

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED SIX PAGES.**

NAME André Hoelz		POSITION TITLE Professor of Chemistry	
eRA COMMONS USER NAME hoelza			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of Freiburg, Freiburg, Germany	B.Sc.	06/93	Chemistry
University of Freiburg, Freiburg, Germany	M.Sc.	02/97	Chemistry/Biochemistry
The Rockefeller University, New York, NY, USA	Ph.D.	06/04	Biochemistry/Biophysics

A. Personal Statement

The research in my group focuses on the structural and functional characterization of large and dynamic macromolecular assemblies. Prior to joining the California Institute of Technology (Caltech) in November 2010 as an assistant professor, I had already been working towards this aim for 6 years as a semi-independent investigator at The Rockefeller University, leading my own research group as part of Günter Blobel's laboratory. I have received extensive interdisciplinary training in molecular biology, biochemistry, biophysics, cell biology, and structural biology. My graduate studies in John Kuriyan's group focused on the structural and functional characterization of two important protein kinases that are key regulators of human physiology. At Rockefeller, my group pioneered the structural and functional characterization of the ~120 MDa nuclear pore complex (NPC), a ~1000 protein assembly that is the sole mediator of nucleocytoplasmic transport, composed of ~34 different proteins that occur in multiple copies. Over the last decade, my group has determined about half of its structured mass in ~40 crystal structures of individual nucleoporins (nups) or nup complexes. One major focus has been the structural and functional characterization of the NPC coat and its evolutionary relationship to other vesicle coats. Another major effort of my group has been the elucidation of the molecular mechanism of mRNA export events occurring at the cytoplasmic face of the human NPC that are a frequent target of malignant genetic mutations. An additional more recent focus has been the structural and functional characterization of the symmetric NPC core that harbors the central transport channel. In 2010 and again last year, I was invited to write a review on the current status of the structural characterization of the NPC for the Annual Reviews of Biochemistry series, an honor recognizing our pioneering contributions and our status at the forefront of the field.^{1,2} In parallel to the work on the NPC and its associated cellular machineries, my group determines structure-function relationships of various important histone-modifying enzymes, including demethylases, acetyltransferases and deacetylases. In total, I am the senior author of ~65 deposited crystal structure entries in the protein data bank (PDB). This expertise and experience in conjunction with my demonstrated track record of productive research projects uniquely qualifies me to lead the proposed work.

1. **Hoelz, A.,***** Debler, E.W., Blobel, G. (2010). Structure of the Nuclear Pore Complex. **Annu. Rev. Biochem.** 80, 613-643. [* corresponding author, ** invited author] PMID: 21495847
2. **Lin, D.H., Hoelz, A. ***** (2019). Structure of the Nuclear Pore Complex (An Update). **Annu. Rev. Biochem.** *in press*. [* corresponding author, ** invited author]

B. Positions and Honors

Appointments

1997 – 1997	Research Associate, Karl Decker Laboratory, University of Freiburg, Germany
1997 – 2004	Graduate Fellow, John Kuriyan Laboratory, The Rockefeller University, USA
2004 – 2004	Postdoctoral Fellow, Thomas P. Sakmar Laboratory, The Rockefeller University, USA
2004 – 2007	Postdoctoral Fellow, Günter Blobel Laboratory, The Rockefeller University, USA
2007 – 2009	Research Associate, Günter Blobel Laboratory, The Rockefeller University, USA
2009 – 2010	Research Assistant Professor, The Rockefeller University, USA
2010 – 2016	Assistant Professor of Chemistry, California Institute of Technology, USA
2015 – present	Investigator, Heritage Medical Research Institute
2016 – present	Professor of Chemistry, California Institute of Technology
2016 – present	Faculty Scholar, Howard Hughes Medical Institute

Awards & Honors

1991	Award of the 'Fonds der Chemischen Industrie', Germany
1997 – 1999	Rockefeller Graduate Student Pre-Doctoral Fellowship
1999 – 2003	Burroughs Wellcome Fund, Pre-Doctoral Fellowship, Interfaces in Science Program
2003 – 2004	Murray Foundation Postdoctoral Fellowship
2007	Science Highlight, National Synchrotron Light Source, Brookhaven National Laboratory
2008	Science Highlight, Advanced Light Source, Lawrence Berkeley National Laboratory
2009	Science Highlight, Advanced Photon Source, Argonne National Laboratory
2010 – 2012	Albert Wyrick V Scholar Award, V Foundation for Cancer Research
2011 – 2014	54 th Mallinckrodt Scholar Award, Edward Mallinckrodt, Jr. Foundation
2012 – 2014	Kimmel Scholar Award, Sidney Kimmel Foundation for Cancer Research
2015 – 2018	Inaugural Heritage Principal Investigator, Heritage Medical Research Institute
2015 – 2020	Camille Dreyfus Teacher-Scholar Award, Camille & Henry Dreyfus Foundation
2015	Science Highlight 2015, Advanced Photon Source, Argonne National Laboratory
2016	Science Highlight 2016, Stanford Synchrotron Radiation Lightsource
2016	Science Highlight 2016, Advanced Photon Source, Argonne National Laboratory
2016 – 2021	Faculty Scholar, Howard Hughes Medical Institute

C. Contribution to Science, selected publications

1. Lin, D. H., Correia, A.C., Cai, S.W., Huber, F.M., Jette, C.A., **Hoelz, A.*** (2018). Structural and functional analysis of mRNA export regulation by the nuclear pore complex. **Nat. Commun.**, 2319. PMCID: 5998080
2. Huber, F.M., **Hoelz, A.*** (2017). Molecular basis for protection of ribosomal protein L4 from cellular degradation, **Nat. Commun.** 8, 14354. PMCID: 5296656
3. **Hoelz, A.*** Glavy, J.,* Beck, M.* (2016). Towards the atomic structure of the Nuclear Pore Complex: When top down meets bottom up, **Nat. Struct. Mol. Biol.** 23, 624-630. PMCID: 5156573
4. Lin, D.,[#] Stuwe, T.,[#] Schilbach, S., Rundlet, E.J., Perriches, T., Mobbs, G., Fan, Y., Thierbach, K., Huber, F.M., Collins, L.N., Davenport, A.M., Jeon, Y.E., **Hoelz, A.*** (2016). Architecture of the symmetric core of the nuclear pore, **Science** 352, aaf1015. [** featured on the **COVER** and highlighted in **CELL**] PMCID: 5207208
5. Stuwe, T.,[#] Bley, C.J.,[#] Thierbach, K.,[#] Petrovic, S.,[#] Schilbach, S., Mayo, D.J., Perriches, T., Rundlet, E.J., Jeon, Y.J., Collins, L.N., Huber, F.M., Lin, D.H., Paduch, M., Koide, A., Lu, V., Fischer, J., Hurt, E., Koide, S., Kossiakoff, A., **Hoelz, A.*** (2015). Architecture of the fungal nuclear pore inner ring complex, **Science** 350, 56-64. [** featured with a **PERSPECTIVE** by Katharine S. Ullman and Maureen A. Powers] PMCID: 4826903
6. Stuwe, T., Correia, A., Lin, D. H., Paduch, M., Lu, V. T., Kossiakoff, A. A., **Hoelz, A.*** (2015). Architecture of the nuclear pore complex coat. **Science** 347, 1148-1152. PMCID: 5180592
7. Stelter, P.,[#] Huber, F.M.,[#] Kunze, R., Flemming, D., Hoelz, A.*, Hurt, E.* (2015). Coordinated Ribosomal L4 Protein Assembly into the Pre-Ribosome Is Regulated by Its Eukaryote-Specific Extension, **Mol. Cell** 58, 854-862. [COVER] PMID: 25936803
8. Stuwe, T., Lin, D. H., Collins, L. N., Hurt, E., **Hoelz, A.*** (2014). Evidence for an evolutionary connection between the large adaptor nucleoporin Nup192 and karyopherins. **Proc. Natl. Acad. Sci. USA**, 111, 2530-2535. PMCID: 24505056
9. Davenport, A.M., Huber, F.M., **Hoelz, A.*** (2014). Structural and functional analysis of human SIRT1. **J. Mol. Biol.**, 426, 526-541. [COVER] PMCID: 24120939
10. Hsia, K.C., **Hoelz, A.*** (2010). Crystal structure of α -COP in complex with ϵ -COP provides insight into the architecture of the COPI vesicular coat. **Proc. Natl. Acad. Sci. USA** 107, 11271-11276. PMCID: 20534429
11. Debler, E.W., Ma, Y., Seo, H.S., Hsia, K.C., Noriega, T.R., Blobel, G.*, **Hoelz, A.*** (2008). A Fence-Like Coat for the Nuclear Pore Membrane. **Mol. Cell** 32, 815-826. [COVER] PMCID: 19111661
12. Hsia, K.C., Stavropoulos, P., Blobel, G.* and **Hoelz, A.*** (2007) Architecture of a coat for the nuclear pore membrane. **Cell** 131, 1313-1326. PMCID: 18160040
13. Melcak, I., **Hoelz, A.***, Blobel, G.* (2007). Structure of Nup58/45 Suggests Flexible Nuclear Pore Diameter by Intermolecular Sliding. **Science** 315, 1729-1732. PMCID: 17379812

Complete List of Published Work in MyBibliography: (43 peer-reviewed publications)

<http://www.ncbi.nlm.nih.gov/sites/myncbi/andre.hoelz.1/bibliography/47297582/public/>

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Petrovic, Stefan**

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

POSITION TITLE: **Graduate Student Research Assistant**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Bucknell University	BA	08/2010	05/2014	Cell Biology and Biochemistry
California Institute of Technology	PHD	08/2014	present	Molecular Biophysics and Biochemistry

A. Personal Statement

My research interests are centered around using biochemical, genetic, structural, and computational tools to answer questions about the molecular workings of cellular machinery. Throughout my graduate training as a member of the Hoelz group at Caltech, I have strived to apply and expand my background in quantitative and physical disciplines in function of addressing long-standing questions about the nuclear pore complex (NPC) structure. I have witnessed and contributed to paradigm-shifting advancements in our understanding of how the architecture of this large molecular machine contributes to its function, namely the regulation of transport of matter and information between the nucleus and the rest of the cell. Beyond attaining advanced training in biochemical reconstitution and biophysical characterization of large protein complexes, x-ray crystallography and single particle cryo-EM, yeast genetics and mammalian cell biology, I have had the opportunity to hone my skills in oral and written communication, grant writing, project management and mentoring of undergraduate and junior graduate students.

- a. Stuwe T[#], Bley C. J[#], Thierbach K[#], **Petrovic S[#]**, Schilbach S, Mayo D. J, Perriches T, Rundlet E. J, Jeon Y. J, Collins L. N, Huber F. M, Lin D. H, Paduch M, Koide A, Lu V, Fischer J, Hurt E, Koide S, Kossiakoff A, Hoelz A. Architecture of the fungal nuclear pore inner ring complex. *Science*. 2015; 350, 56-64. PMCID: 4826903 # authors contributed equally to this work

B. Positions and Honors**Positions and Employment**

2011 - 2014	Peer Tutor, Organic Chemistry I & II courses, Bucknell University
2012 - 2014	Peer Tutor, Intro to Genetics course, Bucknell University
2011 - 2014	Teaching Assistant, General, Inorganic, Analytical Chemistry courses, Bucknell University
2013 - 2014	Teaching Assistant, Classical & Modern Physics, Bucknell University
2015	Teaching Assistant, Intro to Cell Biology course, Caltech
2016	Teaching Assistant, Biophysical/Structural Methods course, Caltech
2017 - 2018	Teaching Assistant, Macromolecular Structure Determination with Modern X-ray Crystallography Methods course, Caltech
2018	Teaching Assistant, Principles of Biology course, Caltech

Other Experience and Professional Memberships

2011 -	Member, Alpha Lambda Delta Honor Society
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- 2014 - Member, Phi Sigma Biological Science Society
- 2014 - Member, Phi Beta Kappa Honors Society
- 2016 Attendee, Cold Spring Harbor Lab: X-ray Methods in Structural Biology

Honors

- 2008 - 2010 Scholarship, United World College of the Adriatic
- 2011 Scholarship, Kales Undergrad Research Fund at Bucknell University
- 2012 - 2013 Scholarship, Walthour Undergrad Research Fund at Bucknell University
- 2010 - 2014 Scholarship, Gary & Sandy Sojka at Bucknell University
- 2010 - 2014 Scholarship, Shelby Davis UWC Scholars Program
- 2013 Award, McKnight Prize in Biochemistry at UT Southwestern finalist
- 2014 Award, Bucknell Prize in Cell Biology / Biochemistry
- 2014 Award, Teaching Assistant Excellence Award, Bucknell Chemistry Dept
- 2014 Award for Academic Excellence, Phi Beta Kappa at Bucknell University
- 2014 *Summa cum laude* with Honors Thesis, Bucknell University
- 2014 - 2015 Fellowship, Amgen Graduate Fellows at Caltech
- 2016 - 2018 Fellowship, Boehringer Ingelheim Foundation Graduate Fellows

C. Contribution to Science

2. **High School Research:** I spent a summer under the supervision of Dr. Davorin Medakovic at the Rudjer Boskovic Marine Research Institute in Croatia, using powder X-ray diffraction to study the biomineralization and shell-formation in the mussel *Mytilus galloprovincialis* as part of the European COST Project TD0903.
3. **Undergraduate Research:** My research question revolved about determining the reaction mechanism of a novel phospholipase C isolated from *Streptomyces antibioticus*, with Dr. Thomas L. Selby at Bucknell University as my advisor on the project. I performed a mutational study of the enzyme's active site, develop a kinetic assay for measuring activity, and carried out an in-depth $^1\text{H}/^{31}\text{P}$ NMR analysis of the reaction substrates.
 - a. **Petrovic S**, Selby L. T. Mechanistic Characterization of the *Streptomyces antibioticus* Phospholipase C Enzyme. ACS Middle Atlantic Regional Meeting; 2012; Baltimore, MD.
 - b. **Petrovic S**, Selby L. T. Chemical Rescue of Lysine-to-Alanine Mutations in the Ca^{2+} -dependent PI-PLC from *Streptomyces antibioticus*. 245th ACS National Meeting; 2013; New Orleans, LA.
4. **Graduate Research:** My ongoing predoc research is focused on structure-function studies of the nuclear pore complex (NPC). More specifically, I have contributed to the solution of the channel nucleoporin trimer (CNT) structure that sustains a large portion of the selective diffusion barrier at the center of the NPC transport channel. This work refuted a popular hypothesis that held the NPC capable of regulating the diameter of the transport channel through structural rearrangements of its component proteins. I have continued working on elucidating the architecture of the entire inner ring of the NPC with single residue precision and complementing my biochemical and structural findings with *in vivo* functional assays; this is work which I expect to culminate with the submission of high impact manuscript in the next six months.
 - a. Stuwe T[#], Bley C. J[#], Thierbach K[#], **Petrovic S**[#], Schilbach S, Mayo D. J, Perriches T, Rundlet E. J, Jeon Y. J, Collins L. N, Huber F. M, Lin D. H, Paduch M, Koide A, Lu V, Fischer J, Hurt E, Koide S, Kossiakoff A, Hoelz A. Architecture of the fungal nuclear pore inner ring complex. *Science*. 2015; 350, 56-64. ^{# authors contributed equally}
 - b. **Petrovic S**, Perriches T, Samanta D, Thierbach K, Hoelz A. Nic96 recruits and positions the CNT to establish a functional diffusion barrier of the NPC. "Life at the Edge: The nuclear envelope in nucleocytoplasmic transport and genome organization" DGZ Meeting; 2018; Potsdam, Germany.