

**BIOGRAPHICAL SKETCH**

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NAME: Gopalakrishnan, Vanathi

eRA COMMONS USER NAME (credential, e.g., agency login): VANATHI

POSITION TITLE: Associate Professor of Biomedical Informatics (tenured), Intelligent Systems (Director), Computational & Systems Biology, Bioengineering, Clinical and Translational Science

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
BMS College of Engineering, Bangalore, India	B.E.	1988	Computer Engineering
University of Pittsburgh, Pittsburgh, PA	M.S.	1991	Computer Science
University of Pittsburgh, Pittsburgh, PA	Ph.D.	1999	Computer Science

**A. Personal Statement**

I am a computer scientist with over two decades of research experience in bioinformatics and biomedical data analysis, following my passion for developing intelligent systems to reduce the burden of disease. I develop and apply novel rule learning algorithms for the predictive and integrative modeling of biomedical data obtained from molecular profiling studies, radiologic imaging and/or clinical textual reports. I am fundamentally interested in technologies for data mining and discovery that allow incorporation of prior knowledge. Research areas of interest involve extensions to rule learning via the incorporation of: (1) Bayesian Statistics, (2) prior rule models, and (3) knowledge obtained through mining of ontologies or the literature. I have an extensive background in developing and testing real-world models from large datasets in collaboration with biomedical scientists. I have created via scientific collaboration, the unique hybrid Bayesian Rule Learning (BRL) methods that combine the strengths of Bayesian networks with rule inferencing, thereby encoding the uncertainty in the validity of a rule as a posterior probability. As the principal investigator on NIH-funded R01's, I have overseen their application to biomarker discovery and validation for the early detection of ALS, lung cancer, and esophageal adenocarcinoma.

I am currently the elected Director of the Intelligent Systems Program (ISP), a premier multidisciplinary graduate program at the University of Pittsburgh dedicated to applied artificial intelligence (AI). The ISP has focused primarily on doctoral training for 33 years, comprising now of around 35 faculty members (secondary appointments) from across 11 departments within the University. My current focus is on founding and directing CHAI, Center for Humans and Artificial Intelligence, which will build on the existing infrastructure provided by the ISP, and expand its research and training programs to act as a nexus for innovations in multidisciplinary AI.

I direct the PRoBE laboratory for **P**attern **R**ecognition from **B**iomedical **E**vidence, which aims to accelerate Biomedical knowledge discovery to reduce disease burden by developing and applying novel hybrid AI methods that learn from multimodal data and prior knowledge. A few well-cited and recent papers from our laboratory are:

- A1. Ranganathan, S., Williams, E., Ganchev, P., **Gopalakrishnan, V.**, Urbinelli, L., Newhall, K., Cudkowicz, M.E., Brown, R.H. Jr., Bowser, R. Proteomic Profiling of Cerebrospinal Fluid Identifies Biomarkers for Amyotrophic Lateral Sclerosis, *J Neurochem.* 2005 Dec;95(5):1461-71. PMID: 16313519 PMCID: PMC1540444. (Cited 241 times as per google scholar on 9/2/2020).

- A2. H Ryberg, J An, S Darko, JL Lustgarten, M Jaffa, **Gopalakrishnan, V.**, Lacomis, D., Cudkowicz, M.E. Bowser, R. Discovery and verification of amyotrophic lateral sclerosis biomarkers by proteomics. *Muscle & nerve, Muscle & Nerve.* 42: 104–111, 2010. PMID: 20583124 PMCID: PMC2975276. (Cited 118 times as per google scholar on 9/2/2020).
- A3. Bigbee, W. L\*, **Gopalakrishnan, V.\***, Weissfeld J, L., Wilson, D. O., Dacic, S. Lokshin, A. E., Siegfried, J. M. A Multiplexed Serum Biomarker Immunoassay Panel Discriminates Clinical Lung Cancer Patients from High-Risk Individuals Found to be Cancer-Free by CT Screening. *J Thorac Oncol.* 2012 Apr;7(4):698-708. (**\*These authors contributed equally to the study**). PMID: 22425918 PMCID: PMC3308353. (Cited 82 times as per google scholar on 9/2/2020).
- A4. Liu Y, Manners J, Bittar Y, Chou SH, **Gopalakrishnan V.** Towards precision critical care management of blood pressure in hemorrhagic stroke patients using dynamic linear models. *PLoS One.* 2019;14(8):e0220283. PMCID: PMC6681940
- A5. Balasubramanian JB, Boes RD, **Gopalakrishnan V.** A novel approach to modeling multifactorial diseases using Ensemble Bayesian Rule Classifiers. *Journal of Biomedical Informatics.* 2020. Jul;107:103455. PMID: 32497685

## B. Positions and Honors

### Positions and Employment

- 1988 – 1989 Systems Executive, Wipro Information Technology Limited, Bangalore, India.
- Summer 1991 Software Engineer, Systems Modeling Corporation, Sewickley, PA.
- 1989 – 1997 Research Assistant, Intelligent Systems Laboratory, University of Pittsburgh, Pittsburgh, PA.
- 1996 – 1998 Co-founder of Intelligent Systems, M.D., Inc., Florida, USA. (now NASDAQ:ICAD)
- Spring 2000 Part-Time Faculty, Intelligent Systems Program, University of Pittsburgh. Introduced and taught a new Graduate level core course called Introduction to Bioinformatics.
- 7/2000 – 7/2002 Visiting Assistant Professor, Department of Medicine, Section of Medical Informatics (SMI), University of Pittsburgh, Pittsburgh, PA
- 7/2000 – 7/2002 Visiting Assistant Professor of Intelligent Systems, University of Pittsburgh (UPitt)
- 8/2002 – 6/2006 Assistant Professor, Department of Medicine (SMI), UPitt (tenure-track)
- 7/2006 – 11/2011 Assistant Professor, Department of Biomedical Informatics, UPitt (tenure-track)
- 8/2002 – 11/2011 Assistant Professor of Intelligent Systems, UPitt (secondary appointment)
- 7/2006 – 11/2011 Assistant Professor of Computational Biology, UPitt (joint appointment)
- 12/2011 – now Associate Professor (tenured) of Biomedical Informatics, Intelligent Systems and Computational & Systems Biology, University of Pittsburgh, School of Medicine.
- 6/2012 - 6/2014 Director (& mentor) of the Computer Science, Biology and Biomedical Informatics (CoSBBI) Summer Program for High School Students (rising Juniors and Seniors) for the first two years of this University of Pittsburgh Cancer Institute’s innovative program.
- 2/2017 - present Co-Director of the Bioengineering, Biotechnology and Innovation (BBI) Area of Concentration for Medical Curriculum within the School of Medicine, UPitt.
- 2/2018 – present Associate Professor of Bioengineering, Swanson School of Engineering, UPitt.
- 2/2019 – present Associate Professor of Clinical and Translational Science, UPitt
- 9/2018 – present Director of the Intelligent Systems Program, School of Computing and Information, UPitt. (First year was in-training as co-director with Dr. Diane Litman)

### Other Select Experience and Memberships (non-consecutive) in Professional and Scientific Societies

- 2000 - The International Society for Computational Biology (ISCB)
- 2004 - Association for Computing Machinery (ACM)
- 2004 - American Association for Advancement of Science (AAAS)
- 2000 - The American Association for Artificial Intelligence (AAAI)
- 2000 - The American Medical Informatics Association (AMIA)
- 2006 - Lung & Thoracic Malignancies Program, University of Pittsburgh Cancer Institute (UPCI)  
Peer Review Experience Overview
- 2009 NIH (NCRR/NCATS) SBIR Grants and Contracts Review Study Section
- 2011 NSF Review Panelist (Informatics / BIG Data)
- 2013 NIH P41 Special Review Panelist and NIH P51 Review Panelist
- 2014 Expert Committee Review: Canada Foundation for Innovation: Integrating ‘Big Data’ for Health

- 2015 NIH Winter BDMA Study Section Review Panelist,
- 2015 NIH Special emphasis panelist: Imaging and Biomarkers for Early Cancer Detection
- 2016 NIH Academic Industrial Partnership (AIP) Review Meeting
- 2017 NIH Special emphasis panelist: Imaging and Biomarkers for Early Detection of Aggressive Cancer
- 2018 NIH Maximizing Investigators' Research Award for Early Stage Investigators
- 2018 NIH BDMA Winter study section panelist
- 2019 NIH K99 Reviewing for NIGMS
- 2020 NIH Several Panels including S10 Instrumentation grant reviews and Rapid SARS-CoV-2 proposals

### **Honors**

- 1988 Best Trainee Award, Wipro Information Technology Limited, Bangalore, India.
- 1994 W.M. Keck Fellowship in Computational Biology
- 2006 Pitt Innovator Award (for licensing RL-Wrap: Wrapper-based Rule Learning)
- 2011 AMIA Translational Bioinformatics (TBI) Distinguished Paper Award: Co-and Senior Author (**see C2c**)
- 2015 AMIA TBI Marco Ramoni Distinguished Paper Award: Co-author and Senior Author (**see C3d**)
- 2018 Pitt Innovator Award (for Coronary Artery Disease intelligent detection via Metabolomic Expression)
- 2020 Distinguished Alumni Honor, B.M. S. College of Engineering, Computer Science & Engineering Dept.

### **International Patent Application Filing**

Zaidi AH, Jobe BA, Zeng X, Balasubramanian JB, Gopalakrishnan V, Bigbee WL, inventors; Methods for the detection of Esophageal Adenocarcinoma. PCT Application Filed by University of Pittsburgh (Dec 2014).

### **C. Contributions to Science**

1. Novel computational frameworks for enabling macromolecular crystallization: The art of growing a good X-ray diffractable quality crystal of a protein or other macromolecule can be infused with scientific theory to enable bench scientists to better understand how protein nucleation and growth take place. My first contribution to interdisciplinary science began with my doctoral dissertation work which produced novel insights into the process of macromolecular crystallization via the development and assessment of computational models. This pioneering research in a niche area of bioinformatics was published in important conferences and journals (see 1a – 1d), and led to new research by other groups and robotic companies to improve the science of macromolecular crystallization to provide better monitoring tools and experimental design conditions.

- a. Hennessy, D., **Gopalakrishnan, V.**, Buchanan, B.G., Subramanian, D., Rosenberg, J.M. Induction of Rules for Biological Macromolecule Crystallization, In: Proceedings of the Second International Conference on Intelligent Systems for Molecular Biology (1994) 179-187.
- b. **Gopalakrishnan, V.**, Buchanan, B.G., Rosenberg, J.M. Intelligent Aids for Parallel Experiment Planning and Macromolecular Crystallization. In: Proceedings of the Eight International Conference on Intelligent Systems for Molecular Biology (2000) 171-180.
- c. **Gopalakrishnan, V.**, Buchanan, B.G., Rosenberg, J.M. A Simple Simulator of Protein Crystallization, Journal of Applied Crystallography 35(6) (2002) 727-733.
- d. **Gopalakrishnan, V.**, Livingston, G., Hennessy, D., Buchanan, B., Rosenberg, J.M. Machine-Learning Techniques for Macromolecular Crystallization Data, Acta Crystallogr D Biol Crystallogr 60 (2004)1705-1716.

2. Development of novel rule learning methodologies for predictive modeling and classifier construction from both data and prior knowledge: Over the past two decades, I have collaborated with world-renowned faculty at the University of Pittsburgh to develop and test hybrid machine learning methods that combine the strengths of Bayesian network learning with symbolic rule-based inference to provide clinicians and bench scientists with predictive models that are parsimonious, easily interpretable, and accurately capture uncertainty. My laboratory has produced many innovative methods for modeling biomedical data that include new and efficient methods for discretizing continuous valued data, and transfer learning of classification rules between two related datasets. Moreover, we use ontologies and literature mining methods to capture prior knowledge and use them as input to our classification algorithms (b, d, and e). I have previously successfully received two separate R01s from two institutes of the NIH (NLM and NIGMS) for work related to a and c below.

- a. **Gopalakrishnan, V.**, Lustgarten, J. L., Visweswaran, S., Cooper, G.F. Bayesian Rule Learning for Biomedical Data Mining. Bioinformatics. 26(5) (2010) 668-675. PMID: 20080512; PMCID: PMC2852212.

- b. Lu, X., Zhai, C., **Gopalakrishnan, V.**, Buchanan, B.G. Automatic annotation of protein motif function with Gene Ontology terms, BMC Bioinformatics 5 (2004) 122. PMID: PMC517493.
- c. Ganchev, P., Malehorn, D., Bigbee, W. L., Gopalakrishnan, V. Transfer Learning of Classification Rules for Biomarker Discovery and Verification from Molecular Profiling Studies. J Biomed Inform. 2011 Dec;44 Suppl 1:S17-23. Epub 2011 May 6. (Won a Distinguished Paper Award at the AMIA TBI Summit on Translational Bioinformatics in 2011). PMID: 21571094 PMID: PMC3706089.
- d. Jordan, R, Visweswaran, S, **Gopalakrishnan, V.** Semi-automated literature mining to identify putative biomarkers of disease from multiple biofluids. J Clin Bioinformatics. 2014, 4:13. PMID: PMC4215335.
- e. Ogoe, H.A., Visweswaran, S., Lu, X., Gopalakrishnan, V. Knowledge Transfer via Classification Rules using Functional Mapping for Integrative Modeling of Gene Expression Data. BMC Bioinformatics. 16 (2015): 226. PMID: 26202217. PMID: PMC4512094.

3. Application of our methods to biomarker discovery and validation from omic data: I have been collaborating locally, regionally and nationally with several research groups to apply our novel predictive modeling methods to discover and validate biomarkers for early detection and monitoring of various diseases including Amyotrophic Lateral Sclerosis, Ulcerative Colitis and Cancers of the Lung, Breast and Esophagus. Five representative publications are given below:

- a. Ranganathan, S., Williams, E., Ganchev, P., **Gopalakrishnan, V.**, Urbinelli, L., Newhall, K., Cudkowicz, M.E., Brown, R.H. Jr., Bowser, R. Proteomic Profiling of Cerebrospinal Fluid Identifies Biomarkers for Amyotrophic Lateral Sclerosis, J Neurochem. 2005 Dec;95(5):1461-71. PMID: 16313519 PMID: PMC1540444. (Cited 226 times as per google scholar on 3/1/2019).
- b. Bigbee, W. L\*., **Gopalakrishnan, V.\***, Weissfeld J, L., Wilson, D. O., Dacic, S. Lokshin, A. E., Siegfried, J. M. A Multiplexed Serum Biomarker Immunoassay Panel Discriminates Clinical Lung Cancer Patients from High-Risk Individuals Found to be Cancer-Free by CT Screening. J Thorac Oncol. 2012 Apr;7(4):698-708. (\*These authors contributed equally to the study). PMID: 22425918 PMID: PMC3308353. (Cited 69 times as per google scholar on 3/1/2019).
- c. Zaidi, A.H, **Gopalakrishnan, V.**, Kasi, P. M., Zeng, X., Malhotra, U., Balasubramanian, J., Visweswaran, S., Sun, M., Flint, M. S., Davison, J. M., Hood, B. L., Conrads, T. P., Bergman, J.J., Bigbee, W. L., Jobe, B. A. Evaluation of a 4-protein serum biomarker panel – biglycan, annexin-A6, myeloperoxidase and protein S100-A9 (B-AMP©) – for the detection of esophageal adenocarcinoma. Cancer. 2014 Aug 5. PMID: 25100294. PMID: PMC4441619 (Impact Factor = 5.201).
- d. Lopez Pineda, A., **Gopalakrishnan, V.** Novel Application of Junction Trees to the Interpretation of Epigenetic Differences among Lung Cancer Subtypes. Winner of the 2015 Marco Ramoni Distinguished Paper Award in Translational Bioinformatics. AMIA Jt Summits Transl Sci Proc. 2015 Mar 23;2015:31-5. eCollection 2015. San Francisco, CA, USA. PMID: 2630622 PMID:PMC4525224.
- e. Pineda, A.L, Ogoe, H. A., Balasubramanian, J.B., Rangel Escareno, C., Visweswaran, S., Herman, J. G., **Gopalakrishnan, V.** On predicting lung cancer subtypes using 'omic' data from tumor and tumor-adjacent histologically-normal tissue. BMC Cancer.16 (2016):184. PMID: 26944944 PMID: PMC4778315.

4. Mining big imaging data sets for clinically relevant information and image-derived markers related to injuries and diseases of brain and heart. I am highly interested in research that involves combining omic-biomarkers and imaging-derived markers to increase the precision for disease detection, monitoring and treatment. Towards that end, my laboratory has been developing novel methods to extract image-derived markers from fMRI data, brain tumor diffusion MR data (4a) and cardiac MRI data (4b and c).

- a. Ceschin, R. Panigraphy, A., **Gopalakrishnan, V.** sfDM: Open Source Software for Temporal Analysis and Visualization of Brain Tumor Diffusion MR using Serial Functional Diffusion Mapping. Cancer Inform. 2015 Feb 1;14(Suppl 2):1-9. doi: 10.4137/CIN.S17293. eCollection 2015. PMID: PMC4315050.
- b. Menon, P. G., Morris, L., Staines, M., Lima, J., Lee, D. C., **Gopalakrishnan, V.** Novel MRI-derived quantitative biomarker for cardiac function applied to classifying ischemic cardiomyopathy within a Bayesian rule learning framework. Proceedings of the SPIE 9034, Medical Imaging 2014: Image Processing, 90341L (21 March 2014) pp: 90341L-90341L-6. PMID: PMC4440803.
- c. **Gopalakrishnan, V.**, Menon, P.G., Madan, S. cMRI-BED: A novel informatics framework for cardiac MRI biomarker extraction and discovery applied to pediatric cardiomyopathy classification. Biomed Eng Online. 2015;14 Suppl 2:S7. Epub 2015 Aug 13. PMID: PMC4547147.

5. Training next generation of scientists. The UPCI runs a highly selective program in the summer to train high school students in laboratory and computational work. Students whom I mentored have won best poster awards, and gone on to present in national conferences. A sample publication in the Journal of Pathology Informatics illustrates this service to science, while also bringing out novel contributions made by these students and their research mentors.

- a. Dutta-Moscato, J., **Gopalakrishnan, V.**, Lotze, M. T., Becich, M.J. Creating a Pipeline of Talent for Informatics: STEM Initiative for High School Students in Computer Science, Biology and Biomedical Informatics (CoSBBI). Journal of Pathology Informatics. 2014; Editorial in J Pathol Inform 2014;5:12. PMID: 24860688. PMCID: PMC4030307.

#### **Complete List of Published Work in MyBibliography:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/vanathi.gopalakrishnan.1/bibliography/41925325/public/?sort=date&direction=descending>

#### **D. Additional Information: Research Support and/or Scholastic Performance**

##### **Ongoing Research Support**

NONE

##### **Completed Research Support (over the past few years)**

R01LM10950 Gopalakrishnan (PI) 08/15/11 – 06/30/15

Bayesian Rule Learning Methods for Disease Prediction and Biomarker Discovery

The objective of this project is to develop, evaluate, and refine novel Bayesian Rule Learning (BRL) methods that are algorithmically efficient, result in parsimonious models and accurately estimate predictive uncertainty from high-dimensional biomedical datasets for early detection of disease.

Role: Principal Investigator

P50 CA0904440 Herman (PI) 09/16/11 – 08/31/16

SPORE in Lung Cancer

The major goals of the UPCI Lung Cancer SPORE are to improve detection and treatment of lung cancer and to understand the mechanisms of increased susceptibility of women to lung cancer.

Role: Co-Director of the Biostatistics and Bioinformatics CORE

R01GM100387 Gopalakrishnan (PI) 09/24/12 – 03/31/20

Transfer Rule Learning for Knowledge Based Biomarker Discovery and Predictive Biomedicine  
Funded Competitive Renewal Project Title: Transfer Rule Learning with Functional Mapping for Integrative Modeling of Panomics Data

The major goal of this project is develop, apply, and evaluate novel Transfer Rule Learning (TRL) methods for integrative biomarker discovery from related biomedical data sets.

Role: Principal Investigator

Pittsburgh Health Data Alliance Gopalakrishnan (PI) 04/01/18 - 03/31/19

CADidME: Coronary Artery Disease Intelligent Detection via Metabolomic Expression

The goal of this scope of work is to develop an algorithm that will ensure proper discretization of physiological and metabolic biomarkers, and to create a knowledge base (KB) of cardiovascular disease risk factors that indicate personalized cardiovascular risk.

Role: Principal Investigator