H. Schwalbe

*The author presented on this page has published more than **25 articles** since 2000 in Angewandte Chemie, most recently:*
"Characterization of the Simultaneous Decay Kinetics of Metarhodopsin States II and III in Rhodopsin by Solution-State NMR Spectroscopy": J. Stehle, R. Silvers, K. Werner, D. Chatterjee, S. Gande, F. Scholz, A. Dutta, J. Wachtveitl, J. Klein-Seetharaman, H. Schwalbe, *Angew. Chem.* **2014**, *126*, 2110–2116; *Angew. Chem. Int. Ed.* **2014**, *53*, 2078–2084.

Harald Schwalbe

Date of birth:	March 26, 1966
Position:	Professor of Organic Chemistry, University of Frankfurt
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Education:	1985–1990 Diploma, University of Frankfurt 1990–1993 PhD with Prof. C. Griesinger, University of Frankfurt 1993–1995 Postdoctoral fellow with Prof. C. Dobson, University of Oxford 1996–1999 Working on habilitation, University of Frankfurt
Awards:	**2001** Pew Scholar of Biomedical Science; Sloan Research Fellow, A. P. Sloan Foundation; **2002**–present Mentor of the Studienstiftung des deutschen Volkes; **2006** 1822 Award for teaching (Frankfurt University)
Current research interests:	Studying structure and functional dynamics of proteins, RNA, and DNA by NMR spectroscopy Contributing to drug development by using the versatility of chemical synthesis, NMR spectroscopy, and X-ray crystallography
Hobbies:	Singing, playing the piano, reading

My own favorite saying is … "There are 1000 ways of getting no signal".

I admire … my co-workers.

The secret of being a successful scientist is … unclear to me. I would love to know it.

My science "heroes" are … in chemistry: E. J. Corey, F. Crick, C. M. Dobson, M. Eigen, C. Griesinger, and V. Ramakrishnan.

My future I see … as undecided. Time (and destiny) will tell.

My favorite authors are … Thomas Mann, Shakespeare, Goethe, Schiller, Kafka, Musil, and so many authors of poetry (Eichendorff, Celan, Domin, Hesse, Fontane, Keller, C. F. Mayer, etc.).

My favorite painters are … Grünewald (*Resurrection of Christ*); Michaelangelo (the touching fingers in the *Creation of Adam*); Caravaggio (many; e.g., *Calling of Saint Matthew*) and Monet (many; e.g., the drawings of water lilies).

My favorite composers/musicians are … J. S. Bach, W. A. Mozart, L. van Beethoven, and F. Zappa.

My favorite books are … *Faust* by Goethe and *Dr. Faustus* by Thomas Mann.

The natural talent I would like to be gifted with … the ability to write poems, to paint, and to run 100 m in 10 seconds.

My motto is … "Life is beautiful", and I have been blessed to meet so many wonderful people (family, friends, teachers, mentors, colleagues, co-workers, students).

The greatest scientific advance of the last decade was … understanding the (dynamic) structure of the ribosome.

I am waiting for the day when someone will discover … "beaming". I have suggested this Nobel Prize worthy project to many people; I fear nobody will take on the challenge so I might have to do it myself!

The biggest challenge facing scientists is … to identify an interesting question, keep going, understand how it really works, and, after a nights' thought, start again, since everything still remains unclear.

Young people should study chemistry because … it is simply the best preparation for becoming an observer of nature, an inventor of something new, and a designer of new molecules with great properties. And there's nothing else that is as much fun.

Looking back over my career, I … think it has been OK, but there is still so much out there to do.

The two most significant historic events of the past 100 years were … manned flights to the moon and German reunification.

If I could be anyone for a day, I would be … Angela Merkel.

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Has your approach to publishing your results changed since the start of your career?

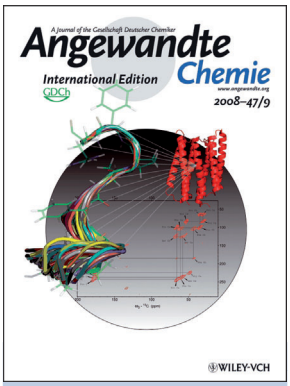
I guess I have become a little more experienced. And I wish to really show what can be learned for a given system within a single paper. There are now many disturbing aspects in publishing: pressure to speed up the reviewing process, and to shift too much data that ought to be in the main text into the supporting information, changing from passive to active voice, being forced to write science in the style of a renarration. I always thought that experiments are objective, time-independent, and thus, use of "we" as personalization of science is incorrect. But then, I read reviews of my manuscripts stating that I should avoid passive voice, so I also use "we". Then, of course, making impact factors of journals important criteria is very unscientific.

What do you think the future holds for your field of research?

NMR will be used to study conformational transitions. We will arrive at the site-resolved description of functional dynamics of proteins, RNA, and DNA. Such a description would include a complete determination of timescales, amplitudes of motions, and enthalpic and entropic contributions for each atom to the stability and kinetics of the system. The experiments will be conducted under increasingly physiological conditions, within cells and their compartments. The interpretation of the results will not only interface with long-timescale molecular dynamics simulations, but also with rigorous kinetic experiments and modeling. Such investigations will lead to an understanding of how cellular processes are regulated, among others by RNA.

My 5 top papers:

1. "Long-Range Interactions within a Nonnative Protein": J. Klein-Seetharaman, M. Oikawa, S. B. Grimshaw, J. Wirmer, E. Duchardt, T. Ueda, T. Imoto, L. J. Smith, C. M. Dobson, H. Schwalbe, *Science* **2002**, *295*, 1719–1722. The paper describes the unfolded state of a protein at atomic resolution. This work, together with C. Dobson, unambiguously shows the presence of secondary and tertiary structure in the unfolded state of a protein. We probed this nonrandom structure by site-directed mutagenesis and explain the native and nonnative interactions on the basis of our general model for the random coil state of proteins.
2. "Kinetic Investigation of Photoinduced RNA Refolding by Real-Time NMR Spectroscopy": P. Wenter, B. Fürtig, A. Hainard, H. Schwalbe, S. Pitsch, *Angew. Chem.* **2005**, *117*, 2656–2659; *Angew. Chem. Int. Ed.* **2005**, *44*, 2600–2603. Together with S. Pitsch, we characterized RNA refolding at atomic resolution by real-time NMR spectroscopy. Different to proteins, RNA molecules can adopt more than one single stable conformation, which often have very similar stability but their interconversion is slow due to high energetic barriers separating the conformational states. This concept of bistable RNAs had been put forward by R. Micura. The Pitsch group had developed RNA chemistry to block Watson–Crick base pairing at specific nucleotide positions by a photolabile group. Introducing a blocked nucleotide into a bistable RNA then led to the complete destabilization of one of the two bistable conformations. By laser irradiation, we could release the photolabile group, track the return to the bistable equilibrium, and derive the kinetics of RNA refolding. The process is four orders of magnitude (!) slower than RNA folding from the random coil.
3. "Time-resolved NMR methods resolving ligand-induced RNA folding at atomic resolution": J. Buck, B. Fürtig, J. Noeske, J. Wöhnert, H. Schwalbe, *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 15699–15704. Together with J. Wöhnert, we then continued to study the ligand-induced folding of a large RNA structure by time-resolved NMR spectroscopy. We initiated folding of riboswitch RNA by releasing the cognate ligand from a synthetic, photocaged precursor and followed the build-up of ca. 20 different RNA reporter signals. We detected different kinetics for different structural elements, and integrated the kinetics into a restrained molecular dynamics simulation to provide a molecular picture of how a single, highly compact ligand-bound state accumulates.
4. "Three-state mechanism couples ligand and temperature sensing in riboswitches": A. Reining, S. Nozinovic, K. Schlepckow, F. Buhr, B. Fürtig, H. Schwalbe, *Nature* **2013**, *499*, 355–359. Riboswitches regulate gene expression in response to binding of a specific, low-molecular-weight metabolite. Prior to our work, the generally accepted model assumed a two-state regulation mechanism: ligand binding induces an allosteric conformational transition. Together with B. Fürtig, we showed that translational riboswitches can populate three long-lived states. Such three-state behavior confers stability of the cellular regulation circuit over a broad range of temperatures and simultaneously integrates a chemical and a physical signal.
5. "Characterization of the Simultaneous Decay Kinetics of Metarhodopsin States II and III in Rhodopsin by Solution-State NMR Spectroscopy": J. Stehle, R. Silvers, K. Werner, D. Chatterjee, S. Gande, F. Scholz, A. Dutta, J. Wachtveitl, J. Klein-Seetharaman, H. Schwalbe, *Angew. Chem.* **2014**, *126*, 2110–2116; *Angew. Chem. Int. Ed.* **2014**, *53*, 2078–2084. Together with J. Wachtveitl and J. Klein-Seetharaman, we followed the light cycle of rhodopsin, a G-protein coupled receptor and the primary light receptor in the eyes of vertebrates. Based on our time-resolved NMR data and by integrating previous X-ray data, we developed a molecular movie on the light-induced kinetics of the visual process. It was the first time where we really needed to develop a moving picture to describe our results. We show that rhodopsin's photodecay involves a parallel kinetic partitioning, previously proposed, but structurally uncharacterized pathway in the light cycle.



The work of H. Schwalbe has been featured on the inside cover of Angewandte Chemie:
"The Structure of the Neuropeptide Bradykinin Bound to the Human G-Protein Coupled Receptor Bradykinin B2 as Determined by Solid-State NMR Spectroscopy": J. J. Lopez, A. K. Shukla, C. Reinhart, H. Schwalbe, H. Michel, C. Glaubitz, *Angew. Chem.* **2008**, *120*, 1692–1695; *Angew. Chem. Int. Ed.* **2008**, *47*, 1668–1671.

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