

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
<i>Sylvia Nagl</i>	
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
<i>Hiroaki Kitano</i>	
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
<i>Richard Begent</i>	
3.1 Background	45
3.2 The challenge	46
3.3 The UK National Cancer Research Institute (NCRI) informatics platform	47

vi	CONTENTS	
3.4	Developing the informatics platform	49
3.5	Benefits of the platform	51
3.6	Conclusions	53
SECTION II	<i>In silico</i> MODELS	57
4	Mathematical Models of Cancer	59
	<i>Manish Patel and Sylvia Nagl</i>	
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
	<i>Philip Maini and Robert A. Gatenby</i>	
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
	<i>Georgios S. Stamatakos and Nikolaos Uzunoglu</i>	
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
	<i>Stephen Neidle</i>	
7.1	Introduction	127
7.2	Macromolecular crystallography	129
7.3	Molecular modelling	135
7.4	Conclusions	138

SECTION III	<i>In vivo</i> MODELS	141
8	The Mouse Tumour Biology Database: an Online Resource for Mouse Models of Human Cancer	143
	<i>Carol J. Bult, Debra M. Krupke, Matthew J. Vincent, Theresa Allio, John P. Sundberg, Igor Mikaelian and Janan T. Eppig</i>	
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
	<i>Cheryl L. Marks and Sue Dubman</i>	
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
	<i>Ricardo Brentani, Anamaria A. Camargo, Helena Brentani and Sandro J. De Souza</i>	
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
	<i>Kirstine Knox, Amanda Taylor and David J. Kerr</i>	
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

viii	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
	<i>Don Gotterbarn and Simon Rogerson</i>	
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
	<i>Dipak Kalra and David Ingram</i>	
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
	<i>Mary Anderlik Majumder and Mark Rothstein</i>	
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