

A complex 3D molecular model of a protein structure, featuring a dense network of atoms represented by small spheres (white for carbon, red for oxygen, blue for nitrogen) and connected by sticks. Large, flat, colored surfaces (red, orange, yellow, green, blue) represent the protein's secondary structure elements, such as alpha-helices and beta-sheets, which are intertwined and folded. The background is a light blue gradient.

Biothermodynamics

The Role of Thermodynamics
in Biochemical Engineering

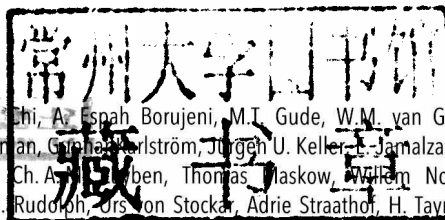
Edited by Urs von Stockar

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The Role of Thermodynamics in Biochemical Engineering

Edited by Urs von Stockar



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PREFACE

Biotechnology is a fascinating yet complex area with enormous potential for enhancing the well-being of mankind and of the environment. For those applications under development that aim to bring this potential to fruition, biotechnologists and biochemical engineers seek those fundamental principles that provide insight into the immensely complicated behaviour of the biological and biochemical world and that can be used for planning experimental research and interpreting results.

In the early 90s, the Steering Committee of the European Science Foundation (ESF) program on Process Integration in Biochemical Engineering (PIBE) recognized that thermodynamics represents one set of such fundamental principles, but which had hitherto only rarely been applied in biotechnology, although quite a substantial body of knowledge and results had already been published. It therefore decided to develop a course for advanced graduate students and researchers in order to make the field of thermodynamics as applied to biotechnology better known, and in order to stimulate its use.

Since then, this graduate course on *Thermodynamics in Biochemical Engineering* has taken place six times: 1994 in Toulouse (F), 1996 in Braga (P), 1998 in Nijmegen (NL), 2000 on Monte Verità above Ascona (CH), 2005 in Mürren (CH) and 2008 in Biedenkopf (D). Table 1 lists the lecturers who taught these courses. They were organized and coordinated by L.A.M. van der Wielen and / or U. von Stockar.

In all these years, a considerable amount of course material has accumulated. The aim of this book is to make this available to a larger audience in an up-dated and edited format. The book will also serve as a formal basis for future advanced courses on thermodynamics in biochemical engineering.

The very nature of such an endeavour makes the perfect matching of writing and presentation styles for the individual chapters impossible. The fact that thermodynamics has not yet been very widely applied in biotechnology, and that consequently many biotechnologists are unfamiliar with thermodynamics, made it necessary to include quite a number of chapters intended as introductions to particular topics and written in a pedagogical manner. At the same time, a growing number of research projects on the application of thermodynamics to biochemical engineering are carried out and published. In an attempt to inform the reader on the state of art in this field, other chapters represent reviews of cutting edge research and results.

For the courses, a large number of problems and assignments for the participants have been developed as well. Some of these are included in certain chapters as

Table 1 List of speakers who have lectured in one or several advanced courses on Thermodynamics in Biochemical Engineering.

Lecturers	Affiliation	Country
J. de Swaan Arons	Delft University of Technology (TUD)	The Netherlands
F. Franks	Pafra Ltd, Cambridge	United Kingdom
E. Gnaiger	University Hospital	Austria
P. J. Halling	University of Strathclyde, Glasgow	United Kingdom
C. A. Haynes	University of British Columbia, Vancouver	Canada
J. J. Heijnen	Delft University of Technology (TUD)	The Netherlands
J. Keller	Universität Siegen	Germany
T. Maskow	Umwelt Forschungszentrum (UFZ) Leipzig	Germany
W. NORde	Wageningen University (WUR)	The Netherlands
J. M. Prausnitz	University of California, Berkeley	USA
T. Randolph	University of Colorado, Boulder	USA
S. Rudolph	Delft University of Technology (TUD)	The Netherlands
A. J. J. Straathof	Delft University of Technology (TUD)	The Netherlands
L. A. M. van der Wielen	Delft University of Technology (TUD)	The Netherlands
U. von Stockar	Swiss Federal Institute of Technology Lausanne	Switzerland
H. Wennerström	University of Lund	Sweden

sample calculations or examples, and we are convinced that the reader will appreciate these as highly valuable help in understanding difficult topics. A larger number of assignments and worked results, however, remain in our files. Space restrictions for this current volume do not allow us to publish the exercises together in a single volume, so in order to help the interested reader a selection of these will be made available as Mathcad files in the summer of 2013 (information concerning the availability of this supplementary material can be found at the publisher's website: <http://www.epflpress.org>, on the page dedicated to this book). These very same exercises will be elaborated and edited in book form at some later date.

Many people have contributed toward the present work. The authors are indebted to a large number of graduate students, postdocs and secretaries who have helped us to organize, prepare and teach the various international courses. We acknowledge DECHEMA in Frankfurt for having organized the last course in Biedenkopf. The authors would like to thank those colleagues who have taken the time to read and review the manuscripts. We are grateful to Lars Regestein, RWTH Aachen, for having advised us on the assignment problems after having conducted a critical evaluation of the full set.

Luuk van der Wielen
Course coordinator

Urs von Stockar
Editor, Course coordinator

ABOUT THE AUTHORS

John F. Carpenter joined the faculty at the University of Colorado School of Pharmacy in 1993 where he is currently Professor of Pharmaceutical Sciences and Co-Director of the University of Colorado Center for Pharmaceutical Sciences. His research interests include stabilization and degradation of therapeutic protein during processing, formulation and delivery, and development of new analytical methods for protein aggregation and particle formation.

Eva Y. Chi received a Ph.D. degree in Chemical Engineering from the University of Colorado, during which she worked with Prof. Theodore Randolph on the thermodynamics of protein aggregation. She is now an Assistant Professor of Chemical Engineering at the University of New Mexico. Her current research interests include physical properties and self-assembly behaviors of proteins, polymers, and biomembranes, where biomolecular thermodynamics plays a central role.

Charles Haynes is Professor at the Michael Smith Laboratories of the University of British Columbia, Canada. His laboratory runs the Centre for Biological Calorimetry, a federally funded centre which provides Canada with state-of-the-art methods for measuring the delicate energetics of biological interactions in solution or at interfaces.

Sef J. J. Heijnen is professor and group leader for Bioprocess Technology, Department of Biotechnology, Faculty of Applied Sciences, Delft University of Technology, The Netherlands. He has worked in the fermentation industry (1973-1988) and at TU-Delft (1988) in bioprocess technology. His interest is in design based on thermodynamic/kinetic/transport modelling of industrial processes and for micro-organisms (cell systems engineering).

Jürgen U. Keller is professor at the Institute for Fluid Dynamics and Thermodynamics, University of Siegen, Germany.

Marcel L. Jansen is Manager of the department Process Support and Development at Sanquin Blood Supply Foundation, Division of Plasma Products in Amsterdam, The Netherlands. After doctoral studies at the Delft University of Technology, he started R&D career in downstream processing in the biopharmaceutical industry in 1996. He

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Hans-Olof Johansson is in the Department of Biochemistry and Structural Biology, Lund University, Sweden. His main interest is modeling the thermodynamic driving forces of protein-polymer interactions. His two main areas of research are aqueous two-phase systems for bioseparation and surface-tethered polymers and proteins.

Gunnar Karlström is professor in the Department of Theoretical Chemistry, Lund University, Sweden. His main areas of activity are macroscopic properties of dipolar systems as described by quantum chemistry and intermolecular interactions in condensed phases.

Karel Ch.A.M. Luyben is Rector Magnificus of the Delft University of Technology. In 1983 he was appointed as professor in Biochemical Engineering at the Delft University of Technology. From 1985-1990, he was Chairman of the Netherlands Biotechnology Society (NBV). He was Scientific Director of the Graduate School 'Biotechnological Sciences Delft Leiden' (BSDL) from its foundation in 1993 up until 1998.

Thomas Maskow is head of the Group Biocalorimetry/Ecothermodynamics, Department of Environmental Microbiology at the Helmholtz Center for Environmental Research-UFZ, Germany.

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John M. Prausnitz is Professor in the Graduate School, Department of Chemical and Biomolecular Engineering, University of California, Berkeley. He is author of the widely-used textbook *Molecular Thermodynamics of Fluid-Phase Equilibria*. He is a member of the National Academy of Sciences, the National Academy of Engineering, and the American Academy of Arts and Sciences. He has received honorary doctoral degrees from four universities: L'Aquila, Padua, Berlin and Princeton. In 2005, he received the National Medal of Science.

Theodore W. Randolph accepted the Patton Associate Professor chair in the Department of Chemical Engineering at the University of Colorado, where he currently serves as the Gillespie Professor of Bioengineering and co-Director of the University of Colorado's Center for Pharmaceutical Biotechnology. His research interests

include biopharmaceutical formulation, lyophilization of proteins, protein-solvent interactions in non-aqueous environments, and protein refolding.

Urs von Stockar has been professor at the Swiss Federal Institute of Technology in Lausanne (EPFL) since 1977, where he has conducted research on gas-liquid mass transfer, integrated bioprocessing and biocalorimetry. He is an individual member of the scientific committee of the Swiss Academy of Technical Sciences.; chairman of the Swiss Coordination Committee for Biotechnology; and executive committee member of the European Federation of Biotechnology since 1990. Since 2007, he is honorary professor of the Swiss Federal Institute of Technology, Lausanne and adjunct professor of the Dublin City University.

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