

**BIOGRAPHICAL SKETCH**

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NAME: Rama Reddy Goluguri

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

POSITION TITLE: Postdoctoral scholar

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)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Andhra University, India	BS	07/2003	07/2006	Biochemistry, Biotechnology, Chemistry
University of Hyderabad, India	MS	07/2006	07/2008	Biochemistry
National Centre for Biological Sciences, India	PhD	08/2011	03/2018	Biology
University of California, Merced, USA	Postdoctoral	06/2018	9/2021	Biochemistry/ Biophysics
Stanford University School of Medicine, USA	Postdoctoral	10/2021	Present	Biochemistry/ Biophysics

**A. Personal Statement**

My long-term research interest is to understand the relationship between protein conformational dynamics and its function. I am particularly interested in how the sequence of a protein codes for its conformational dynamics and how these motions in the proteins are functionally relevant. Changes in protein sequence due to mutation result in change in their stability and conformational dynamics, and in some cases such changes result in diseases. I have gained expertise in experimental methodologies to quantify the motions in the protein over different timescales during my doctoral and postdoctoral studies.

I studied the protein folding reaction in my graduate studies in Prof. Jayant Udgaonkar's lab at National Centre for Biological Sciences, India. I developed a microsecond mixer to study fast events (deadtime of 35  $\mu$ s) during folding reaction which were impossible to study using commercial stopped flow mixer. I used this methodology to study the fast-folding events for three different proteins (monellin, SH3 domain of PI3 Kinase and mouse prion protein) which resulted in 4 publications. Then I went on to develop the fluorescence correlation spectroscopy methodology to investigate protein dynamics under equilibrium conditions. I studied mouse prion protein using this methodology and investigated what causes the mutant proteins to undergo aggregation and found out that the protein samples partially unfolded conformations which are more prone to aggregations. The mutations that cause aggregation stabilizes these partially unfolded conformations. This led to my 5<sup>th</sup> publication from my PhD.

I then joined Prof. Victor Munoz's lab at UC Merced as postdoctoral scholar in 2018. My research at UC Merced was focused on understanding protein-DNA interactions by utilizing single molecule FRET and optical tweezers. I have established the optical tweezers methodology in the lab, using which we have been able to show the importance of a protein's folding mechanism in its function. We have studied the effect of transcriptional factors structural dynamics on their ability to scan the DNA for its target site. I also worked on the mechanism of protein fold switching, where a single protein exists in two different structures depending on the solution conditions. I am currently working on three manuscripts with Victor which will be out in the next one year.

I recently joined the Spudich lab (October 2021) to learn about motor protein myosin. I am interested in how point mutations in myosin result in disease phenotypes at molecular level. Currently, I am interested in developing a fluorescence-based sensor to characterize the clinically relevant folded-back state of myosin and how it relates to HCM and DCM pathogenesis. I am using my expertise in site specific labeling of proteins and single molecule techniques to design the sensor. I am also interested in establishing transient kinetic assays to study different steps of chemo mechanical cycle of myosin in Spudich lab. The end-goal of my postdoctoral training is to have an independent academic career in an institute which has both research and teaching opportunities. Spudich lab provides me with the opportunities to collaborate and discuss my work with leaders in the field of motor proteins. I am also planning on presenting my work in various conferences focused on biophysics and motor proteins. I am also looking for opportunities to improve my writing and teaching skills. I am planning on taking courses on teaching offered by Stanford University. I am hoping my experience at Spudich lab and Stanford university will help me reach my career goal of becoming an independent researcher in the field of protein biophysics.

## **B. Positions, Scientific Appointments and Honors**

2008-2011 Technical Trainee, Junior Scientist, Assistant Manager at Dr. Reddy's Laboratory, an Indian multinational pharmaceutical company.  
2011-2018 Graduate student Prof. Jayant Udgaonkar's lab at National Center for Biological Sciences, India  
2018-2021 Postdoctoral Scholar Prof. Victor Munoz lab at UC Merced, United States  
2021- Postdoctoral Scholar Prof. James Spudich lab at Stanford University

## **C. Contributions to Science**

### **Associate manager Dr.Reddy's Laboratories**

I worked at Dr. Reddy's Laboratories Ltd, which is one of India's largest pharmaceutical companies, based in Hyderabad, for three years (2008-11). I joined the company after my masters as a Technical Trainee and was soon promoted to the post of a Junior Scientist and finally the Associate Manager. During the three years that I spent in the Research and Development department of Dr. Reddy's Labs, I was involved mostly in method development. I extensively used various HPLC-based analytical methods and capillary electrophoresis methods to assess the purity of pharmaceutical proteins. I developed a new method to estimate the number of protein molecules with their C-terminal lysine residues cleaved in an ensemble, for which I received the Stellar performance award from Dr. Reddy's Laboratories.

### **Graduate Studies:**

As a graduate student in Prof. Jayant Udgaonkar's lab I worked on answering important questions related to protein folding and protein aggregation. We aimed at understanding the role of polypeptide chain compaction during folding reaction. The polypeptide chain compaction happens within a millisecond of initiating folding reaction and can not be captured by commercial stopped flow mixers which have a mixing dead time of few milliseconds. To address this technological limitation, I constructed a microsecond mixer with a mixing dead time of 35 microseconds. We used this methodology to look at the early events of folding for 3 different proteins and these experiments resulted 4 publications. I presented my work at different conference in India

- Moullick, R., **Goluguri, R.** and Udgaonkar, J. B. (2018) Ruggedness in the Free Energy Landscape Dictates Misfolding of the Prion Protein. *JMB*, vol 431, issue 4, 807-824.
- Sen, S., **Goluguri, R.** and Udgaonkar, J. B. (2017) A dry transition state more compact than the native state is stabilized by non-native interactions during the unfolding of a small protein. *Biochemistry* 56, 3699-3703.
- **Goluguri, R.** and Udgaonkar, J. B. (2016) Microsecond rearrangements of hydrophobic clusters in an initially collapsed globule prime structure formation during the folding of a small protein. *J. Mol. Biol.* 428, 3102-3117.
- **Goluguri, R.** and Udgaonkar, J. B. (2015) Rise of the helix from a collapsed globule during the folding of monellin. *Biochemistry* 54, 5356-5365.

In the last two years of my graduate training, I established fluorescence correlation spectroscopy methodology in the lab. Using this methodology, we studied the dynamics of the mouse prion protein under equilibrium conditions and try to understand the link between protein dynamics and protein aggregation. I have trained several undergraduate and graduate students in the lab.

- **Goluguri, R.,** Sen, S. and Udgaonkar, J. B. (2019) Microsecond sub-domain motions and folding and misfolding of mouse prion protein. *eLife*, e44766

#### **Post-doctoral fellow in Prof. Victor Munoz's lab.**

During my first postdoc training in Munoz lab, I have studied protein dynamics and their relation to function. I have initiated optical tweezers methodology in the lab. I worked on transcription factor Engrailed homeodomain and looked at the mechanism by which it searches for its target site on DNA and how conformational dynamics of the protein effect the DNA scanning function of transcription factors. I have presented this work in different international conferences and currently two manuscripts under preparation.

- **Goluguri, R.,** Sadqi, M., and Muñoz, V., DNA scanning mechanism of a eukaryotic transcription factor. (Manuscript under preparation)
- **Goluguri, R.,** Sadqi, M., Tanielian, B., and Muñoz,V., Functional role of protein disorder in eukaryotic gene regulation. (Manuscript under preparation)

#### **Post-doctoral fellow in Prof. James Spudich lab.**

In Spudich lab I am working on how point mutations in cardiac myosin results in cardiomyopathy phenotype at molecular level. It was hypothesized that the inactive state of the cardiac myosin called super relaxed state (SRX) plays a major role in pathomechnism of several cardiomyopathies. I am working on developing a fluorescence-based sensor to quantify the SRX state in solution. I mentored a undergraduate student during summer 2022 for the Stanford Cardiovascular Institute summer program.

#### **Academic and Professional Honors and Awards**

- 2022-Rapidfire talk in Biological fluorescence subgroup in Biophysical Society meeting
- **2021-** Best poster award in Biochemistry section at UC Chemical symposium
- **2017-**Invited talk FCS 2017, National workshop on fluorescence and Raman spectroscopy, Guwahati,India;December 17-21, 2017.
- **2010-**Stellar performance award from Dr.Reddy's Laboratory
- **2010-** Pingali Mohan Reddy medal for Best Overall Performance in School of Life Sciences, University of Hyderabad, 2006-2008 batch.
- **2010-** Prof. A. N. Radhakrishnan Memorial Medal, for best performance in Biochemistry department, University of Hyderabad, 2006-2008 batch.
- 2006-08 Achievers award scholarship during masters at University of Hyderabad.

#### **Other Experiences and Professional Memberships**

- 2018- Member, The Protein Society
- 2021 - Member, The Biophysical Society
- 2022- Member, American Heart Association

#### **D. Scholastic Performance**

Scientific computing course by Prof. Michael colvin at UC Merced

I have taken the following courses at National Centre for Biological Sciences during my graduate studies in the year 2011-2012. Only a pass or fail grade is given which are indicated beside the course name

- Developmental Biology (P)
- Introduction to Laboratory Practices (P)
- Mathematics: Pre-calculus and differential calculus (P)
- Physical Biochemistry (P)
- Scientific Communication (Mandatory course; no grade given)

#### **Conference Abstracts**

Goluguri, R. R., Sadqi, M., & Munoz, V. (2022). Transcriptional factors control their diffusion on DNA by modulating their dynamics. *Biophysical Journal*, 121(3), 457a.

Goluguri, R. R., Sadqi, M., Nagpal, S., & Munoz, V. (2021, October). Functional Role of Protein Disorder in Eukaryotic Gene Regulation. In *PROTEIN SCIENCE* (Vol. 30, pp. 64-64). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY.

Moulick, R., Goluguri, R. R., & Udgaonkar, J. B. (2017). Role of Folding Intermediates in Initiating Aggregation of the Prion Protein. *The FASEB Journal*, 31, 763-6.

Moulick, R., Goluguri, R. R., & Udgaonkar, J. B. (2018). pH-Induced Frustration in the FREE Energy Landscape Dictate Misfolding of the Prion Protein. *Biophysical Journal*, 114(3), 415a.