

BIOGRAPHICAL SKETCH

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NAME Heinrich Roder, Ph.D.		POSITION TITLE Senior Member, Adjunct Professor	
eRA COMMONS USER NAME			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Eidgenössische Technische Hochschule (ETH), Zürich, Switzerland	Diploma	1978	Physics
Eidgenössische Technische Hochschule (ETH), Zürich, Switzerland (Advisor: Kurt Wüthrich)	Ph.D.	1981	Biophysics

A. POSITIONS

Research Associate, Department of Physics, University of Illinois at Urbana-Champaign, 1981-1984
Urbana, IL (with H. Frauenfelder)

Research Assistant Professor, Department of Biochemistry and Biophysics, 1984-1987
University of Pennsylvania, Philadelphia, PA

Assistant Professor, Department of Biochemistry and Biophysics, University of 1987-1990
Pennsylvania, Philadelphia, PA

Associate Professor (with tenure), Department of Biochemistry and Biophysics, 1990-1991
University of Pennsylvania, Philadelphia, PA

Member (with tenure), Institute for Cancer Research, Fox Chase Cancer Center, 1991-1998
Philadelphia, PA

Adjunct Associate Professor/Adjunct Professor, Department of Biochemistry and 1991/1994
Biophysics, University of Pennsylvania, Philadelphia, PA -date

Molecular and Cellular Biophysics Study Section, NIH 1994

NIH Site Visit, Yale University, New Haven, CT 1995

Senior Member, Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia, PA 1998-date

NSF Molecular Biophysics Panel 2001-2005

NIH Center for Scientific Review, Special Emphasis Panels (8 meetings) 1997-date

Program Leader, Biomolecular Structure and Function Program, Fox Chase Cancer Center 2002-date

B. PEER-REVIEWED PUBLICATIONS (selected from a total of 90)

Roder, H., Berendzen, J., Bowne, S.F., Frauenfelder, H., Sauke, T.B., Shyamsunder, E., Weissman, M.B.
Comparison of the magnetic properties of deoxy- and photodissociated myoglobin. *Proc. Natl. Acad. Sci. U.S.A.* **81**:2359-2363, 1984.

Roder, H., Wagner, G., Wüthrich, K. Amide proton exchange in proteins by EX₁ kinetics: Studies of the basic
pancreatic trypsin inhibitor at variable p²H and temperature. *Biochemistry* **24**:7396-7407, 1985.

Roder, H., Wüthrich, K. Protein folding kinetics by combined use of rapid mixing techniques and NMR
observation of individual amide protons. *Proteins: Struct. Funct. Genet.* **1**:34-42, 1986.

Roder, H., Elöve, G.A., Englander, S.W. Structural characterization of folding intermediates in cytochrome c
by H-exchange labeling and proton NMR. *Nature* **335**:700-704, 1988.

Roder, H. Structural characterization of protein folding intermediates by proton magnetic resonance and
hydrogen exchange. *Methods Enzymol.* **176**:446-473, 1989.

Feng, Y., **Roder, H.**, Englander, S.W. Redox-dependent structure change and hyperfine nuclear magnetic
resonance shifts in cytochrome c. *Biochemistry* **29**:3494-3504, 1990.

Jeng, M.-F., Englander, S.W., Elöve, G.A., Wand, A.J., **Roder, H.** Structural description of acid-denatured
cytochrome c by hydrogen exchange and 2D NMR. *Biochemistry* **29**:10433-10437, 1990.

Paterson, Y., Englander, S.W., **Roder, H.** Definition of antibody binding sites on protein antigens by hydrogen
exchange and two-dimensional NMR. *Science* **249**:755-759, 1990.

B. PEER-REVIEWED PUBLICATIONS – HEINRICH RODER, Ph.D. (continued)

- Baldwin, R.L., **Roder, H.** Characterizing protein folding intermediates. *Current Biol.* **1**:218-220, 1991.
- Briggs, M.S., **Roder, H.** Early hydrogen-bonding events in the folding reaction of ubiquitin. *Proc. Natl. Acad. Sci. U.S.A* **89**:2017-2021, 1992.
- Elöve, G.A., Chaffotte, A.F., **Roder, H.**, Goldberg, M.E. Early steps in cytochrome c folding probed by time-resolved circular dichroism and fluorescence spectroscopy. *Biochemistry* **31**:6876-6883, 1992.
- Jones, C.M., Henry, E.R., Hu, Y., Chan, C.-K., Luck, S.D., Bhuyan, A., **Roder, H.**, Hofrichter, J., Eaton, W.A. Fast events in protein folding initiated by nanosecond laser photolysis. *Proc. Natl. Acad. Sci. U.S.A* **90**:11860-11864, 1993.
- Khorasanizadeh, S., Peters, I.D., Butt, T.R., **Roder, H.** Folding and stability of a tryptophan-containing mutant of ubiquitin. *Biochemistry* **32**:7054-7063, 1993.
- Moore, K.S., Wehrli, S., **Roder, H.**, Rogers, M., Forrest, J.N., Mc Crimmon, D., Zasloff, M. Squalamine An Aminosterol antibiotic from the shark. *Proc. Natl. Acad. Sci. U.S.A* **90**:1354-1358, 1993.
- Wu, L., Laub, P.B., Elöve, G.A., Carey, J., **Roder, H.** A Noncovalent peptide complex as a model for an early folding intermediate of cytochrome c. *Biochemistry* **32**:10271-10276, 1993.
- Elöve, G.A., Bhuyan, A.K., **Roder, H.** Kinetic mechanism of cytochrome c folding: involvement of the heme and its ligands. *Biochemistry* **33**:6925-6935, 1994.
- Gochin, M., **Roder, H.** Protein structure refinement based on paramagnetic NMR shifts: applications to wild-type and mutant forms of cytochrome c. *Protein Sci.* **4**:296-305, 1995.
- Roder, H.** Watching protein folding unfold. *Nature Struct. Biol.* **2**:817-820, 1995.
- Zhang, Y.-Z., Paterson, Y., **Roder, H.** Rapid amide proton exchange rates in peptides and proteins measured by solvent quenching and two-dimensional NMR. *Protein Sci.* **4**:804-814, 1995.
- Khorasanizadeh, S., Peters, I.D., **Roder, H.** Evidence for a 3-state model of protein folding from kinetic analysis of ubiquitin variants with altered core residues. *Nature Struct. Biol.* **3**:193-205, 1996.
- Colón, W., Elöve, G.A., Wakem, L.P., Sherman, F., **Roder, H.** Side chain packing of the N- and C-terminal helices plays a critical role in the kinetics of cytochrome c folding. *Biochemistry* **35**:5538-5549, 1996.
- Colón, W., **Roder, H.** Kinetic intermediates in the formation of the cytochrome c molten globule. *Nature Struct. Biol.* **3**:1019-1025, 1996
- Sauder, J.M., MacKenzie, N.E., **Roder, H.** Kinetic mechanism of folding and unfolding of *Rhodobacter capsulatus* cytochrome c₂. *Biochemistry* **35**:16852-16862, 1996.
- Colón, W., Wakem, L.P., Sherman, F., **Roder, H.** Identification of the predominant non-native histidine ligand in unfolded cytochrome c. *Biochemistry* **36**:12535-12541, 1997.
- Park, S.-H., O'Neil, K.T., **Roder, H.** An early intermediate in the folding reaction of the B1 domain of protein G contains a native-like core. *Biochemistry* **36**:14277-14283, 1997.
- Pinheiro, T.J.T., Elöve, G.A., Watts, A., **Roder, H.** Structural and kinetic description of cytochrome c unfolding induced by the interaction with lipid vesicles. *Biochemistry* **36**:13122-13132, 1997.
- Roder, H.**, Colón, W. Kinetic role of early intermediates in protein folding. *Curr. Opin. Struct. Biol.* **7**:15-28, 1997.
- Walkenhorst, W.F., Green, S.M., **Roder, H.** Kinetic evidence for folding and unfolding intermediates in Staphylococcal nuclease. *Biochemistry* **63**:5795-5805, 1997.
- Houry, W.A., Sauder, J.M., **Roder, H.**, Scheraga, H.A. Definition of amide protection factors for early kinetic intermediates in protein folding. *Proc. Natl. Acad. Sci. U.S.A* **95**:4299-4302, 1998.
- Sauder, J.M., **Roder, H.** Amide protection in an early folding intermediate of cytochrome c. *Folding & Design* **3**:293-301, 1998.
- Shastri, M.C.R., Luck, S.D., **Roder, H.** A continuous-flow capillary mixer to monitor reactions on the microsecond time scale. *Biophys. J.* **74**:2714-2721, 1998.
- Shastri, M.C.R., **Roder, H.** Evidence for barrier-limited protein folding kinetics on the microsecond time scale. *Nature Struct. Biol.* **5**:385-392, 1998.
- Shastri, M.C.R., Sauder, J.M., **Roder, H.** Kinetic and structural analysis of submillisecond folding events in cytochrome c. *Acct. Chem. Res.* **31**:717-725, 1998.
- Walsh, S.T.R., Cheng, H., Bryson, J.W., **Roder, H.**, DeGrado, W.F. Solution structure and dynamics of a *de novo* designed three helix bundle protein. *Proc. Natl. Acad. Sci. U.S.A.* **96**:5486-5491, 1999.
- Park, S.-H., Shastri, M.C.R., **Roder, H.** Folding dynamics of the B1 domain of protein G explored by ultrarapid mixing. *Nature Struct. Biol.* **6**:943-947, 1999.

B. PEER-REVIEWED PUBLICATIONS – HEINRICH RODER, Ph.D. (continued)

- Roder, H., Shastry, M.C.R. Methods for exploring early events in protein folding. *Curr. Opin. Struct. Biol.* **9**:620-626, 1999.
- Pinheiro, T.J., Cheng, H., Seeholzer, S.H., Roder, H. Direct evidence for the cooperative unfolding of cytochrome c in lipid membranes from H-(2)H exchange kinetics. *J. Mol. Biol.* **303**:617-626, 2000.
- Talaga, D.S., Lau, W.L., Roder, H., Tang, J., Jia, Y., Degrado, W.F., Hochstrasser, R.M. Dynamics and folding of single two-stranded coiled-coil peptides studied by fluorescent energy transfer confocal microscopy. *Proc. Natl. Acad. Sci. U.S.A.* **97**:13021-13026, 2000.
- Capaldi, A.P., Shastry, M.C.R., Kleanthous, C., Roder, H., Radford, S.E. Ultrarapid mixing experiments reveal that Im7 folds via an on-pathway intermediate. *Nature Struct. Biol.* **8**:68-72, 2001.
- Kuwata, K., Shastry, M.C.R., Cheng, H., Hoshima, M., Batt, C.A., Goto, Y., Roder, H. Structural and kinetic characterization of early folding events in β -lactoglobulin. *Nature Struct. Biol.* **8**:151-155, 2001.
- Cheng, R.P., Suich, D.J., Cheng, H., Roder, H., DeGrado, W.F. Template-constrained somatostatin analogues: a biphenyl linker induces a type-V' turn. *J. Amer. Chem. Soc.* **123**:12710-12711, 2001.
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- Hagen, S.J., Latypov, R.F., Dolgikh, D.A., Roder, H. Rapid intrachain binding of histidine-26 and histidine-33 to heme in unfolded ferrocytochrome C. *Biochemistry* **41**:1372-1380, 2002.
- Teilum, K., Maki, K., Kragelund, B.B., Poulsen, F.M., Roder, H. Early kinetic intermediate in the folding of Acyl-Coenzyme A binding protein detected by fluorescence labeling and ultrarapid mixing. *Proc. Natl. Acad. Sci. U.S.A.* **99**:9807-9812, 2002.
- Abdullaev, Z., Bodrova, M. E., Chernyak, B. V., Dolgikh, D. A., Kluck, R. M., Pereverzev, M. O., Arseniev, A. S., Efremov, R. G., Kirpichnikov, M. P., Mokhova, E. N., Newmeyer, D. D., Roder, H. & Skulachev, V. P. A cytochrome c mutant with high electron transfer and antioxidant activities but devoid of apoptogenic effect. *Biochem. J.* **362**:749-54, 2002.
- Zhang, Y.Z., Cheng, H., Gould, K.L., Golemis, E.A., Roder, H. Structure, stability and function of hDim1 investigated by NMR, circular dichroism and mutational analysis. *Biochemistry* **42**:9609-9618, 2003.
- Gianni, S., Travaglini-Allocatelli, C., Cutruzzola, F., Brunori, M., Shastry, M.C., Roder, H. Parallel pathways in cytochrome c(551) folding. *J. Mol. Biol.* **330**:1145-1152, 2003.
- Kuwata, K., Matumoto, T., Cheng, H., Nagayama, K., James, T.L., Roder, H. NMR-detected hydrogen exchange and molecular dynamics simulations provide structural insight into fibril formation of prion protein fragment 106-126. *Proc. Natl. Acad. Sci. U.S.A.* **100**:14790-14795, 2003.
- Zhu, Y., Alonso, D.O., Maki, K., Huang, C.Y., Lahr, S.J., Daggett, V., Roder, H., DeGrado, W.F., Gai, F. Ultrafast folding of alpha3D: a *de novo* designed three-helix bundle protein. *Proc. Natl. Acad. Sci. U.S.A.* **100**:15486-15491, 2003.
- Roder, H. Stepwise helix formation and chain compaction during protein folding. *Proc. Natl. Acad. Sci. U.S.A.* **101**:1793-1794, 2004.
- Maki, K., Cheng, H., Dolgikh, D.A., Shastry, M.C.R., Roder, H. Early events during folding of wild-type staphylococcal nuclease and a single-tryptophan variant studied by ultrarapid mixing. *J. Mol. Biol.* **338**:383-400, 2004.
- Roder, H., Maki, K., Cheng, H., Shastry, M.C.R. Rapid mixing methods for exploring the kinetics of protein folding. *Methods* **34**:15-27, 2004.
- Pabit, S.A., Roder, H., Hagen, S.J. Internal friction controls the speed of protein folding from a compact configuration. *Biochemistry* **43**:12532-12538, 2004.
- Welker, E., Maki, K., Shastry, M.C.R., Juminaga, D., Bhat, R., Scheraga, H.A., Roder, H. Ultrarapid mixing experiments shed new light on the characteristics of the initial conformational ensemble during the folding of ribonuclease A. *Proc. Natl. Acad. Sci. USA* **101**:17681-17686, 2004.
- Garcia, P., Bruix, M., Rico, M., Ciofi-Baffoni, S., Banci, L., Shastry, M.C.R., Roder, H., de Lumley-Woodyear, T., Johnson, C.M., Ratner, V., Fersht, A.R., Baker, P.D. Effect of heme on the structure of the denatured state and folding kinetics of cytochrome b₅₆₂. *J. Mol. Biol.* **346**:331-344, 2005.

B. PEER-REVIEWED PUBLICATIONS – HEINRICH RODER, Ph.D. (continued)

Kurchan, E., Roder, H., Bowler, B.E. Kinetics of loop formation and breakage in the denatured state of iso-1-cytochrome *c*. *J. Mol. Biol.* **353**:730-743, 2005.

Roder, H., Maki, K., Cheng, H. Early events in protein folding explored by rapid mixing methods. *Chem. Rev.* **106**:1836-1861, 2006.

Latyov, R.F., Cheng, H., Roder, N.A., Zhang, J., Roder, H. Structural characterization of an equilibrium unfolding intermediate in cytochrome *c*. *J. Mol. Biol.* **357**:1009-1025, 2006.

Apetri, A. C., Maki, K., Roder, H. & Surewicz, W. K. Early intermediate in human prion protein folding as evidenced by ultrarapid mixing experiments. *J. Am. Chem. Soc.* **128**:11673-8, 2006.

SELECTED BOOK CHAPTERS

Roder, H., Shastry, M.C.R., Sauder, J.M., Park, S.-H. Kinetic and structural characterization of early events in protein folding. Old and new views of protein folding. E (Kuwajima, K., Arai, M. eds.), Amsterdam: Elsevier, 1999.

Roder, H., Elöve, G.A., Shastry, R.M.C. Early stages of protein folding. In *Mechanisms of protein folding* (Pain, R. H. eds.), pp. 65-104. Oxford University Press, New York, 2000.

Roder, H., Maki, K., Latypov, R.F., Cheng, H., Shastry, M.C.R. Early events in protein folding explored by rapid mixing methods. In *Protein Folding Handbook* (Buchner, J., Kiefhaber, T., eds.), pp. 491-535. Wiley-VCH, Weinheim, 2005.

C. RESEARCH SUPPORT**Ongoing Research Support**

R01 GM056250 (PI: Roder)

05/01/2006 – 04/30/2010

NIH

Kinetics of Early Events in Protein Folding

The major goals of this project are: 1) To monitor the formation of specific tertiary interactions during folding of staphylococcal nuclease (SNase) and cytochrome *c* (cyt *c*) from tens of microseconds to minutes in an effort to understand the nature of (early) folding events and structural properties of intermediates; 2) To characterize the structure and dynamics of early intermediates during folding of cyt *c* and SNase by ultrafast quenched-flow H/D exchange and NMR; 3) To characterize the structure of equilibrium intermediates in protein folding in order to understand the basis of structural cooperativity and the relationship between thermodynamic and kinetic intermediates; and 4) To explore the conformational properties of the denatured state by fluorescence and hydrodynamic methods.

Role: Principal Investigator

P30 CA06927 (PI: Young)

09/10/2005 – 06/30/2010

NIH

Comprehensive Cancer Center Program at Fox Chase

This Cancer Center Support Grant provides salary support to Dr. Roder as Facility Director of the Spectroscopy Support Facility and Major Program Leader.

Role: Program Leader and Facility Director

Completed Research Support

MCB-0079148 (PI: Roder)

08/01/2000 – 07/31/2004

NSF

Structural and Kinetic Characterization of Barriers and Intermediates in Folding of Cytochrome *c*

The major goal of this project is to elucidate: 1) The properties and origin of the kinetic barrier encountered during the initial collapse of the polypeptide chain; 2) The role of intermediates in directing folding; 3) The nature of the rate-limiting energy barrier; and 4) The cooperativity in folding/unfolding transitions.

Role: Principal Investigator