Freie Universität Berlin
Fachbereich Chemie
Institut für Kristallographie

Simulation and Analysis of Docking and Molecular Dynamics of Electron-Transfer Protein Complexes

Dissertation zur Erlangung der Doktorwürde des Fachbereiches Chemie der Freien Universität Berlin

vorgelegt von

G. Matthias Ullmann

1. Gutachter: Prof. Dr. Ernst-Walter Knapp
2. Gutachter: Prof. Dr. Wolfram Saenger

Berlin, 27. August 1998

Acknowledgments

This work was done in the group of Professor Ernst-Walter Knapp at the Free University of Berlin. Professor Ernst-Walter Knapp enabled me to work on dynamic properties of electron-transfer protein complexes. With his ideas and interest he constantly supported my work. Thank to him, I had excellent working conditions throughout my time in Berlin. Professor Nenad M. Kostić (Iowa State University Ames) awaked my interest on protein-mediated electron transfer. He always found time to answer my questions and was open for new ideas. All members of our group in Berlin helped me in many respects. Specially, I am thankful to Dr. Daniel Hoffmann who always had time to give me advises and to discuss problems in the beginning of my PhD work, Björn Rabenstein for his collaboration in the calculations of the electron-transfer and protonation reactions at the bacterial photosynthetic reaction center, Dr. Markus Hauswald and Dr. Axel Jensen (Bayer AG) for their collaboration in superimposing plastocyanin and cytochrome c_6 as well as ferredoxin and flavodoxin, and Bernd Melchers for keeping our network running and for installing many useful programs. It was a pleasure to contribute to the experimental work of Dr. Tatjana N. Parac, Maja M. Ivković-Jensen, Ekaterina V. Sokerina, and Milan Crnogorac of Professor Kostić's group. The discussions we had personally and via email helped me a lot. I thank Mandy Colditz and Christa Ullmann for proof reading my thesis. Programs with which parts of the data in this thesis have been calculated were kindly provided by Prof. Donald Bashford (MEAD), Dr. Paul Beroza (MCTI), Dr. Jeffrey J. Regan (GREENPATH), and Dr. Per Kraulis (MOLSCRIPT).

I am grateful to the Boehringer Ingelheim Fonds for financial support of this work. Particularly I thank Monika Beutelsbacher and Dr. Hermann Fröhlich for their help in many respects and for organizing the wonderful Boehringer Ingelheim Fonds meetings in Hirschegg and Blaubeuren.

Especially I thank my parents, Konrad and Christa Ullmann, and my sister Barbara Ullmann. They always encouraged and supported me during my whole study and raised my interest for life science and physics.

Contents

Curriculum Vitae

Name:	G. Matthias Ullmann
Address:	Roonstr. 23 12203 Berlin Germany Tel. +49-30-838-2842
Nationality:	German
Date of Birth:	September 26, 1970
Birthplace:	Stollberg/Erzgebirge (Saxony)
Marital-Status:	not married
Profession:	Biochemist

Education

September 1977 - August 1987	Primary and secundary school in Lugau (Final Exam – Grade: A)
September 1987 - August 1989	High school ('Gymnasium') in Stollberg (Abitur – Grade: A)
September 1989 - August 1990	Military Service in Delitzsch and Leipzig
September 1990 - September 1992	Study of Biology at the *Friedrich-Schiller-University Jena* (Prediploma – Grade: A)
Oktober 1992 - Juli 1995	Study of Biochemistry at the *University of Witten/Herdecke* (Audited Account: Diplom-Biochemist)
August 1993 - Novenber 1993	Research Visit in the laboratory of Prof. Dr. Nenad M. Kostić *Iowa State University Ames* (Electron-Transfer in the Plastocyanin-Cytochrome *c* -Complex)
Januar 1995 - Juli 1995	exteral Diploma Thesis at the *Free University Berlin* (Institute for Crystallography, AG Prof. Ernst-Walter Knapp) (Analysis of Conformations of Amino Acids Sidechains to Simulate the Long-Term Dynamic of Proteins using a Monte-Carlo Method.) (Diploma – Grade: A)
October 1995 - April 1996	Researcher in the group of Prof. Dr. Ernst-Walter Knapp (*Free University Berlin*) (Cluster-Algorithms and Rotamer Libraries)
May 1996 - June 1996	Research Visit in the laboratory of

	Prof. Dr. Nenad M. Kostić *Iowa State University Ames* (Electron-Transfer in the Plastocyanin-Cytochrome *f* -Complex)
since April 1996	PhD work in the group Prof. Dr. Ernst-Walter Knapp (*Free University Berlin*) (Simulation and Analysis of Docking and Dynamics of Electron-Transfer Protein-Complexes)

Fellowships

January 1991 - September 1995	German National Merit Foundation Fellowship (Studienstiftung)
since July 1996	Boehringer Ingelheim Fonds Fellowship

Teaching Activities

1995-1998	Supervising several practial trainings on computational biochemistry and biophysics
1997	Supervising the diploma study of B. Rabenstein („Protonation and Redox States of the Quinones in the Bacterial Reaction Center of Rhodopseudomonas viridis.")
1998	Supervising the diploma study of M. Franke („Simulation of the Self-Exchange Electron Transfer of Rubredoxin.")

Berlin, November 4, 1998

Publications

Journal Articles

1. G. Matthias Ullmann and Nenad M. Kostić (1995): Electron Tunneling Paths in Various Electrostatic Complexes between Cytochrome *c* and Plastocyanin. Anisotropy of the Copper-Ligand Interactions and Dependence of the Iron-Copper Electronic Coupling on the Metalloprotein Orientation. *J. Am. Chem. Soc.*, **117**: 4766-4774

2. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić (1997): Computational Simulation and Analysis of the Dynamic Associtión between Plastocyanin and Cytochrome *f*. Consequences for the Electron-transfer Reaction. *J. Am. Chem. Soc.*, **119**: 42-52

3. G. Matthias Ullmann, Markus Hauswald, Axel Jensen, Nenad M. Kostić, and Ernst-Walter Knapp (1997): Comparison of the Physiologically-Equivalent Proteins Cytochrome c_6 and Plastocyanin on the Basis of Their Electrostatic Potentials. Tryptophane 63 in Cytochrome c_6 May Be Isofunctional with Tyrosine 83 in Plastocyanin. *Biochemistry*, **36**: 16187-16196

4. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp (1998): Energetics of Electron Transfer and Protonation Reactions of Quinons in the Photosynthetic Reaction Center of *Rhodopseudomonas viridis*. *Biochemistry*, **37**: 2488-2495

5. Maja M. Ivković-Jensen, G. Matthias Ullmann, Simon Young, Örjan Hansson, Milan Crnogorac, Mikael Ejdebäck, and Nenad M. Kostić (1998): Effects of Single and Double Mutations in Plastocyanin on the Rate Constant and Activation Parameters of the Gated Electron-Transfer Reaction between the Triplet State of Zinc Cytochrome *c* and Cupriplastocyanin. *Biochemistry*, **37**: 9557-9569

6. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp: Calculation of Protonation Patterns in Proteins with Conformational Relaxation - Application to the Photosynthetic Reaction Center. *Eur. Biophys. J.*, **27**: 628-637

7. Ekaterina V. Sokerina, G. Matthias Ullmann, Gertie van Pouderoyen, Gerard W. Canters, and Nenad M. Kostić: Electrostatic Effects on the Kinetics of Photoinduced Electron-Transfer Reactions of the Triplet State of Zinc Cytochrome *c* with Wild-Type and Mutant Forms of *Pseudomonas aeruginosa* Azurin. *submitted*

8. Tatjana N. Parac, G. Matthias Ullmann, and Nenad M. Kostić: New Regioselectivity in the Cleavage of Histidine-Containing Peptides by Palladium(II) Complexes by Kinetic Experiments and Molecular Dynamics Simulations. *submitted*

9. Maja M. Ivković-Jensen, G. Matthias Ullmann, Milan Crnogorac, Mikael Ejdebäck, Simon Young, Örjan Hansson, and Nenad M. Kostić (1998): Comparing the Rates and the Activation Parameter for the Forward Reaction between the Triplet State of Zinc Cytochrome *c* and Cupriplastocyanin and the Back Reaction between the Zinc Cytochrome *c* Cation Radical and Cuproplastocyanin. *submitted*

10. Maja M. Ivković-Jensen, G. Matthias Ullmann, Simon Young, and Örjan Hansson (1998): Electrostatic Interactions Between the Triplet State of Zinc Cytochrome *c* and Cupriplastocyanin in the Bimolecular Electron-Transfer Reaction. Effects of Ionic Strength and Plastocyanin Mutation on the Bimolecular Rate Constant. *submitted*

11. G. Matthias Ullmann and Ernst-Walter Knapp: Electrostatic Computations of Protonation and Redox Equilibria in Proteins. *Invited Review* in *Eur. Biophys. J., in preparation*

12. G. Matthias Ullmann, Markus Hauswald, Axel Jensen, and Ernst-Walter Knapp: Superposition of Ferredoxin and Flavodoxin Using Their Electrostatic Potentials. Implications for Their Interactions with Photosystem I and Ferredoxin:NADP Reductase. *in preparation*

13. G. Matthias Ullmann, Michael Rempel, and Ernst-Walter Knapp: A New Type of Algorithm for Clustering Molecular Structures. *in preparation*

14. G. Matthias Ullmann: The Coupling of Protonations and Oxidations in Proteins. A Computational Investigation of the Redox Bohr-Effect in Cytochrome c_3. *in preparation*

Talkes at International Conferences

1. G. Matthias Ullmann (1996): Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. EUROBIC 3 Noordwijkerhout August 4-10 1996, 3rd European Conference on Bio-inorganic Chemistry.

2. G. Matthias Ullmann (1996): Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. IUPAB XII Amsterdam August 11-16 1996, XIIth International Biophysics Congress.

3. G. Matthias Ullmann (1997) Electron Transfer in the Plastocyanin-Cytochrome *f*-Complex. May 8-11 1997, Joint Meeting of the Italian and German Biophysical Society. Hünfeld.

Book Articles

1. G. Matthias Ullmann, Ingo Muegge, and Ernst-Walter Knapp (1996): Shifts of the Special Pair Redox Potential of Mutants of *Rhodobacter sphaeroides* calculated with Delphi and Charmm Energy Functions. In: *Reaction Centers of Photosynthetic Bacteria. Structure and Dynamics. Michel-Beyerle, E. M. (Ed.)* pg. 143-155 Springer Verlag Heidelberg.

2. G. Matthias Ullmann (1999): Mechanisms of Charge Transfer in Biomaterials. *In: Handbook of Advanced Electronic and Photonic Materials. H. S. Nalwa (Ed.) in prepraration* (Invited Review) Academic Press.

Articles in Conference Proceedings etc.

1. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić (1996): Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. *Prog. Biophys. Mol. Biol.* **65(Sup.)**:153

2. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp (1997): Protonation and Redox States of the Quinones in the Reaction Center of *Rhodopseudomonas viridis*. *Eur. Biophys. J.* **26**:122

3. G. Matthias Ullmann (1996): Simulation and Analysis of Docking and Dynamics of Electron-Transfer Protein-Complexes. *Futura* **3/96**: 219-220

4. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić (1997): Electron Transfer in the Plastocyanin-Cytochrome *f* and the Cytochrome c_6-Cytochrome *f* Complex. *J. Inorg. Biochem.* **67**: 401

Thesis

1. G. Matthias Ullmann (1995): Analyse und Auswahl von Konformationen der Aminosäureseitenketten zur Simulation der Langzeitdynamik von Proteinen mit einer Monte-Carlo-Methode. *Diploma Thesis. Universität Witten/Herdecke*

2. G. Matthias Ullmann (1998): Simulation and Analysis of Docking and Dynamics of Electron-Transfer Protein-Complexes. *PhD Thesis (not accepted yet). Freie Universität Berlin*

Contributions at International Conferences

1. G. Matthias Ullmann and Nenad M. Kostić. Electron-Tunneling Paths in Various Electrostatic Complexes between Cytochrome c and Plastocyanin. Hünfeld-Conference, May 11-14 1995, Meeting of the German Society of Biophysics. *Poster*

2. G. Matthias Ullmann and Nenad M. Kostić. Theoretical Analysis of Electron-Transfer Pathways and pK_a-Values in the Electrostatic Complex between Plastocyanin and Cytochrome *f*. ICBIC 7 Lübeck September 3-8 1995, International Congress on Bioinorganic Chemistry. *Poster*

3. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić. Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. EUROBIC 3 Noordwijkerhout August 4-10 1996, 3rd European Conference on Bio-inorganic Chemistry. *Poster and Oral Presentation*

4. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić. Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. IUPAB XII Amsterdam August 11-16 1996, XIIth International Biophysics Congress. *Poster and Oral Presentation*

5. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić. Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. NATO Advanced Workshop, San Mineato, Italy, March 15-21 1997 *Poster*

6. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić. Electron Transfer in the Plastocyanin-Cytochrome *f*-Complex. May 8-11 1997, Joint Meeting of the Italian and German Biophysical Society. Hünfeld. *Poster and Oral Presentation*

7. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić. Modelling of the Plastocyanin-Cytochrome *f*-Complex. Simulations and Calculations of Electron-Transfer Pathways. Second International Symposium on Algorithms for Macromolecular Modelling, May 21 - 24 1997, Berlin. *Poster*

8. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp. Protonation and Redox States of the Quinones in the Reaction Center of Rps. viridis. 2nd European Biophysics Congress, EBSA 97, Orléans July 13-17 1997. *Oral Presentation (Björn Rabenstein)*

9. G. Matthias Ullmann, Ernst-Walter Knapp, and Nenad M. Kostić. Electron Transfer in the Plastocyanin-Cytochrome *f* and the Cytochrome c_6-Cytochrome *f* Complex. ICBIC 8 Yokohama July 27 - August 1 1997, International Congress on Bioinorganic Chemistry. *Poster*

10. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp. Energetics of Electron and Proton Transfer Reactions of the Quinones in the Photosynthetic Reaction Center of *Rhodopseudomonas viridis*. Workshop: Hydrogen Transfer - Experiment and Theory; Berlin, September 10-13 1997. *Poster*

11. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp. Triple Moves in Monte Carlo Titration of Systems with Strongly Coupled Titratable Groups - Application to the Reaction Center of *Rhodopseudomonas viridis* with a Low Dielectric Constant. Workshop: Monte Carlo Approach to Biopolymers and Protein Folding. HLRZ, Forschungszentrum Jülich, December 3-5 1997. *Poster*

12. G. Matthias Ullmann, M. Hauswald, A. Jensen, Nenad M. Kostić, and Ernst-Walter Knapp. Comparison of Protein Structures on the Basis of Electrostatic Potentials. The Isofuctional Proteins Cytochrome c_6 and Plastocyanin. European Conference on Computational Chemistry and the Living World From Sequence to Function, Chambery, April 20-24 1998. *Oral Presentation (Ernst-Walter Knapp)*

13. G. Matthias Ullmann and Ernst-Walter Knapp. Coupling of Electron and Proton Transfer. Computational Investigation of the Redox Bohr-Effect in Cytochrome c_3. EBEC 98, Göteborg, June 27 – July 2, 1998. *Poster*

14. G. Matthias Ullmann, M. Hauswald, Nenad M. Kostić, and Ernst-Walter Knapp. Superposition of Isofunctional Proteins on the Basis of Their Electrostatic Potentials. Application to Plastocyanin and Cytochrome c_6 and to Ferredoxin and Flavodoxin. EUROBIC 4. Seville, July 20-25 1998. *Poster*

15. Björn Rabenstein, G. Matthias Ullmann, and Ernst-Walter Knapp. Protonation Patterns of the Photosynthetic Reaction Center and Energetics of the Different Charge and Protonation States of the Quinones. XIth International Congress on Photosynthesis. Budapest, August 17-22 1998. *Poster*

16. G. Matthias Ullmann and Ernst-Walter Knapp. Coupling of Electron and Proton Transfer. Computational Investigation of the Redox Bohr-Effect in Cytochrome c_3. Coupling of Electron and Protons in Photosynthesis. Seregélyes, August 14-17 1998. Satellite Meeting of the XIth International Congress on Photosynthesis. *Poster*

17. G. Matthias Ullmann and Ernst-Walter Knapp. Electrostatic superposition of Ferredoxin and Flavodoxin. XIth International Congress on Photosynthesis. Budapest, August 17-22 1998. *Poster*

18. G. Matthias Ullmann, M. Hauswald, Nenad M. Kostić, and Ernst-Walter Knapp. Superposition of Isofunctional Proteins on the Basis of Their Electrostatic Potentials. Application to Plastocyanin and Cytochrome c_6 and to Ferredoxin and Flavodoxin. Talking Proteins: an EMBO Workshop. Heidelberg, September 16-19 1998 *Poster*

19. G. Matthias Ullmann, M. Hauswald, Nenad M. Kostić, and Ernst-Walter Knapp. Superposition of Isofunctional Proteins on the Basis of Their Electrostatic Potentials. Application to Plastocyanin and Cytochrome c_6 and to Ferredoxin and Flavodoxin. Annual Meeting of the German Biophisics Society. Frankfurt, September 20-23 1998. *Poster*