## BIOGRAPHICAL SKETCH

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NAME: Vidhya Rangaraju

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

POSITION TITLE: Research Group Leader

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 |
|---|---|---|---|---|
| **Anna University** Chennai, India | B. Tech | 07/2002 | 05/2006 | Industrial Biotechnology |
| **National Center for Biological Sciences** Bengaluru, India | | 06/2006 | 05/2007 | Chemical Biology |
| **Cornell University** Ithaca, NY, USA | | 07/2007 | 06/2008 | Chemistry and Chemical Biology |
| **Weill Cornell Medicine (WCM)** New York, NY, USA | PhD | 07/2008 | 01/2014 | Chemical Biology and Neuroscience |
| **Max Planck Institute for Brain Research (MPIBR)** Frankfurt, Germany | Postdoc | 02/2014 | 12/2019 | Neuroscience |

**A. Personal Statement**

I am a Research Group Leader at the Max Planck Florida Institute for Neuroscience (MPFI). My lab seeks to **bridge the knowledge gap between mitochondria and memory formation**. Our findings indicate that mitochondria undergo structural remodeling and synthesize energy on demand in response to synaptic plasticity (a, b, c). We have also shown that mitochondria are locally stabilized near synapses to meet the immediate and local energy demands of synaptic plasticity (b, c, d, e). We employ several cutting-edge approaches, including subcellular proteomics, CRISPR-based proteomic screening, **state-of-the-art ATP** and calcium imaging in the spine and mitochondria, and various genetic and biochemical tools to **identify the fundamental mitochondrial mechanisms that drive synaptic plasticity**. We investigate different forms and stages of learning and memory (spatial, motor, short-term, and long-term). I have mentored several trainees over my six-year career as an independent investigator, all of whom have been successful in their academic pursuits. I lead an eight-member, multi-disciplinary research team with a skill set that spans cellular and molecular biology, super-resolution and electron microscopy, advanced proteomics, in vivo imaging, and animal behavior in rodent, human, and disease models. Our group is ideally positioned with the wealth of additional expertise at the MPFI.

During my Ph.D. in Timothy Ryan's lab at Weill Cornell Medicine, **I developed and employed a novel luciferase-based ATP reporter** (U.S. Patent 9487819 B2) and demonstrated that ATP is locally produced at synaptic terminals in response to neuronal activity. I found that the synaptic vesicle cycling pathway consumes the most energy in nerve terminals. Even brief perturbations in activity-driven ATP synthesis dramatically affected the synaptic vesicle cycling pathway and the subsequent synaptic communication (a). As such neuronal defects have been observed in many neurological disorders, these results emphasize the **importance of synthesizing ATP on demand to support synaptic function**.

This work further inspired me to understand the mechanisms underlying energy supply during memory formation in postsynaptic spines. As a postdoc in Erin Schuman's lab at the Max Planck Institute for Brain Research in Germany, I developed novel approaches to visualize newly synthesized proteins in spines using two-photon glutamate uncaging, locally manipulate mitochondrial function via optogenetics, and image live mitochondria using super-resolution. As a result, I showed that mitochondria form stable compartments that serve as the local energy supply for synaptic plasticity. Furthermore, I demonstrated the **importance of a local energy source, mitochondria, in fueling the molecular players required for protein synthesis and memory formation, the absence of which could result in memory impairment** (d).

Consistent with my track record of tackling uncharted research questions with novel approaches, we continue to address our research questions rigorously. The publications listed below are selected to highlight my expertise in the methods and questions we address in our research program:

a. **Vidhya Rangaraju**, Nathaniel Calloway, Timothy A. Ryan, Activity-Driven Local ATP Synthesis Is Required for Synaptic Function, ***Cell*** 156, 825 (2014). PMCID: PMC3955179. Number of citations: 889.
b. Ilika Ghosh, Ruolin Fan, Monil Shah, Ojasee Bapat, **Vidhya Rangaraju***, Synapses drive local mitochondrial ATP synthesis to fuel plasticity, ***bioRxiv*** 10.1101/2025.04.09.648032, in revision. Number of citations: 3. *corresponding author.
c. Monil Shah, Ilika Ghosh, Luca Pishos, Valentina Villani, Tristano Pancani, Ryohei Yasuda, Chao Sun, Naomi Kamasawa, **Vidhya Rangaraju***, Mitochondria structurally remodel near synapses to fuel the sustained energy demands of plasticity, ***bioRxiv*** 10.1101/2025.08.27.672715 (2025), in review. PMID: 40909516. PMCID: PMC12407993. *corresponding author.
d. **Vidhya Rangaraju**, Marcel Lauterbach, Erin M. Schuman, Spatially Stable Mitochondrial Compartments Fuel Local Translation during Plasticity, ***Cell*** 176, 73 (2019). PMID: 30612742. Number of citations: 393. *Special commentary:* Crosstalk of local translation and mitochondria: powering plasticity in axons and dendrites, *Neuron* 101, 204 (2019).
e. Ojasee Bapat, Tejas Purimetla, Sarah Kruessel, Monil Shah, Ruolin Fan, Christina Thum, Fiona Rupprecht, Julian D. Langer, **Vidhya Rangaraju***, VAP spatially stabilizes dendritic mitochondria to locally support synaptic plasticity, ***Nature Communications***, 15, 205 (2024). PMCID: PMC10766606. Number of citations: 36. *corresponding author.

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

Positions and Scientific Appointments

| | |
|---|---|
| 01/2020 – present | Research Group Leader, Rangaraju Neuroenergetics Lab, MPFI, USA |
| 10/2020 – present | Affiliate Faculty, Charles E. Schmidt College of Science, Florida Atlantic University, USA |
| 02/2014 – 12/2019 | Postdoctoral Fellow, Erin M. Schuman Lab, MPIBR, Germany |
| 07/2008 – 01/2014 | Graduate Student, Timothy A. Ryan Lab, Weill Cornell Medicine, USA |
| 01/2008 – 05/2008 | Project Assistant, Barbara Baird Lab, Cornell University, USA |
| 06/2006 – 05/2007 | Junior Research Fellow, National Centre for Biological Sciences, India |
| 05/2004 – 06/2004 | CSIR Program on Youth for Leadership in Science, CLRI, India |

Honors

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|---|---|
| 05/2025 | McKnight Scholars Program Finalist |
| 12/2024 – 12/2025 | Chan Zuckerberg Neuroscience Collaboration Supplement |
| 09/2024 – 08/2029 | NIH Director's New Innovator Award (DP2) |
| 09/2024 | Society for Neuroscience Janett Rosenberg Trubatch Career Development Award |
| 10/2023 | CZI Ben Barres Early Career Acceleration Award |
| 03/2023 | HHMI Freeman Hrabowski Scholars Program Finalist |
| 07/2022 – 09/2023 | Louis D. Srybnik and F.O.R.E Foundation Grant |
| 07/2021 – 09/2023 | Louis D. Srybnik Foundation Grant |
| 10/2020 | Peter and Patricia Gruber International Research Award, Society for Neuroscience |
| 12/2019 | Scientific Discovery of the Year, MPIBR |
| 09/2019 | GRADE Brain Travel Grant |
| 04/2019 | MacGillavry Fellowship, University of Amsterdam (declined) |

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|---|---|
| 06/2018 | Lindau Nobel Laureate Meeting Award |
| 09/2015 | GlaxoSmithKline Stiftung Travel Grant |
| 09/2015 | EMBO Workshop Travel Grant |
| 03/2015 | Humboldt Research Fellowship for Postdoctoral Researchers (declined) |
| 02/2015 | Marie Curie Actions Individual Fellowship 2016-2017 |
| 12/2014 | EMBO Long-Term Postdoctoral Fellowship 2015 |
| 04/2012 | Vincent du Vigneaud Award of Excellence, WCM, USA |
| 11/2007 | Best Poster Prize, Chemical Biology Student Symposium, Cornell University, USA |
| 06/2006 – 06/2007 | Junior Research Fellowship, National Centre for Biological Sciences, India |
| 06/2001 – 06/2004 | CSIR Program for Youth on Leadership in Science fellowship, CSIR, India |

Memberships of Scientific Societies

| | |
|---|---|
| From 02/2018 | Lindau Nobel Laureate Meetings Alumni |
| From 01/2016 | Marie Curie Fellows |
| From 01/2015 | EMBO Long-Term Fellows |
| 01/2011 – 12/2011 | Society for Neuroscience |

Service

| | |
|---|---|
| Manuscript Reviewer | Science, PNAS, Nature Biotechnology, Nature Neuroscience, Nature Communications, Nature Microbiology, Cell Reports, EMBO Reports, Current Opinion in Cell Biology, Cell Calcium, iScience, Frontiers in Cell and Developmental Biology, PLOS Biology, Seminars in Cell and Developmental Biology, BMC Biology, Neurophotonics, Journal of Cellular Physiology, Biochemical Society transactions, Histology and Histopathology. |
| Grant Reviewer | Human Frontier Science Program (HFSP) Postdoc Fellowships, France; Motor Neurone Disease Association, UK; NIH, F03A Study Section, Center for Scientific Review, USA; Minerva Foundation GmbH, Germany; NIH Early Career Reviewer, NDPR Study Section, Center for Scientific Review, USA; Israeli Ministry of Innovation, Science, and Technology, Israel; Israel Science Foundation, Israel; Human Frontier Science Program (HFSP) Research Grants, France; Chan Zuckerberg Initiative Collaborative Pairs Program, USA |
| External Board | EMBO Reports, Germany; NeuroNex2, NSF grant, USA |
| Selection Committee | Faculty search, Okinawa Science and Technology, Japan; Faculty search, UF Scripps Neuroscience, USA; Peter Gruss Young Investigator Award, MPFI, USA; NeuroMEETS, MPFI, USA; IMPRS graduate program, MPFI, USA; IMPRS graduate program, MPIBR, Germany |
| Thesis Committee | Michael Maibach, Lohmann Lab, NINS, Netherlands; Brittni R. Walker, Moraes Lab, U Miami, USA; Yiwei Hua, Tian Lab, MPFI, USA; Carlos C. Ramos, Morais Lab, Univer. de Lisboa, Portugal; Yibo Zhao, Puthanveettil Lab, UF Scripps |
| Lecturer | Advanced Neuroimaging Techniques, MPFI imaging course, USA; IMPRS graduate program, MPIBR, Germany; MPIBR Teaching Lab, Germany |
| Seminar Chair | Organelle Biology and Metabolism, CZI Neuroscience 2024, USA; Trafficking Club, Department of Biochemistry, WCM, USA |
| Career Seminar | iJOBS, Rutgers Robert Wood Johnson Medical School, USA; Johns Hopkins School of Medicine, USA; MPFI Postbaccalaureate Program, USA; Max Planck Career Day, MPIBR, Germany |
| Panel Discussion | Music and Mind with opera legend Renée Fleming, Kravis Center, USA; Celebration of Women in Neuroscience, Society for Neuroscience, USA; Future of Dendritic Research, EMBO Workshop, Greece; Tri-I PhD Program in Chemical Biology retreat, USA; Network for Women in Science, MPFI, USA |
| Public Lecturer | Science Meets Music, MPFI, USA; MPFI Institute Breakfast, Board of Trustees Meeting, USA; Night of Science, Germany; Bar of Science, Germany; Cornell Alumni Ivy Circle, Germany |
| Others | IACUC Scientific Member, MPFI, USA; Founder and Postdoctoral Association Representative, MPIBR, Germany; Neuroscience Study Guide Author & Editor, German Neuroscience Olympiad, Germany |

**C. Contributions to Science**

**1. Identified the energy consumers and the mechanisms of energy synthesis in presynaptic terminals**

The brain consumes 20% of the human body's total energy to perform critical functions, including learning and memory formation. While neuronal synapses are hotspots of energy consumption, the locus of metabolic control was unknown. To address this question, I developed an optical reporter (U.S. Patent, see 4a) to visualize and measure changes in ATP levels in individual living nerve terminals. In addition, I custom-built a highly sensitive microscope, as conventional microscopes could not measure the luminescence signal produced by the luciferase. Using these novel approaches, I found that **ATP is locally produced at synaptic terminals in response to neuronal activity to fuel synaptic transmission**. Furthermore, I genetically disrupted the synaptic vesicle cycling pathway and showed that synaptic vesicle cycling consumes the most energy in nerve terminals. This research, published in *Cell*, shed new light on the **molecular balance between electrical activity and synaptic energy synthesis** (1a). Our findings started a new paradigm for studying the metabolic control of cognition and neurodegeneration (1b), changed the research direction of the Ryan Lab (Ph.D. lab), and inspired me to establish my lab to study Neuroenergetics. I have presented this work at conferences, including the Society for Neuroscience and The Gordon Research Conference for Cell Biology of the Neuron (1c, 1d).

a. **Vidhya Rangaraju**, Nathaniel Calloway, Timothy A. Ryan, Activity-Driven Local ATP Synthesis Is Required for Synaptic Function, ***Cell*** 156, 825 (2014). PMCID: PMC3955179.
b. Sen Yang, Zhen-Xian Niou, Andrea Enriquez, Jacob LaMar, Jui-Yen Huang, Karen Ling, Paymaan Jafar-Nejad, Jonathan Gilley, Michael P. Coleman, Jason M. Tennessen, **Vidhya Rangaraju***, Hui-Chen Lu, NMNAT2 supports vesicular glycolysis via NAD homeostasis to fuel fast axonal transport, ***Molecular Neurodegeneration*** 19, 13 (2024). PMCID: PMC10823734. *senior author
c. **Vidhya Rangaraju,** Timothy A. Ryan. Syn-ATP: A Novel Optical Reporter of Presynaptic ATP Levels. ***Society for Neuroscience*** (2011).
d. **Vidhya Rangaraju,** Timothy A. Ryan. Syn-ATP: A Novel Optical Reporter of Presynaptic ATP Levels. ***Gordon Research Conference, Cell Biology of the Neuron*** (2012).

**2. Discovered the local mechanisms of energy synthesis in postsynaptic spines and dendrites**

Memory formation is highly energy-consuming but its energy supply was unknown. I addressed this question for my postdoctoral work by developing tools to label newly made proteins in spines following spine stimulation, locally disrupt mitochondrial function by optogenetics, and resolve live mitochondrial structures by super-resolution. Using these new approaches, **I showed that locally stable mitochondria fuel the protein synthesis required for synaptic plasticity, a cellular correlate for memory formation,** published in *Cell* (2a). Using an unbiased proteomic screening approach, we identified that **VAP (Vesicle-Associated Membrane protein-associated Protein), a protein implicated in amyotrophic lateral sclerosis, is a molecular glue that stabilizes mitochondria by tethering them to actin,** published in *Nature Communications* (2b). We developed novel imaging tools and strategies to measure ATP within individual spines and mitochondria to show that the **locally stable mitochondria near dendritic spines generate instant and sustained ATP to support synaptic plasticity** (2c). We recently developed a CLEM/ET pipeline along with machine learning based EM image segmentations and quantification to show that the locally stable **mitochondria near spines undergo substantial structural remodeling in their inner cristae structure, energy synthesis machinery, and their associations with endoplasmic reticulum and ribosomes to generate the ATP** needed to support neuronal plasticity (2d).

a. **Vidhya Rangaraju,** Marcel Lauterbach, Erin M. Schuman, Spatially Stable Mitochondrial Compartments Fuel Local Translation during Plasticity, ***Cell*** 176, 73 (2019). PMID: 30612742.
b. Ojasee Bapat, Tejas Purimetla, Sarah Kruessel, Monil Shah, Ruolin Fan, Christina Thum, Fiona Rupprecht, Julian D. Langer, **Vidhya Rangaraju***, VAP spatially stabilizes dendritic mitochondria to locally support synaptic plasticity, ***Nature Communications***, 15, 205 (2024). PMCID: PMC10766606. *corresponding author.
c. Ilika Ghosh, Ruolin Fan, Monil Shah, Ojasee Bapat, **Vidhya Rangaraju***, Synapses drive local mitochondrial ATP synthesis to fuel plasticity, ***bioRxiv*** 10.1101/2025.04.09.648032 (2025), in revision. *corresponding author.
d. Monil Shah, Ilika Ghosh, Luca Pishos, Valentina Villani, Tristano Pancani, Ryohei Yasuda, Chao Sun, Naomi Kamasawa, **Vidhya Rangaraju***, Mitochondria structurally remodel near synapses to fuel the sustained energy demands of plasticity, ***bioRxiv*** 10.1101/2025.08.27.672715 (2025), in review. PMID: 40909516. PMCID: PMC12407993. *corresponding author.

**3. Characterized the cellular mechanisms of dendrites during plasticity**

As neurons have a complex morphology, it was unclear how they accomplish the large-scale resource allocation of proteins and RNAs to meet local demands during plasticity, given a fixed global budget for protein production. It was unclear how local spine stimulation influence the size of the translation compartments, including the spatial spread of the nascent protein and RNA. We used metabolic labeling and DNA-PAINT to visualize and quantify nascent proteins during plasticity. We discovered a **local 'neighborhood' of synapses that are allotted with newly made proteins during spine plasticity**, published in *Science Advances* (3a). We also showed that **long non-coding RNAs are recruited to plasticity-induced spines for mediating structural plasticity and fear memory consolidation**, published in *Nature Communications* (3b). With our ongoing interest in unraveling the significance of the mitochondria and endoplasmic reticulum in cellular mechanisms within dendrites, we showed that: (i) **ER forms a ladder-like array along dendrites to enable long-range calcium propagation important for dendritic computations and plasticity** (3c); (ii) as mitochondria can serve as calcium regulators, we showed the significance of **mitochondria in maintaining spine and dendritic calcium to maintain long-term memory using state-of-the-art mitochondrial calcium imaging** (3d).

a. Chao Sun, Andreas Nold, Claudia M. Fusco, **Vidhya Rangaraju*,** Tatjana Tchumatchenko, Mike Heilemann, Erin M. Schuman. The Prevalence and Specificity of Local Protein Synthesis during Neuronal Synaptic Plasticity, ***Science Advances*** 7, eabj0790 (2021). PMCID: PMC8448450. *senior author.
b. Isabel Espadas, Jenna L. Wingfield,…Ryohei Yasuda, **Vidhya Rangaraju***, Sathyanarayanan Puthanveettil, Synaptically-targeted long non-coding RNA SLAMR promotes structural plasticity by increasing translation and CaMKII activity, ***Nature Communications*** 15, 2694 (2024). PMCID: PMC10973417. *senior author.
c. Lorena Benedetti, Ruolin Fan, …Harald F. Hess, Stephan Saalfeld, **Vidhya Rangaraju***, David E. Clapham, Pietro De Camilli, Timothy A. Ryan, Jennifer Lippincott-Schwartz, Periodic ER-plasma membrane junctions support long-range Ca2+ signal integration in dendrites, ***Cell*** 188, 484 (2025). *senior author.
d. Anjali Amrapali Vishwanath, …Thomas Preat, Tim P. Vogels, **Vidhya Rangaraju***, Arnau Busquets-Garcia, Pierre-Yves Placais, Alice Pavlowsky, Jaime de Juan-Sanz, Mitochondrial Ca2+ efflux controls neuronal metabolism and long-term memory across species, ***Nature Metabolism***, in press (2025).

**4. Developed genetically encoded tools to probe energy synthesis and protein synthesis mechanisms in neurons**

I have actively contributed to neuroscience by developing novel tools to dissect different mechanisms of neuronal biology. **I designed, optimized, and characterized a novel ATP reporter based on the firefly enzyme luciferase to quantify ATP concentrations in living nerve terminals** (4a, 4b). This work influenced my Ph.D. mentor Tim Ryan to veer his research direction toward synaptic metabolism, encouraging a new generation of trainees from his and other labs to establish their careers on neuronal metabolism and disease. We modified this presynaptic ATP reporter by targeting it to postsynaptic-(Homer2) and mitochondria-(COX8) targeting proteins to **measure ATP levels in spines and mitochondria**, respectively (4c). During my postdoctoral work, I developed a **genetically encoded protein synthesis inhibitor to inhibit protein synthesis and memory formation in a single neuron**, published in *Nature Methods* (4d). The development of this reporter allows for the manipulation of structural plasticity in a cell-type-specific manner, a process widely known to be part of memory consolidation. Recently, we developed a **new palette of organellar calcium sensors for endoplasmic reticulum and mitochondria to study organellar function in neurons** (4d).

a. **Vidhya Rangaraju**, Nathaniel Calloway, Timothy A. Ryan, Activity-Driven Local ATP Synthesis Is Required for Synaptic Function, ***Cell*** 156, 825 (2014). PMCID: PMC3955179; Measuring subcellular concentrations *in vivo*. ***U.S. Patent No. 9487819 B2***; Submitted in Addgene
b. Ilika Ghosh, Ruolin Fan, Monil Shah, Ojasee Bapat, **Vidhya Rangaraju***, Synapses drive local mitochondrial ATP synthesis to fuel plasticity, ***bioRxiv*** 10.1101/2025.04.09.648032 (2025), in revision. *corresponding author.
c. Maximilian Heumüller, Caspar Glock, **Vidhya Rangaraju**, Anne Biever, Erin M Schuman, A genetically encodable cell-type-specific protein synthesis inhibitor, ***Nature Methods*** 16, 699 (2019). PMID: 31308551.
d. Agathe Moret, Helen Farrants, Ruolin Fan, Kelsey G. Zingg, Bryon Silva, Camilla Roselli, Thomas G. Oertner, Christine E. Gee, Dafni Hadjieconomou, **Vidhya Rangaraju**, Eric Schreiter, Jaime de Juan-Sanz, An expanded palette of bright and photostable organellar Ca2+ sensors, ***eLife***14:RP107845 (2025).

**Complete List of Published Work in MyBibliography**

https://www.ncbi.nlm.nih.gov/myncbi/vidhya.rangaraju.1/bibliography/public/