

THE NATIONAL ACADEMIES™

Advisers to the Nation on Science, Engineering, and Medicine

The nation turns to the National Academies—National Academy of Sciences, National Academy of Engineering, Institute of Medicine, and National Research Council—for independent, objective advice on issues that affect people's lives worldwide.

www.national-academies.org

ISBN 0-309-09584-0



9 780309 095846

90000

EXECUTIVE SUMMARY	1
1 THE NATURE OF THE FIELD	12
Introduction,	12
The Mathematics-Biology Interface,	12
What Has Changed in Recent Years?,	15
What Makes Computational Biology Problems Hard?,	19
Factors Common to Successful Interactions Between the Mathematical Sciences and the Biosciences,	20
Preparing the Ground for Improved Synergies of Benefit to Both Fields,	22
Structure of This Report,	27
References,	27
2 HISTORICAL SUCCESSES	29
The Beginnings of Population Biology,	29
Inference of Gene Function by Homology,	30
Evolutionary Processes in Populations,	32
Modeling,	33
Medical and Biological Imaging,	34
Summary,	35
References,	36

3	UNDERSTANDING MOLECULES	38
	Introduction, 38	
	The Mathematics-Biology Connection, 39	
	Areas of Mathematical Applications for Molecules, 41	
	Sequence Analysis, 41	
	Structure Analysis, 43	
	Dynamics, 45	
	Interactions, 47	
	Future Directions, 48	
	References, 49	
4	UNDERSTANDING CELLS	51
	Introduction, 51	
	Exemplification of These Issues, 52	
	Cellular Structures, 55	
	Discovery of Cellular Networks and Their Functions, 57	
	From Networks to Cellular Functions, 60	
	From Cells to Tissues, 66	
	Data Integration, 68	
	Biological Considerations, 70	
	Future Directions, 72	
	References, 73	
5	UNDERSTANDING ORGANISMS	80
	Cardiac Physiology, 81	
	Circulatory Physiology, 84	
	Respiratory Physiology, 85	
	Information Processing, 86	
	Endocrine Physiology, 87	
	Morphogenesis and Pattern Formation, 88	
	Locomotion, 90	
	Cancer, 91	
	Delivery of Therapy to Target Tumor Cells, 91	
	Mechanisms of Drug Action, 92	
	Growth and Differentiation of Cell Populations, 92	
	Development of Resistance, 92	
	In Vivo Dynamics of the HIV-1 Infection, 93	
	Future Directions, 94	
	References, 95	

6	UNDERSTANDING POPULATIONS	99
	Population Genetics, 99	
	Ecological Aspects of Populations, 104	
	A Synthesis of Ecology and Evolution, 106	
	References, 108	
7	UNDERSTANDING COMMUNITIES AND ECOSYSTEMS	110
	Computation, 116	
	Future Directions, 117	
	References, 122	
8	CROSSCUTTING THEMES	127
	The “Small n , Large P ” Problem, 127	
	Finding Patterns in Gene-Expression Data, 128	
	Supervised Learning, 131	
	Unsupervised Learning, 132	
	Analysis of Ordered Systems, 134	
	Applications of Hidden Markov Models to the Analysis of DNA, RNA, and Protein Sequences, 134	
	Profile HMMs, 135	
	HMMs in Gene Finding, 136	
	Applications of Monte Carlo Methods in Computational Biology, 138	
	Gibbs Sampling in Motif Finding, 139	
	Inference of Regulatory Networks, 139	
	Sampling Protein Conformations, 140	
	Lessons from Mathematical Themes of Current Import, 140	
	Processing of Low-Level Data, 142	
	Epilogue, 144	
	References, 145	