

Contents

Preface xi

Acknowledgments xv

List of Abbreviations xvii

1. Introduction: Respiration, phosphorylation, and mechanism 1
 - 1.1 Respiration, photosynthesis, and bioenergetics 2
 - 1.2 Vitalism 3
 - 1.3 Historical questions 5
 - 1.4 Phosphorylation 13
 - 1.5 Mechanisms 14
 - 1.6 The relevance of cell bioenergetics to the question of mechanism 15
2. From physiology to biochemistry: Respiration and oxidation from 1600 to 1900 17
 - 2.1 Initiation of the experimental study of respiration 18
 - 2.2 John Mayow's *Tractatus Quinque* 20
 - 2.3 Stephen Hales's *Vegetable Staticks* 22
 - 2.4 Respiration and combustion 23
 - 2.5 The location of respiration 26
 - 2.6 Thermodynamic questions 28
 - 2.7 Bernard's criticism of slow combustion 31
 - 2.8 Hofmeister's integration of cell biology 32
 - 2.9 O_2 and oxidation 33
 - 2.10 Spectroscopy, hemoglobin, and animal pigments 35
 - 2.11 Cell-free systems 38
3. Relating phosphorylation, respiration, and oxidation: 1900–1945 41
 - 3.1 Resolving nineteenth-century questions 41
 - 3.2 Achievements of the first half of the twentieth century 42
 - 3.3 Yeast and animal juices: The importance of phosphate 43
 - 3.4 Thunberg, Wieland, and the nature of biological oxidation 47
 - 3.5 Warburg's *Atmungsferment* 51
 - 3.6 Keilin's cytochrome 54
 - 3.7 DPN (NAD) and its oxidation 59
 - 3.8 Muscle, lactic acid, and energy 61
 - 3.9 Adenosine triphosphate and muscle phosphates 62
 - 3.10 Aerobic ATP synthesis: Engelhardt and Kalckar 65

3.11	Phosphorylation linked to respiration: Belitzer and Ochoa	68
3.12	Lipmann: The significance of phosphorylation	69
4.	Emergence of the field of cell bioenergetics: 1945-1960	73
4.1	Emergence of a new field	73
4.2	The mitochondrion as the location of respiratory activity	74
4.3	Further elucidation of the respiratory chain	76
4.4	Phosphorylation	82
4.5	Sites for phosphorylation	85
4.6	Seeking to understand the mechanism of phosphorylation	87
4.7	The phosphorylating enzyme	91
4.8	Fragmenting mitochondria	91
4.9	Physiological aspects of mitochondria	94
5.	Defining the mechanism: 1960-1977	97
5.1	What mechanism?	97
5.2	The first proton theory: Robert J. P. Williams	99
5.3	The chemiosmotic hypothesis of Peter Mitchell	100
5.4	Revising the respiratory chain	104
5.5	Exploring the ATP synthase	108
5.6	Reconstituting oxidative phosphorylation	111
5.7	Bacteriorhodopsin	112
5.8	Conformational theories	113
5.9	Mitochondrial membranes	117
5.10	Ion movements across the mitochondrial membrane	119
5.11	Resolving the mechanism	122
6.	Discovering photosynthesis	128
6.1	The development of ideas on photosynthesis	128
6.2	Initial studies of photosynthesis	129
6.3	The importance of water and CO ₂	131
6.4	Energy	132
6.5	Discovering chlorophyll and chloroplasts	133
6.6	Understanding the nature of photosynthesis	137
6.7	Photosynthetic bacteria and an oxidation-reduction mechanism	139
6.8	Light and dark reactions	141
6.9	O ₂ evolution and the Hill reaction	143
6.10	CO ₂ assimilation	146
6.11	Discovering photophosphorylation	149
7.	Elucidating the photosynthetic light reaction	154
7.1	The fourth period of photosynthetic history	154
7.2	Seeking a coherent model of photosynthesis	155
7.3	The photosynthetic unit	158

7.4	Two light reactions and a reaction center	161
7.5	The Z-scheme and two photosystems	162
7.6	The contribution from bacterial photosynthesis	167
7.7	The chloroplast electron-transport chain	171
7.8	Chloroplast photophosphorylation	175
8.	The impact of protein technology: 1977–1997	181
8.1	The fifth period of investigation	181
8.2	The chemiosmotic mechanism for oxidative and photosynthetic phosphorylation	182
8.3	The Q cycle	183
8.4	Stoichiometric problems in mitochondria	186
8.5	Uncoupling and uncoupling proteins in mitochondria	188
8.6	Bacteriorhodopsin, a bioenergetic protein	190
8.7	Understanding the respiratory chain	194
8.8	Elucidating the mechanism of respiratory chain complexes	195
8.9	Photosynthetic complexes	200
8.10	Adenine nucleotide transport	205
8.11	The ATP synthase	207
9.	The search for mechanism	214
9.1	Photosynthetic and oxidative biochemistry—the relationship	214
9.2	The course of bioenergetics history	216
9.3	Does methodology drive bioenergetics?	218
9.4	The significance of the membrane	223
9.5	Membrane proteins	224
9.6	The concept of mechanism	225
9.7	Revolution, hypothesis, and crisis	229
9.8	Resolving the crisis: Accepting the chemiosmotic theory	233
	References	237
	Index	267