselimiting conditions", BMC Genomics 2017 Apr 17;18(1):301. doi: 10.1186/s12864-017-3676-8.

4. Kalantari, R., Hicks, J., Li, L., Gagnon, K., Sridhara, V., Lemoff, A., Mirzaei, H., and Corey, D. R. "Stable Association of RNAi Machinery is Conserved Between the Cytoplasm and Nucleus of Human Cells", RNA. 2016 Jul;22(7):1085-98. doi: 10.1261/rna.056499.

5. Houser, J. R., et. al., Controlled measurement and comparative analysis of cellular components in E. coli reveals broad regulatory changes under long-term starvation. PLOS Computational Biology 2015 Aug 14;11(8):e1004400.

6. Sridhara, V., Meyer AG, Rai P, Barrick JE, Ravikumar P, Segre D, and Wilke C.O. " Predicting growth conditions from internal metabolic fluxes in an in-silico model of E. coli." (PLoS One. 2014 Dec 12;9(12):e114608.).

7. Sridhara, V., Joshi, R. P. "Evaluations of a mechanistic hypothesis for the influence of extracellular ions on electroporation due to high-intensity, nanosecond pulsing." Biochimica Biophysica Acta - Biomembranes, Vol. 1838, no. 7, Jul 2014, pp. 1793-1800.

8. Sridhara, V., Joshi, R. P. "Numerical study of lipid translocation driven by nanoporation due to multiple high-intensity, ultrashort electrical pulses." Biochimica Biophysica Acta - Biomembranes, Vol. 1838, no. 7, Mar 2014, pp. 902-909.

9. Sridhara, V., Dina L. Bai, An Chi, Jeffrey Shabanowitz, Donald F. Hunt, Stephen H. Bryant and Lewis Y. Geer "Increasing peptide identifications and decreasing search times for ETD spectra by pre-processing and calculation of parent precursor charge." Proteome Science 2012, 10:8.

10. Sridhara, V., Aron Marchler-Bauer, Stephen H. Bryant and Lewis Y. Geer, "Automatic annotation of experimentally derived, evolutionarily conserved post-translational modifications onto multiple genomes." Database (Oxford), 2011, bar019.

11. Joshi, R.P., Sridhara, V., Song, J., Schoenbach, K.H "Aspects of Lipid Membrane BioResponses to Subnanosecond, Ultrahigh Voltage Pulsing." IEEE Trans. Dielectrics & Electrical Insulation, Vol. 16, no. 5, Oct 2009, pp. 1243-1250.

12. Allen L. Garner, George Chen, Nianyong Chen, Viswanadham Sridhara, Juergen F. Kolb, R. James Swanson, Stephen J. Beebe, Ravindra P. Joshi, and Karl H. Schoenbach "Changes in the Dielectric Properties of Jurkat Cells Induced by Ultrashort Electrical Pulses," Biochemical Biophysical Research Communications Vol. 362, Issue. 1, Oct. 2007, pp. 139-144.

13. Joshi, R.P., Nguyen, A., Sridhara, V., Nuccitelli, R., and Schoenbach, K.H., "Simulations of Calcium Release Dynamics in Response to a High-Intensity, Ultra-Short Electric Pulse," Physical review. E, Statistical, nonlinear, and soft matter physics 2007; 75(4 Pt 1):041920.

14. Pliquett, U., Joshi, R.P., Sridhara, V., Schoenbach, K.H. "High Electrical Field effects on Cell Membranes." Bioelectrochemistry Vol. 70, Oct. 2006, pp. 275-282.

15. Joshi, R.P., Sridhara, V., Schoenbach, K.H "Microscopic Calculations of Local Lipid Membrane Permittivities and Diffusion Coefficients for Application to Electroporation Analyses." Biochemical Biophysical Research Communications Vol. 348, Issue. 2, Sept. 2006, pp. 643648.

16. Qin Hu, Sridhara, V., R. P. Joshi, J. Kolb and K.H, Schoenbach, "Molecular Dynamics Analysis of High Electric Pulse effects on Bilayer Membranes Containing DPPC and

DPPS." (invited paper) IEEE Transactions on Plasma Science, Vol. 34, no. 4, Aug. 2006, pp. 1405-1411.

17. Hu, Q., Sridhara, V., Joshi, R.P., Schoenbach, K.H., Beebe, S.J., Blackmore, P.F. "Simulations of transient membrane behavior in cells subjected to a high-intensity ultrashort electric pulse." Physical Review E - Statistical, Nonlinear, and Soft Matter Physics, Vol. 71,no. 3, March 2005, pp. 031914(1-7).

18. Joshi, R. P., Sridhara, V., Jogai, B., Shah, P., Del Rosario, R.D. "Analysis of dislocation scattering on electron mobility in GaN high electron mobility transistors." Journal of Applied Physics, Vol. 93, no. 12, Jun 15, 2003, pp. 10046-10052.

19. Joshi, R. P., Sridhara, V., Shah, P., Del Rosario, R.D. "Monte Carlo analysis of GaN-based Gunn oscillators for microwave power generation." Journal of Applied Physics, Vol. 93, no. 8, Apr 15, 2003, pp. 4836-4842.

CONFERENCE PROCEEDINGS

1. Sridhara, V., Joshi, R.P., Hu, Q., Nguyen, A., and Schoenbach, K.H. "Simulations of cell response to high intensity, ultrashort electrical pulses" (invited paper) Bio-Electromagnetic Society Conference, Cancun, Mexico, June 11-15, 2006.

2. Pliquett, U., et. al., "Monitoring intrastructural changes in Jurkat cells after nanosecond pulsed electric field application." Electromed 2005 Conference, Portland, OR, May 15-18 , 2005.

3. Garner, A.L., et. al., "Changes in the Dielectric Properties of Jurkat and HL-60 cells after Electrical Pulses." Electromed 2005 Conference, Portland, OR, May 15-18, 2005.

POSTERS

SCD(FDA) 2020, AACR 2017, Proceedings of the AACR 2016, EMBL Conference 2014, Synthetic Biology: Engineering, Evolution and Design (SEED), ASMS 2010, ASMS 2009, ASMS 2008

GRANT REVIEWER

National Science Foundation (NSF)

JOURNALS REFEREED

Journal of Proteome Research, PLoS Pathogens, Journal of Theoretical Biology, Biology Direct, PLoS Computational Biology, International Journal of Bioinformatics Research and Applications

PROFESSIONAL MEMBERSHIPS

- American Association for Cancer Research
- American society for mass spectrometry

AWARDS	• June 2007: NIH Postdoctoral Fellowship
	• April 2007: Outstanding Graduate Researcher Award (Ph. D.)
	• June 2006: Old Dominion University BCET Scholarship
	• April 2006: Honorary Mention for ODU Research Foundation Day Poster Presentation
	• 1996-2000: National Merit Scholarship, College of Engineering, Osmania University
	• 1994-1996: College Scholarship, St. Thomas Samhita Jr. College
	• May 1994: Certificate of merit in Math

SAMPLE PROJECTS

ML-LDA	Database (Oxford) paper summarizing ML + bioinformatics [URL: https://www.ncbi.nlm.nih.gov/pubmed/22321509]
ML-Regularization	PLoS One paper - Regularization and metabolic network models [URL: https://www.ncbi.nlm.nih.gov/pubmed/25502413]
Cancer-Proteogenomics	AACR poster [URL: https://sivome.github.io/Poster_PDFs/ Proteogenomic_AACR_Poster.pdf]
single-cell FDA-project	SCD (FDA) poster [URL: https://sivome.github.io/Poster_PDFs/ SingleCellMSC_SCD_Poster.pdf]
Visualization-R	Nature Biomedical Engineering paper - Designing probes for genome capture [URL: https://www.ncbi.nlm.nih.gov/pubmed/29152409]
Neural networks	Neural Networks blog - 10X single cell data [URL: https://sivome.github.io/genomics/2019/ 11/17/Denoising-Single-Cell-Data-With-Autoencoders.html]
Jupyter	Jupyter notebook - Summarizing proteomics results [URL: https://sivome.github.io/ proteomics/2019/03/11/Reporting_Proteomics_Results.html]
R Markdown	Tidyverse R - OMSSA [URL: https://sivome.github.io/proteomics/2019/03/15/universe-of-proteomics-with-tidyverse.html]