Contents

Preface ix
List of Contributors xi

SECTION I  CANCER SYSTEMS 1

1 A Path to Knowledge: from Data to Complex Systems Models of Cancer 3
Sylvia Nagl
1.1 Conceptual foundations: biological complexity 7
1.2 A taxonomy of cancer complexity 9
1.3 Modelling and simulation of cancer systems 14
1.4 Data standards and integration 20
1.5 Concluding remarks 24

2 Theory of Cancer Robustness 29
Hiroaki Kitano
2.1 Robustness: the fundamental organizational principle of biological systems 30
2.2 Underlying mechanisms for robustness 31
2.3 Intrinsic features of robust systems: evolvability and trade-offs 32
2.4 Cancer as a robust system 34
2.5 Therapy strategies 36
2.6 A proper index of treatment efficacy 38
2.7 Computational tools 39
2.8 Conclusion 40

3 Developing an Integrated Informatics Platform for Cancer Research 45
Richard Begent
3.1 Background 45
3.2 The challenge 46
3.3 The UK National Cancer Research Institute (NCRI) informatics platform 47
CONTENTS

3.4 Developing the informatics platform 49
3.5 Benefits of the platform 51
3.6 Conclusions 53

SECTION II  In silico MODELS 57

4 Mathematical Models of Cancer 59
Manish Patel and Sylvia Nagl
4.1 Growth models 62
4.2 A very brief tour of cellular automata 72
4.3 Angiogenesis models 73
4.4 Treatment response models 78
4.5 Dynamic pathways models 83
4.6 Other models 86
4.7 Simulations of complex biological systems 86
4.8 Concluding remarks 87

5 Some Mathematical Modelling Challenges and Approaches in Cancer 95
Philip Maini and Robert A. Gatenby
5.1 Introduction 95
5.2 Multiscale modelling 96
5.3 Tumour vascular modelling 98
5.4 Population models 100
5.5 Conclusion 103

6 Computer Simulation of Tumour Response to Therapy 109
Georgios S. Stamatakos and Nikolaos Uzunoglu
6.1 Introduction 109
6.2 Tumour growth simulation 111
6.3 Radiotherapy response simulation 114
6.4 Chemotherapy response simulation 118
6.5 Simulation of tumour response to other therapeutic modalities 119
6.6 Simulation of normal tissue response to antineoplastic interventions 120
6.7 Integration of molecular networks into tumour behaviour simulations 120
6.8 Future directions 120

7 Structural Bioinformatics in Cancer 127
Stephen Neidle
7.1 Introduction 127
7.2 Macromolecular crystallography 129
7.3 Molecular modelling 135
7.4 Conclusions 138
SECTION III  In vivo MODELS  141

8 The Mouse Tumour Biology Database: an Online Resource for Mouse Models of Human Cancer  143
Carol J. Bult, Debra M. Krupke, Matthew J. Vincent, Theresa Allio, John P. Sundberg, Igor Mikaelian and Janan T. Eppig
8.1 Introduction  143
8.2 Background  143
8.3 Database content  145
8.4 Data acquisition  145
8.5 Using the MTB database  148
8.6 Connecting the MTB database with related databases  150
8.7 Summary  152

9 Bioinformatics Approaches to Integrate Cancer Models and Human Cancer Research  155
Cheryl L. Marks and Sue Dubman
9.1 Background  155
9.2 The MMHCC Informatics at the outset of the programme  156
9.3 Initial NCI bioinformatics infrastructure development  158
9.4 Future directions for informatics support  164
9.5 Summary  167

SECTION IV  DATA  169

10 The FAPESP/LICR Human Cancer Genome Project: Perspectives on Integration  171
Ricardo Brentani, Anamaria A. Camargo, Helena Brentani and Sandro J. De Souza
10.1 Introduction  171
10.2 The FAPESP/LICR Human Cancer Genome Project  172
10.3 An integrated view of the tumour transcriptome  175
10.4 Summary  182

11 Today’s Science, Tomorrow’s Patient: the Pivotal Role of Tissue, Clinical Data and Informatics in Modern Drug Development  185
Kirstine Knox, Amanda Taylor and David J. Kerr
11.1 Introduction  185
11.2 A new national strategy for the provision of tissue annotated with clinical information to meet current and future needs of academic researchers and industry  187
CONTENTS

11.3 The NCRI National Cancer Tissue Resource for cancer biology and treatment development 191
11.4 A potential future world-class resource integrating research and health service information systems and bioinformatics for cancer diagnosis and treatment 194
11.5 A proposed information system architecture that will meet the challenges and deliver the required functionality: an overview 195
11.6 Consent and confidentiality: ensuring that the NCTR is embedded in the UK’s legal and ethical framework 204
11.7 Concluding remarks: future challenges and opportunities 208

SECTION V ETHICS 211

12 Software Design Ethics for Biomedicine 213
Don Gotterbarn and Simon Rogerson

12.1 The problem: software and research 213
12.2 Risk identification 214
12.3 Biomedical software example 216
12.4 Is an ethical risk analysis required? 217
12.5 Details of SoDIS 218
12.6 A SoDIS analysis of the biomedical software example 224
12.7 Conclusion 230

13 Ethical Issues of Electronic Patient Data and Informatics in Clinical Trial Settings 233
Dipak Kalra and David Ingram

13.1 Introduction 233
13.2 Ethical aspects of using patient-identifiable health data 233
13.3 Legislation and policies pertaining to patient-identifiable health data 240
13.4 Using anonymized and pseudonymized data 250
13.5 Protecting personal health data 252

14 Pharmacogenomics and Cancer: Ethical, Legal and Social Issues 257
Mary Anderlik Majumder and Mark Rothstein

14.1 Introduction 257
14.2 Getting pharmacogenomic tests and drugs to market 258
14.3 Cost and coverage issues 261
14.4 Ethical challenges of pharmacogenomics 264
14.5 Conclusion 270

Index 275