BIOGRAPHICAL SKETCH

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NAME: Shah, Premal

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

POSITION TITLE: Assistant Professor

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)	END DATE MM/YYYY	FIELD OF STUDY
Anna University, Chennai, Tamil Nadu	BS	05/2006	Biotechnology
University of Tennessee, Knoxville, Tennessee	PHD	05/2011	Ecology and Evolutionary Biology
University of Pennsylvania, Philadelphia, Pennsylvania	Postdoctoral Fellow	12/2015	

A. Personal Statement

My research has focused on understanding the dynamics and evolution of translational regulation in a wide range of model and non-model organisms. We take a multidisciplinary approach by integrating expertise from molecular, evolutionary and computational biology to study how natural selection for efficient and accurate protein synthesis influences the evolution of genomic patterns, and how regulation of protein synthesis itself evolves during adaptation and speciation. This expertise puts me in a position to successfully lead the generation of high-throughput genomic datasets as well as the computational aspects of the proposed research. I have previously developed Bayesian models to estimate codon-specific elongation and mutation rates from genomic and gene expression datasets. My work also challenged a long-standing assumption in the field that codons with higher tRNA abundances have lower missense error rates, and that selection for accuracy is the primary force in shaping patterns of codon bias. I built upon this foundation to develop whole-cell models of protein translation parametrized with ribosome-profiling datasets. Our research currently focuses on generating ribosome-profiling and RNA-seq datasets and integrating them in a synthetic whole-cell modeling framework to understand the evolution and dynamics of translational regulation in E. coli, yeast, mouse, and humans. In addition, we use high-content live microscopy and flow-cytometry to study how post-transcriptional processes influence cell-to-cell variation in mRNA and protein abundances.

Ongoing and recently completed projects that I would like to highlight include:

NIH/NIGMS R35GM124976 09/14/17 – 08/31/22
Dynamics and evolution of translational regulation
Role: PI

NSF/BBSRC 1936046 07/01/19 – 06/30/22
RiboViz for reliable, reproducible and rigorous quantification of protein synthesis from ribosome profiling data
Role: PI

NIH/NIDDK R01DK124369 04/01/20 – 31/03/25
Defining post-transcriptional regulons in intestinal epithelial regeneration
Role: Sub-contract (PI: Kathryn Hamilton)

NIH/NIDDK R01DK056645-17A1 12/01/17 – 11/31/22
The LIN28b-Let7-IMP1 axis in colonic epithelial biology
Role: Sub-contract (PI: Anil Rustgi)

1. Cope,Alexander,L, Anderson,Felicity,, Favate,John,S, Jackson,Michael,, Mok,Amanda,, Kurowska,Anna,, MacKenzie,Emma,, Shivakumar,Vikram,, Tilton,Peter,, Winterbourne,Sophie,M, Xue,Siyin,, Kavoussanakis,Kostas,, Lareau,Liana,F, Shah,Premal,, Wallace,Edward,. riboviz 2: A flexible and robust ribosome profiling data analysis and visualization workflow. bioRxiv [Preprint]. 2021 May 17. Available from: http://dx.doi.org/10.1101/2021.05.14.443910 DOI: 10.1101/2021.05.14.443910
2. Favate,John,S, Liang,Shun,, Yadavalli,Srujana Samhita,, Shah,Premal,. The landscape of transcriptional and translational changes over 22 years of bacterial adaptation.. bioRxiv [Preprint]. 2021 January 13. Available from: http://dx.doi.org/10.1101/2021.01.12.426406 DOI: 10.1101/2021.01.12.426406
3. Morishita,Yoshikazu,, Fuentes,Ileana,, Favate,John,S, Zushida,Ko,, Nishi,Akinori,, Hevi,Charles,, Goldsmith,Noriko,, Buyske,Steve,, Sullivan,Stephanie,E, Miller,Courtney,A, Kandel,Eric,R, Uchida,Shusaku,, Shah,Premal,, Shumyatsky,Gleb,P. The gastrin-releasing peptide regulates stress-enhanced fear and dopamine signaling.. bioRxiv [Preprint]. 2021 January 01. Available from: http://dx.doi.org/10.1101/2020.12.31.424996 DOI: 10.1101/2020.12.31.424996
4. Carja O, Xing T, Wallace EWJ, Plotkin JB, Shah P. riboviz: analysis and visualization of ribosome profiling datasets. BMC Bioinformatics. 2017 Oct 25;18(1):461. PubMed Central PMCID: PMC5657068.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2016 -	Assistant Professor, Department of Genetics, Rutgers University, Piscataway, NJ
2011 - 2015	Postdoctoral Fellow, University of Pennsylvania, PHILADELPHIA, PA
2009 - 2011	Graduate Research Assistant, National Institute for Mathematical and Biological Synthesis, University of Tennessee, Knoxville, TN

Honors

2011	Jim Tanner Award for Outstanding Dissertation, Dept. of Ecology and Evolutionary Biology at University of Tennessee
2000	National Scholarship, Central Board of Secondary Education, New Delhi awarded to top 0.01% in Mathematics at the National level.

C. Contribution to Science

1. A major focus of my research has been to understand how various factors such as patterns of codon usage, transcript abundance, domain architecture, gene length, initiation and elongation rates jointly modulate the global pace of protein synthesis in a cell. To address this question, we have developed a mathematical and computational modeling framework that tracks every single ribosome, tRNA and mRNA molecule within a cell defined by its biophysical parameters and allows us to determine how translation of each gene is influenced by all other genes. By integrating these models with ribosome-profiling datasets, we have characterized the dynamics of translation in both healthy and stressed cells.

a. Favate,John,S, Liang,Shun,, Yadavalli,Srujana Samhita,, Shah,Premal,. The landscape of transcriptional and translational changes over 22 years of bacterial adaptation.. bioRxiv [Preprint]. 2021 January 13. Available from: http://dx.doi.org/10.1101/2021.01.12.426406 DOI: 10.1101/2021.01.12.426406
b. Carja O, Xing T, Wallace EWJ, Plotkin JB, Shah P. riboviz: analysis and visualization of ribosome profiling datasets. BMC Bioinformatics. 2017 Oct 25;18(1):461. PubMed Central PMCID: PMC5657068.
c. Weinberg DE, Shah P, Eichhorn SW, Hussmann JA, Plotkin JB, Bartel DP. Improved Ribosome-Footprint and mRNA Measurements Provide Insights into Dynamics and Regulation of Yeast Translation. Cell Rep. 2016 Feb 23;14(7):1787-1799. PubMed Central PMCID: PMC4767672.
d. Shah P, Ding Y, Niemczyk M, Kudla G, Plotkin JB. Rate-limiting steps in yeast protein translation. Cell. 2013 Jun 20;153(7):1589-601. PubMed Central PMCID: PMC3694300.

2. Evolution of biased codon usage

   Synonymous codons of an amino acid are used unequally across a genome. Several factors such as mutational biases, selection for translational accuracy and efficiency, mRNA folding etc., have been proposed to explain these patterns. However, their relative contributions to the observed codon usage patterns have been hard to quantify. As part of my graduate studies, I focused on developing a framework to tease apart the relative importance of various factors in determining codon bias. By integrating biochemical kinetics of tRNAs within a ribosome to their effects on translation errors and evolution of CUB, we revealed inherent trade-offs between translational accuracy and efficiency of a codon. As a result, this work challenged a long-standing assumption in the field that codons with higher tRNA abundances have lower missense error rates and that selection for accuracy is the primary force in shaping patterns of codon bias. Moreover, by nesting a model based on efficient ribosome usage during translation in a population-genetic framework, I was able to simultaneously estimate biases in mutation rates among codons, and codon-specific elongation rates. In addition to explaining the observed variation in codon usage across various genomes, these models have allowed us to tease apart the relative importance of adaptive and non-adaptive forces in shaping genomic codon choice.

   a. Cope,Alexander,L, Shah,Premal,. Intragenomic variation in mutation biases causes underestimation of selection on synonymous codon usage. bioRxiv [Preprint]. 2021 November 11. Available from: https://www.biorxiv.org/content/10.1101/2021.10.29.466462v1 DOI: 10.1101/2021.10.29.466462
   b. Gilchrist MA, Chen WC, Shah P, Landerer CL, Zaretzki R. Estimating Gene Expression and Codon-Specific Translational Efficiencies, Mutation Biases, and Selection Coefficients from Genomic Data Alone. Genome Biol Evol. 2015 May 14;7(6):1559-79. PubMed Central PMCID: PMC4494061.
   c. Shah P, Gilchrist MA. Explaining complex codon usage patterns with selection for translational efficiency, mutation bias, and genetic drift. Proc Natl Acad Sci U S A. 2011 Jun 21;108(25):10231-6. PubMed Central PMCID: PMC3121864.
   d. Shah P, Gilchrist MA. Effect of correlated tRNA abundances on translation errors and evolution of codon usage bias. PLoS Genet. 2010 Sep 16;6(9):e1001128. PubMed Central PMCID: PMC2940732.

3. Role of epistasis in protein evolution

   Understanding the nature of epistatic interactions between sites in a gene will allow us to address basic questions in biology at the molecular scale – such as how large a role does history play in molecular evolution? Do later events depend critically on specific earlier events, or do all events occur more or less independently? My research has explored these ideas in the context of protein evolution. My work has shown that amino-acid substitutions are typically contingent on the presence of prior substitutions and that substitutions that occur early in evolution become entrenched and difficult to modify as subsequent substitutions accrue. Such models provide key insights into the structure of a protein's fitness landscape and the effects of historical contingency on protein evolution.

   a. McCandlish DM, Shah P, Plotkin JB. Epistasis and the Dynamics of Reversion in Molecular Evolution. Genetics. 2016 Jul;203(3):1335-51. PubMed Central PMCID: PMC4937490.
   b. Shah P, McCandlish DM, Plotkin JB. Contingency and entrenchment in protein evolution under purifying selection. Proc Natl Acad Sci U S A. 2015 Jun 23;112(25):E3226-35. PubMed Central PMCID: PMC4485141.
   c. McCandlish DM, Rajon E, Shah P, Ding Y, Plotkin JB. The role of epistasis in protein evolution. Nature. 2013 May 30;497(7451):E1-2; discussion E2-3. PubMed PMID: 23719465.

4. Molecular phylogenetics

   Phylogenetic trees have long been important tools to study macroevolutionary patterns and in particular, to study how diversification rates vary through both time and across lineages. I have developed parametric methods to identify shifts in diversification rates in phylogenies. Such inferences are important to understand patterns of adaptive radiations and inform us about how specific geological or climatic events have shaped our current species diversity.

a. Fordyce JA, Shah P, Fitzpatrick BM. iteRates: An R Package for Implementing a Parametric Rate Comparison on Phylogenetic Trees. Evol Bioinform Online. 2014;10:127-30. PubMed Central PMCID: PMC4125422.
b. Niemiller ML, Fitzpatrick BM, Shah P, Schmitz L, Near TJ. Evidence for repeated loss of selective constraint in rhodopsin of amblyopsid cavefishes (Teleostei: Amblyopsidae). Evolution. 2013 Mar;67(3):732-48. PubMed PMID: 23461324.
c. Shah P, Fitzpatrick BM, Fordyce JA. A parametric method for assessing diversification-rate variation in phylogenetic trees. Evolution. 2013 Feb;67(2):368-77. PubMed PMID: 23356610.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/premal.shah.1/bibliography/public/