BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Huber, Thomas	Research Associate
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Munich, Munich, Germany	M.D.	1988-1995	Medicine
University of Munich, Munich, Germany	Ph.D.	1995-1999	Medicine
University of Munich, Munich, Germany	Postdoc.	1999-2000	Biochemistry
University of Arizona, Tucson, AZ	Postdoc.	2000-2002	Physical Chemistry
The Rockefeller University, New York, NY	Postdoc.	2002	Mol. Biol. and Biochem.

A. Positions and Honors.

Positions and Employment

1990–1994 Research Assistant, Institute for Physical Biochemistry, University of Munich.
1995–1999 Scientific Assistant, Institute for Physical Biochemistry, University of Munich.
1996–2000 Seminar group leader within the program of preclinical education for medical students covering the entire field of Medical Biochemistry (72 hrs per year), Institute for Physiological Chemistry, University of Munich
1999–2000 Postdoctoral Research Fellow, Institute for Metabolic Biochemistry, University of Munich.
2000–2002 Postdoctoral Research Fellow, Department of Chemistry, University of Arizona.
2002– Visiting Scientist, Department of Chemistry, University of Arizona.
2002 Postdoctoral Research Fellow, Laboratory of Molecular Biology and Biochemistry, Rockefeller University, New York, NY.
2002–2004 Associate, Howard Hughes Medical Institute, Laboratory of Molecular Biology and Biochemistry, Rockefeller University, New York, NY.
2004– Research Associate, Laboratory of Molecular Biology and Biochemistry, Rockefeller University, New York, NY.

Other Experience and Professional Memberships (selected)

Biophysical Society, Bethesda, MD.

B. Peer-Reviewed Publications (in chronological order).

1) Huber, T., M. Klingenberg, and K. Beyer. (1999). Binding of nucleotides by the mitochondrial ADP/ATP carrier as studied by ^{1}H nuclear magnetic resonance spectroscopy. Biochemistry. 38, 762-769.
2) Huber, T. (1999). Untersuchungen zur mikroskopischen Struktur einer biologischen Membran numerische Modellrechnungen als methodische Erweiterung physikalischer Experimente. Ph.D. thesis. Ludwig-Maximilians-Universität, München.
3) Hahnel, D., T. Huber, V. F. Kurze, K. Beyer, and B. Engelmann. (1999). Contribution of copper binding to the inhibition of lipid oxidation by plasmalogen phospholipids. Biochem. J. 340, 377-383.
4) Beyer, K., and T. Huber. (1999). Mixed micelle formation between gramicidin-S and a nonionic detergent: a nuclear magnetic resonance model study of peptide/detergent aggregation. Eur. Biophys. J. Biophys. Lett. 28, 166-173.
5) Kurze, V. F., B. Steinbauer, T. Huber, and K. Beyer. (2000). A ^{2}H NMR study of macroscopically aligned bilayer membranes containing interfacial hydroxyl residues. Biophys. J. 78, 2441-2451.
6) Guo, W., V. F. Kurze, T. Huber, N. H. Afdhal, K. Beyer, and J. A. Hamilton (2002), A solid-state NMR study of phospholipid-cholesterol interactions: sphingomyelin-cholesterol binary systems. Biophys. J. 83, 1465-1478.

7) Huber, T., K. Rajamoorthi, V. F. Kurze, K. Beyer, and M. F. Brown. (2002). Structure of docosahexaenoic acid-containing phospholipid bilayers as studied by ^{2}H NMR and molecular dynamics simulations. J. Am. Chem. Soc., 124, 298-309.
8) Huber, T., A. V. Botelho, K. Beyer, and M. F. Brown. (2004). Membrane model for the GPCR rhodopsin: hydrophobic interface and dynamical structure. Biophys. J., 86, 2078-2100.
9) Botelho, A. V., T. Huber, T. P. Sakmar, and M. F. Brown. (2006). Curvature and Hydrophobic Forces Drive Oligomerization and Modulate Activity of Rhodopsin in Membranes. Biophys. J., 91, 4464-4477.
10) Periole, X., T. Huber, S.-J. Marrink, T. P. Sakmar. (2007). G Protein-Coupled Receptors Self-Assemble in Dynamics Simulations of Model Bilayers. J. Am. Chem. Soc., 129, 10126-10132.
11) Banerjee, S., T. Huber, and T. P. Sakmar. (2008). Rapid incorporation of functional rhodopsin into nanoscale apolipoprotein bound bilayer (NABB) particles. J. Mol. Biol., 377, 1067-1081.
12) Louis, M., T. Huber, R. Benton, T. P. Sakmar, and L. B. Vosshall. (2008). Bilateral olfactory sensory input enhances chemotaxis behavior. Nat. Neurosci., 11, 187-199.
13) Vogel, R., M. Mahalingam, S. Lüdeke, T. Huber, F. Siebert, and T. P. Sakmar. (2008). Functional role of the "ionic lock"—an interhelical hydrogen-bond network in family A heptahelical receptors. J. Mol. Biol., 380, 648-655.
14) Ye, S. X., C. Köhrer, T. Huber, M. Kazmi, P. Sachdev, E. C. Y. Yan, A. Bhagat, U. L. RajBhandary, and T. P. Sakmar. (2008). Site-specific incorporation of keto amino acids into functional G protein-coupled receptors using unnatural amino acid mutagenesis. J. Biol. Chem., 283, 1525-1533.
15) Huber, T., and T. P. Sakmar. (2008). Rhodopsin's active state is frozen like a DEER in the headlights. Proc. Natl. Acad. Sci. U.S.A., 105, 7343-7344.
16) Huber, T., S. T. Menon, and T. P. Sakmar. (2008). Structural Basis for Ligand Binding and Specificity in Adrenergic Receptors: Implications for GPCR-targeted Drug Discovery. Biochemistry, 47, 11013-11023.
17) Ye, S., T. Huber, R. Vogel, and T. P. Sakmar. (2009). Azido labels enable FTIR analysis of rhodopsin activation. Nat. Chem. Biol., 5, 397-399.

Invited Reviews and Book Chapters

1) Huber, T., and T. P. Sakmar. (2005). The Photoreceptor Membrane as a Model System in the Study of Biological Signal Transduction. In Advances in Planar Lipid Bilayers and Liposomes, Eds. A. Ottava and H. T. Tien, Elsevier, San Diego, CA. 1, 181-206.
2) Sakmar, T. P., and T. Huber. (2009). Rhodopsin. In New Encyclopedia of Neuroscience, Eds. L. R. Squire, Oxford: Academic Press, Elsevier, San Diego, CA. 8, 365-372.

Abstracts

1) Huber, T., and K. Beyer. (2000). Multiscale properties of the aqueous boundary of biological membranes from simulation. Biophys. J., 78, 182a.
1) Beyer, K., V. F. Kurze, B. Steinbauer, and T. Huber. (2000). Interfacial membrane dynamics as studied by ^{2}H-NMR using exchange labeled hydroxyl residues. Biophys. J., 78, 181a.
2) Huber, T., A. V. Botelho, K. Beyer, and M. F. Brown. (2002). Structural Principles and Applications of ^{2}H NMR and Molecular Dynamics to Biomembranes. Biophys. J., 82, 152a.
3) Huber, T., A. V. Botelho, and M. F. Brown. (2002). Critical Evaluation of Influences of Membrane Lipid Properties on Rhodopsin Function. Biophys. J., 82, 27a. (Talk)
4) Huber, T., A. V. Botelho, and M. F. Brown. (2002). Hydrophobic interface of the GPCR prototype rhodopsin. Biophys. J., 82, 225a.
5) Botelho, A. V., T. Huber, and M. F. Brown. (2002). Hydrophobic Matching of Lipids and Rhodopsin in Membranes Probed by ^{2}H NMR and Flash Photolysis Spectroscopy. Biophys. J., 82,146a.
6) Botelho, A. V., T. Huber, and M. F. Brown. (2002). Lipid-Protein Interactions-New Biomembrane Model. Biophys. J., 82,152a.
7) Botelho, A. V., T. Huber, and M. F. Brown. (2003). Flexible Surface Model for Lipid-Rhodopsin Interactions: Further Analysis. Biophys. J., 84, 55a.
8) Huber, T., A. V. Botelho, and M. F. Brown. (2003). Membrane Model for the GPCR Rhodopsin: Dynamical Structure and Generalized Molecular Surface. Biophys. J., 84, 272a.

9) Huber, T., B. S. W. Chang, and T. P. Sakmar. (2003). Structure and Dynamics of Archosaur Rhodopsin and Other Ancestral Visual Pigments. Biophys., J. 84, 271a.
10) Botelho, A. V., T. Huber, and M. F. Brown. (2004). Free energy additivity for modeling lipid-protein interactions. Biophys. J., 86, 563a.
11) Brown, M. F., A. V. Botelho, T. Huber, and H. I. Petrache. (2004). Polyunsaturated bilayers: What's the difference? Biophys. J., 86, 367a. (Talk).
12) Huber, T., B. S. W. Chang, A. V. Botelho, T. P. Sakmar, and M. F. Brown. (2004). Phase space sampling – A long journey towards realistic biomembrane models. Biophys. J., 86, 417a.
13) Banerjee, S., T. P. Sakmar, and T. Huber. (2005). Incorporation of Rhodopsin into a Nanoscale Apolipoprotein Bound Bilayer. Biophys. J., 88, 2845-Pos.
14) Botelho, A. V., T. Huber, T. P. Sakmar, and M. F. Brown. (2005). Direct Effect of Membrane Stress on Lipid-Rhodopsin Organization and Function. Biophys. J., 88, 2846-Pos.
15) Huber, T., K. M. Gunnison, M. A. Kazmi, B. S. W. Chang, and T. P. Sakmar. (2005). Identification of the Primary Entry Site in Visual Rhodopsins: an Intramembranous Pathway from Mutagenesis and MD Simulations. Biophys. J., 88, 2482-Pos.
16) A. V. Botelho, V. F. Kurze, K. Beyer, M. F. Brown, and T. Huber. (2006) Collective Order Fluctuations from Deuterium NMR Studies of Hydration Effects on POPC–d_{31} Membranes. Biophys. J., 90, 365a. 1744-Pos.
17) Huber, T., A. V. Botelho, T. P. Sakmar, M. F. Brown. (2006). Curvature and Hydrophobic Mismatch Drive Non-Ideal Mixing and Activation of Rhodopsin in Membranes. Biophys. J., 90, 15a. 64-Plat. (Talk).
18) Huber, T., K. M. Gunnison, M. A. Kazmi, B. S. W. Chang, and T. P. Sakmar. (2006). Closing the visual cycle – exit and entry of retinal in opsin. Biophys. J. 90, 331a., 1599-Plat. (Talk).
19) Huber, T., and T. P. Sakmar. (2006). Chromophore Entry and Release in Visual Pigments. Keystone Symposium on G Protein-Coupled Receptors: Evolving Concepts and New Techniques. (Talk).
20) Huber, T., A. V. Botelho, T. P. Sakmar, and M. F. Brown. (2007). Functional consequences of seven-transmembrane receptor association in bilayers. Biophys. J., 92, 198A.
21) Huber, T., K. M. Gunnison, M. A. Kazmi, B. S. W. Chang, and T. P. Sakmar. (2007). Thermodynamic analysis of the ligand binding pathway in the seven-transmembrane (7-TM) receptor rhodopsin. Biophys. J., 92, 186A.
22) Huber, T., X. Periole, S. J. Marrink, and T. P. Sakmar. (2007). Seven-transmembrane (7-TM) receptors self-assemble in coarse grain molecular dynamics (CGMD) simulations of model bilayers. Biophys. J., 92, 250A.
23) Banerjee, S., T. Huber, and T. P. Sakmar. (2008). Imaging Heptahelical Receptors in Nanoscale Apolipoprotein Bound Bilayers. Biophys. J., 94, 477a.
24) Louis, M., T. Huber, R. Benton, T. P. Sakmar, and L. Vosshall. (2009). Mechanisms of chemotactic navigation in Drosophila larvae. J. Neurogenetics, 23, S75-S75.
25) Ye, S., T. Huber, R. Vogel, T. P. Sakmar. (2009). Probing conformational changes in rhodopsin with site-specific azido labels. Biophys. J., 96, 6a.
26) Banerjee, S., A. Grunbeck, T. Huber, P. Sachdev, T. P. Sakmar. (2009). Rapid incorporation of heterologously expressed GPCR CCR5 in nanoscale apolipoprotein bound bilayers (NABBs). Biophys. J., 96, 51a.
27) Huber, T., T. P. Sakmar. (2009). Structural basis of lipid effects on G-protein-coupled receptor (GPCR) activation. Biophys. J., 96, 592a-593a.
28) Ye, S., T. Huber, T. P. Sakmar. (2009). Unnatural amino acid mutagenesis for site-specific incorporation of keto and azido functionalities into functional G protein-coupled receptors. Biophys. J., 96, 632a.
29) Periole, X., T. Huber, S.-J. Marrink, T. P. Sakmar. (2009). Membrane proteins-bilayer interplay: insights from coarse-grained self-assembly and potential of mean force simulations of rhodopsin in model bilayers. Biophys. J., 96, 673a.

C. Research Support

Ongoing Research Support

National Science Foundation's Partnerships for Advanced Computational Infrastructure (NFS PACI) Medium Resource Allocation Committee (MRAC) Renewal grant MCB060033 Huber (PI) 2008-2009
"Ligand binding mechanism in the visual photoreceptor opsin, a G-protein-coupled receptor (GPCR)"
The long-term goal of our research is to provide comprehensive understanding of ligand recognition in seven-transmembrane (7-TM) helical G-protein coupled receptors (GPCRs). The determination of the first high resolution structure of a GPCR, the visual photoreceptor rhodopsin, in the year 2000 was a hallmark that enabled us to study GPCRs by molecular dynamics (MD) simulations. We built models of receptors in a native-like phospholipid bilayer environment. These all-atom models contain typically about 50,000 atoms, and can be routinely simulated on a sub-microsecond timescale using massive parallel processing (MPP) architectures on the TeraGrid, such as the PSC BigBen Cray XT3. Along with biochemical and biophysical experiments to map the thermodynamics of ligand binding in rhodopsin, this research aims at formulating methods to study the mechanism of ligand binding and recognition for GPCRs in general. In contrast to computational 'alchemy' studies to determine the absolute free energy of ligand binding, we utilize in a conceptual framework that focuses on thermally accessible ligand binding pathways and the role of receptor conformational changes in gating the ligand access. In the past year, publication of a series of high resolution crystal structures of additional GPCRs led to dramatic advances in the field. The new structures include β_2-adrenergic receptor, squid rhodopsin, and most recently, opsin, the ligand-free form of bovine rhodopsin. Due to the importance of the β_2-adrenergic receptor structure, we used the majority of the 300,000 service units (SUs) of from the previous application period to simulate several models of β_2-adrenergic receptor with the inverse agonist carazolol and the natural agonist epinephrine (adrenaline) for more than 600 nanoseconds simulation time in total. Here we apply for TeraGrid Wide Roaming Access with 500,000 SUs in order to continue the studies on 11-cis-retinal binding to opsin, which we would like to supplement with comparative studies on ligand binding in β_2-adrenergic receptor. The computational resources will be used for conventional MD simulations to study the equilibrium dynamics of several receptor structures, as well as for biased MD simulations to probe the free energy landscape of the ligand binding pathway.
Role: PI

Completed Research Support

National Science Foundation's Partnerships for Advanced Computational Infrastructure (NFS PACI) Medium Resource Allocation Committee (MRAC) Renewal grant MCB060033 Huber (PI) 2007-2008
"Ligand binding mechanism in the visual photoreceptor opsin, a G-protein-coupled receptor (GPCR)"
Role: PI

NFS PACI Medium Resource Allocation Committee (MRAC) grant MCB060033 Huber (PI) 2006-2007
"Ligand binding mechanism in the visual photoreceptor opsin, a G-protein-coupled receptor (GPCR)"
Role: PI

NSF PACI Development grant MCB020015P Huber (PI) 2002-2003
"Dynamics of phospholipids in G protein-coupled receptor containing membranes"
Role: PI

NSF PACI Development grant MCB020017N Huber (PI) 2002-2003
"Molecular dynamics simulations of a Biomembrane model comprising the G protein-coupled receptor rhodopsin in a polyunsaturated lipid bilayer membrane"
Role: PI

NSF PACI Alliance Allocations Board (AAB) grant MCB020034 Huber (PI) 2002-2003
"Rhodopsin–the single quantum detector and its unique environment"
Role: PI

NFS PACI Alliance Allocations Board (AAB) grant MCB030026 Huber (PI) 2003-2005
"Biomembrane models of G protein-coupled receptor signaling"
Role: PI