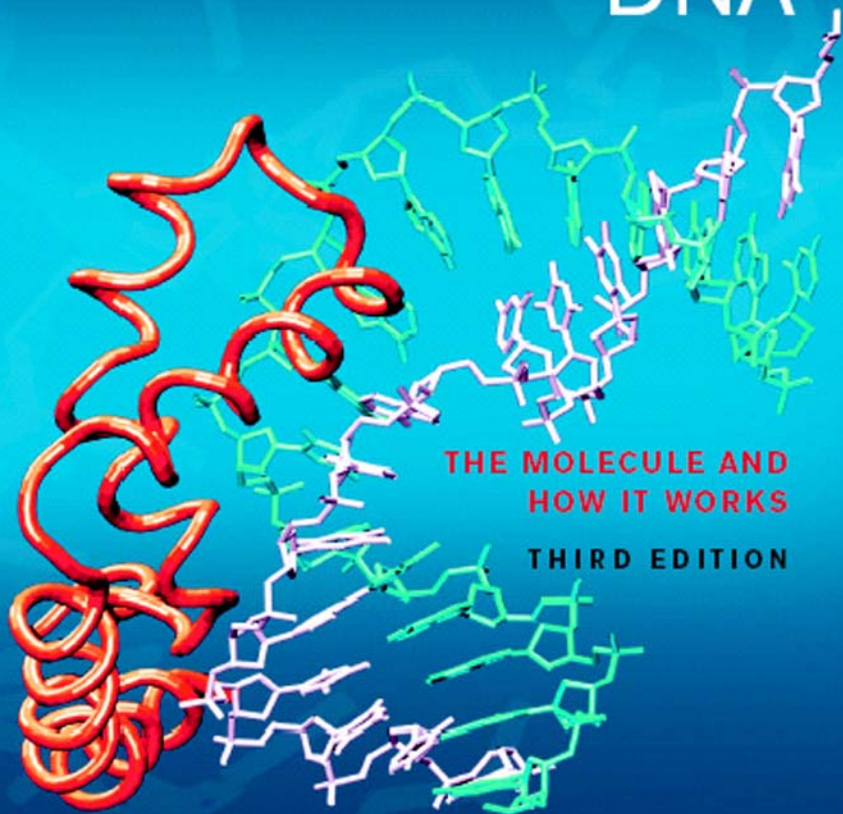




# Understanding DNA



**THE MOLECULE AND  
HOW IT WORKS**

**THIRD EDITION**

Chris R Calladine  
Horace R Drew  
Ben F Luisi  
Andrew A Travers

# UNDERSTANDING DNA

The Molecule & How It Works

**Third Edition**

## From reviews of earlier editions

A systematic and comprehensive analysis of the structure of DNA from a wonderfully fresh perspective. The book is a systematic effort to understand this fascinating molecule from the inside out, building from the first, and simplest, principles ... I recommend it very highly.

*Trends in Genetics*

We see DNA structures so often that it is often taken for granted that the molecule should not be anything but an aesthetically appealing, spiraling helix. But why should it assume such a nice structure? The book offers an absolutely delightful answer to this and other similarly mischievous questions. 'Understanding DNA' is a great book that will surely prove to be a valuable teaching tool.

*The Biochemist*

Among the strengths of the book are the clarity of the explanations of some quite difficult concepts and the novel way in which certain ideas are treated, perhaps causing the reader to think again about certain aspects of DNA structure. I enjoyed reading this book and would encourage colleagues working in the general area of DNA research to read it.

*Heredity*

Stylish ... beautifully crafted, with a logical step-by-step approach to the subject. A book from which the advanced undergraduate will benefit, and which will also generate a refreshing perspective for experts.

*Nature*

Authoritative and lucid.

*Aaron Klug*

# UNDERSTANDING DNA

## The Molecule & How It Works

**Third Edition**

by

**Chris R. Calladine**

Department of Engineering  
University of Cambridge, Cambridge, UK

**Horace R. Drew**

CSIRO Division of Molecular Science  
Sydney Laboratory, Australia

**Ben F. Luisi**

Department of Biochemistry  
University of Cambridge, Cambridge, UK

**Andrew A. Travers**

Medical Research Council Laboratory of Molecular Biology  
Cambridge, UK



**ELSEVIER**  
ACADEMIC  
PRESS

Amsterdam Boston Heidelberg London New York Oxford Paris  
San Diego San Francisco Singapore Sydney Tokyo

This book is printed on acid-free paper.

First Edition 1992

Second Edition 1997

Third Edition 2004

Copyright © 2004, Elsevier Ltd. 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 or otherwise, without the prior written permission of the publisher.

Permissions may be sought directly from Elsevier's Science & Technology Rights Department in Oxford, UK: phone: (+44) 1865 843830, fax: (+44) 1865 853333, e-mail: [permissions@elsevier.co.uk](mailto:permissions@elsevier.co.uk). You may also complete your request on-line via the Elsevier homepage (<http://www.elsevier.com>), by selecting 'Customer Support' and then 'Obtaining Permissions'.

Elsevier Academic Press  
525 B Street, Suite 1900, San Diego, California 92101-4495, USA  
<http://www.elsevier.com>

Elsevier Academic Press  
84 Theobald's Road, London WC1X 8RR, UK  
<http://www.elsevier.com>

**British Library Cataloguing in Publication Data**

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

**Library of Congress Cataloging-in-Publication Data**

A catalog record for this title is available from the Library of Congress

ISBN 0-12-155089-3

Typeset by Charon Tec Pvt Ltd, Chennai, India  
Printed and bound in Italy

04 05 06 07 08 9 8 7 6 5 4 3 2 1

The cover picture shows a complex between a protein called 'HMG-D' from fly chromosomes, and a particular sequence of DNA to which it binds strongly.

The two strands of double-helical DNA are shown in white and yellow respectively, while the protein is shown with less detail in red.

The strongly curved and untwisted structure of DNA in this complex illustrates our modern understanding of the molecule's biological action, in terms of its three-dimensional structure, which may be recognized and bound specifically by a regulatory protein.

Thus the DNA structure itself contains important information, in addition to the well-known one-dimensional Genetic Code written in the sequence of bases A, T, C and G.

*This page intentionally left blank*

# Contents

Preface .....	xi
Chapter 1    An Introduction to Molecular Biology for Non-Scientists .....	1
Chapter 2    Why a Helix? .....	18
Chapter 3    Different Kinds of Double Helix .....	39
Chapter 4    Twisting and Curving .....	64
Chapter 5    Curving in Three Dimensions .....	94
Chapter 6    DNA Supercoiling .....	116
Chapter 7    The Assembly of DNA into Chromosomes .....	139
Chapter 8    Specific DNA–Protein Interactions .....	173
Chapter 9    Methods Used to Study the Structure of DNA .....	203
Chapter 10   DNA in Disease, Diagnostics, and Medicine .....	235
Chapter 11   Cytosine Methylation and DNA Epigenetics .....	270
Postscript   .....	295
Appendix 1: Notes on the Derivation of Some Technical Terms .....	299
Appendix 2: The Chemical Theory of Base-stacking Interactions in DNA .....	301
Appendix 3: How to modify Gene Expression Using Anti-sense Oligonucleotides, Ribozymes or Small Interfering-RNA .....	312
Answers to Selected Exercises .....	323
Index .....	327



*This page intentionally left blank*

## About the authors

Chris Calladine is Emeritus Professor of Structural Mechanics at the University of Cambridge. In addition to researching many aspects of structural engineering, he has applied the methods of structural mechanics to the study of bacterial flagella, DNA and proteins.

Horace Drew solved several of the first DNA crystal X-ray structures with Richard Dickerson at Caltech, and subsequently spent 5 years researching DNA and chromosome structures with Aaron Klug at the MRC Laboratory of Molecular Biology in Cambridge, England. He now lives in Australia and is a Principal Research Scientist at CSIRO Molecular Science, Sydney Laboratory.

Ben Luisi studied hemoglobin structure with Max Perutz in Cambridge, and protein–DNA interactions with Paul Sigler at Yale University. He is a Wellcome Trust Senior Fellow in the Department of Biochemistry, University of Cambridge.

Andrew Travers is a staff scientist at the MRC Laboratory of Molecular Biology in Cambridge, England. He has studied transcriptional control in bacteria and flies, the wrapping of DNA in nucleosomes, and the role of HMG proteins in cells.