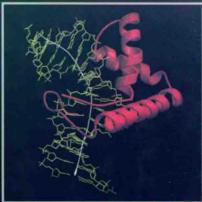
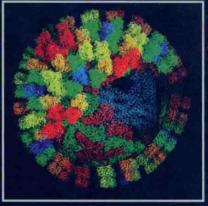


Structure, Function and Methods







Editors Michael M. Cox and George N. Phillips, Jr.



Volume 1

Handbook of Proteins: Structure, Function and Methods

Volume 1

Editors

Michael M Cox and George N Phillips, Jr University of Wisconsin, Madison, Wisconsin, USA



Copyright © 2007

John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England

Telephone (+44) 1243 779777

Email (for orders and customer service enquiries): cs-books@wiley.co.uk Visit our Home Page on www.wileyeurope.com or www.wiley.com

Protein Motifs: the Leucine Zipper, pp. 132–138; Gel Electrophoresis: One-dimensional, pp. 879–881; Gel Staining Techniques, pp. 884–889; Protein Production for Biotechnology, pp. 931–936; Flow Cytometers, pp. 1011–1016; and Structural Genomics, pp. 1185–1188, are US government works in the public domain and not subject to copyright.

All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except under the terms of the Copyright, Designs and Patents Act 1988 or under the terms of a licence issued by the Copyright Licensing Agency Ltd, 90 Tottenham Court Road, London W1T 4LP, UK, without the permission in writing of the Publisher. Requests to the Publisher should be addressed to the Permissions Department, John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England, or emailed to permreq@ wiley.co.uk, or faxed to (+44) 1243 770620.

This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is sold on the understanding that the Publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

Other Wiley Editorial Offices

John Wiley & Sons Inc., 111 River Street, Hoboken, NI 07030, USA

Jossey-Bass, 989 Market Street, San Francisco, CA 94103-1741, USA

Wiley-VCH Verlag GmbH, Boschstr. 12, D-69469 Weinheim, Germany

John Wiley & Sons Australia Ltd, 42 McDougall Street, Milton, Queensland 4064, Australia

John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop #02-01, Jin Xing Distripark, Singapore 129809

John Wiley & Sons Canada Ltd, 6045 Freemont Boulevard, Ontario, Canada L5R 4J3

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

Library of Congress Cataloguing-in-Publication Data

Handbook of proteins: structure, function, and methods / editors, Michael M. Cox and George N. Phillips Jnr.

p. ; cm.

Includes bibliographical references and index.

ISBN 978-0-470-06098-8 (hb)

1. Proteins-Handbooks, manuals, etc. I. Cox, Michael M. II. Phillips, George N.

[DNLM: 1. Proteins. QU 55 H236 2007]

QP551.H32 2007

572'.6--dc22

2007039325

ISBN 978-0-470-06098-8 (HB)

Typeset by Macmillan India Limited, Bangalore, India.

Printed and bound in Singapore by Markono Print Media Pte Ltd, Singapore.

This book is printed on acid-free paper responsibly manufactured from sustainable forestry in which at least two trees are planted for each one used for paper production.

Cover images. Main picture: Green fluorescent protein (GFP) rendered in blue with reflective, glowing chromophore and green mist. © 1996 Tod D. Romo. Top right: Lymphoid enhancer factor 1 (red) is an architectural protein that bends DNA away from its surface by side-chain intercalation. The structure was solved in the laboratories of R. Grosschedl and P. Wright. Bottom right: The structure of the Bluetongue virus (BTV) core has a diameter of 700 Å and represents the largest particle to date solved by X-ray crystallography. The structure illustrates in atomic detail how nearly 1000 protein subunits self-assemble and interact to form a transcriptionally active compartment.

Handbook of Proteins: Structure, Function and Methods



The Handbook of Proteins: Structure, Function and Methods re-publishes a selection of recent and topical articles from Wiley's landmark Encyclopedia of Life Sciences (ELS), the leading resource in the life sciences. Spanning the entire spectrum of life sciences, ELS features more than 4,000 peer-reviewed articles, which are regularly updated, making it an essential read for life scientists and a valuable resource for teaching. Aimed at students and teachers, and also at researchers outside academia, articles provide comprehensive and authoritative coverage, written by leaders in the field. The entire Encyclopedia is available online at http://www.els.net, in full colour, with new and updated articles added regularly.

Contributors

Peter Agre Johns Hopkins University School of Medicine, Baltimore, Maryland, USA Water Channels

Robert A Alberty Massachusetts Institute of Technology, Cambridge, Massachusetts, USA
Thermodynamics in Biochemistry

Bairoch Amos Swiss Institute of Bioinformatics, Geneva, Switzerland *Protein Databases*

Vernon E Anderson Case Western Reserve University, Cleveland, Ohio, USA

Ground State Destabilization

Brigitte M Angres CLONTECH Laboratories Inc., Palo Alto, California, USA

Green Fluorescent Protein (GFP)

Gerritsen Viviennoe Baillie Swiss Institute of Bioinformatics, Geneva, Switzerland Protein Databases

Winona C Barker National Biomedical Research Foundation, Washington, DC, USA *Protein Sequence Databases*

Alan J Barrett Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK Proteases

Adrian H Batchelor Walter and Eliza Hall Institute, Royal Melbourne Hospital, Victoria, Australia Crystallization of Protein—DNA Complexes

Ronald C Bates University of Maryland Baltimore County, Maryland, USA Chromatofocusing

Jeremy Berg National Institute of General Medical Sciences, Maryland, USA

Structural Genomics

Helen M Berman Rutgers, The State University of New Jersey, New Brunswick, New Jersey, USA
Structural Databases of Biological Macromolecules

Steven M Berry University of Illinois at Urbana-Champaign, Urbana, IL, USA

Protein Structure Design and Engineering

Gregg Bogosian Monsanto Company, Chesterfield, Missouri, USA *Protein Synthesis: Measuring Errors*

Squire J Booker Pennsylvania State University, University Park, Pennsylvania, USA Enzymatic Free Radical Reactions

Philip E Bourne University of California San Diego, La Jolla, California,

Primary Protein and Nucleic Acid Three-dimensional Structure Databases

Sinead Boyce Trinity College, Dublin, Ireland *Enzyme Classification and Nomenclature*

Thomas Braun University of Basel, Basel, Switzerland Two-dimensional Electron Crystallography

Joan B Broderick Michigan State University, East Lansing, Michigan, USA Coenzymes and Cofactors

Barbara Brodsky Robert W Johnson Medical School, Piscataway, New Jersey, USA *Proline Residues in Proteins*

Doug A Brooks Women's and Children's Hospital, North Adelaide, South Australia. Australia

Protein: Cotranslational and Posttranslational Modification in Organelles

Wolfgang Buckel Philipps-Universität, Marburg, Germany Cobalamin Coenzymes and Vitamin B_{12}

Timothy DH Bugg University of Warwick, Coventry, UK *Enzymes: General Properties*

Neil J Bulleid University of Manchester, Manchester, UK *Permeabilized Mammalian Cell Systems for Protein* Synthesis

Konrad Büssow Max Planck Institute of Molecular Genetics, Berlin, Germany Array-based Proteomics

Julio E Celis Danish Centre for Human Genome Research, University of Aarhus, Aarhus, Denmark

Gel Electrophoresis of Proteins: High-resolution Two-dimensional; Electroelution of Proteins from Polyacrylamide Gels; Autoradiography and Fluorography; Protein Identification: Overlay Procedures

Hue Sun Chan University of Toronto, Toronto, Canada *Amino Acid Side Chain Hydrophobicity*

John-Marc Chandonia University of California, San Francisco, California, USA

Protein Secondary Structures: Prediction

Jennifer Cheek University of South Carolina, Columbia, South Carolina, USA

Coenzymes: Haem

Guang Chen PENN Center for Bioinformatics, University of Pennsylvania, Philadelphia, USA
Interaction Networks of Proteins

Deepak Chhabra Institute for Biomedical Research, University of Sydney, Australia

Fluorescence Resonance Energy Transfer

Roberta Chiaraluce University of Rome, Rome, Italy Chaperones, Chaperonin and Heat-Shock Proteins; Chaperonins

Wah Chiu Baylor College of Medicine, Houston, Texas, USA *Electron Cryomicroscopy and Three-dimensional Computer Reconstruction of Biological Molecules*

Theodora Choli-Papadopoulou School of Chemistry, Aristotle University of Thessaloniki, Thessaloniki, Greece Proteins: Postsynthetic Modification – Function and Physical Analysis

Shaorong Chong New England Biolabs Inc., Beverly, Massachusetts, USA

Proteins: Affinity Tags

Cyrus Chothia MRC Laboratory of Molecular Biology, Cambridge, UK *Immunoglobulin Fold: Structures of Proteins in the Immunoglobulin Superfamily*

Andreas Chrambach National Institute of Child Health and Human Development, Bethesda, Maryland, USA Gel Electrophoresis: One-dimensional

W Wallace Cleland University of Wisconsin, Madison, Wisconsin, USA Enzyme Kinetics: Steady State

Frank R Collart Argonne National Laboratory, Argonne, IL, USA Protein Production for Biotechnology

Valerio Consalvi University of Rome, Rome, Italy Chaperones, Chaperonin and Heat-Shock Proteins; Chaperonins

Robert A Copeland DuPont Pharmaceuticals, Wilmington, Delaware, USA Enzymology Methods

Kevin Cowtan University of York, UK

Phase Problem in X-ray Crystallography, and its Solution

Alain J Cozzone Institute of Biology and Chemistry of Proteins, CNRS, Lyon, France

Proteins: Fundamental Chemical Properties

Merlin Crossley University of Sydney, Sydney, Australia *Protein Motifs: Zinc-fingers*

Matthew P Crump University of Southampton, Southampton, UK Enzymes: Phosphopantetheine Dependent; Enzymes: Coenzyme A dependent

Cynthia Maria Borges Damasceno Cornell University, Ithaca, New York, USA

Tandem-affinity Purification (TAP) Tags

Shailesh V Date PENN Center for Bioinformatics, University of Pennsylvania School of Medicine, Philadelphia, USA Interaction Networks of Proteins

Victor L Davidson University of Mississippi Medical Center, Jackson, Mississippi, USA *Protein-derived Cofactors*

John H Dawson University of South Carolina, Columbia, South Carolina, USA
Coenzymes: Haem

Martijn de Jager Leiden University, Leiden, The Netherlands Atomic Force Microscopy

Charles M Deber Hospital for Sick Children, University of Toronto, Ontario, Canada
Proline Residues in Proteins

Claire Delahunty The Scripps Research Institute, La Jolla, California, USA Proteomics: A Shotgun Approach without Two-dimensional Gels

Louis TJ Delbaere University of Saskatchewan, Saskatoon, Saskatchewan, Canada Protein Motifs: ATP-binding Motifs

Charles DeLisi Boston University, Boston, Massachusetts, USA Amino Acid Substitutions: Effects on Protein Stability

J Fred Dice Tufts University School of Medicine, Boston, Massachusetts, USA
Lysosomal Degradation of Proteins

Mensur Dlakic University of Michigan, Ann Arbor, Michigan, USA DNA Structure Changes Coupled to Protein Binding

Chen Y Dong Massachusetts Institute of Technology, Cambridge, Massachusetts, USA Fluorescence Spectrophotometry

Cristobal G dos Remedios Institute for Biomedical Research, University of Sydney, Australia
Fluorescence Resonance Energy Transfer

Jan Drenth University of Groningen, The Netherlands X-ray Diffraction: Principles

Jacques Dubochet University of Lausanne, Lausanne, Switzerland Electron Cryomicroscopy

A Keith Dunker Indiana University School of Medicine, Indianapolis, Indiana, USA
Unstructured Proteins

Michael F Dunn University of California, Riverside, California, USA Protein—Ligand Interactions: General Description

Ben M Dunn University of Florida College of Medicine, Gainsville, Florida, USA Engineered Enzymes

H Jane Dyson The Scripps Research Institute, La Jolla, California, USA Spectroscopic Techniques

Jason Eames Queen Mary, University of London, London, UK Metalloenzymes and Electrophilic Catalysis

Dale E Edmondson Emory University, Atlanta, Georgia, USA Flavin Coenzymes

M Raafat El-Gewely University of Tromsø, Tromsø, Norway Mutagenesis: Site-specific

Andreas Engel University of Basel, Basel, Switzerland *Two-dimensional Electron Crystallography*

David R Engelke University of Michigan Medical School, Ann Arbor, Michigan, USA

Protein—RNA Interactions

Peter G Fajer Florida State University, Tallahassee, Florida, USA Electron Paramagnetic Resonance (EPR) and Spin-labelling

Chris Fenton University of Tromsø, Tromsø, Norway *Mutagenesis: Site-specific*

Anthony L Fink University of California, Santa Cruz, California, USA Molten Globule

Daniel Finley Harvard Medical School, Boston, Massachusetts, USA *Protease Complexes*

Harvey F Fisher VA Medical Center, Kansas City, Missouri, USA Protein–Ligand Interactions: Molecular Basis

John M Flanagan Pennsylvania State University at Hershey Medical Center, Hershey, Pennsylvania, USA Enzlyme Activity: Control

Brian G Fox University of Wisconsin, Madison, Wisconsin, USA Iron Cofactors: Non-haem

Willard M Freeman Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA Phosphorimager

Douglas D Frey University of Maryland, Baltimore County, Maryland, USA

Chromatofocusina

Eric T Fung Ciphergen Biosystems, Inc., Fremont, California, USA Molecular Entry Point: Strategies in Proteomics

Israel M Gelfand Rutgers University, Piscataway, New Jersey, USA Immunoglobulin Fold: Structures of Proteins in the Immunoglobulin Superfamily

David Gell University of Sydney, Sydney, Australia *Protein Motifs: Zinc-fingers*

Kris Gevaert Ghent University, Ghent, Belgium Protein Characterization: Analytical Approaches and Applications to Proteomics

Eman Ghanem Texas A&M University, College Station, Texas, USA *Enzymes: The Active Site*

Sandro Ghisla University of Konstanz, Konstanz, Germany Flavin Coenzymes

Hiram F Gilbert Baylor College of Medicine, Houston, Texas, USA *Peptide Bonds, Disulfide Bonds and Properties of Small Peptides*

Sarah E Giuliani Argonne National Laboratory, Argonne, IL, USA *Protein Production for Biotechnology*

Jörn Glökler Max Planck Institute of Molecular Genetics, Berlin, Germany Array-based Proteomics

Isa Gokce Gaziomanpasa University, Tokat, Turkey *Protein–Protein Interactions*

Richard L Grantham Université Lyon, Villeurbanne, France Codon Usage in Molecular Evolution

Karl Otto Greulich Institute of Molecular Biotechnology, Jena, Germany Single-molecule Light Microscopy; Optical Tweezers

Gerald R Grimsley Texas A&M University, College Station, Texas, USA *Protein Stability*

Pavel S Gromov Danish Centre for Human Genome Research, University of Aarhus, Aarhus, Denmark

Gel Electrophoresis of Proteins: High-resolution Two-dimensional; Electroelution of Proteins from Polyacrylamide Gels; Autoradiography and Fluorography; Protein Identification: Overlay Procedures

Marianne Grunberg-Manago Institute of Physico-chemical Biology, Paris, France

Protein Synthesis Initiation in Bacteria

Florent Guillain CNRS, Grenoble, France *ATPases: Ion-motive*

J Mitchell Guss University of Sydney, New South Wales, Australia Macromolecular Structure Determination: Comparison of Crystallography and NMR

Martin Guttenberger University of Tübingen, Tübingen, Germany Protein Determination

David L Hacker École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland Protein Production in Mammalian Cells

Lars Hagel Amersham Pharmacia Biotech AB, Uppsala, Sweden Gel Filtration

Per Hammarström Linköping University, Linköping, Sweden *Protein Denaturation and the Denatured State*

F Ulrich Hartl Max-Planck Institute of Biochemistry, Martinsried, Germany Protein Folding In Vivo

Leila D Hebshi CLONTECH Laboratories Inc., Palo Alto, California, USA *Green Fluorescent Protein (GFP)*

Lizbeth Hedstrom Brandeis University, Waltham, Massachusetts, USA *Enzyme Specificity and Selectivity*

Stefan H Heinemann Friedrich Schiller University, Jena, Germany Sodium, Calcium and Potassium Channels

John R Helliwell University of Manchester, Manchester, UK X-ray Diffraction at Synchrotron Light Sources

Richard H Henchman School of Chemistry, University of Manchester, UK

Protein Structural Flexibility: Molecular Motions

Judith Herzfeld Brandeis University, Waltham, Massachusetts,

Hydrophobic Effect

Chien Ho Carnegie Mellon University, Pittsburgh, PA, USA Haemoglobin: Cooperativity in Protein-Ligand Interactions

Heinz Hohenberg Heinrich Pette Institute for Experimental Virology and Immunology, Hamburg, Germany Immuno-electron Microscopy

Felicia Houser-Scott University of Michigan Medical School, Ann Arbor, Michigan, USA Protein-RNA Interactions

Su-Ming Hu Academia Sinica, Taipei, Taiwan Expression Tags for Protein Production

Roderick E Hubbard University of York, York, UK Hydrogen Bonds in Proteins: Role and Strength

Graeme K Hunter University of Western Ontario, London, Ontario, Canada History of Protein Chemistry

Thomas D Hurley Indiana University School of Medicine, Indianapolis, Indiana, USA NADP + Binding to Dehydrogenases

Joachim Jaeger Wadsworth Center, Albany, New York, USA Macromolecular Structure Determination by X-ray Crystallography

Bing K Jap Lawrence Berkeley National Laboratory, Berkeley, California, USA

Crystallization of Proteins: Two-dimensional

Herbert P Jennissen University of Duisburg-Essen, Essen, Germany Hydrophobic Interaction Chromatography

George C-T Jiang Wake Forest University, Winston-Salem, North Carolina, USA Enzyme Activity: Control

Kenneth A Johnson University of Texas, Austin, Texas, USA Enzyme Kinetics: Transient Phase

Susan Jones University College, London, UK Protein Quaternary Structure: Subunit-Subunit Interactions

Bengt-Harald Jonsson Linköping University, Linköping, Sweden Protein Denaturation and the Denatured State

Ralph C Judd University of Montana, Missoula, Montana, USA Peptide Mapping

Steven R Kain Agilent Technologies, Santa Clara, California, USA Green Fluorescent Protein (GFP)

Lydia E Kavraki Department of Computer Science, Rice University Houston, Texas, USA Protein-Ligand Interactions: Computational Docking

James L Keck University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA Protein-Protein Interactions: Identification

David Keeling Astra Hässle, Mölndal, Sweden Ion Motive ATPases: V- and P-type ATPases

George L Kenyon University of California - San Francisco, San Francisco, California, USA Covalent Nucleophilic Catalysis

Tom K Kerppola Howard Hughes Medical Institute and University of Michigan Medical School, Ann Arbor, Michigan, USA Protein-DNA Interactions: Energetics; DNA Structure Changes Coupled to Protein Binding

Landon S King Johns Hopkins University School of Medicine, Baltimore, Maryland, USA Water Channels

Glenn F King University of Connecticut Health Center, Farmington, Connecticut, USA Macromolecular Structure Determination: Comparison of Crystallography and NMR

Anthony John Kirby University of Cambridge, Cambridge, UK Acid-Base Catalysis by Enzymes

Alexander E Kister Rutgers University, Piscataway, New Jersey, USA Immunoglobulin Fold: Structures of Proteins in the Immunoglobulin Superfamily

Elisabeth Kjeldsen University of Tromsø, Tromsø, Norway Mutagenesis: Site-specific

Judith P Klinman University of California - Berkeley, Berkeley, California, Quinone Cofactors

Charles W Knopf Deutsches Krebsforschungszentrum, Heidelberg, DNA-binding Enzymes: Structural Themes

Lars Konermann University of Western Ontario, London, Ontario, Protein Unfolding and Denaturants

Zoltan Konthur Max Planck Institute of Molecular Genetics, Berlin, Germany Array-based Proteomics

Lakshmi P Kotra Wayne State University, Michigan, USA Transition State Stabilization

Dmitry Krylov National Cancer Institute, Bethesda, Maryland, Protein Motifs: the Leucine Zipper

Sandeep Kumar Frederick Cancer Research and Development Center National Cancer Institute, Frederick, Maryland, USA Induced Fit

Emmanuel Lacroix European Molecular Biology Laboratory, Heidelberg, Germany *Protein Design*

Jeremy H Lakey University of Newcastle-upon-Tyne, UK *Protein–Protein Interactions*

Joseph R Lakowicz University of Maryland, Baltimore, Maryland, USA Fluorescent Analogues in Biological Research

Y Amy Lam Johns Hopkins University, Baltimore, Maryland, USA Ubiquitin Pathway

Elizabeth V Landorf Argonne National Laboratory, Argonne, IL, USA *Protein Production for Biotechnology*

Thomas Maxon Laue University of New Hampshire, Durham, New Hampshire, USA
Sedimentation

Juliette T J Lecomte Pennsylvania State University, University Park, Pennsylvania, USA Protein Structure: Unusual Covalent Bonds

Alastair C Lewis University of York, York, UK Chromatographic Techniques

Guangpu Li University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA *Protein Motifs: GTP-binding Loop*

Jiayin Li National Institute of General Medical Sciences, Maryland, USA Structural Genomics

Xianqiang L Li Genemed Biotechnologies Inc., San Francisco, California, USA

Green Fluorescent Protein (GFP)

Hanjo Lim Aventis Pharmaceuticals Inc., Bridgewater, New Jersey, USA Mass Spectrometry: Analysis of Two-dimensional Protein Gels

Matthew E Lopper University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA Protein–Protein Interactions: Identification

Yi Lu University of Illinois at Urbana-Champaign, Urbana, IL, USA Protein Structure Design and Engineering

Steven J Ludtke Baylor College of Medicine, Houston, Texas, USA *Electron Cryomicroscopy and Three-dimensional Computer Reconstruction of Biological Molecules*

Angelika Lueking Max Planck Institute of Molecular Genetics, Berlin, Germany

Array-based Proteomics

Jonathan A Lukin Carnegie Mellon University, Pittsburgh, PA, USA Haemoglobin: Cooperativity in Protein–Ligand Interactions

Buyong Ma Frederick Cancer Research and Development Center National Cancer Institute, Frederick, Maryland, USA Induced Fit **Joel Mackay** University of Sydney, Sydney, Australia *Protein Motifs: Zinc-fingers*

Jacob V Maizel Frederick Cancer Research and Development Center, Frederick, Maryland, USA Protein–Ligand Interactions: Energetic Contributions and Shape Complementarity

Mohammad Azam Mansoor Agder University College, Kristiansand, Norway Liquid Chromatography

Francesca M Marassi The Wistar Institute, Philadelphia, PA, USA Nuclear Magnetic Resonance (NMR): Solid State

Mark Marsh University College London, London, UK Clathrin-coated Vesicles and Receptor-mediated Endocytosis

Bruce L Martin University of Minnesota, Twin Cities, Minneapolis, MN, USA

Regulation by Covalent Modification

Allan Matte University of Saskatchewan, Saskatoon, Saskatchewan, Canada
Protein Motifs: ATP-binding Motifs

Brian W Matthews Howard Hughes Medical Institute and University of Oregon, Eugene, OR, USA

Protein Motifs: the Helix-Turn-Helix Motif; Hydrophobic Interactions in Proteins

John C Maule MRC Human Genetics Units, Edinburgh, UK Pulsed-field Gel Electrophoresis

J Andrew McCammon Howard Hughes Medical Institute, University of California at SanDiego, USA

Protein Structural Flexibility: Molecular Motions

Alexander McPherson University of California, Irvine, California, USA *Crystallization of Proteins and Protein–Ligand Complexes*

Jarošaw Meller Cornell University, Ithaca, New York, USA and Nicholas Copernicus University, Toruń, Poland Molecular Dynamics

Carl R Merril National Institutes of Health, Bethesda, Maryland, USA Gel Staining Techniques

Elisabeth Mintz CEA, Grenoble, France ATPases: Ion-motive

Julie C Mitchell University of Wisconsin, Madison, Wisconsin, USA Protein–Protein Interactions: Prediction

Osamu Miyashita Department of Biochemistry and Molecular Biophysics, The University of Arizona, Tucson, USA Normal Mode Analysis Techniques in Structural Biology

Shahriar Mobashery Wayne State University, Michigan, USA *Transition State Stabilization*

Amram Mor Hebrew University of Jerusalem, Jerusalem, Israel *Peptides: Biological Activities of Small Peptides*

Scott W Morrical University of Vermont, Burlington, Vermont, USA

Protein Motifs for DNA Binding

John F Morrison Australian National University, Canberra, Australia Enzyme Activity: Reversible Inhibition

Richard Mott University of Oxford, Oxford, UK *Alignment: Statistical Significance*

Ishita Mukerji Wesleyan University, Middletown, Connecticut, USA Resonance Raman Spectroscopy

Nicola J Mulder European Molecular Biology Laboratory Outstation – European Bioinformatics Institute, Wellcome Trust Genome Campus, United Kingdom Protein Family Databases

Kenneth P Murphy University of Iowa, Iowa, USA Calorimetry

Shorena Nadaraia Pennsylvania State University at Hershey Medical Center, Hershey, Pennsylvania, USA Enzyme Activity: Control

Chittoor R Narahari University of Maryland Baltimore County, Maryland, USA Chromatofocusing

Knud H Nierhaus Max-Planck Institute for Molecular Genetics, Berlin, Germany

Protein Synthesis Inhibitors

Raquel Norel Tel Aviv University, Tel Aviv, Israel Protein—Ligand Interactions: Energetic Contributions and Shape Complementarity

John Norvell National Institute of General Medical Sciences, Maryland, USA

Structural Genomics

Ruth Nussinov Frederick Cancer Research and Development Center, National Cancer Institute, Frederick, Maryland, USA and Tel Aviv University, Tel Aviv, Israel

Protein—Ligand Interactions: Energetic Contributions and Shape Complementarity; Induced Fit

Siobhan O'Sullivan University College Cork, Mardyke, Cork, Ireland *Ion Exchange Chromatography*

Donald J Olbris Brandeis University, Waltham, Massachusetts, USA *Hydrophobic Effect*

Stanley J Opella University of Pennsylvania, Philadelphia, PA, USA *Nuclear Magnetic Resonance (NMR): Solid State*

Norman J Oppenheimer University of California, San Francisco, California, USA

NAD⁺ and NADP⁺ as Prosthetic Groups for Enzymes

Christine A Orengo University College London, London, UK *Evolution of Protein Domains; Protein Structure Classification*

Johannes Orphal CNRS, Université de Paris-Sud, France Fourier Transform Infrared C Nick Pace Texas A&M University, College Station, Texas, USA Protein Stability

Mark Page Medeva Development, London, UK Immunoglobulin Purification

David AD Parry Massey University, Palmerston North, New Zealand Mass Measurements by Scanning Transmission Electron Microscopy

Frances MG Pearl University College London, London, UK *Protein Structure Classification*

James E Penner-Hahn The University of Michigan, Ann Arbor, Michigan, USA
X-ray Absorption Spectroscopy

Control of the Park of the State of

Nikolaus Pfanner University of Freiburg, Freiburg, Germany *Protein Translocation Across Membranes*

Cecile M Pickart Johns Hopkins University, Baltimore, Maryland, USA *Ubiquitin Pathway*

Derek E Piper Howard Hughes Medical Institute and the Johns Hopkins University School of Medicine, Baltimore, Maryland, USA *Crystallization of Protein–DNA Complexes*

Vladimir K Pliška Swiss Federal Institute of Technology (ETH), Zürich, Switzerland Substrate Binding to Enzymes

Carol B Post Purdue University, West Lafayette, Indiana, USA
Transition States: Substrate-induced Conformational Transitions

Nicholas C Price University of Stirling, Scotland, UK Circular Dichroism: Studies of Proteins

Jaime Prilusky Weizmann Institute of Science, Rehovot, Israel Mining Biological Databases

Daniel M Quinn University of Iowa, Iowa City, Iowa, USA *Enzymatic Rate Enhancements*

Frank M Raushel Texas A&M University, College Station, Texas, USA Enzymes: The Active Site

Neil D Rawlings Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK
Proteases

Reinhart AF Reithmeier University of Toronto, Ontario, Canada *Membrane Proteins*

David Rickwood University of Essex, Colchester, UK Centrifugation Techniques

Pier Giorgio Righetti University of Verona, Verona, Italy Capillary Electrophoresis

Daniel J Robertson Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA Phosphorimager

Peter Roepstroff University of Southern Denmark, Odense, Denmark Mass Spectrometry Instrumentation in Proteomics Marianne Rooman Free University of Brussels, Brussels, Belgium Protein–DNA Interactions

Jocelyn Kenneth Campbell Rose Cornell University, Ithaca, New York, USA

Tandem-affinity Purification (TAP) Tags

Michael T Ryan La Trobe University, Melbourne, Australia Protein Translocation Across Membranes

Fred Sablitzky The University of Nottingham, Institute of Genetics, Nottingham, UK

Protein Motifs: the Helix-Loop-Helix Motif

George Sachs UCLA, Los Angeles, California, USA *Ion Motive ATPases: V- and P-type ATPases*

Ruth M Saecker UW-Madison, Madison, Wisconsin, USA Protein—DNA Interactions: Polyelectrolyte Effects; Protein—DNA Complexes: Nonspecific

Margareta Sahlin Stockholm University, Stockholm, Sweden Radical Enzymes

Jerome Salem University of Pennsylvania, Philadelphia, Pennsylvania, USA

Enzymes: Purification

Kirstie Saltsman National Institute of General Medical Sciences, Maryland, USA Structural Genomics

Mark SP Sansom University of Oxford, Oxford, UK Hydrophobicity Plots

Gary Sawers John Innes Centre, Norwich, UK *Amino Acid Degradation*

Karl-Heinz Scheidtmann University of Bonn, Germany *Immunoprecipitation Techniques*

Georgios Scheiner-Bobis Justus Liebig University, Giessen, Germany Gene Expression in Yeast

Franz-Xaver Schmid University of Bayreuth, Germany Biological Macromolecules: UV-visible Spectrophotometry

Marion Schmidt Albert Einstein College of Medicine, Bronx, New York, USA

Protease Complexes

Ulrich Schneider Scienion AG, Berlin, Germany *Array-based Proteomics*

K Barbara Schowen University of Kansas, Lawrence, Kansas, USA Thiamin Diphosphate and Vitamin B_1

Richard L Schowen University of Kansas, Lawrence, Kansas, USA *Thiamin Diphosphate and Vitamin B* $_1$

Susana K Schowen University of Kansas, Lawrence, Kansas, USA Thiamin Diphosphate and Vitamin B₁

Benjamin Schwartz University of California - Berkeley, Berkeley, California, USA *Quinone Cofactors*

Heinz Schwarz Max Planck Institute for Developmental Biology, Tübingen, Germany *Immuno-electron Microscopy*

David Schwarz Department of Computer Science, Rice University Houston, Texas, USA

Protein-Ligand Interactions: Computational Docking

Robert K Scopes La Trobe University, Bundoora, Victoria, Australia Enzyme Activity and Assays

Nancy L Scott Pennsylvania State University, University Park, Pennsylvania, USA Protein Structure: Unusual Covalent Bonds

Luis Serrano European Molecular Biology Laboratory, Heidelberg, Germany *Protein Design*

David Sheehan University College Cork, Mardyke, Cork, Ireland *Ion Exchange Chromatography*

Peter M Shoolingin-Jordan University of Southampton, Southampton, UK

Enzymes: Coenzyme A dependent; Enzymes: Phosphopantetheine Dependent

R Steven Sikorski University of Iowa, Iowa City, Iowa, USA Enzymatic Rate Enhancements

Neeti Sinha Frederick Cancer Research and Development Center National Cancer Institute, Frederick, Maryland, USA Induced Fit

Britt-Marie Sjöberg Stockholm University, Stockholm, Sweden *Radical Enzymes*

Henry S Slayter Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA *Transmission Electron Microscopy: Preparation of Specimens*

John Bryan Smith Celltech Chiroscience plc, Slough, UK Peptide Sequencing by Edman Degradation

Peter TC So Massachusetts Institute of Technology, Cambridge, Massachusetts, USA Fluorescence Spectrophotometry; Two-photon Fluorescence Light Microscopy

Henning Stahlberg University of Basle, Basle, Switzerland
Electron Cryomicroscopy

John A Steinkamp Los Alamos National Laboratory, Los Alamos, New Mexico, USA Flow Cytometers

U Stelzl Max-Planck Institute for Molecular Genetics, Berlin, Germany Protein Synthesis Inhibitors

Ronald E Stenkamp University of Washington, Seattle, Washington, USA Protein Quaternary Structure: Symmetry Patterns

Lance Stewart deCODE biostructures, Inc., Washington, USA Gene Synthesis for Protein Production

Barry L Stoddard Fred Hutchinson Cancer Research Center, Seattle, Washington, USA *Time-resolved X-ray Crystallography*

Mark A Strauch University of Maryland, Baltimore, Maryland, USA Protein–DNA Complexes: Specific; Protein–DNA Interactions: Techniques Used

Muttaiya Sunderalingam Ohio State University, Columbus, Ohio, USA

Protein—Nucleic Acid Interaction: Major Groove Recognition Determinants

Florence Tama Department of Biochemistry and Molecular Biophysics, The University of Arizona, Tucson, USA Normal Mode Analysis Techniques in Structural Biology

Sarah Teter University of California at Davis, Davis, California, USA Protein Folding In Vivo

Janet M Thornton European Bioinformatics Institute, Hinxton, Cambridge, UK and University College, London, UK Protein Structure Classification; Protein Quaternary Structure: Subunit–Subunit Interactions

Keith F Tipton Trinity College Dublin, Ireland Enzymes: Irreversible Inhibition; Enzyme Classification and Nomenclature

Michael D Toney University of California–Davis, California, USA Binding and Catalysis

Thomas Traut University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA Enzyme Activity: Allosteric Regulation

Jill Trewhella Los Alamos National Laboratory, New Mexico, USA Low Angle Scattering of Neutrons and X-rays

Chung-Jung Tsai Frederick Cancer Research and Development Center, National Cancer Institute, Frederick, Maryland, USA Protein–Ligand Interactions: Energetic Contributions and Shape Complementarity; Induced Fit

Volker Uhl Institute of Molecular Biotechnology, Jena, Germany Single-molecule Light Microscopy

John van Noort Leiden University, Leiden, The Netherlands Atomic Force Microscopy

Joël Vandekerckhove Ghent University, Ghent, Belgium
Protein Characterization: Analytical Approaches and Applications to
Proteomics

Charles R Vinson National Cancer Institute, Bethesda, Maryland, USA Protein Motifs: the Leucine Zipper

Monique M van Oers Wageningen University, Wageningen, The Netherlands Baculovirus Expression Systems

Just M Vlak Wagneningen University, Wageningen, The Netherlands *Baculovirus Expression Systems*

Alfred Völkl University of Heidelberg, Heidelberg, Germany *Ultracentrifugation*

Kent E Vrana Pennsylvania State University at Hershey Medical Center, Hershey, Pennsylvania, USA - Formerly of Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA Enzyme Activity: Control; Phosphorimager

Waldemar Waldeck Deutsches Krebsforschungszentrum, Heidelberg, Germany DNA-binding Enzymes: Structural Themes

Peter J Walian Lawrence Berkeley National Laboratory, Berkeley,

Crystallization of Proteins: Two-dimensional

California, USA

Gerald Walter Biorchard Limited, c/o Cornupia Capital Ltd, London, UK *Array-based Proteomics*

Andrew H-J Wang Academia Sinica, Taipei, Taiwan Expression Tags for Protein Production

Ting-Fang Wang Academia Sinica, Taipei, Taiwan *Expression Tags for Protein Production*

Michael Watkinson Queen Mary, University of London, London, UK Metalloenzymes and Electrophilic Catalysis

JThrock Watson Michigan State University, East Lansing, Michigan, USA Mass Spectrometry: Peptide Sequencing

Henry Weiner Purdue University, West Lafayette, Indiana, USA *NADP* * *Binding to Dehydrogenases*

Zhiping Weng Boston University, Boston, Massachusetts, USA *Amino Acid Substitutions: Effects on Protein Stability*

Milton H Werner The Rockefeller University, New York, USA Nuclear Magnetic Resonance (NMR) Spectroscopy: Structural Analysis of Proteins and Nucleic Acids

DN Wilson Max-Planck Institute for Molecular Genetics, Berlin, Germany *Protein Synthesis Inhibitors*

René Wintjens Free University of Brussels, Brussels, Belgium Protein—DNA Interactions

Donald J Winzor University of Queensland, Brisbane, Australia Binding Constants: Measurement and Biological Range

Brigitte Wittmann-Liebold Wittmann Institute of Technology and Analysis, WITA GmbH, Teltow, Germany Proteins: Postsynthetic Modification – Function and Physical Analysis

Cynthia Wolberger Howard Hughes Medical Institute and the Johns Hopkins University School of Medicine, Baltimore, Maryland, USA *Crystallization of Protein–DNA Complexes*

Haim J Wolfson Tel Aviv University, Tel Aviv, Israel
Protein–Ligand Interactions: Energetic Contributions and Shape
Complementarity; Induced Fit

Florian M Wurn École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland Protein Production in Mammalian Cells

Kurt Wüthrich Swiss Federal Institute of Technology (ETH), Zürich, Switzerland

Nuclear Magnetic Resonance (NMR) Spectroscopy of Proteins

Yong Xiong Ohio State University, Columbus, Ohio, USA Protein–Nucleic Acid Interaction: Major Groove Recognition Determinants

Hao Xu University of Tromsø, Tromsø, Norway *Mutagenesis: Site-specific*

Hang Xu University of Vermont, Burlington, Vermont, USA Protein Motifs for DNA Binding

Chi C Yang SynPep Corporation, California, USA Solid-phase Peptide Synthesis: Fmoc

John R Yates III The Scripps Research Institute, La Jolla, California, USA

Mass Spectrometry: Analysis of Two-dimensional Protein Gels; Proteomics: A Shotgun Approach without Two-dimensional Gels

Corin A Yeats University College London, London, UK Evolution of Protein Domains

George J Yohrling IV Johnson and Johnson, Pharmaceutical Research and Development, Spring House, Pennsylvania, USA *Enzyme Activity: Control*

Hongyu Zhang Celera Genomics, Rockville, Maryland, USA *Protein Tertiary Structures: Prediction from Amino Acid Sequences*

Preface

The *Handbook of Proteins* was conceived as a specialized reference work designed to serve a wide range of researchers and students in the molecular life sciences. The two volumes draw on the rich resources of Wiley's *Encyclopedia of Life Sciences* (ELS). First published online in 2001, ELS now includes over 4,000 articles by eminent scientists in every discipline related to Biology. However, the very breadth and depth of information in ELS can be daunting when the answer to a simple question is needed quickly. This *Handbook* provides a focused and accessible resource that assembles the more than 200 ELS articles dealing with a topic of fundamental importance – the proteins.

Proteins are involved in almost every function in a cell. Every scientist and student interested in the molecular underpinnings of life regularly finds themselves dealing with proteins on some level. Understanding proteins is one of the prerequisites for advanced study in any area of biochemistry and molecular biology. This reference work has been developed with those researchers and students in mind.

There are few aspects of protein structure, function, or chemistry that are not illuminated by one or more articles in this volume. Numerous articles also provide an introduction to almost every method used to purify proteins, determine their structures and properties, and catalogue them in databases. The emphasis placed on methods has led to the inclusion of articles covering topics from chromatography to crystallography to calorimetry to centrifugation to circular dichroism. And that only covers the Cs. Dozens of additional articles detail important aspects of enzymatic catalysis and protein-ligand interactions. Many others deal with protein structure. Our goal has been to create a resource that will command a

prominent place on the shelf of students and working scientists, and that will encourage frequent retrieval.

The articles speak for themselves. The authors were commissioned in recognition of their expertise, and all of the articles were peer-reviewed. Many of the articles were already a part of ELS. A few dozen were newly commissioned or updated to make this work as complete a resource as possible. An outstanding editorial staff helped to ensure readability and quality.

The compilation of the *Handbook* before you was a team effort, and would not have been possible without the work and help of the following people. First, we thank the Editorial Advisory Boards for the Biochemistry and Structural Biology sections of ELS, Aseem Ansari, Samuel Butcher, Perry Frey, Joachim Frank, Richard Gourse, James Ntambi, and Olivier Lichtarge. These individuals not only advised us in the selection of topics and potential authors, but also read and reviewed significant numbers of articles. We also thank the editors at John Wiley & Sons, particularly Fionnuala Rose (Project Editor), Andrea Baier (Commissioning Editor), and Kate Osborne (Assistant Editor). We are sure we tested their patience on more than one occasion, but Fionnuala, Andrea and Kate kept the project on track and provided pleasant encouragement and advice at all the right times.

Finally, we thank all of the authors for their splendid contributions. The real joy of this project has come in reading these many articles. They have provided hours of informative inspiration for us, and we anticipate they will do the same for the users of the *Handbook*.

Michael M. Cox and George N. Phillips, Jr.

Madison, Wisconsin

December 2007

How to use this book

Articles are divided into two categories indicating their level of complexity: Introductory and Advanced. Introductory articles have been written primarily for

undergraduates and non-specialists requiring the basic concepts of a particular subject. Advanced articles provide a more detailed discussion of specialist subjects, equivalent to that found in graduate level texts.

Contents

Volume 1		Protein Databases	92
RITTI		Gerritsen Vivienne Baillie and Bairoch Amos	
Contributors	xi	Protein Denaturation and the Denatured State	98
Preface	XXI	Per Hammarström and Bengt-Harald Jonsson	98
How to Use This Book	XXI	2 of 11 and 50 of the 2018 11 and 50 of 50 of	
		Protein Design	105
Introduction		Emmanuel Lacroix and Luis Serrano	
History of Protein Chemistry	3	Protein Family Databases	109
Graeme K Hunter		Nicola J Mulder	109
A few and the second of the few areas of the few			
Protein Structure		Protein Motifs: ATP-binding Motifs	114
Amino Acid Side Chain Hydrophobicity	9	Allan Matte and Louis TJ Delbaere	
Hue Sun Chan		Protein Motifs: GTP-binding Loop	118
Amino Acid Substitutions: Effects on Protein Stability	15	Guangpu Li	110
Zhiping Weng and Charles DeLisi	1.5		
		Protein Motifs: the Helix-Loop-Helix Motif	123
Evolution of Protein Domains	23	Fred Sablitzky	
Corin A Yeats and Christine A Orengo		Protein Motifs: the Helix-Turn-Helix Motif	127
Hydrogen Bonds in Proteins: Role and Strength	32	Brian W Matthews	127
Roderick E Hubbard		II.C. description	
Hydrophobic Effect	37	Protein Motifs: the Leucine Zipper	132
Judith Herzfeld and Donald J Olbris		Dmitry Krylov and Charles R Vinson	
Applied to		Protein Motifs: Zinc-fingers	138
Hydrophobic Interactions in Proteins	45	David Gell, Merlin Crossley and Joel Mackay	130
Brian W Matthews		741 A	
Immunoglobulin Fold: Structures of Proteins in the		Protein Quaternary Structure: Subunit-Subunit	
Immunoglobulin Superfamily	51	Interactions	143
Israel M Gelfand, Cyrus Chothia and Alexander E Kister		Susan Jones and Janet M Thornton	
Mining Biological Databases	58	Protein Quaternary Structure: Symmetry	
Jaime Prilusky	30	Patterns Chalant Laurianid demonstra	149
		Ronald E Stenkamp	
Molten Globule	60	Dantain Consender Chamber David	101
Anthony L Fink		Protein Secondary Structures: Prediction John-Marc Chandonia	154
Peptide Bonds, Disulfide Bonds and Properties		John-Mare Chandonia	
of Small Peptides	66	Protein Sequence Databases	159
Hiram F Gilbert		Winona C Barker	
and the second second second second second	10.2	in Depression in Depression in the Control of the C	17.1
Peptides: Biological Activities of Small Peptides Amram Mor	73	Protein Stability	162
Amrum Mor		C Nick Pace and Gerald R Grimsley	
Primary Protein and Nucleic Acid Three-dimensional		Protein Structural Flexibility: Molecular Motions	166
Structure Databases	81	Richard H Henchman and J Andrew McCammon	
Philip E Bourne			will.
Proline Residues in Proteins	06	Protein Structure Classification	172
Charles M Deber and Barbara Brodsky	86	Frances MG Pearl, Christine A Orengo and Janet M Thornton	
The same of the sa		A normon	

Protein Structure: Unusual Covalent Bonds $Nancy\ L\ Scott\ and\ Juliette\ T\ J\ Lecomte$	181	Proteases Alan J Barrett and Neil D Rawlings	311
Protein Tertiary Structures: Prediction from Amino		Ubiquitin Pathway	318
Acid Sequences	191	Y Amy Lam and Cecile M Pickart	
Hongyu Zhang			
Section of Design Court Responsible	100	Enzymes	
Protein Unfolding and Denaturants Lars Konermann	198	Binding Constants: Measurement and Biological	
Luis Konermann		Range	327
Protein: Cotranslational and Posttranslational		Donald J Winzor	4
Modification in Organelles	204		
Doug A Brooks		Engineered Enzymes	333
Proteins: Fundamental Chemical Properties	209	Ben M Dunn	4
Alain J Cozzone	207	Enzymatic Rate Enhancements	340
		Daniel M Quinn and R Steven Sikorski	
Structural Databases of Biological Macromolecules	218		
Helen M Berman		Enzyme Activity: Control	347
Unstructured Proteins	223	Shorena Nadaraia, George J Yohrling IV, George C-T Jiang, John M Flanagan and Kent E Vrana	
A Keith Dunker	223	Jung, John W Flanagan and Kent L France	
A Kem Dance		Enzyme Classification and Nomenclature	355
Burney Committee of the		Sinead Boyce and Keith F Tipton	
Protein Synthesis		Francisco Vination Standy State	265
Chaperones, Chaperonin and Heat-Shock Proteins	235	Enzyme Kinetics: Steady State W Wallace Cleland	365
Valerio Consalvi and Roberta Chiaraluce		The manage Creama	
Chaperonins	241	Enzyme Kinetics: Transient Phase	370
Valerio Consalvi and Roberta Chiaraluce	211	Kenneth A Johnson	
		Enzyme Specificity and Selectivity	376
Codon Usage in Molecular Evolution	246	Lizbeth Hedstrom	370
Richard L Grantham			
Protein Folding In Vivo	252	Enzymes: General Properties	383
Sarah Teter and F Ulrich Hartl	100	Timothy DH Bugg	
		Enzymes: Purification	390
Protein Synthesis Inhibitors	258	Jerome Salem	\$
D N Wilson, U Stelzl and Knud H Nierhaus			
Protein Synthesis Initiation in Bacteria	270	Enzymes: The Active Site	396
Marianne Grunberg-Manago		Eman Ghanem and Frank M Raushel	
		Radical Enzymes	403
Proteins: Postsynthetic Modification – Function and	276	Britt-Marie Sjöberg and Margareta Sahlin	
Physical Analysis Phisita Witten and Liebald and Theodora Chali	276		410
Brigitte Wittmann-Liebold and Theodora Choli- Papadopoulou		Substrate Binding to Enzymes Vladimir K Pliška	417
Тиринорошой		v taaimii K I tiska	
Protein Degradation		Enzyme Activity	
Amino Acid Degradation	287	Acid-Base Catalysis by Enzymes	429
Gary Sawers	20,	Anthony John Kirby	127
and the best of the property of the party of the party of		Construction and Table 1994 and daniely	
Lysosomal Degradation of Proteins	294	Binding and Catalysis	436
J Fred Dice		Michael D Toney	
Protease Complexes	301	Covalent Nucleophilic Catalysis	441
Marion Schmidt and Daniel Finley		George L Kenyon	