Kishore Hari

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RESEARCH INTERESTS

Network Biology, Design Principles, Data Analysis, Multi-scale modelling

RESEARCH STATEMENT

My research interests are *Network Biology, Transcriptomics, Multi-scale modeling, and Design Principles of phenotypic heterogeneity.* I have experience in identifying design principles in biological networks that allow the prediction of their dynamics with little to no simulations. I have also worked with agent-based models and transcriptomic data. During my Ph.D., I have identified that most understanding of cancer metastasis is highly singular and modular. Given the complexity of the metastatic system, there is an urgent requirement for extensive coupling of various important aspects of metastasis, such as mutations with the landscape of non-genetic heterogeneity, various axes of phenotypic plasticity, and temporal and spatial dynamics. I am interested in integrating transcriptomic data and genomic data to establish regulatory networks specific to cancer metastasis and develop a multi-scale cancer metastasis model, including these networks, that leads to a comprehensive understanding of the invasion and colonization of cancer cells.

EDUCATION

Indian Institute of Science   Bengaluru, India
PhD in Computational Systems Biology; GPA 8.6/10   Aug 2018 - Jul 2023
Thesis: *Elucidating design principles of phenotypic hetergeneity in cancer metastasis*

Indian Institute of Technology Bombay   Mumbai, India
M.Sc. – Biotechnology; GPA: 9.13/10   Aug 2015 – May 2017
Thesis: *Stochastic modelling of GAL system in* Saccharomyces cerevisiae

Indian Institute of Technology Roorkee   Roorkee, India
B.Tech. – Biotechnology; GPA: 7.54/10   Aug 2010 – May 2014
Thesis: *Preparation, characterization and in-vitro studies of Gefitinib loaded Albumin Nanoparticles*

EXPERIENCE

Indian Institute of Science   Bengaluru
Research Scholar   August 2018 – July 2023

- **Design Principles of Biological Networks underlying phenotypic robustness and plasticity**:
  * Modelled the gene regulatory networks (GRNs) underlying Epithelial-Mesenchymal Plasticity (EMP) in cancer metastasis to understand the emergence of phenotypic robustness and plasticity.
  * Simulated the dynamics of the GRNs using various methods such as ODE-based simulations, Boolean simulations, and stochastic simulations. Experience in tools such as RACIPE and DSGRN that allow for comprehensive mapping of the steady state space of a GRN.
  * Identified design principles in GRNs that can affect the steady state dynamics, phenotypic plasticity, phenotypic heterogeneity, and robustness. These design principles have implications both in predicting steady-state dynamics of GRNs without simulation as well as identifying viable therapeutic targets for cancer metastasis.
- **Data analysis**:
  * Analysed high-throughput biological data of diverse characteristics, including cell-fate tracking data, RNA sequencing data for various collaborative projects
  * Elucidated patterns such as patient survival, cell growth kinetics and ecological interactions from the data using statistical methods
- **Agent based modelling**:
  * Developed a grid-based ABM for a 2-d culture establishing the role of contact inhibition of proliferation on mitochondrial activity by incorporating cell division as a function of density in its neighborhood.

TEACHING AND MENTORSHIP EXPERIENCE

MS Ramaiah University of Applied Sciences   Bengaluru, India
Lecturer: Inferential Statistics   January 2023 – May 2023

MS Ramaiah University of Applied Sciences   Bengaluru, India
Lecturer: Introduction to Programming through R   August 2022 – December 2022

Indian Institute of Science   Bengaluru
Research Scholar   August 2018 – July 2023

- Mentored over 10 undergraduate students with various academic backgrounds towards the successful completion of their projects with peer-reviewed publications.

- ○ Co-organized a mini-symposium in the *Society for Mathematical Biology Annual conference, 2021*
- ○ Led the organization of BSSE Annual research symposium 2022.
- ○ Organized multiple iterations of the workshop on *Practical Statistics and Programming for Biologists*, focused on data analysis and visualization in R.

Work Experience

- **Cytel** — Pune
  Associate software developer — *June 2017 – July 2018*

- **HPCL Green R&D Center** — Bengaluru
  Project Assistant — *Jan 2015 – May 2015*

Contributed talks and Posters

- Contributed talk, NetSci 2023, Vienna, Austria, July 2023

- Contributed talk, Cellular Lineages and Plasticity Conference, Alleppey, April 2022

- Poster, European Conference on Mathematical and Theoretical Biology (ECMTB 2022), Heidelberg, Germany, September 2022

- Contributed talk, American Physical Society Satellite Meeting, International Center for Theoretical Sciences, April 2022

- Contributed talk, Society of Mathematical Biology Conference (SMB 2021), Virtual, June 2021

- Poster, Systems Approaches to Cancer Biology Conference, Virtual, November 2020

- Poster, Society of Mathematical Biology Conference (SMB 2020), Virtual, August 2020

- Poster, Phenotypic heterogeneity as a driver of cancer progression, MRDG, Indian Institute of Science, January 2020

- Contributed talk, 16th International Conference on Molecular Systems Biology, De La Salle University, Manila, Philippines, October 2019

Awards and Achievements

- Open Arms Travel Grant - *NetSci 2023* – Jul 2023

- Travel Grant - *Physics of Life 2023* – Mar 2023

- Landahl-Busenberg Award - *ECMTB 2023* – Sep 2022

- Best Poster Award - *Phenotypic heterogeneity as a driver of cancer progression* – Jan 2020
- Best Poster Award - *BSSE Annual Symposium* – Jan 2020
- *Prime Minister's Research Fellowship* – May 2019 to July 2023
- *All India Rank 1* , GATE 2017
- *All India Rank 1* , JAM 2015

Full List of Publications and Preprints

*, †for equal contribution

Publications

- K. Hari, B. Sabuwala, B. V. Subramani, C. A. La Porta, S. Zapperi, F. Font-Clos, and M. K. Jolly. Identifying inhibitors of epithelial–mesenchymal plasticity using a network topology-based approach. **npj Systems Biology and Applications**, 6(1):15, 2020

- K. Hari, V. Ullanat, A. Balasubramanian, A. Gopalan, and M. K. Jolly. Landscape of epithelial-mesenchymal plasticity as an emergent property of coordinated teams in regulatory networks. **eLife**, 11:e76535, 2022

- K. Hari, W. Duncan, M. A. Ibrahim, M. K. Jolly, B. Cummins, and T. Gedeon. Assessing biological network dynamics: Comparing numerical simulations with analytical decomposition of parameter space. **npj Systems Biology and Applications** *(Accepted in Principle)*, 2023

- K. Hari*, M. Rashid*, J. Thampi, N. K. Santhosh, and M. K. Jolly. Network topology metrics explaining enrichment of hybrid epithelial/mesenchymal phenotypes in metastasis. **PLoS Computational Biology**, 18(11):e1010687, 2022

- B. Sabuwala*, K. Hari*, A. S. Vengatasalam, and M. K. Jolly. Coupled mutual inhibition and mutual activation motifs as tools for cell-fate control. **Cells Tissues Organs**, Feb. 2023

- K. Hari*, P. Harlapur*, A. Gopalan, V. Ullanat, A. S. Duddu, and M. K. Jolly. Emergent properties of coupled bistable switches. **Journal of Biosciences**, 47(4):1–14, 2022

- <u>K. Hari</u>, U. Ram, and M. K. Jolly. Identifying "more equal than others" edges in diverse biochemical networks. ***PNAS***, 118(16):e2103698118, 2021

- J. Foo, D. Basanta, R. C. Rockne, ..., <u>K Hari</u>, M. Jolly, et al. Roadmap on plasticity and epigenetics in cancer. ***Physical Biology***, 19(3):031501, 2022

- A. Hebbar*, A. Moger*, <u>K Hari</u>, and M. K. Jolly. Robustness in phenotypic plasticity and heterogeneity patterns enabled by EMT networks. ***Biophysical Journal***, pages 3600–3615, 2022

- L. Chauhan*, U. Ram*, <u>K. Hari</u>, and M. K. Jolly. Topological signatures in regulatory network enable phenotypic heterogeneity in small cell lung cancer. ***eLife***, 10:e64522, 2021

- A. C. Dhadve, <u>K. Hari</u>, B. Rekhi, M. K. Jolly, A. De, and P. Ray. Decoding molecular interplay between runx1 and foxo3a underlying the pulsatile igf1r expression during acquirement of chemoresistance. ***Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease***, 1866(6):165754, 2020

- A. Chedere, <u>K. Hari</u>, S. Kumar, A. Rangarajan, and M. K. Jolly. Multi-stability and consequent phenotypic plasticity in ampk-akt double negative feedback loop in cancer cells. ***Journal of clinical medicine***, 10(3):472, 2021

- H. C. Naik, <u>K. Hari</u>, D. Chandel, S. Mandal, M. K. Jolly, and S. Gayen. Semicoordinated allelic-bursting shape dynamic random monoallelic expression in pregastrulation embryos. ***iScience***, 24(9):102954, 2021

- H. C. Naik, <u>K. Hari</u>, D. Chandel, M. K. Jolly, and S. Gayen. Single cell analysis reveals x upregulation is not global in pre-gastrulation embryos. ***iScience***, page 104465, 2022

- K. Vipparthi, <u>K. Hari</u>, P. Chakraborty, S. Ghosh, A. K. Patel, A. Ghosh, N. K. Biswas, R. Sharan, P. Arun, M. K. Jolly, et al. Emergence of hybrid states of stem-like cancer cells correlates with poor prognosis in oral cancer. ***iScience***, 25(5):104317, 2022

- S. S. Varankar, <u>K Hari</u>, S. Kartika, S. A. Bapat, and M. K. Jolly. Cell geometry distinguishes migration-associated heterogeneity in two-dimensional systems. ***Computational and Systems Oncology***, 2(3), 2022

- M. Khot, D. Sreekumar, S. Jahagirdar, A. Kulkarni, <u>K. Hari</u>, E. E. Faseela, R. Sabarinathan, M. K. Jolly, and K. Sengupta. Twist1 induces chromosomal instability (cin) in colorectal cancer cells. ***Human molecular genetics***, 29(10):1673–1688, 2020

- A. Iyer, K. Gupta, S. Sharma, <u>K. Hari</u>, Y. F. Lee, N. Ramalingam, Y. S. Yap, J. West, A. A. Bhagat, B. V. Subramani, et al. Integrative analysis and machine learning based characterization of single circulating tumor cells. ***Journal of Clinical Medicine***, 9(4):1206, 2020

- S. Sahoo, A. Mishra, H. Kaur, <u>K. Hari</u>, S. Muralidharan, S. Mandal, and M. K. Jolly. A mechanistic model captures the emergence and implications of non-genetic heterogeneity and reversible drug resistance in er+ breast cancer cells. ***NAR cancer***, 3(3):zcab027, 2021

- S. Sahoo, S. P. Nayak, <u>K. Hari</u>, P. Purkait, S. Mandal, A. Kishore, H. Levine, and M. K. Jolly. Immunosuppressive traits of the hybrid epithelial/mesenchymal phenotype. ***Frontiers in immunology***, 12, 2021

- A. Nam, A. Mohanty, S. Bhattacharya, S. Kotnala, S. Achuthan, <u>K. Hari</u>, S. Srivastava, L. Guo, A. Nathan, R. Chatterjee, et al. Dynamic phenotypic switching and group behavior help non-small cell lung cancer cells evade chemotherapy. ***Biomolecules***, 12(1):8, 2021

- S. S. Khumukcham, V. Penugurti, A. Soni, V. Uppala, <u>K. Hari</u>, M. K. Jolly, A. Dwivedi, A. S. Pk, C. Padala, S. Mukta, et al. A reciprocal feedback loop between hif-1α and hpip controls phenotypic plasticity in breast cancer cells. ***Cancer letters***, 526:12–28, 2022

- P. Harlapur, A. S. Duddu, <u>K Hari</u>, P. Kulkarni, and M. K. Jolly. Functional resilience of mutually repressing motifs embedded in larger networks. ***Biomolecules***, 12(12):1842, 2022

Preprints

- B. Thurakkal, <u>K. Hari</u>, R. Marwaha, S. Karki, M. K. Jolly, and T. Das. Collective heterogeneity of mitochondrial potential in contact inhibition of proliferation. *bioRxiv (accepted in Biophysical Journal)*, 525600, Jan. 2023

- <u>K. Hari</u>*†, P. Harlapur*, A. Saxena, A. Girish, H. Levine, and <u>M. K. Jolly</u>†. Low dimensionality of phenotypic space as an emergent property of coordinated teams in biological regulatory networks. *bioRxiv*, 526930, Feb. 2023