

CONTENTS

<i>Contributors</i>	<i>xi</i>
<i>The journey from discovering cell volume regulation of euryhaline fish to the identification of key mechanisms of cell volume homeostasis</i>	<i>xv</i>

Section 1

General Principles of Cell Volume Regulation

1. Water Homeostasis and Cell Volume Maintenance and Regulation	3
Eric Delpire and Kenneth B. Gagnon	
1. Introduction	4
2. Whole Body Water Homeostasis	6
3. Cell Volume Homeostasis	12
Acknowledgments	40
References	40
2. Search for Upstream Cell Volume Sensors: The Role of Plasma Membrane and Cytoplasmic Hydrogel	53
Sergei N. Orlov, Aleksandra Shiyani, Francis Boudreault, Olga Ponomarchuk, and Ryszard Grygorczyk	
1. Introduction	54
2. Cell Volume-Sensing by the Plasma Membrane	55
3. Cell Volume Sensing by the Cytoplasm	65
4. Delayed Volume Sensors: Role of Elevated $[Na^+]_i/[K^+]_i$ Ratio	69
5. Conclusions and Perspective	73
Acknowledgments	75
References	75
3. Cytoskeletal Contribution to Cell Stiffness Due to Osmotic Swelling; Extending the Donnan Equilibrium	83
Pei-Chuan Chao, Mettupalayam Sivaselvan, and Frederick Sachs	
1. Introduction	84
2. Modeling	85
3. Equilibrium of Chemical Potential and Osmotic Pressure Due to Fixed Charge	86

4. Mechanical Equilibrium	87
5. Numerical Results	89
6. Summary	91
7. Discussion	91
References	94
4. Membrane Stiffening in Osmotic Swelling: Analysis of Membrane Tension and Elastic Modulus	97
Manuela A.A. Ayee and Irena Levitan	
1. Introduction	98
2. Membrane Tension	102
3. Elastic Properties	113
4. Conclusions	117
Acknowledgments	118
References	118
5. Molecular Identities and ATP Release Activities of Two Types of Volume-Regulatory Anion Channels, VSOR and Maxi-Cl	125
Yasunobu Okada, Toshiaki Okada, Md. Rafiqul Islam, and Ravshan Z. Sabirov	
1. Introduction	126
2. Two Types of Volume-Regulatory Anion Channels: VSOR and Maxi-Cl	127
3. Molecular Identities of VSOR	132
4. Molecular Identities of Maxi-Cl	145
5. ATP Release Activities of VSOR and Maxi-Cl	152
6. Conclusions and Future Directions	158
Acknowledgments	159
References	160
6. Molecular Biology and Physiology of Volume-Regulated Anion Channel (VRAC)	177
James Osei-Owusu, Junhua Yang, Maria del Carmen Vitery, and Zhaozhu Qiu	
1. Introduction	178
2. LRRC8 Heteromers as VRAC	180
3. Physiological Role of SWELL1 and VRAC	187
4. Future Studies of VRAC	192
Acknowledgments	196
References	196

Section 2

Regulation of Intracellular Chloride and Water Homeostasis

7. Role of WNK Kinases in the Modulation of Cell Volume	207
Paola de los Heros, Diana Pacheco-Alvarez, and Gerardo Gamba	
1. Introduction	208
2. Principles of Cell Volume Regulation	208
3. With No Lysine Kinases (WNKs)	219
4. The WNK Kinases as Intracellular Chloride Sensors	222
5. WNKs and Cell Volume Regulation	227
References	229
8. Intracellular Macromolecules in Cell Volume Control and Methods of Their Quantification	237
Michael A. Model and Jonathan C. Petrucci	
1. Introduction	238
2. The Components of Cell Volume and the Main Relationships	240
3. Methods for Measurement of W , A_T , and A_S (Non-QPI)	245
4. Quantitative Phase Imaging (QPI)	251
5. Biological Questions	263
6. Conclusion	273
Acknowledgments	274
References	274

Section 3

Cell Volume Regulation in the Airways

9. Slippery When Wet: Airway Surface Liquid Homeostasis and Mucus Hydration	293
Megan J. Webster and Robert Tarran	
1. Introduction	294
2. Airway Surface Liquid (ASL) Composition	299
3. Airway Surface Liquid Volume Regulation	300
4. pH Homeostasis of the ASL	316
5. CF Lung Disease	319
6. Conclusions	324
References	324

10. Physiology of the Gut: Experimental Models for Investigating Intestinal Fluid and Electrolyte Transport **337**

Isha Dey and Neil A. Bradbury

- | | |
|--|-----|
| 1. Introduction | 338 |
| 2. Epithelial Ion and Fluid Secretion | 343 |
| 3. Intestinal Ion and Fluid Transport | 348 |
| 4. Model Systems for Studying Intestinal Ion Transport | 352 |
| 5. A "Swell" Ing Assay | 363 |
| 6. Summary | 370 |
| References | 371 |

Section 4

Cell Volume Regulation in the Brain

11. Cell Volume Control in Healthy Brain and Neuropathologies **385**

Corinne S. Wilson and Alexander A. Mongin

- | | |
|---|-----|
| 1. Common and Unique Aspects of Osmotic Balance Within the CNS | 387 |
| 2. RVD in the CNS Cells | 395 |
| 3. RVI in the CNS Cells | 404 |
| 4. Cell Volume Changes During Normal Brain Functioning | 405 |
| 5. A Special Case for Astrocytic Swelling and Cell Volume Control | 409 |
| 6. Failure of Cell Volume Control in Brain Pathologies | 415 |
| 7. VRAC as a Villain in Neuropathologies | 427 |
| 8. The Evolving Understanding of VRAC Identity: Progress and Perspectives | 430 |
| Acknowledgments | 436 |
| References | 436 |

12. Cytotoxic Swelling of Sick Excitable Cells – Impaired Ion Homeostasis and Membrane Tension Homeostasis in Muscle and Neuron **457**

Catherine E. Morris

- | | |
|---|-----|
| 1. Membrane Injury, Na^+ -Loading, Swelling Death. Or Not? | 459 |
| 2. Membrane Tension Homeostasis and Membrane Fragility | 461 |
| 3. Safeguarding the Bilayer – Tension Buffering | 465 |
| 4. Mammalian Neuron Osmoresistivity Revisited | 469 |
| 5. Donnan the Elephant (in the Sick Excitable Room) | 470 |

6. Cytotoxic Swelling of Skeletal Muscle	472
7. Excitotoxic Insults Stiffen Neurons. Then They Swell, Bleb, Soften, Die	476
8. Cytotoxic Swelling of Neurons	478
9. Modeling Excitotoxic Swelling in Neurons	480
10. Mechanistic Model for Excitotoxic Neuronal Swelling During SD	485
11. Conclusion: IH and MTH Working Together	486
References	489