Contents

Preface vii

Foreword ix

1. Introduction 1

1.1 Background 1
1.2 Aims and Target Audience 4
1.3 Why Model? 5
1.4 Historical Perspectives 9
1.5 Anatomy and Function of the Heart 18
  1.5.1 Macroscopic Description 18
  1.5.2 Basic Cardiac Cellular Electrophysiology 21
  1.5.3 Cardiac Structure and Electrophysiology 27
  1.5.4 The Electrocardiogram (ECG) 30
  1.5.5 Cardiac Contraction 35
1.6 Role of Mathematical Modelling in the Heart 36
1.7 Notation 40
1.8 Open Questions, Issues and Challenges 41

2. Geometric Modelling 43

2.1 Introduction 43
2.2 Finite Element Basis Functions 45
  2.2.1 Local Coordinate System 45
  2.2.2 Linear Lagrange Basis Functions 46
  2.2.3 Quadratic Lagrange Basis Functions 49
  2.2.4 Basis Functions in Higher-Dimensions 51

2.2.5 Cubic Hermite Basis Functions 55
2.3 Fitting Techniques 61
2.3.1 Data Projection 61
2.3.2 Linear Field Fitting 63
2.3.3 Iterative Linear Field Fitting 64
2.3.3.1 Sobolev Smoothing 65
2.4 Geometric Models 68
2.4.1 Heart Models 68
2.4.2 Torso Models 71
2.4.3 Patient-Specific Models 71
2.5 Open Questions, Issues and Challenges 73

3. Cell Modelling 77

3.1 Introduction 77
3.1.1 Units 79
3.2 Biophysically-Based Models 81
3.2.1 Cell Membrane 82
3.2.2 Hodgkin and Huxley (HH) 82
3.2.3 The Noble 1962 Model 88
3.2.4 The Beeler-Reuter Model (BR) 91
3.2.5 The Beeler-Reuter-Drouhard-Roberge Model (BRDR) 97
3.2.6 The DiFrancesco-Noble Model (DFN) 101
3.2.7 The Luo-Rudy I Model (LRI) 107
3.2.8 The Luo-Rudy II Model (LRII) 116
3.2.9 The Noble, Varghese, Kohl and Noble Model (NVKN) 122
3.2.10 Biophysical Cell Model Summary 128
3.3 Simplified Models of Cardiac Myocytes 131
3.3.1 Polynomial Model 131
3.3.2 FitzHugh-Nagumo Model 132
3.3.3 Rogers-Modified FitzHugh-Nagumo Model 133
3.3.4 van Capelle-Durrer Model 136
3.3.5 Fenton-Karma Model (FK) 137
3.4 Solution of Cell Models 142
3.5 CellML 146
3.6 Open Questions, Issues and Challenges 147

4. Tissue Modelling 151

4.1 Introduction 151

4.2 Tissue Structure 152
4.3 Modelling Electrical Activity 154
  4.3.1 The Cable Model 154
  4.3.2 The Bidomain Model 159
4.4 Numerical Solution Techniques 166
4.5 Finite Element-Derived Finite Difference Method 166
  4.5.1 Domain Metrics 167
  4.5.2 Describing the Microstructure 172
  4.5.3 Expressing the Laplacian Terms 174
  4.5.4 Numerical Approximations 176
  4.5.5 Evaluation of the Bidomain Laplacian Coefficients . 179
  4.5.6 Element Branching 183
  4.5.7 Bidomain Boundary Conditions 184
  4.5.8 Implicit and Explicit Formulations 186
  4.5.9 Deformation 188
4.6 Alternative Solution Techniques 188
  4.6.1 Finite Difference Solution of the Bidomain Equations 189
  4.6.2 Finite Element Solution of the Bidomain Equations . 191
  4.6.3 Finite Volume Solution of the Bidomain Equations . 195
4.7 Testing the Solution Method 196
  4.7.1 The Laplacian Operator 196
  4.7.2 One-Dimensional Propagation 199
  4.7.3 Deforming Fibre 202
  4.7.4 Three-Dimensional Isotropic Propagation 203
  4.7.5 Anisotropic Three-Dimensional Propagation 205
4.8 Examples of Tissue Excitation 206
  4.8.1 Excitation in Two Dimensions 207
  4.8.2 Excitation in Three Dimensions 213
4.9 General Comments 219
4.10 Open Questions, Issues and Challenges 221

5. Whole-Heart Modelling 223

5.1 Introduction 223
5.2 Equivalent Source Models 224
5.3 Empirical Models 225
5.4 Bidomain Models 228
5.5 Tissue Types 231
5.6 Illustrative Examples 231
  5.6.1 Ventricular Excitation 232

5.6.2 Atrial Excitation 234
5.7 Open Questions, Issues and Challenges 236

6. Organ in the Body – The Forward Problem of Electrocardiology 239

6.1 Introduction 239
6.2 The Electrocardiogram 240
6.3 Electrical Activity in the Torso 245
6.3.1 Torso Boundary Conditions 247
6.3.2 Summary of the Integrated Model 248
6.4 Geometric Torso Model 249
6.5 Torso Solution – The Finite Element Method (FEM) 250
6.5.1 Gaussian Quadrature 257
6.5.2 Analytic Test Problem 259
6.6 Torso Solution – The Boundary Element Method (BEM) . . 260
6.6.1 Numerical Solution Procedures for the Boundary Integral Equation 268
6.6.2 Numerical Evaluation of Coefficient Integrals 270
6.6.3 Conductivity Tensor 274
6.6.4 The Derivative BEM 275
6.6.4.1 Fundamental Solution Derivatives 276
6.6.4.2 Derivative Boundary Element Identities . . 276
6.6.4.3 Singularity on the Domain Boundary 277
6.6.4.4 Discretisation 283
6.6.4.5 Conductivity Tensor 287
6.6.5 Source Terms 288
6.6.6 Accuracy and Computational Efficiency 292
6.7 From Cell to Body Surface 296
6.7.1 Common Approaches 297
6.7.2 Dipole Source Calculation 298
6.7.3 Coupled and Uncoupled Solutions 299
6.7.4 Coupling Approaches 300
6.7.4.1 Boundary Iteration Method 301
6.7.4.2 Direct Assembly 304
6.7.5 Two-Dimensional Fully-Coupled Forward Simulations 308
6.8 Three-Dimensional Torso Simulations 316
6.8.1 Dipole from Experimental Recordings 317
6.8.2 Dipoles from Cellular Current Density 320
6.8.3 Solution Visualisation 321
6.9 Open Questions, Issues and Challenges 326

7. The Inverse Problem of Electrocardiology 329

- 7.1 Introduction . . . 329
- 7.2 The Inverse Problem . . . 332
- 7.3 Transfer Matrices . . . 333
- 7.4 Singular Value Decomposition (SVD) . . . 339
- 7.5 Potential-based Inverse Algorithms . . . 340
  - 7.5.1 Tikhonov Regularisation . . . 342
  - 7.5.2 Truncated SVD (TSVD) . . . 343
  - 7.5.3 Greensite Potential-Based Inverse . . . 345
- 7.6 Activation-based Inverse Algorithm . . . 347
- 7.7 Determining the Regularisation Parameters . . . 354
  - 7.7.1 Optimal Criterion . . . 354
  - 7.7.2 L-Curve Criterion . . . 355
  - 7.7.3 CRESO Criterion . . . 356
  - 7.7.4 Zero-Crossing Criterion . . . 357
- 7.8 Validation Approaches . . . 357
  - 7.8.1 Simulation Studies . . . 357
  - 7.8.2 Experimental Validation . . . 364
- 7.9 Modelling Aspects . . . 369
- 7.10 The Outlook . . . 371
- 7.11 Open Questions, Issues and Challenges . . . 372

8. Modelling Other Cardiac Processes 375

- 8.1 Ventricular Mechanics . . . 375
- 8.2 Electro-mechanics . . . 378
- 8.3 Ventricular Blood Flow . . . 378
- 8.4 Coronary Blood Flow . . . 381
- 8.5 Ischaemia . . . 383
- 8.6 Re-entry and Cardiac Arrhythmias . . . 383
- 8.7 Re-entry and Mechanics . . . 388
- 8.8 The Future of Cardiac Modelling . . . 388
- 8.9 Open Questions, Issues and Challenges . . . 390

Appendix A Finite Element Example 393

- A.1 Element Stiffness Matrix . . . 394
- A.2 Global Stiffness Matrix . . . 395
- A.3 Boundary Conditions . . . 396
- A.4 Irregular Geometries . . . 397

Bibliography 399

Index 417