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Website:
https://www.mithunnag.com/

Technical Skills

In-Vitro

- *Protein purification (native and denaturing conditions)*
- *Thermodynamic analysis of folding and ligand binding*
- *NMR spectroscopy and X-ray crystallography*
- *TR-FRET, Fluorescence Polarization, Intrinsic Fluorescence, circular dichroism, and BLI*
- *Mass spectrometry (LC-MS, MALDI-TOF)*
- *DLS and MALS for size and aggregation*
- *Atomic force microscopy*
- *Cloning: Gibson assembly and site-directed mutagenesis*
- *Western blotting for protein detection and validation*

In-Vivo

- *Mammalian cell culture (HEK293T, 3T3-L1)*
- *Transfection-based reporter assays*
- *Functional validation of drug binding (luciferase assays)*
- *Flow cytometry for cellular profiling and analysis*
- *Scanning and transmission electron microscopy (SEM, TEM)*

In-Silico

- *Molecular dynamics simulations (GROMACS, AMBER),Pymol, Chimera*
- *Python-based data pipelines (on Jupyter notebook)*
- *GraphPad Prism for statistical analysis and data visualization*
- *Bioinformatics tools for sequence analysis and structural modeling*
- *AI-guided protein and peptide design Progen2, Boltz-2, Bioemu*

Mithun Nag K.G.

Personal Statement

With a foundation in structural biology and biophysics, I have **developed unique experimental and computational strategies to identify, characterize, and stabilize high-energy transient intermediates** that govern protein function. My PhD integrated thermodynamic analysis with ancestral reconstruction to reshape folding landscapes and engineer caspases with tunable specificity by selectively stabilizing intermediate states. During my postdoctoral training, I uncovered ligand-induced conformational dynamics in nuclear receptors, demonstrating that ligands bind transient intermediate ensembles and actively remodel the conformational landscape, as revealed by NMR and complementary biophysical and computational approaches. By integrating in vitro, in vivo, and in silico methods, my work provides mechanistic insight into how ligand binding exploits dynamic protein ensembles to enable structure-guided drug discovery.

Research Experience

Vanderbilt University - Postdoctoral Fellow
Nashville, TN
08/2023 - 06/2025

I investigated the **conformational dynamics of nuclear receptors** which are **transcription factors targeted by ~15% of FDA-approved drugs**. My work focused on **PPARγ**, involved in **diabetes and cancer**, and **Nurr1**, a promising target in **neurodegenerative diseases like Alzheimer's**.

- Contributed to characterizing **the structural and dynamic effects of FX-909 on PPARγ**, a covalent **inverse agonist from Fair Therapeutics in clinical trials for bladder cancer**, which stabilizes the receptor in a transcriptionally repressive conformation
- Helped show that **SR33065 and SR36708, analogs of T0070907, shift PPARγ into a repressive conformation** but still allow ligand binding, revealing a limitation of current inverse agonists and **informing the design of more effective covalent inhibitors** for diabetes and cancer therapy
- Discovered that **polyunsaturated fatty acids bind a high-energy intermediate of Nurr1 and PPARγ**, revealing a druggable disordered state relevant to neurological disorders and diabetes, and **supporting strategies like Sibylla Biotech that target intermediate conformational states** rather than static binding pockets

These studies reflect my core strength **in integrating protein dynamics into drug discovery**. With deep **expertise in high-energy states, conformational ensembles, NMR, and computational modeling**, I go beyond static structural snapshots to uncover how ligands reshape protein energy landscapes—driving **ensemble-based approaches** for more selective and effective therapeutics.

University of Texas at Arlington - Graduate Research
Arlington, TX

Education

05/2023
Ph.D.
Quantitative Biology
University of Texas At Arlington
Arlington, TX, USA

12/2017
M.S.
Bioengineering
University of Texas at Arlington
Arlington, TX, USA

05/2015
B.E.
Biotechnology
BMS College of Engineering
Bangalore, Karnataka, India

08/2018 - 05/2023

Caspases are central regulators of apoptosis and inflammation, with emerging roles in cancer, immune signaling, and cell differentiation. My PhD research explored how **folding mechanisms, evolutionary pressures, and conformational dynamics shape** caspase **function and regulation** across subfamilies.

- Investigated the folding landscapes of caspases-8 and cFLIP**, identifying a conserved high-energy intermediate**, a pH-dependent conformational switch, and early unfolding of the small subunit suggesting an evolutionary drive toward dimerization in effector caspases
- **Reconstructed and characterized an ancestral carnivora inflammatory caspase**, uncovering evolutionary tradeoffs in IL-1β and gasdermin D cleavage specificity
- **Mapped conserved allosteric networks and intermediate states across 500 million years of caspase evolution** using ancestral reconstruction, MD simulations, and network analysis

This work shaped my view of macromolecules as dynamic ensembles, including high energy intermediates, and equipped me with evolutionary tools to design biologics such as peptides, antibodies, or proteins using epistatic mutations for tunable specificity.

Harvard University SEAS - Lab Engineer
03/2018 - 08/2018
Designed microfluidics-based sensors with Arduino to monitor soil nutrients for environmental applications, and **mentored international students in building low-cost water purification systems**. **Taught undergraduates to operate HPLC** systems and analyze chemical contaminants, and **developed 3D Matrigel-based cell culture modules** for the Biostar Summer Program to better simulate in vivo physiology.

Everest Biotech - Laboratory Assistant
05/2015 - 09/2015
Research on chitosan derivatives for antibiotic properties and purification of kokum butter for use as ointment base

Awards and Leadership

Received the NSF XSEDE Startup Award and a FASEB Conference Travel Award (2022). Served as Academic Co-Chair of the Vanderbilt Postdoc Association and Postdoc Liaison for the Biochemistry Postdoc Association, co-organizing the 18th and 19th Vanderbilt Postdoc Symposia and presenting research at multiple international conferences through oral and poster presentations.

CREATIVE SCIENCE COMMUNICATION

Animations using MD trajectories and Adobe tools (Illustrator, Animate and Premier Pro) to communicate research findings