

CURRICULUM VITAE

Name/ Position

Name PD Dr. rer. nat. Peter Hildebrand
born 14.11.1968 in Burglengenfeld, Germany
married, three children

Position: Head of the ProteinFormatics laboratory,
Institute of Medical Physics and Biophysics,
Charité Universitätsmedizin Berlin



Education and Training

1989-1992 Studies in biology, University of Regensburg

1991 Pree-degree in biology

1993-1994 Studies in biology/ecology, University of Sevilla, Spain

1994 Two months practicum at the Institute of Natural and Nutritional Science of Sevilla, Spain

1995-1997 Studies in biology, University of Regensburg, final examination 1997

1997-1998 Diploma thesis at the Ecological Faculty of the Humboldt University Berlin

1998 Award of the diploma in biology by the Humboldt University Berlin

1999-2002 PhD student at the graduate college 'Model Studies of Structure, Behaviour and Recognition of Biomolecules in Atomic Resolution'.

2003 Award of the title Doktor rerum naturalium (Dr. rer. nat.) at the Humboldt University Berlin. Title of the work: 'tertiary structure modelling of helical membrane proteins'

2008-2011 Preparation of the habilitation dissertation: 'structure-function relationships of helical membrane proteins: implications for 3D modelling'

2011 Habilitation in biophysics at the Charité Universitätsmedizin Berlin

2010-2012 Advanced education in the ESF-Qualifying program for teaching

Academic Positions

2003-2005 Post-doctoral fellow at the Institute of Biochemistry of the Humboldt University Berlin, in the Protein Structure Theory laboratory of Prof. Dr. Cornelius Frömmel

- 2005-2007 Post-doctoral fellow at the Institute of Molecular Biology and Bioinformatics of the Free University Berlin, in the Structural Bioinformatics laboratory of PD Dr. Robert Preißner
- 2008-dato Head of the ProteinFormatics laboratory at the Institute of Medical Physics and Biophysics, Charité Universitätsmedizin Berlin.
- 2009-2010 Guest scientist at the Los Alamos National Laboratory, New Mexico, USA

Funded Projects

- 2010-2014 DFG: Tertiary structure modeling of active G protein coupled receptors (renewal requested) (250 T).
- 2011-2014 SFB 740: From molecules to modules: organisation of functional units in cells, subproject B6: permanent vs. transient interactions between biopolymers in modular function (220 T).
- 2015-2018 SFB 740: From molecules to modules: organisation of functional units in cells, subproject B6: structural elucidation of the GPCR allosteric machine (280 T).
- 2013-2015 DFG: Molecular principles of patho- physiological mechanisms of the incretin receptors with general implications for family B GPCRs (215 T)
- 2012-2013 Contingent at the HLRN high performance cluster (280 T)

Selected Talks AG Hildebrand

- 06 / 2009 Seminar at the Center for Bioinformatics, University of Saarbrücken: 'analysis and prediction of helical membrane proteins'
- 06 / 2010 Course of lecture of the German Pharmaceutical Society, University of Freiburg: 'a G protein coupled receptor at work: the rhodopsin model'
- 12 / 2010 Seminar at the Rudolf Boehm Institute for Pharmacology and Toxicology, University of Leipzig: 'a G protein coupled receptor at work: the rhodopsin model'
- 12 / 2010 Seminar at the Department of Theoretical and Computational Biophysics, Max Planck Inttitute, Göttingen: 'a G protein coupled receptor at work: the rhodopsin model'
- 04 / 2011 MGMS Meeting on Membrane Proteins: Structure and Function, University of Oxford, England: 'a G protein coupled receptor at work: the rhodopsin model'
- 06 / 2011 Seminar at the Bart de Strooper laboratory, K. U. Leuven, Belgium: 'in silico analysis of APP-TM dimerisation and its interruption by gamma-secretase modulators'

- 08 / 2011 Course of lecture of the Network of Inflammation in Context of Pain and Disease, Berlin: 'a G protein coupled receptor at work: the rhodopsin model'
- 09 / 2011 7th FABISCH Symposium for Cancer Research and Molecular Cell Biology, Berlin: 'in silico analysis of APP-TM dimerisation and its interruption by gamma-secretase modulators'
- 03 / 2012 Seminar at DESRES (DE Shaw Laboratory), New York, USA: 'a ligand channel through the G protein coupled receptor rhodopsin'
- 02 / 2012 Mini-Symposium of the Leibniz Graduate School of Molecular Biophysics Berlin: 'computational modelling of secondary and tertiary structure interactions of helical membrane proteins'
- 01 / 2013 Biophysical Society Meeting: 'Dynamics of C-Terminal Gt alpha and Gs alpha Peptides in the Binding Cavity of Active GPCRs'
- 10 / 2013 Seminar at the SFB 740: 'Conformational Dynamics During GPCR / G-Protein Coupling'
- 11 / 2014 Biophysical Society Meeting: 'Conformational Dynamics During GPCR - G Protein Coupling'
- 01 / 2015 Gordon Research Conference on Molecular Pharmacology: 'Position of transmembrane helix 6 determines receptor g protein coupling specificity' (Poster presentation)
- 04 / 2015 Neurocure seminar at Charité: 'A structural model of Gs vs. Gi signaling by the β 2-adrenergic receptor'
- 02 / 2016 CECAM workshop: Models for Protein Dynamics 1976-2016: 'Role of structural dynamics at the receptor G protein interface for signal transduction'

Awards

2016: 'secundo loco' W2 professorship for computer simulations at University Leipzig.

Selected publications

1. Szczepek, M., Beyrière, F., Hofmann, K. P., Elgeti, M., Kazmin, R., Rose, A., Bartl, F. J., Stetten von, D., Heck, M., Sommer, M. E., **Hildebrand, P. W.** and Scheerer, P (2014). Crystal structure of a common GPCR binding interface for G protein and arrestin, *Nat. Commun.*, 10, 4801.
2. Rose A.S., Elgeti M., Zacchariae U., Grubmüller H., Hofmann K.P., Scheerer P. and **Hildebrand P.W.** (2014) Position of transmembrane helix 6 determines receptor g protein coupling specificity. *J Am Chem Soc*, 32, 11244-7.
3. Budkevich T.V., Giesebrecht J., Ramrath D., Mielke T., Ismer J., **Hildebrand P.W.**, Tung C.S., Nierhaus K.H., Sanbonmatsu K.Y. and Spahn C.M.T. (2014) Regulation of the mammalian elongation cycle by 40S subunit rolling: a eukaryotic-specific ribosome rearrangement, *Cell*, 1, 121-31.
4. Elgeti M., Rose A.S., Bartl F.J., **Hildebrand P.W.**, Hofmann K.P. and Heck M. (2013) Precision vs. flexibility in GPCR signalling. *J Am Chem Soc*, 33, 12305-12.
5. Munter L.M., Sieg H., Bethge T., Liebsch F., Bierkandt F.S., Schleege M., Bittner H.J., Heberle J., Jakubowski N., **Hildebrand P.W.**, Multhaup G. (2013) Model peptides uncover the role of the BACE1 transmembrane sequence in metal-ion mediated oligomerization, *J Am Chem Soc*, 51, 19354-61.
6. Richter, L., Munter, L.M., Ness, J., **Hildebrand, P.W.**, Dasari, M., Unterreitmeier, S., Bulic, B., Beyermann, M., Gust, R., Reif, B. et al. (2010) Amyloid beta 42 peptide (Abeta42)-lowering compounds directly bind to Abeta and interfere with amyloid precursor protein (APP) transmembrane dimerization. *Proc Natl Acad Sci U S A*, 107, 14597-14602.
7. **Hildebrand, P.W.**, Scheerer, P., Park, J.H., Choe, H.W., Piechnick, R., Ernst, O.P., Hofmann, K.P. and Heck, M. (2009) A ligand channel through the G protein coupled receptor opsin. *PLoS ONE*, 4, e4382.
8. Scheerer, P., Heck, M., Goede, A., Park, J.H., Choe, H.W., Ernst, O.P., Hofmann, K.P. and **Hildebrand, P.W.** (2009) Structural and kinetic modeling of an activating helix switch in the rhodopsin-transducin interface. *Proc Natl Acad Sci U S A*, 106, 10660-10665.
9. Scheerer, P., Park, J.H., **Hildebrand, P.W.**, Kim, Y.J., Krauss, N., Choe, H.W., Hofmann, K.P. and Ernst, O.P. (2008) Crystal structure of opsin in its G-protein-interacting conformation. *Nature*, 455, 497-502.
10. **Hildebrand, P.W.**, Rother, K., Goede, A., Preissner, R. and Frommel, C. (2005) Molecular packing and packing defects in helical membrane proteins. *Biophys J*, 88, 1970-1977.

Teaching experiences

Lectures in biochemistry and biophysics (since 2010):

1. Monosaccharide / Stereochemie, 2. Di- und Polysaccharide, 3. Aromaten, Heterozyklen, Nucleotide, 4. Aminosäuren und Peptide, 5. Proteine, 6. Grundlagen chemischer Reaktionen (Kinetik, Thermodynamik), 7. Funktionelle Gruppen, 8. Glucose – ein zentrales Biomolekül

Lectures in molecular medicine (since 2014):

1. Structure and evolution of proteins

Seminars in biochemistry / biophysics (since 2008):

1. Chemie der Kohlenhydrate, 2. Struktur und Funktion ausgewählter Mono-, Di- und Polysaccharide, 3. Chemie der Triacylglycerine und Phospholipide, 4. Lipide als Energiespeicher und Membranbaustein, 5. Molekulare Eigenschaften biologischer Membranen, 6. Chemie der Aminosäuren und Peptide, 7. Synthese und Abbau von Proteinen der Membran, 8. Struktur und Funktion von Nukleotiden, 9. Grundlagen des Säure-Basen-Haushaltes, 10. Hämoglobin und Myoglobin, 11. Chemiosmotische Kopplung

COMPLETE LIST OF PUBLICATIONS

38. Sprink T., Ramrath D, Yamamoto H., Yamamoto K., Loerke J., Ismer J., **Hildebrand P.W.**, Scheerer P., Bürger J., Mielke T. and Spahn CMT (2016) Structures of ribosome-bound initiation factor 2 reveal the mechanism of subunit association, *Science Advances*, accepted
37. Rose A., Zacchariae U., Grubmüller H., Hofmann K.P., Scheerer P. and **Hildebrand P.W.** (2015) Role of Structural Dynamics at the Receptor G Protein Interface for Signal Transduction, *PLoS ONE*, 10(11):e0143399
36. Yamamoto H., Collier M., Loerke J., Ismer J., et al., **Hildebrand P.W.**, Scheerer P. and Spahn C.M.T. (2015), Molecular architecture of the ribosome-bound Hepatitis C virus internal ribosomal entry site RNA, *EMBOJ*, 34(24):3042-58
35. Barucker C. et al., **Hildebrand P.W.** McKinney A. and Multhaup G. (2015) A β 42-oligomer interacting peptides (AIPs) render toxic amyloid- β 42 species non-toxic and suppress the formation of fibrils, *Sci Rep*, 29;5:15410
34. Brehm, A., et al., **Hildebrand P.W.**, Brogan P., Krüger E., Aksentijevich I., Goldbach-Mansky R. (2015) Diverse proteasome subunit mutations link proteasome dysfunction and Type I interferon induction in CANDLER/PRAAS, *J Clin Invest*, 125(11):4196-211
33. Prade E., Bittner H.J., Sarkar R., Amo J.M.L., Althoff-Ospelt G., **Hildebrand P.W.** and Reif B. (2015) Structural mechanism of the interaction of Alzheimer's disease A β fibrils with the NSAID sulindac sulfide, *JBC*, Epub ahead of print

32. Kazmin R, Rose A, Szczepek M, Elgeti M, Ritter E, Piechnick R, Hofmann K.P., Scheerer P and **Hildebrand P.W.** and Bartl (2015) The activation pathway of human rhodopsin in comparison to bovine rhodopsin, *JBC*, 14;290(33):20117-27
31. Rose, A. S. and **Hildebrand P.W.** (2015) A web application for molecular visualization, *Nucleic Acids Res*, 41, D576-9.
30. Österreich, F., Bittner, H., Weise, C., Grohmann, L., Janke, L. K., **Hildebrand, P.W.**, Multhaup, G., Munter, L. (2015) Impact of Amyloid Precursor Protein Hydrophilic Transmembrane Residues on Amyloid-beta Generation, *Biochemistry*, 17, 2777-84.
29. Sommer, M. E., Elgeti, M., **Hildebrand, P. W.**, Szczepek, M., Hofmann, K. P and Scheerer, P (2015) Structure-based biophysical analysis of the interaction of rhodopsin with G Protein and arrestin, *Methods Enzymol.*, 556, 563-608.
28. Szczepek, M., Beyrière, F., Hofmann, K. P., Elgeti, M., Kazmin, R., Rose, A., Bartl, F. J., Stetten von, D., Heck, M., Sommer, M. E., **Hildebrand, P. W.** and Scheerer, P (2014) Crystal structure of a common GPCR binding interface for G protein and arrestin, *Nat. Commun.*, 10, 4801.
27. Rose A.S., Elgeti M., Zacchariae U., Grubmüller H., Hofmann K.P., Scheerer P. and **Hildebrand P.W.** (2014) Position of transmembrane helix 6 determines receptor g protein coupling specificity. *J Am Chem Soc*, 32, 11244-7.
26. Barucker C., Harmeier A., Weiske J., Fauler B., Albring K.F., Prokop S., **Hildebrand P.W.**, Lurz R., Heppner F.L., Huber O., Multhaup G. (2014) Nuclear translocation uncovers the amyloid Peptide aβ42 as a regulator of gene transcription, *J Biol Chem*, 29, 20182-91.
25. Budkevich T.V., Giesebrecht J., Ramrath D., Mielke T., Ismer J., **Hildebrand P.W.**, Tung C.S., Nierhaus K.H., Sanbonmatsu K.Y. and Spahn C.M.T., Regulation of the mammalian elongation cycle by 40S subunit rolling: a eukaryotic-specific ribosome rearrangement, *Cell*, 1, 121-31.
24. Munter L.M., Sieg H., Bethge T., Liebsch F., Bierkandt F.S., Schleegeer M., Bittner H.J., Heberle J., Jakubowski N. and **Hildebrand P.W.**, Multhaup G. (2013) Model peptides uncover the role of the BACE1 transmembrane sequence in metal-ion mediated oligomerization, *J Am Chem Soc*, 51, 19354-61.
23. Rose, A., Theune, D., Goede, A. and **Hildebrand, P.W.** (2013) MP:PD – A data base of internal packing densities, internal waters and internal cavities in helical membrane proteins. *Nucleic Acids Res*, 42, D347-51.
22. Elgeti M., Rose A.S., Bartl F.J., **Hildebrand P.W.**, Hofmann K.P. and Heck M. (2013) Precision vs. flexibility in GPCR signalling. *J Am Chem Soc*, 33, 12305-12.
21. Ismer, J., Rose, A., Goede, A., Johanna K. S. Tiemann, Rother, K. and **Hildebrand, P.W.** (2012) Voronoia4RNA – A database of atomic packing densities of RNA structures and their complexes. *Nucleic Acids Res*, 41, D280-4.

20. Kaden, D., Harmeyer, A., Weise, C., Munter, L.M., Althoff, V., Rost, B.R., **Hildebrand, P.W.**, Schmitz, D., Schaefer, M., Lurz, R., et al. (2012) Novel APP/A β mutation K16N produces highly toxic heteromeric A β oligomers. *EMBO Mol Med*, 7, 647-59.
19. Piechnick, R., Ritter, E., **Hildebrand, P.W.**, Ernst, O.P., Scheerer, P., Hofmann, K. and Heck, M. (2012) The effect of channel mutations on the uptake and release of the retinal ligand in opsin. *Proc Natl Acad Sci U S A*, 109, 5247-52.
18. Botev, A., Munter, L.M., Wenzel, R., Richter, L., Althoff, V., Ismer, J., Gerling, U., Weise, C., Kokscha, B., **Hildebrand, P.W.** et al. (2011) The Amyloid Precursor Protein C-Terminal Fragment C100 Occurs in Monomeric and Dimeric Stable Conformations and Binds gamma-Secretase Modulators. *Biochemistry*, 50, 828-35.
17. Muhs, M., Yamamoto, H., Ismer, J., Takaku, H., Nashimoto, M., Uchiumi, T., Nakashima, N., Mielke, T., **Hildebrand, P.W.**, Nierhaus, K.H. et al. (2011) Structural basis for the binding of IRES RNAs to the head of the ribosomal 40S subunit. *Nucleic Acids Res.*, 39, 5264-75.
16. Ratje, A.H., Loerke, J., Mikolajka, A., Brunner, M., **Hildebrand, P.W.**, Starosta, A.L., Donhofer, A., Connell, S.R., Fucini, P., Mielke, T. et al. (2010) Head swivel on the ribosome facilitates translocation by means of intra-subunit tRNA hybrid sites. *Nature*, 468, 713-716.
15. Richter, L., Munter, L.M., Ness, J., **Hildebrand, P.W.**, Dasari, M., Unterreitmeier, S., Bulic, B., Beyermann, M., Gust, R., Reif, B. et al. (2010) Amyloid beta 42 peptide (A β 42)-lowering compounds directly bind to A β and interfere with amyloid precursor protein (APP) transmembrane dimerization. *Proc Natl Acad Sci U S A*, 107, 14597-14602.
14. Rose, A., Goede, A. and **Hildebrand, P.W.** (2010) MPlot--a server to analyze and visualize tertiary structure contacts and geometrical features of helical membrane proteins. *Nucleic Acids Res*, 38, W602-8.
13. Munter, L.M., Botev, A., Richter, L., **Hildebrand, P.W.**, Althoff, V., Weise, C., Kaden, D. and Multhaup, G. (2010) Aberrant amyloid precursor protein (APP) processing in hereditary forms of Alzheimer disease caused by APP familial Alzheimer disease mutations can be rescued by mutations in the APP GxxxG motif. *J Biol Chem*, 285, 21636-21643.
12. **Hildebrand, P.W.**, Scheerer, P., Park, J.H., Choe, H.W., Piechnick, R., Ernst, O.P., Hofmann, K.P. and Heck, M. (2009) A ligand channel through the G protein coupled receptor opsin. *PLoS ONE*, 4, e4382.
11. Scheerer, P., Heck, M., Goede, A., Park, J.H., Choe, H.W., Ernst, O.P., Hofmann, K.P. and **Hildebrand, P.W.** (2009) Structural and kinetic modeling of an activating helix switch in the rhodopsin-transducin interface. *Proc Natl Acad Sci U S A*, 106, 10660-10665.
10. Harmeyer, A., Wozny, C., Rost, B.R., Munter, L.M., Hua, H., Georgiev, O., Beyermann, M., **Hildebrand, P.W.**, Weise, C., Schaffner, W. et al. (2009) Role of amyloid-beta glycine 33 in oligomerization, toxicity, and neuronal plasticity. *J Neurosci*, 29, 7582-7590.

9. Rose, A., Lorenzen, S., Goede, A., Gruening, B. and **Hildebrand, P.W.** (2009) RHYTHM--a server to predict the orientation of transmembrane helices in channels and membrane-coils. *Nucleic Acids Res*, 37, W575-580.
8. **Hildebrand, P.W.**, Goede, A., Bauer, R.A., Gruening, B., Ismer, J., Michalsky, E. and Preissner, R. (2009) SuperLooper--a prediction server for the modeling of loops in globular and membrane proteins. *Nucleic Acids Res*, 37, W571-574.
7. Hofmann, K.P., Scheerer, P., **Hildebrand, P.W.**, Choe, H.W., Park, J.H., Heck, M. and Ernst, O.P. (2009) A G protein-coupled receptor at work: the rhodopsin model. *Trends Biochem Sci*, 34, 540-552.
6. Rother, K., **Hildebrand, P.W.**, Goede, A., Gruening, B. and Preissner, R. (2009) Voronoia: analyzing packing in protein structures. *Nucleic Acids Res*, 37, D393-395.
5. Scheerer, P., Park, J.H., **Hildebrand, P.W.**, Kim, Y.J., Krauss, N., Choe, H.W., Hofmann, K.P. and Ernst, O.P. (2008) Crystal structure of opsin in its G-protein-interacting conformation. *Nature*, 455, 497-502.
4. **Hildebrand, P.W.**, Gunther, S., Goede, A., Forrest, L., Frommel, C. and Preissner, R. (2008) Hydrogen-bonding and packing features of membrane proteins: functional implications. *Biophys J*, 94, 1945-1953.
3. **Hildebrand, P.W.**, Lorenzen, S., Goede, A. and Preissner, R. (2006) Analysis and prediction of helix-helix interactions in membrane channels and transporters. *Proteins*, 64, 253-262.
2. **Hildebrand, P.W.**, Rother, K., Goede, A., Preissner, R. and Frommel, C. (2005) Molecular packing and packing defects in helical membrane proteins. *Biophys J*, 88, 1970-1977.
1. **Hildebrand, P.W.**, Preissner, R. and Frömmel, C. (2004) Structural features of transmembrane helices. *FEBS Lett*, 559, 145-151.



11.02.16

PD Dr. Peter Hildebrand