

CONTENTS

<i>Preface to the Second Edition</i>	<i>xi</i>
<i>Foreword from the First Edition</i>	<i>xvii</i>
<i>Preface from the First Edition</i>	<i>xxi</i>
<i>List of Figures</i>	<i>xxxiii</i>
<i>List of Tables</i>	<i>xxxix</i>
Chapter 1 Biomedical Data	1
1.1 The Nature and Representation of Biomedical Data	5
1.1.1 What Can Be Represented in a Computer?.....	18
1.1.2 Cells, DNA, Proteins, and the Genetic Code	37
1.1.3 Anatomy.....	54
1.1.4 Medical Laboratory Data	56
1.1.5 Medical Images.....	63
1.1.6 Metadata.....	83
1.2 Objects, Metadata, and Serialization	87
1.2.1 A Simple Solution Using Tags (Keywords).....	88
1.2.2 An Object-Oriented Design	90
1.2.3 A Better Solution Using Metaobjects	102
1.2.4 Medical Images: Incorporating Binary Data.....	111
1.2.5 Drug Interactions: Organizing Drugs into Classes	118
1.2.6 XML.....	124
1.3 Database Concepts and Systems.....	133
1.3.1 The Relational Model	134
1.3.2 Indexing and Tree Structures	143
1.3.3 Time-Oriented Data and Interval Trees.....	150
1.3.4 The Entity-Attribute-Value (EAV) Model.....	155
1.3.5 Online Analytical Processing (OLAP).....	156
1.4 Data Quality	165
1.5 Data, Information, and Knowledge.....	169
1.6 Summary	173
1.7 Exercises	173
Chapter 2 Symbolic Biomedical Knowledge	179
2.1 Biomedical Theories and Computer Programs.....	182
2.1.1 A World Class Reasoning Example	182

CONTENTS

2.1.2	Biological Examples	183
2.1.3	Symbolic Theories	184
2.2	Logic and Inference Systems	187
2.2.1	Predicate Calculus	189
2.2.2	Unsound Inference: Abduction and Induction	218
2.2.3	First Order Logic (FOL)	219
2.2.4	Rule-Based Programming for FOL	230
2.2.5	Example: Predicting Drug Interactions by Logical Inference	237
2.2.6	Truth Maintenance Systems	242
2.2.7	Electronic Medical Records and Guidelines	254
2.2.8	Example: Cancer Radiotherapy Planning	255
2.2.9	Example: Rule-Based Nursing Knowledge	272
2.2.10	Limitations of FOL	277
2.3	Frames, Semantic Nets, and Ontologies	281
2.3.1	A Simple Frame System	281
2.3.2	Extensions to Frame Systems	303
2.3.3	Frame System Implementations, Interfaces, and APIs	306
2.3.4	The UW Foundational Model of Anatomy	307
2.3.5	Representing Drug Information in Frames	313
2.3.6	Frames and Object-Oriented Programming Languages	316
2.3.7	Example: The Gene Ontology	318
2.4	Description Logics	321
2.4.1	Description Logics and Notation Systems	325
2.4.2	Example: GALEN	326
2.4.3	The Semantic Web	330
2.4.4	Example: Enhancing Queries With LOINC	333
2.4.5	Back to the Future	335
2.5	Summary	335
2.6	Exercises	337
Chapter 3	Probabilistic Biomedical Knowledge	343
3.1	Probability and Statistics	344
3.1.1	Probability	345
3.1.2	Statistics	346
3.1.3	The Laws of Probability	347
3.1.4	Conditional Probability	350
3.1.5	Independence	351
3.1.6	Random Variables and Estimation	352
3.2	Bayes' Rule, Bayes Nets, and Probabilistic Inference	364
3.2.1	Simple Bayesian Inference	365
3.2.2	Non-Boolean Variables	367
3.2.3	Bayes Nets	368
3.2.4	Example: Radiation Therapy Planning	373
3.3	Utility and Decision Modeling	375
3.3.1	A Decision Analysis Vignette	376

3.3.2	Graph Structure and Probability Assignment	377
3.3.3	Determining Utilities	378
3.3.4	Computation of Expected Values	381
3.4	Information Theory	382
3.4.1	Encoding of Messages	382
3.4.2	Entropy and Information	386
3.4.3	Efficient Encoding	388
3.4.4	Error Detection and Correction	391
3.4.5	Information Theory in Biology and Medicine	391
3.5	Summary	395
3.6	Exercises	395
Chapter 4 Biomedical Information Access		397
4.1	Information Retrieval Systems	398
4.1.1	IR System Design	402
4.1.2	Indexing	403
4.1.3	Processing Queries	410
4.1.4	Searching and Matching	410
4.1.5	Ranking the Results	410
4.1.6	Performance Evaluation	411
4.2	Beyond Text Documents	413
4.2.1	Biomedical Images	413
4.2.2	Electronic Medical Records	414
4.3	Networks and Biomedical Data Communication	415
4.3.1	Networks and Protocols	418
4.3.2	HL7: Clinical Data Encoding and Transmission	424
4.3.3	DICOM: Medical Image Data Encoding and Transmission	433
4.3.4	Network Access to Biomedical Documents and Data	445
4.3.5	Network Access to an Ontology: The FMA	458
4.4	Summary	476
4.5	Exercises	476
Chapter 5 Computational Models and Methods		479
5.1	Computing with Genes, Proteins, and Cells	480
5.1.1	Mapping Genes to Proteins	480
5.1.2	Computing with Protein Sequences	485
5.2	Search	496
5.2.1	A General Framework for Search	497
5.2.2	Uninformed Search Strategies	503
5.2.3	Informed Search Strategies	505
5.2.4	Path Search	508
5.2.5	Example: DNA Sequence Alignment	509
5.2.6	Example: Biochemical Pathways	515
5.3	Natural Language Processing	523
5.4	State Machines and Dynamic Models	525

CONTENTS

5.4.1 State Machines	526
5.4.2 A Simple State Machine	529
5.4.3 Example: Simulating the Cell Cycle in Yeast	533
5.4.4 Example: Implementing DICOM with a State Machine.....	540
5.5 Stochastic Processes	562
5.5.1 Markov Chains.....	563
5.5.2 Example: Prostate Cancer	565
5.5.3 Example: Radiotherapy Clinical Target Volume.....	567
5.6 Summary.....	575
5.7 Exercises.....	576
Chapter 6 Biomedical Data, Knowledge, and Systems in Context	579
6.1 A Bit of Personal History and Perspective	580
6.2 Medical Device Safety.....	583
6.2.1 Radiation Therapy Planning Systems	583
6.2.2 Who is Master, the Human or the Computer?	585
6.2.3 The Therac-25: A Real-Time Disaster	586
6.2.4 Prism	587
6.2.5 The UW Neutron Therapy Facility	588
6.2.6 Safety by Design: Radiotherapy Machines.....	589
6.3 System and Data Security	595
6.3.1 Real Life Examples.....	595
6.3.2 Security Management – the Context.....	597
6.3.3 Ideas for a Security Program.....	599
6.4 Summary.....	601
6.5 Exercises	601
Chapter 7 Epilogue.....	603
7.1 The Halting Problem—A Metaphoric Version	604
7.2 Where Do New Ideas Come From?.....	604
7.3 Making A Difference	605
Appendix A Notes on Lisp, Other Languages, and Resources	607
A.1 Lisp Notes	608
A.1.1 CLOS and MOP.....	609
A.1.2 Optimization	612
A.1.3 Books on Lisp	615
A.1.4 Common Lisp Systems, Libraries, and Resources	616
A.2 Other Programming Languages	617
A.2.1 The Factorial Function: A Snapshot Language Comparision	617
A.3 Other Resources.....	619
A.4 Exercises	620
Bibliography.....	627
Index.....	647