BIOGRAPHICAL SKETCH

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NAME: Petry, Sabine

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

POSITION TITLE: Associate 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
Goethe Universität Frankfurt am Main	BS	07/2000	Biochemistry
Goethe Universität Frankfurt am Main and Max-Planck Institute of Biophysics	MS	07/2003	Biophysics
University of Cambridge and MRC Laboratory of Molecular Biology	PHD	07/2007	Structural Studies
UCSF/HHMI, San Francisco, CA	Postdoctoral Fellow	08/2013	Cell Biology

A. Personal Statement

The mission of my laboratory is to understand how cells obtain their shape, position organelles, move materials, and segregate chromosomes. Each of these functions relies on the microtubule (MT) cytoskeleton attaining a specific architecture. Despite its central biological role, we do not yet understand how a particular MT architecture is established in a cell. Moreover, we still lack a basic understanding of how a cell makes microtubules in the first place, even though their building block, tubulin, was discovered in the 1960s. In order to address these complex questions, my laboratory studies how the MT cytoskeleton is built, using elements of multiple disciplines including cell biology, biochemistry, biophysics, structural biology and engineering. Having been trained in Prof. Hartmut Michel's department and by Dr. Venki Ramakrishnan, I am an expert in X-ray crystallography; I was able to solve the first structure of the 70S ribosome during the translation cycle, while participating in efforts to apply high-resolution cryo-electron microscopy to the ribosome. As a post-doctoral fellow in Prof. Ron Vale's laboratory, I became proficient in light microscopy, established the Xenopus extract system to resolve individual nucleation events, and discovered that MTs branch during mitosis, which is critical for spindle assembly and cell division.

Since I started my laboratory at Princeton in 2013, we have achieved the following milestones: We recently solved a long-standing mystery of how microtubules are nucleated in cells by identifying a novel MT nucleation factor which is part of the universal nucleation module. Next, we uncovered how this MT nucleation module gets to the right location and is turned on at the right time to give rise to a cellular MT network. By reconstituting this MT nucleation pathway in vitro and determining its building plan, we can explain branching MT nucleation from its molecular components to its resulting 3D architecture which is critical for spindle assembly and chromosome segregation. Based on my laboratory's expertise and track record in MT nucleation, branching MT nucleation and spindle assembly, we are in an ideal position to successfully execute the proposed aims.

My laboratory consists of eight outstanding members: four Ph.D. students, three post-doctoral scholars and one senior thesis student. Besides the NIH Pathways to Independence Award, I received the Pew Award for Biomedical Research, the Sidney Kimmel Award for Cancer Research, the Packard Award for Science and Engineering, and the NIH New Innovator Award (DP2). Most recently, I was awarded ASCB's WICB Junior Award for Research Excellence, which is given annually to one Assistant Professor within seven years of starting her laboratory, as well as the inaugural Biophysics Award of the Oswaldt Foundation. Since July 1, 2020, I am Associate Professor with tenure.

Ongoing projects that I would like to highlight include:

Princeton Catalysis Initiative (PIs: Petry, Shaevitz)
07/01/2020 - 06/30/2023
Using optical tweezers to perform chromosome segregation

Princeton University SEAS Innovation Research Grants (PIs: Petry, Stone)
03/03/21-08/28/23
Mathematical modeling and mechanism of mitotic spindle assembly

Princeton University E&W Schmidt Transformative Technology Fund (PIs: Petry, Stone)
7/1/2021 – 06/30/2024
Microtubule-Enabled Nano Technology (MENT) Pulling, Pushing and Separating on the Nanoscale

Princeton University Biomolecular Condensate Initiative (PIs: Petry, Shaevitz, Stone)
09/01/21-08/31/23
Capillary bundling of biological filaments: mechanism and function

New Jersey Alliance for Clinical and Translational Science (PIs: Petry, Shen)
10/13/2021-10/12/2022
Targeting of mitotic spindle assembly factor TPX2 for cancer therapy

Foundation for Health Advancement: Seed Funding for Business Venture of NJ Health Foundation (PI: Petry)
11/30/2021-11/29/2022
Treating and Curing Cancer – A novel screen for a new class of cancer drug targets and therapeutics

1R01 GM141100 - 01A1
National Institutes of Health (PI: Petry)
2/1/22-1/31/26
Investigating Regulation and Mechanisms of Microtubule Nucleation in Acentrosomal Spindle Assembly

Completed projects that I would like to highlight include:

2014-40376
The Lucile & David Packard Foundation (PI: Petry)
10/30/2014-11/30/2022
Building the Microtubule Cytoskeleton via Microtubule Nucleation

1DP2GM123493
NIH DP2 New Innovator Award (PI: Petry)
9/30/2016 – 05/31/2021
Building the Chromosome Segregation Machinery from Scratch

Princeton University E&W Schmidt Transformative Technology Fund (PIs: Shaevitz, Petry, and Yang)
7/1/2016 - 12/31/2021
Revolutionizing Cell Biology with a Combined 3D Imaging and Force Microscope

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2020 -	**Associate Professor (with tenure) Dep. of Molecular Biology, Princeton University**
2019/(20)	Physiology Course Faculty, Marine Biology Laboratory, *Woods Hole, MA*
2018	Electron Microscopy Boot Camp Rutgers University, *New Brunswick, NJ*
2017 -	Member, Biophysical Society
2017	Kugee Womens' Leadership Course, *Princeton NJ*
2016	HHMI Gilliam URM Mentoring Workshop, HHMI, *Chevy Chase, MD*
2015 -	Member, American Association for the Advancement of Science
2014 - 2015	Member, American Genetics Society
2013 -	Associated Faculty Member, Department of Chemistry, Princeton University
2013 -	Associated Faculty Member, Dep. of Chemical & Biological Engineering, Princeton University
2013 - 2020	**Assistant Professor, Department of Molecular Biology, Princeton University**
2013	EMBO Laboratory Management Course for Group Leaders, *Leimen, Germany*

2011	Scientific Leadership & Management, UCSF Office of Career and Prof. Development, *CA*
2009 - 2012	(Summers), Marine Biological Laboratory, *Woods Hole, MA /* Collaborators: Prof. Timothy Mitchison (Harvard Medical School), Dr. Francois Nedelec (EMBL) / Topic: Functional Studies of the Augmin Complex in *Xenopus* Egg Extracts
2009	Analytical and Quantitative Light Microscopy, Marine Biological Laboratory, *Woods Hole MA*
2008 -	Member, American Society for Cell Biology
2008 - 2013	**Post-doctoral Fellow, University of California at San Francisco /** Mentor: Prof. Ronald D. Vale / Topic: Structural and Functional Analysis of Microtubule Nucleation within the Mitotic Spindle
2006 - 2007	RNA society
7 – 8/2003	**World Health Organization**, *Geneva, Switzerland* Summer Associate, solely responsible for the section UV Radiation in the Department for the Protection of the Human Environment
2003 - 2007	**Ph.D. Student, MRC Laboratory of Molecular Biology**, *Cambridge, UK*
2002 - 2003	Diploma (M.Sc.) Student, Max Planck Institute of Biophysics, *Frankfurt am Main, Germany* Advisors: Prof. Carola Hunte and Prof. Hartmut Michel. Diploma Thesis: Generation and Characterization of Single-Chain-Fv Fragments specific for the Cytochrome bc1 Complex
7/2001	**Genoscope**, the National Sequencing Center, *Evry, France* Research Associate involved in high-throughput sequencing and genome analysis
8 – 10/2000	**Max-Planck-Institute of Biophysics**, *Frankfurt am Main, Germany* Research Associate with Dr. Guenter Frisch and Prof. Dr. Hartmut Michel Biochemical and X-ray crystallographic studies of the bacterial reaction center
7 – 8/1999	**Merck KGaA**, *Darmstadt, Germany* Summer Associate in the Environmental Protection Department
1996 – 1998	Professional basketball player with the Aschaffenburg Wild Cats, *Germany*

Honors

2022	**Inaugural Biophysics Award of the Oswaldt Foundation**
2019	**Women in Cell Biology Junior Award for Excellence in Research** by the American Society of Cell Biology (ASCB) awarded once a year to one female Assistant Professor within seven years of starting her laboratory
(i) 2018-20 & (ii) 2020-22	**Catalysis Initiative**, co-PI, Princeton University awarded to PIs from different departments that together start a new research direction
2017 – 2019	**Humboldt University – Princeton University Partnership Grant**, co-PI
2016	**NIH New Innovator Award (DP2)**
2016	**Schmidt Fund Transformative Technology Award**, co-PI, Princeton University
2015 – 2016	**Innovation Award**, co-PI, Department of Molecular Biology Princeton University
2015 – 2016	**Humboldt University – Princeton University Partnership Grant**, co-PI
2014 – 2019	**Packard Fellowship for Science and Engineering**
2014 – 2016	**Pew Scholar in the Biomedical Sciences**
2014 – 2016	**Kimmel Scholar for Cancer Research**
2012 - 2016	**NIH Pathway to Independence Award (K99/R00)**
2009 - 2011	**Postdoctoral HHMI Fellow of the Life Science Research Foundation**
2009	Postdoctoral Fellowship of the Helen Hay Whitney Foundation (declined)
2009	Postdoctoral Fellowship of the Human Science Frontier Program (declined)
2008	**EMBO Long-term Fellowship for Postdoctoral Research**
2007	**FEBS Young Scientist Prize** for best presentation, 7th FEBS Young Scientist Forum *Vienna, Austria*
2006	**Young Investigator Award** for best poster and best lecture, 40th Anniversary Meeting *Spetses, Greece*
2005	**Max Perutz Student Price for Outstanding Research**, MRC Lab. of Molecular Biology *Cambridge, UK*

2003 - 2006 **Ph.D. Scholarship by Boehringer Ingelheim Fonds**
2003 - 2006 **College Scholarship for University of Cambridge** from Medical Research Council, *UK*
2003 **World Health Organization Scholarship**, Bureau for Leaders in International Organizations, *Germany*
2001 - 2003 **German National Merit Foundation / Studienstiftung des Deutschen Volkes** (awarded to the top 0.5% of German University students, with financial support and courses)

C. Contribution to Science

1. Together with Venki Ramakrishnan, I solved the first crystal structures of a classical translation factor bound to the entire ribosome, work which substantially increased our knowledge of how class I release factors recognize stop codons and stimulate peptide release. Shortly after, I was part of the team that solved the high-resolution structure of the 70S ribosome complexed with mRNA and tRNA ligands. Those first structures of functional ribosomal complexes explain many aspects of protein synthesis and are important steps towards obtaining a complete picture of how translation factors drive protein synthesis in the ribosome.

    a. Weixlbaumer A, Jin H, Neubauer C, Voorhees RM, Petry S, Kelley AC, Ramakrishnan V. Insights into translational termination from the structure of RF2 bound to the ribosome. Science. 2008 Nov 7;322(5903):953-6. PubMed Central PMCID: PMC2642913.
    b. Petry S, Weixlbaumer A, Ramakrishnan V. The termination of translation. Curr Opin Struct Biol. 2008 Feb;18(1):70-7. PubMed PMID: 18206363.
    c. Selmer M, Dunham CM, Murphy FV 4th, Weixlbaumer A, Petry S, Kelley AC, Weir JR, Ramakrishnan V. Structure of the 70S ribosome complexed with mRNA and tRNA. Science. 2006 Sep 29;313(5795):1935-42. PubMed PMID: 16959973.
    d. Petry S, Brodersen DE, Murphy FV 4th, Dunham CM, Selmer M, Tarry MJ, Kelley AC, Ramakrishnan V. Crystal structures of the ribosome in complex with release factors RF1 and RF2 bound to a cognate stop codon. Cell. 2005 Dec 29;123(7):1255-66. PubMed PMID: 16377566.

2. Working with Ron Vale, I uncovered that a microtubule (MT) can be nucleated from the sides of a pre-existing MT (branching) and identified its key players using light microscopy. Until this discovery, it was still unknown whether this process even existed in metazoan organisms or in a mitotic spindle of any organism. It explains how MTs are amplified with a defined geometry: a low branch angle and local preservation of polarity make branching MT nucleation well suited for rapid assembly of the spindle and kinetochore fibers, prerequisites for a successful cell division. Microtubule branching helps explain many unresolved aspects of how the mitotic spindle is assembled, and raises new questions about its role in building the microtubule cytoskeleton of the cell.

    a. Petry S, Groen AC, Ishihara K, Mitchison TJ, Vale RD. Branching microtubule nucleation in Xenopus egg extracts mediated by augmin and TPX2. Cell. 2013 Feb 14;152(4):768-77. PubMed Central PMCID: PMC3680348.
    b. Petry S, Vale RD. A new cap for kinetochore fibre minus ends. Nat Cell Biol. 2011 Nov 13;13(12):1389-91. PubMed Central PMCID: PMC3532025.
    c. Petry S, Pugieux C, Nédélec FJ, Vale RD. Augmin promotes meiotic spindle formation and bipolarity in Xenopus egg extracts. Proc Natl Acad Sci U S A. 2011 Aug 30;108(35):14473-8. PubMed Central PMCID: PMC3167534.
    d. Uehara R, Nozawa RS, Tomioka A, Petry S, Vale RD, Obuse C, Goshima G. The augmin complex plays a critical role in spindle microtubule generation for mitotic progression and cytokinesis in human cells. Proc Natl Acad Sci U S A. 2009 Apr 28;106(17):6998-7003. PubMed Central PMCID: PMC2668966.

3. Since I was hired at Princeton University in 2013, my laboratory has focused on the overarching goal of explaining how a cell creates the microtubule architecture that supports most aspects of cell function. Having discovered branching MT nucleation during my post-doctoral work (see Contribution 2), my laboratory has studied and used this MT nucleation pathway to gain insight into the role of its key

molecular players. Upon deciphering the overall roles of augmin and TPX2, we have been able to fully reconstitute this pathway *in vitro* from more than forty proteins. By combining modeling with experiments, we described the kinetic rules and hierarchy that established the building plan of this pathway. These contributions form the rationale and basis of the proposal submitted here.

a. Alfaro-Aco R, Thawani A, Petry S. Biochemical reconstitution of branching microtubule nucleation. Elife. 2020 Jan 14;9 PubMed Central PMCID: PMC6959992.
b. Thawani A, Stone HA, Shaevitz JW, Petry S. Spatiotemporal organization of branched microtubule networks. Elife. 2019 May 8;8 PubMed Central PMCID: PMC6519983.
c. Song JG, King MR, Zhang R, Kadzik RS, Thawani A, Petry S. Mechanism of how augmin directly targets the γ-tubulin ring complex to microtubules. J Cell Biol. 2018 Jul 2;217(7):2417-2428. PubMed Central PMCID: PMC6028527.
d. Alfaro-Aco R, Thawani A, Petry S. Structural analysis of the role of TPX2 in branching microtubule nucleation. J Cell Biol. 2017 Apr 3;216(4):983-997. PubMed Central PMCID: PMC5379942.

4. While researching how branching MT nucleation works, we discovered that one of its essential MT nucleation effectors, the protein TPX2, undergoes a liquid liquid phase separation (LLPS). While such protein phase separations have been routinely described *in vitro*, we were able to define a specific role for this process. By forming a co-condensate with tubulin on the MT lattice, TPX2 spatially biases microtubule nucleation to occur from there and enhances reaction kinetics. Because the latter point was shown in a single reaction, by directly measuring kinetics, and in a physiological environment, we consider this an important contribution to the phase separation field. Most recently, by combining theory with experiments, we have shown that TPX2 behaves on MTs just like a liquid, obeying the Raleigh Plateau Instability, similar to how dew forms drops on a spider web.

   a. Setru SU, Gouveia B, Alfaro-Aco R, Shaevitz JW, Stone HA, Petry S. A hydrodynamic instability drives protein droplet formation on microtubules to nucleate branches. Nature physics. 2021 January 28. Available from: https://doi.org/10.1038/s41567-020-01141-8 PMID: NIHMS1649857; NIHMSID: NIHMS1649857
   b. Alfaro-Aco R, Thawani A, Petry S. Biochemical reconstitution of branching microtubule nucleation. Elife. 2020 Jan 14;9 PubMed Central PMCID: PMC6959992.
   c. King MR, Petry S. Phase separation of TPX2 enhances and spatially coordinates microtubule nucleation. Nat Commun. 2020 Jan 14;11(1):270. PubMed Central PMCID: PMC6959270.

5. In order to generate any MT in any cell, MTs need to be nucleated. Despite the discovery of tubulin 50 years ago, and the discovery of the universal nucleator gamma-tubulin ring complex (γ-TuRC), we do not yet fully understand how γ-TuRC nucleates an MT. In addition, some researchers have questioned whether γ-TuRC is really the only nucleation factor. Recently, we identified a second, essential MT nucleation factor, the previously characterized MT polymerase XMAP215. Most recently, we developed the first single-molecule light microscopy assay to observe single γ-TuRC molecules nucleate in real time. These studies have led us to propose a molecular model for MT nucleation by γ-TuRC, and propose a mechanism for how XMAP215 synergistically helps in this process. These contributions form another major rationale of the proposal submitted here.

   a. Rale M, Romer B, Mahon BP, Travis SM, and Petry S. The conserved centrosomal motif, γTuNA, forms a dimer that directly activates microtubule nucleation by the γ-tubulin ring complex (γTuRC). eLife. Elife. 2022 Dec 14;11:e80053. Doi: 10.7554/eLife.80053
   b. Thawani A, Rale MJ, Coudray N, Bhabha G, Stone HA, Shaevitz JW, Petry S. The transition state and regulation of γ-TuRC-mediated microtubule nucleation revealed by single molecule microscopy. Elife. 2020 Jun 15;9 PubMed Central PMCID: PMC7338055.
   c. Thawani A, Kadzik RS, Petry S. XMAP215 is a microtubule nucleation factor that functions synergistically with the γ-tubulin ring complex. Nat Cell Biol. 2018 May;20(5):575-585. PubMed Central PMCID: PMC5926803.