

Curriculum Vitae

Henning Stahlberg

Prof., Institute of Physics,
School of Basic Sciences, EPFL,
and
Department of Fundamental Microbiology,
Faculty of Biology and Medicine,
University of Lausanne, Switzerland



Date of birth: November 18, 1965
Nationality: Swiss and German
Civil status: Married to Dr. med. Milena Menegola Stahlberg (FMH), from GR, Switzerland.
Three children, born 2000, 2002 and 2007.
Lab Website: <http://lbem.epfl.ch>
DCI Website: <http://dci-lausanne.ch>
ORCID: <http://orcid.org/0000-0002-1185-4592>
ResearcherID: <http://www.researcherid.com/rid/H-1868-2011>
Google Scholar: <https://scholar.google.ch/citations?user=u9D1CicAAAAJ>

EDUCATION

2002 Habilitation, Biozentrum (Prof. **Andreas Engel**), University of Basel, Switzerland
1997 PhD, Chemistry Department (Profs. **Jacques Dubochet** & **Horst Vogel**), EPFL Lausanne, Switzerland
1993 Solid-State Physics, Diploma, Physics Department, Technical University Berlin, Germany

CURRENT POSITION(S)

2021 – pres. Academic Director, *Dubochet Center for Imaging*, Uni Lausanne and EPFL, Switzerland
2020 – pres. Full Professor (Ordinarius), Physics Institute, EPFL, and Dep. Fund. Microbiol., Uni Lausanne, Lausanne, Switzerland

PREVIOUS POSITIONS

2010 – 2020 Director, *Center for Cellular Imaging and NanoAnalytics*, University Basel, Switzerland
2009 – 2021 Full Professor (Ordinarius), Biozentrum, University of Basel, Switzerland
2009 – 2010 Adjunct Assoc. Professor, Molecular and Cellular Biology, UC Davis, CA, USA
2007 – 2009 Associate Professor (tenured), Molecular and Cellular Biology, UC Davis, CA, USA
2003 – 2007 Assistant Professor, Molecular and Cellular Biology, UC Davis, CA, USA
2002 – 2003 Group Leader Structural Biology, Biozentrum, Uni Basel, Switzerland
1998 – 2002 PostDoc, Biozentrum, University of Basel, Switzerland
1990 – 1991 Undergrad Researcher, Neutron Scattering, Hahn-Meitner Institute, Berlin, Germany
1989 – 1990 Software Developer, IWIS Scientific Visualization Softw., Berlin, Germany

PUBLICATIONS

As of January 2022: 209 scientific articles
9'714 citations (h-index 54) [Web of Science], or
13'375 citations (h-index 64) [Google Scholar].

HONORA AND AWARDS

2021	Swiss NanoSciences Institute, honorable member, Univ. Basel, Switzerland
2014	Kachalski Keynote, IUPAC, Brisbane, Queensland, Australia
2009	W. M. Keck Award (US\$ 1.2 Mio), Keck Foundation, TX, USA
2008-2013	UC Davis Chancellor's Fellow Award, CA, USA
2004	NSF CAREER award (US\$ 800k), NSF. Alexandria, VA, USA

CURRENT LAB MEMBERS AT EPFL

PI:	1
Senior Scientists:	4
PostDocs:	5
PhD Students:	5
Technicians:	1
Master Students:	1
<u>Administrators:</u>	<u>1</u>
Total:	18

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

2009 – 2019	PostDocs: 27, PhD Students: 33, Master Students: 21 Biozentrum, University of Basel, Switzerland
2003 – 2010	PostDocs: 7, PhD Students: 9, Master Students: 4 Molecular and Cellular Biology, University of California at Davis, CA, USA

ALUMNI WITH OWN ACADEMIC GROUP

- Prof. Nicholas Taylor, University of Copenhagen, Denmark
- Prof. Sarah Shahmoradian, UT Southwestern, TX, USA
- Prof. Mikhail Kudryashev, Max-Planck Institute for Biophysics, Frankfurt, Germany
- Prof. Po-Lin Chiu, Arizona State University, Tempe, AZ, USA
- Prof. Xiangyan Zeng, Fort Valley State Univ., Georgia, USA
- Prof. Lia Stanciu, Purdue University, West Lafayette, IN, USA
- Prof. Lenin Dominguez, Univ. de las Americas Puebla, Mexico
- Dr. James Evans, PNNL, Richland, WA, USA
- Dr. Ricardo Guerrero-Ferreira, Emory University, Atlanta, USA
- Dr. Christopher Bleck, NHLB, NIH, Bethesda, MD, USA

TEACHING ACTIVITIES

2022 –	Teaching “Physics of Life”, EPFL, Lausanne, Switzerland
2009 – 2020	Teaching “Physics of Life”, “Biophys. Chemistry”, “Struct. Biology”, “NanoSciences”, “BioEnergy”, “Electron Microscopy”, Biozentrum, University of Basel, Switzerland
2003 – 2009	Teaching “Macromolecular Structure and Function”, “Structural Biology”, “Advanced Electron Microscopy and Image Processing”, Mol. Cell. Biol., UC Davis, CA, USA
2000 – 2003	Teaching “Digital Image Processing” and “Linear Algebra”, Biozentrum, University of Basel, Switzerland

INSTITUTIONAL RESPONSIBILITIES

2021 – pres.	Academic Director, Dubochet Center for Imaging, EPFL & UNIL, Switzerland
2020 – pres.	Member of steering board of Center for Interdep. Electron Microsc., EPFL, Switzerland
2020 – 2021	Creation of the Dubochet Center for Imaging, EPFL & UNIL, Switzerland
2016 – 2017	Member of search committee for the Director of the Biozentrum, Uni Basel, Switzerland
2009 – 2018	Member of various (>10) faculty search committees, University of Basel, Switzerland

- 2009 – 2013 “Fellowship for Excellence” selection committee, Biozentrum, Uni Basel, Switzerland
 2007 – 2008 Roadmap planning committee, Molecular and Cellular Biology, UC Davis, CA, USA
 2003 – 2007 Member of various (>4) faculty search committees, UC Davis, CA, USA
 2004 – 2009 Member of various (>5) campus committees, MCB, UC Davis, CA, USA
 2004 Participation in two television ads for UC Davis Health System “There’s a whole university behind every UC Davis doctor”. UC Davis, CA, USA

REVIEWING ACTIVITIES

- 2019 – Chair of SAB, Max Planck Institute for Biophysics, Frankfurt, Germany
 2016 – SAB member, Max Planck Institute for Biophysics, Frankfurt, Germany
 2016 – SAB member, IBS, Grenoble, France
 2017 – SAB member, leadXpro.ch, Villigen, Switzerland
 2004 – Review of grant proposals from various foundations and countries, incl. Australia: Queensland Univ.; Germany: DFG, IMPRES (MPG), VolkswagenStiftung; France: FRM; Netherlands: NeCEN; Switzerland: SNF, Ambitione, Latsis Foundation; South Africa: MRC; USA: NSF, NIH, Energy Biosci. Inst. USA, US Civilian Res.&Devel. Foundation, Duke Univ., LLNL LDRD (Livermore)
 2002 – Review of various manuscripts for journals, incl. ACS Nano, BBA, BioCell, COSB, Comp. Biophys. J., CRDF, eLife, EMBO J., EMBO R., J. Mol. Biol., JoVE, J. Pharmacy Pharmacolo., PLOS, J. Struct. Biol., J. Separation Sci., Micron, Micr. Microanal., Nature, Nature Methods, NSMB, PNAS, Science, Structure, Ultramic., and others.
 2019 – 2020 SAB member, nuonex.com, Basel, Switzerland
 2004 – 2008 Review panel member at various study sections, NIH, Washington, USA

ORGANISATION OF LARGER SCIENTIFIC MEETINGS

- Aug. 2022, 2020, 2018, 2016, 2014, 2012, 2010, 2008: Co-Organizer. “EMBO Cryo-EM workshop”, Biennial 10-day workshops. EMBL, Heidelberg, Germany.
 Mar. 2018, 2016, 2014: Co-Organizer. “Int. Symposium on Cryo-EM 3D Image Analysis”, Biennial 1-week Symposia, Tahoe, CA, USA
 Sept. 2018: Organizer and Chair. “Single Particle Cryo-EM”, Annual 1-week Workshop, University Basel, Switzerland
 Sept. 2018, 2017, 2016, 2015, 2014, 2013, 2012: Organizer and Chair. “International Workshop on Sub-Volume Averaging of Electron Tomography data”, Annual 1-week Workshops, University Basel, Switzerland
 June 2016 Organizer, “ICON: International Conference on Nanoscopy”, Basel, Switzerland
 June 2014 Chair, “Gordon Research Conference on 3D EM”, Barcelona, Spain.
 June 2013 Co-Chair. “Gordon Research Conference on 3D EM”, New London, NH, USA.
 June 2005 Session chair. “Gordon Research Conference on Mechanisms of Membrane Transport”, Tilton School, Tilton, NH, USA.
 Aug. 2016, 2012, 2010, 2008, 2006: Organizer and Chair. “International Workshop on 2dx Image Processing”, 1-week workshops, University Basel, Switzerland (2010,2012), UC Davis, CA, USA (2008,2006).
 Nov. 2005, Mar. 2005, Nov. 2004, Jun. 2004, Mar. 2004: Organizer or co-organizer. “Bay area cryo-EM meeting”, Quarterly 1-day workshops, Stanford, UC Davis, San Francisco, Santa Cruz, Berkeley, CA, USA.

INVITED CONFERENCE TALKS (incomplete list)

- Feb. 2020 LS2 Annual Meeting, Zurich, Switzerland
 Jan. 2020 HOPE Parkinson Congress, Paris, France
 Oct. 2019 3D SSOM Symposium, Engelberg, Switzerland
 Oct. 2019 Cryo-EM Inauguration Symposium, IST, Vienna, Austria

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- Sept. 2019 Cold Spring Harbor Asia Conference on Cross-Scale Biological Structure: From Macromolecular Complexes and Organelles to Cells and Tissues, Suzhou, China
- Sept. 2018 Demystifying Alpha-Synuclein Functions in Health and Diseases, 3-day conference (Lashuel), EPFL, Lausanne, Switzerland
- Aug. 2018 EMBO Cryo-EM workshop: *Cryo-electron microscopy*, EMBL, Heidelberg, Germany
- Mar. 2018 Tahoe Cryo-EM 3D Image Analysis Symposium, Granlibakken Conference Center, Lake Tahoe, CA, USA
- Oct. 2017 SGBM and BIOS International Symposium, Freiburg, Germany
- Sept. 2017 Cryo-EM Symposium, Technical University Delft, The Netherlands
- Sept. 2016 TNT2016, Fribourg, Switzerland
- Aug. 2016 EMBO Cryo-EM workshop: *Cryo-electron microscopy*, EMBL, Heidelberg, Germany
- July 2016 SNI Nanoconvention, Conference Center Basel, Switzerland
- June 2016 Kuo Symposium on 3D Cryo-EM Molecular Imaging, Beijing, China
- Mar. 2016 Tahoe Cryo-EM 3D Image Analysis Symposium, Granlibakken Conference Center, Lake Tahoe, CA, USA
- Jan. 2016 Gordon Research Conference on Ligand Recognition and Molecular Gating, Il Ciocco, Italy
- Oct. 2015 Janelia Conference, *Challenges in Crystallography*, Janelia Research Campus, Ashburn, VA, USA
- Sept. 2015 SNI Annual Meeting, *Keynote, Nanoscale Characterization of Parkinson's Disease*, Lenzerheide, Switzerland
- Aug. 2015 CEASAR Seminar, Bonn, Germany
- June 2015 Gordon Research Conference on Three Dimensional Electron Microscopy, Colby Sawyer, NH, USA
- Jan. 2015 LS2 Annual Meeting, University of Zürich, Switzerland
- Nov. 2014 NRAMM Workshop on Advanced topics in EM Structure Determination, Scripps Research Institute, La Jolla, CA, USA
- Sept. 2014 Int. Conference on the Crystallization of Biological Macromolecules, Hamburg, Germany
- Sept. 2014 EMBO Cryo-EM workshop: *Cryo-electron microscopy*, EMBL, Heidelberg, Germany
- Aug. 2014 Kachalski Keynote Lecture, IUPAC Bioenergetics Conference, Brisbane, Queensland, Australia
- Aug. 2014 IMB Seminar Series Lecture, Brisbane University, Queensland, Australia
- June 2014 Gordon Research Conference on Three Dimensional Electron Microscopy, *Chair*, Girona, Spain
- Mar. 2014 International Symposium on Cryo-EM 3D Image Analysis, Granlibakken Conference Center, Lake Tahoe, CA, USA
- Sept. 2013 EMBO Cryo-EM Course, London, UK
- May 2013 Swiss Nano Convention, *Structural investigations of single cells and their molecular components*, Congress Center Basel, Switzerland
- Nov. 2012 NRAMM Workshop on Advanced Topics in EM Structure Determination, Scripps Research Institute, La Jolla, CA, USA
- Sept. 2012 EMBO Cryo-EM workshop: *Cryo-electron microscopy*, EMBL, Heidelberg, Germany
- May 2012 Max Planck Symposium on the Future of Struct. Biol., Hamburg, Germany
- Mar. 2012 SSOM, *Structure Determination of Membrane Proteins*, Les Diablerets, Switzerland
- Sept. 2011 EMBO Cryo-EM Course, London, UK
- Sept. 2010 iNet NanoEvent Basel: *NanoImaging: State of the Art*, Congress Center, Basel, Switzerland
- Aug. 2010 European Crystallographic Meeting, *Projective Constraint Optimization*, Dammstadt, Germany

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- June 2010 Gordon Research Conference on Three Dimensional Electron Microscopy, *Projective Constraint Optimization*, Il Ciocco, Italy
- Feb. 2010 Haider Symposium: *Development of Phase Contrast STEM for Biological Specimens*, Universität Heidelberg, Heidelberg, Germany
- Feb. 2009 Asia-Pacific Congress on Electron Tomography: *Where Electron crystallography of membrane proteins meets electron tomography and single particle cryo-EM*, Brisbane, Queensland, Australia
- Sept. 2008 EMBO Cryo-EM workshop: *Electron crystallography*, EMBL, Heidelberg, Germany
- Jun. 2008 Gordon Research Conference on Three-Dimensional Electron Microscopy, Il Ciocco, Italy
- Sept. 2007 FEMMS 2007: Aberration corrected imaging of organic/biological samples, Sonoma, CA, USA
- Aug. 2007 Microscopy & Microanalysis 2007: The structure of the CNG potassium channel MloK1, Ft. Lauderdale, FL, USA
- Jul. 2007 JEOL User Meeting: Aberration corrected imaging of biological samples, Peabody, MA, USA
- Aug. 2006 International Workshop on Electron Crystallography, UC Davis, CA, USA
- Aug. 2006 EMBO Workshop "Cryo-electron microscopy and 3D image reconstruction", EMBL, Heidelberg, Germany
- Mar. 2006 3rd International Conference on Structural Analysis of Supramolecular Assemblies by Hybrid Methods, Granlibaken Center, Lake Tahoe, CA
- Mar. 2006 GPCR symposium of the American Chemical Society meeting, Atlanta, GA, USA.
- Sep. 2004 EMBO Workshop "Cryo-electron microscopy and 3D image reconstruction", EMBL, Heidelberg, Germany
- Mar. 2003 Swiss Physical Society Annual Meeting, University Basel, Pharmacenter, Switzerland
- Nov. 2002 Integration of Information about Macromolecular Structure (IIMS) Workshop, European Bioinformatics Institute, Hinxton, Cambridge, UK
- Sep. 2002 Annual Meeting of the German Biophysics Society, Dresden, Germany
- Mar. 2002 CSBMCB 45th Annual Meeting and Winternational Symposium on Membrane, Proteins in Health and Disease, Banff, Canada
- Mar. 2001 ISIR Symposium on Biological Motors and Material Sciences and CREST Mini Symposium on Acidic Organelles and V-ATPases, Osaka, Japan
- Feb. 2001 Workshop on Pumps, Channels and Transporters: Structure and Function, Instituto Juan March, Madrid, Spain
- Oct. 2000 Biozentrum Symposium "The new generation", USB Ausbildungszentrum, Basel, Switzerland
- Jul. 2000 Molecular Biology and Physiology of Water and Solute Transport, Göteborg, Sweden
- Feb. 1999 Biophysical Society, 44th Annual Meeting, Baltimore, USA
- Jun. 1997 Reaction centers of photosynthetic purple bacteria: Structure, spectroscopy, dynamics., Cadarache, France
- Sep. 1996 Molecular Recognition in Photosynthesis, European Science Foundation, Jaca, Spain

10 MOST IMPORTANT PUBLICATIONS FROM LAST 10 YEARS

- ‘Two new polymorphic structures of alpha-synuclein solved by cryo-electron microscopy’, Guerrero-Ferreira, R., Taylor, N., Arteni, A.-A., Kumari, P., Mona, D., Ringler, P., Britschgi, M., Lauer, M.E., Verasdock, J., Riek, R., Melki, R., Meier, B.H., Böckmann, A., Bousset, L., Stahlberg, H., *eLife* 8:e48907, (2019)
<https://doi.org/10.7554/eLife.48907>
- ‘Lewy pathology in Parkinson's disease consists of a crowded organellar membranous medley’, Shahmoradian, S., Lewis, A., Genoud, C., Graff, A., Pérez Navarro, P., Goldie, K., Sütterlin, R., Castano-Diez, D., Ingrassia, A., Rozemuller, A.J.M., Paepe, A.D., Erny, J., Staempfli, A., Hoernschemeyer, J., Niedieker, D., El-Mashtoly, S.F., Gerwert, K., Bohrmann, B., Britschgi, M., Stahlberg, H., van de Berg, W.D.J., Lauer, M.E., *Nature Neuroscience* 22, 1099-1109, (2019)
<https://doi.org/10.1038/s41593-019-0423-2>
- ‘Microfluidic protein isolation and sample preparation for high resolution cryo-EM’, Schmidli, C., Albiez, S., Rima, L., Righetto, R., Mohammed, I., Oliva, P., Kovacik, L., Stahlberg, H., Braun, T. *PNAS* 116(30), 15007-15012, (2019)
<https://doi.org/10.1073/pnas.1907214116>
- ‘Cryo-EM structures of a human ABCG2 mutant trapped in ATP-bound and substrate-bound states’, Manolaridis, I., Jackson, S.M., Taylor, N.M.I., Kowal, J., Stahlberg, H., Locher, K.P., *Nature* 563(7331), 426-430 (2018)
<https://doi.org/10.1038/s41586-018-0680-3>
- ‘Structural basis for regulation of human acetyl-CoA carboxylase’, Hunkeler, M., Hagmann, A., Stüttfeld, E., Chami, M., Guri, Y., Stahlberg, H., Maier, T., *Nature* 558, 470-474 (2018)
<https://doi.org/10.1038/s41586-018-0201-4>
- ‘Structure of the human multidrug transporter ABCG2’, Taylor, N., Manolaridis, I., Jackson, S.M., Kowal, J., Stahlberg, H., Locher, K.P., *Nature* 546, 504-509 (2017)
<https://www.nature.com/articles/nature22345>
- ‘Cullin-RING ubiquitin E3 ligase regulation by the COP9 signalosome’, Cavadini, S., et al., and Stahlberg, H., and Thomae, N.H., *Nature* 531(7596), 598-603 (2016)
<https://www.nature.com/articles/nature17416>
- ‘Atomic structure of bacteriophage T4 baseplate and its function in triggering sheath contraction’, Taylor, N., Prokhorov, N.S., Guerrero-Ferreira, R.C., Shneider, M.M., Browning, C., Goldie, K., Stahlberg, H., Leiman, P.G., *Nature* 533(7603), 346-352 (2016)
<http://www.nature.com/articles/nature17971>
- ‘X-ray structure of the mouse serotonin 5-HT₃ receptor’, Hassaine, G., Deluz, C., Grasso, L., Wyss, R., Tol, M. B., Hovius, R., Graff, A., Stahlberg, H., Tomizaki, T., Desmyter, A., Moreau, C., Li, X. D., Poitevin, F., Vogel, H., Nury, H., *Nature* 512(7514), 276-81 (2014)
<http://www.nature.com/articles/nature13552>
- ‘Ligand-induced structural changes in the cyclic nucleotide-modulated potassium channel MloK1’, Kowal, J., Chami, M., Baumgartner, P., Arbeit, M., Chiu, P. L., Rangl, M., Scheuring, S., Schroder, G. F., Nimigean, C. M., Stahlberg, H., *Nature Comm.* 5, 3106 (2014)
<https://www.nature.com/articles/ncomms4106>

PATENTS

- Stefan Arnold (PhD student C-CINA), Thomas Braun (Senior Scientist C-CINA), and Henning Stahlberg. Title: Lossless cryo-grid preparation by controlled sample evaporation. Invention Disclosure, filed Oct. 10, 2017 to the European Patent Office, The Hague. PCT/EP2017/076467
- Stefan Arnold (PhD student C-CINA), Thomas Braun (Senior Scientist C-CINA), and Henning Stahlberg. Title: Lossless cryo-grid preparation stage for high-resolution electron microscopy. Invention Disclosure, filed July 6, 2015 to the European Patent Office, The Hague. 15745407.5

METHODS / SOFTWARE DEVELOPMENT

- CryoWriter – The Braun team in the Stahlberg group Basel has developed microfluidics-based instrumentation to prepare cryo-EM grids from nanolitre quantities of sample. The cytosol of single, hand-picked cells can be imaged in cryo-EM.
- FOCUS – The Stahlberg group has developed a software system to accompany online cryo-EM data collection. This system performs automated quality analysis and life processing of automatically recorded cryo-EM data, and allows online monitoring of the data collection progress via a web interface. Available at <http://focus-em.org>.
- DYNAMO – The Stahlberg group has developed a software system for user-friendly sub-volume averaging of cryo-electron tomography data. Available at <http://dynamo-em.org>.

OUTREACH

- ‘Mysteries of the Unseen World’ – a National Geographic movie about the things too slow, too fast, or too small to see. Director: Louie Schwartzberg. Narrator: Forest Whitaker. This science documentary movie from 2013 screened in various iMax cinemas in the world. Available in English, Dutch, Spanish and Chinese. Rating: 100% Rotten Tomatoes, 7.6/10 IMDb. Our lab contributed about 15 minutes of electron microscopy imagery to the 39-minute long movie. This movie was accompanied by a “Making of...” movie, in which our lab and the technology behind the movie was described.
- We regularly host 1-week workshops and courses on electron microscopy in our institute. These include workshops on electron tomography and sub-volume averaging (2019, 2018, 2017, 2016, 2015, 2014, 2013, 2012) as well as cryo-EM of membrane proteins (2018, 2016, 2012, 2010, 2008, 2006).
- I have lectured in several lay-level forums about structural biology, cryo-EM, or Parkinson’s disease research, as for example, the “Senioren-Uni” lectures of the University Basel (2018, 2012).
- We develop software tools, which we distribute via web servers. We run <http://focus-em.org>, <http://dynamo-em.org>, <http://openbeb.org>, and host source codes in 29 repositories on <http://github.com/C-CINA>.
- I have lectured on various topics in electron microscopy and image processing. These lectures are available on YouTube at <https://www.youtube.com/channel/UCGDVliRoXAVhdXAc9ZVxFzQ>, and on https://www.youtube.com/channel/UCXOgcEReKdaqKW_TdS3QWeg/playlists

OTHER WEBSITES

- <http://www.dci-lausanne.org/workshops> Organized Workshops
- <http://github.com/C-CINA> Open-source repositories for all software packages developed by our group)
- <http://focus-em.org> Documentation, Download, Support for *FOCUS*

LANGUAGES

- German (mother tongue)
- English (fluent)
- French (fluent)
- Italian (intermediate)
- Portuguese (basic)
- Spanish (basic)
- Latin (basic)

HOBBIES

Violoncello, symphonic orchestra and chamber music (string quartet), ski, mountaineering

PENDING RESEARCH SUPPORT (numbers are direct funding)

1. **SERI Swiss Research Infrastructure Roadmap (PI: Stahlberg; 26 coPIs)** **1.1.2025 – 31.12.2028**
 Requested budget: CHF 55.1 Mio for four years.
EM-Frontiers: A research infrastructure for method development and application in electron microscopy
This is a coordinated network of electron microscopy facilities and researchers in Switzerland from the life sciences and materials sciences disciplines. The network will advance the methods and establish a distributed platform for broad access to this technology for Swiss academia and industry.
2. **SNF Sinergia (PI: Picotti; coPIs: Hondele, Riek, Stahlberg)** **1.7.2022 – 30.6.2026**
 Requested budget: CHF 3.2 Mio for four years (CHF 200k/year for Stahlberg lab).
 LLPS condensates: structure, regulation, cellular interactions and links to age-related degenerative disease

ONGOING RESEARCH SUPPORT (numbers are direct funding)

3. **SNF Division III (PI: Stahlberg)** **1.8.2020 – 31.7.2024**
 CHF 325k/year for Stahlberg lab (Total funding: CHF 1.3 Mio for four years)
 Struct. Studies of Human Brain in Neurodegeneration
4. **SNF Division II (PI: Stahlberg)** **1.4.2021 – 31.3.2025**
 CHF 180k/year for Stahlberg lab (Total funding: CHF 727k for four years)
 Coherent Electron Diffractive Imaging for Vitriified Single Protein Particles
5. **SNF Sinergia (PI: Stahlberg; coPIs: Riek, Picotti)** **1.1.2018 – 30.06.2022**
 CHF 190k/year for Stahlberg lab (Total funding: CHF 3.1 Mio for four years)
 Molecular and Cellular Modulation in Parkinson's Disease
6. **SNF NCCR TransCure (PIs: Abriel, Reymond et al.; Stahlberg is coPI)** **1.11.2010 – 31.10.2022**
 CHF 100k/year for Stahlberg lab
 TransCure – From Transport Physiology to Identification of Therapeutic Targets
7. **Sino-Swiss Collaboration grant (PIs: Stahlberg, Zhang, Vogel)** **1.1.2022 – 31.12.2025**
 CHF 88k/year for Stahlberg lab (Total funding: CHF 700k for four years)
 Deciphering the 3D architecture of the synapse
8. **EPFL Seed Funds (PIs: Ablasser, Stahlberg)** **1.1.2022 – 31.12.2023**
 CHF 50k/year for Stahlberg lab (Total funding: CHF 200k for two years)
 Visualization of STING-mediated innate immune mechanisms
9. **Synapsis Foundation (PI: Lewis, a PostDoc in Stahlberg's group).** **1.1.2021 – 31.12.2022**
 CHF 100k/year for Dr. Lewis (Total funding: CHF 200k for two years)
 Ultrastructure of Parkinson's pathology in post-mortem human brain

COMPLETED RESEARCH SUPPORT

1. **SNF, Division II: (PI: Braun, a senior scientist in Stahlberg's group),** **1.4.2016 – 31.3.2020,**
CHF 558k total funding. Funding in 2019: CHF 137k/yr
Fast protein-complex isolation, sample preparation and data processing
for high- resolution structural analysis and visual proteomics
2. **Swiss Nanosciences Institute (PhD fellowship) (PI: Braun, Stahlberg)** **2016 – 2019**
CHF 65k / year
Microfluidics to study nano-crystallization of proteins
3. **Swiss Nanosciences Institute (PhD fellowship) (PI: Braun, Stahlberg)** **2016 – 2019**
CHF 65k / year
Targeted single cell proteomics using magnetic nanoparticles to study prion-like spreading of
amyloid nanoparticles
4. **Swiss Nanosciences Institute (PhD fellowship): (PI: Braun, Meier)** **2016 – 2019**
CHF 65k / year
Nanomechanical mass and viscosity measurement-platform for cell imaging
5. **Argovia Grant: (PI: Braun):** **2017 – 2019**
CHF 147k / year
Single cell nanoanalytics
6. **SNF, Section 2: (PI: Stahlberg),** **1.4.2016 – 31.3.2019,**
CHF 540k total funding. Funding in 2017: CHF 180k/yr
High-resolution membrane protein structures by cryo-EM
7. **F. Hoffmann-La Roche (PI: Stahlberg)** **2019**
CHF 2.000 Mio (Awarded in July 2018, but cancelled in May 2019 upon departure to Lausanne)
Donation for investment into electron microscopy hardware in C-CINA
8. **Synapsis Foundation: (PI: Stahlberg)** **1.1.2015 – 31.12.2018**
CHF 300k total funding. Funding in 2018: CHF 100k/yr
The structure of prionoid tau
9. **SNF, Section 3: (PI: Braun),** **1.10.2015 – 30.9.2018**
CHF 442k total funding. Funding in 2017: CHF 137k/yr
Fast protein complex isolation
10. **CTI (PI: Stahlberg), with CovalX.ch.** **1.10.2016 – 30.9.2018**
CHF 437k total funding
Knowledge and Technology Transfer grant: New Technology for Epitope Mapping Characterization
11. **SNF Sinergia: (PI: Riek, Rajendran, Ries, and Stahlberg).** **1.4.2014 – 31.1.2018**
CHF 2.160 Mio total direct support. Funding for Stahlberg group: CHF 180k/yr
The Time- and Spatially Resolved Aggregation of a-Synuclein and its Relationship to Cell-Cell
Transmissibility
12. **SNF R'Equip: (PI: Stahlberg and others).** **2015**
CHF 405k total direct support
Cryo-electron microscopy in the ZMB
13. **SystemsX.ch: (PI: Stahlberg, co-PI: several).** **2010 –2014**
CHF 4.100 Mio total direct support for 8 groups
RTD CINA Grant
14. **Donations F. Hoffmann-La Roche (PI: Stahlberg)** **2009 – 2017**
CHF 2.016 Mio total direct support

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15. **SNF, Section 2: (PI: Stahlberg),** **1.10.2013 – 31.3.2016,**
CHF 445k total direct support
Software for electron microscopy of membrane proteins
 16. **SNF, Section 3: (PI: Stahlberg),** **1.4.2013 – 31.3.2016**
CHF 562k total direct support
Electron microscopy of membrane proteins
 17. **SNF CoRe (PI: Rajendran & Stahlberg)** **1.4.2014 – 31.3.2016**
CHF 200k total support. Support for Stahlberg: CHF 50k / year
Structural and functional roles of exosomal nanovesicles in the formation, release and
synaptotoxicity of amyloid proteins
 18. **Roche PostDoctoral Fellowship (PI: Stahlberg)** **2012 – 2015**
CHF 402k total support
Structural investigations of human postmortem brain from Parkinson's disease
 19. **NCCR Nano (PI: Schönenberger, coPI Stahlberg and others)** **2009 – 2013**
CHF 100k / year
 20. **NCCR Structural Biology (PI: Grütter, coPI Stahlberg and others)** **2009 – 2012**
CHF 50k / year
 21. **SNF Sinergia (PI: Cornelis, coPI Stahlberg and others)** **2009 – 2012**
CHF 50k / year
Type III Secretion
 22. **SNF, Section 2: (PI: Stahlberg)** **1.10.2009 – 30.9.2012**
CHF 487k total direct support
Software for Electron Crystallography
 23. **SNF, Section 3: (PI: Stahlberg)** **1.10.2009 – 30.9.2012**
CHF 468k total direct support
Electron Microscopy of Ion Channels
 24. **NSF BIO (PI: Stahlberg)** **2/1/05 – 1/31/10**
NSF CAREER award
\$866,612 t.c.
Creation of a highly automated, user-friendly image processing system for electron crystallography
The major goal of this project was to develop a software package for automated electron
crystallography image processing.
 25. **NIH-NIGMS (PI: Stroud, coPI: Stahlberg and others)** **7/1/05 – 6/30/10**
Specialized Center of the Protein Structure Initiative
\$1,271,023 t.c. Stahlberg lab. (~\$16.5m total)
Center for Structures of Membrane Proteins
The goal of this center was the determination of the structure and function of human membrane
proteins.
 26. **National Nuclear Security Administration (NNSA)** **11/1/05 – 10/31/08**
(PI: Browning, coPI: Stahlberg and Spence)
Enhanced Functionality for Materials Analysis in the DTEM
\$750,000 t.c.
The goal of this project was the construction and operation of a dynamic TEM operating in the
femto-second time resolution range.
 27. **NIH-NIGMS (PI: Stahlberg)** **8/1/07 – 7/31/12**
\$1,448,750 t.c.
Electron Microscopy of Membrane Proteins
The goal of this project was the determination of the structures of two ion channel membrane
proteins, and the development of an enhanced protein crystallization robot.

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28. **UC Davis Chancellor's Fellow Award (PI: Stahlberg)** **8/1/08 – 7/31/13**
\$25,000 t.c.
This award is given by the Chancellor of UC Davis to ~5 PI per year. Awardees become members of the Chancellor's club UC Davis.
29. **UC Lab Fee Research Grant (PI: Barty)** **4/1/09 – 3/31/12**
\$600,000 t.c. Stahlberg lab
The goal of this project was the application of a Free X-ray Laser to biological protein complexes.
30. **Keck (PI: Stahlberg, coPI: Browning.)** **1/1/09 – 12/31/10**
Phase-contrast STEM for biological samples
\$1,200,000 t.c. for 2 years
The goal of this project was the design and construction of technology for high-resolution STEM imaging of beam-sensitive biological weak-phase cryo samples.
31. **CBCRP (PI: Stahlberg, coPI: Heyer)** **7/1/05 – 6/30/07**
California Breast Cancer Research Program
\$100,000 d.c.
Structural analysis of cancer-relevant Brca2 mutations
The major goal of this project was the analysis of structural consequences of breast-cancer relevant mutations in the DNA binding protein Brca2 by cryo electron microscopy.
32. **UC (PI: Stahlberg)** **6/1/04 – 5/31/05**
UC New Faculty Research Grant Program
\$2,000 d.c.
Structural Studies of the Tat protein transport system
This fund was intended and used for supplies for a carbon evaporator for TEM sample preparation.
33. **UC-CRCC (PI: Stahlberg)** **7/1/04 – 6/30/05**
UC Cancer Research Coordinating Committee
\$30,000 d.c.
Analysis of DNA binding by Brca2 and determination of the 3D structure of Brca2 protein-DNA complexes by cryo electron microscopy
The major goal of this project was to structurally characterize the interaction of the breast cancer related soluble protein Brca2 with DNA. This is done by high-contrast single particle cryoEM.

In addition to these grant supports to my lab, several of the students or postdocs in my group have applied for individual fellowships, with my support. Larger awarded fellowships were awarded to James Evans (NIH training grant), Lenin Dominguez (PEW fellowship), or Nicholas Taylor (Uni Basel PostDoctoral 9-months Fellowship).

ACHIEVEMENTS

Establishing the *Dubochet Center for Imaging* in Lausanne

Starting 2020, Stahlberg has created the Dubochet Center for Imaging (DCI) in Lausanne. This involved the planning and construction of a temporary site for electron microscopes in the Cubotron building, EPFL, negotiations with vendors, instrument purchasing, installation, recruitment of facility personnel (5), establishing computer systems for online data processing, and initiation of workflows.

The DCI Lausanne site was inaugurated Nov. 15, 2021, and has determined in its first two weeks of function the 1.38Å structure of apoferritin and the 2.0Å structure of the SARS-CoV2 spike, proving outstanding performance. Preparations for a larger DCI Lausanne site are finished, construction will happen during 2022. The DCI currently consists of the DCI Lausanne (EPFL&UNIL), the DCI Geneva (UNIGE), and the inclusion of a third side, the DCI Bern (UNIBE) is in preparation.

Ultrastructural characterization of Lewy bodies in human brain

We study Parkinson's Disease by analyzing the brain of deceased patients that was collected with a very short post-mortem delay. Our main tool is electron microscopy. Parkinson's disease (PD) is characterized by the presence of aggregates in the human brain of 10 micrometer diameter and more, which are staining strongly for phosphorylated alpha-synuclein (aSyn) protein. These aggregates are called Lewy bodies.

When studying Lewy bodies from fresh human brain with correlative light and electron microscopy (CLEM) and modern sample preparation methods, to our surprise, we found that most Lewy bodies that fulfilled above criteria and strongly stained for aSyn were primarily composed of densely packed membranous aggregates, while only a minority of Lewy bodies showed fibrillar material at the periphery (Shahmoradian et al., Nat. Neurosc., 2019). In contrast, aSyn positive glial cytoplasmic inclusions (GCIs) from Multiple System Atrophy patient brain samples did show dominant fibrillar aggregates. This unexpected finding for Lewy bodies was contradicting the PD research field, but highlighted the importance of membrane and mitochondrial maintenance in PD.

We also characterized other larger aggregates in human brain, such as *Corporae amylacea* (Perez-Navarro et al., Sci. Reports 2018), and we described the impact of different preparation methods for human brain on their appearance in the TEM, documenting that older tissue preparation methods sometimes can produce fibrillar artifacts from membranous material (Lewis et al., Curr. Op. Struct. Biol. 2019).

Ultrastructural characterization of alpha-synuclein fibrils

Our group has studied fibrils of aSyn, which were grown in-vitro, sometimes with seeding from human brain. We have determined the atomic structures of various conformations (prionoid strains) of aSyn fibrils (Guerrero et al., eLife 2018 and eLife 2019). Interestingly, some in-vitro conformations are not compatible with PD-relevant mutations in the gene sequence of aSyn, so that one could argue that persons suffering from familial early-onset Parkinson's disease due to such mutations in aSyn could not form conformation-1-fibrils, but would be able to form conformation 2, 3 or other strain fibrils, which might then be the more pathological forms.

It is unclear, how these fibrils contribute to the development of Parkinson's disease, and why in the human brain we only occasionally find fibrils in the post-mortem brain tissue.

Determination of membrane protein structures

The Stahlberg group has structurally characterized a large number of membrane protein systems by cryo-EM, electron tomography or electron crystallography. Several medium to high-resolution membrane protein structures were investigated, and insight into how the proteins function and are regulated was obtained. Studied membrane protein systems include F-ATPases, K-channels, Cl-channels, citrate/sodium antiporters, sodium/potassium antiporters, ABC transporters, GPCRs, PS-I, PS-II and LHC-RC complexes, serotonin receptors, water channels, glycerol channels, and bacterial type III and type VI secretions systems.

Automation of electron microscopy data analysis

FOCUS: The Stahlberg group has developed the software suite called *FOCUS*, which establishes an interface between cryo-EM data collection and cryo-EM data processing. *FOCUS* typically is installed on a Linux computer directly adjacent to an automated cryo-EM instrument. *FOCUS* will monitor the harddrives of the cryo-EM instrument, pull recorded files and submit them to a fully automated processing pipeline, to analyze data quality (defocus, drift, resolution) and submit to online processing (RELION). *FOCUS* can run in different modi: In the single particle mode, particles are picked, classified, and submitted to 2D or 3D reconstruction. In the tomography mode, recorded tilt series are drift-corrected, re-ordered (Hagen scheme), and subjected to 3D reconstruction. In the 2D crystal mode, the automated electron crystallography processing capability of our former package *2dx* are available. *FOCUS* can also sort, display, and manage recorded datasets, which can become rather large (tens of TB). *FOCUS* also maintains a website to allow online tracking of the progress of data collection and data processing.

Websites:

<http://focus-em.org>

<https://github.com/C-CINA>

(Documentation, Download, Support website for *FOCUS*)
(open-source repositories for *FOCUS*
and other software packages developed by our group)

Microfluidic sample preparation for cryo-EM

Our lab has developed microfluidic methodology to harvest miniature quantities of sample with a narrow capillary. This can be used, for example, to aspire the cytosol of a single, hand-picked neuronal cell, or to aspire small volumes of cytosol into the capillary. A tool chain composed of magnetic beads coupled to Fab antibody fragments can then be used to purify small amounts of protein from the aspired sample. The affinity purification typically results in preparations of outmost purity, as judged by TEM imaging. Finally, the miniature quantities of protein can be written onto a cryo-EM grid, akin to writing ink onto a paper with a pen, whereby loss-less application of the entire sample onto the cryo-EM grid is used, without the use of filter paper blotting as conventionally done for cryo-EM grid preparation. This tool chain was developed by the team of Dr. Thomas Braun, who was a senior scientist in the Stahlberg group in Basel. The toolchain allowed to aspire 900 nanoliters of HeLa cell cytosol, purify endogenous 20S proteasome sample out of that cytosol, and write the resulting 9 nanoliters of pure protein onto a cryo-EM grid, which allowed us to determine the atomic structure of the human 20S proteasome within few hours of data collection with the automated imaging pipeline described above (Schmidli et al., PNAS 2019).

Workshops on cryo-EM

We regularly host one-week workshops on image processing for cryo-EM, for 2D crystals (2006-2016, using *2dx*), for single particle cryo-EM and *FOCUS* (since 2018), and for sub-volume averaging with the *DYNAMO* software tool developed by Dr. Daniel Castaño-Díez in C-CINA (since 2012).

Websites:

<https://www.dci-lausanne.org/workshops>

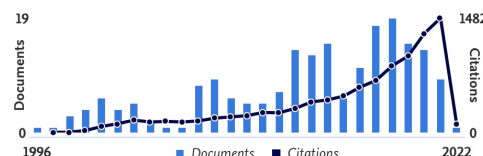
<https://www.dynamo-em.org>

(Websites for Workshops)
(*DYNAMO* software system for sub-volume averaging)

Publication List

ORCID: <http://orcid.org/0000-0002-1185-4592>

As of Jan. 2022: 209 scientific articles
9'714 citations (h-index 54) [Scopus], or
13'375 citations (h-index 64) [Google Scholar].



Publications in international peer-reviewed scientific journals

Underlined authors are members of the Stahlberg lab.

Submitted

1. SARS-CoV-2 Omicron potently neutralized by a novel antibody with unique Spike binding properties
Fenwick, C., Turelli, P., Ni, D., Perez, L., Lau, K., Lana, E., Pellaton, C., Raclot, C., Esteves-Leuenberger, L., Campos, J., Farina, A., Fiscalini, F., Abdelnabi, R., Foo, C.S., Neyts, J., Leyssen, P., LeGrand, R., Levy, Y., Pojer, F., Stahlberg, H., Trono, D., Pantaleo, G.
submitted to **Nature Medicine** (2022)
2. Allosteric control of Type I-A CRISPR-Cas3 complexes and establishment as effective nucleic acid detection and human genome editing tools
Ke, A., Hu, C., Ni, D., Nam, K.H., Majumdar, S., McLean, J., Stahlberg, H., Terns, M.P.
submitted to **Molecular Cell** (2022)
3. Mechanism of cyclic-beta-glucan export by ABC transporter Cgt of *Brucella* revealed by single-particle cryo-EM
Sedzicki, J., Ni, D., Lehmann, F., Wu, N., Zenobi, R., Jung, S., Stahlberg, H., Dehio, C.
submitted to **Nature Struct. Mol. Biol.**, revision requested (2022)
4. Insight into Lipopolysaccharide Translocation by Cryo-EM structures of a LptDE Transporter in Complex with Pro-Macrobodies
Botte, M., Ni, D., Schenck, S., Zimmermann, I., Chami, M., Bocquet, N., Egloff, P., Bucher, D., Trabuco, M., Cheng, R.K.Y., Brunner, J.D., Seeger, M.A., Stahlberg, H., Hennig, M.
submitted, and **bioRxiv** 2021.03.23.436624 (2022)
5. Functional and structural characterization of *Serratia marcescens* ExbB: determinants of the interaction with HasB/TonB
Biou, V., Adaixo, R., Chami, M., Coureux, P., Laurent, B., Ntsogo, Y., Cardoso de Amorim, G., Izadi-Pruneyre, N., Malosse, C., Chamot-Rooke, J., Stahlberg, H., Delepelaire, P.
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6. Cryo-EM structure of alpha-synuclein fibrils amplified by PMCA from PD and MSA patient brains
Burger, D., Fenyi, A., Bousset, L., Stahlberg, H., Melki, R.
submitted to **eLife** (revision requested), and **bioRxiv** 2021.07.08.451588 (2022)
7. Cryo-EM structural studies of the agonist complexed human TRPV4 ion-channel reveals novel structural rearrangements resulting in an open-conformation
Botte, M., Ulrich, A.K.C., Adaixo, R., Gnutt, D., Brockmann, A., Bucher, D., Chami, M., Bocquet, N., Ebbinghaus-Kintscher, U., Puetter, V., Becker, A., Egner, U., Stahlberg, H., Hennig, M., Holton, S.J.
submitted, and **bioRxiv** 2020.10.13.334797 (2022)

In press

8. 2.4 Å structure of the double ring *Gemmatimonas phototrophica* photosystem
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12. Structural analysis of the Spike of the Omicron SARS-COV-2 variant by cryo-EM and implications for immune evasion
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13. FTLT-TDP assemblies seed neoaggregates with subtype-specific features via a prion-like cascade
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14. Identification of a Dps contamination in Mitomycin-C-induced expression of Colicin Ia
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18. Coordination-Driven Monolayer-to-Bilayer Transition in Two-Dimensional Metal-Organic Networks
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19. Single particle analysis for high resolution 2D electron crystallography
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20. Structural investigation of ACE2 dependent disassembly of the trimeric SARS-CoV-2 Spike glycoprotein
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21. Alterations in sub-axonal architecture between normal aging and Parkinson's diseased human brains using label-free cryogenic X-ray nanotomography
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