

<b>ACKNOWLEDGEMENTS</b> .....	<b>VI</b>
<b>ABSTRACT</b> .....	<b>VII</b>
<b>RESUM</b> .....	<b>IX</b>
<b>RESUMEN</b> .....	<b>XI</b>
<b>ABBREVIATIONS AND ACRONYMS</b> .....	<b>XIII</b>
<b>LIST OF FIGURES</b> .....	<b>XIX</b>
<b>CHAPTER 1</b> .....	<b>1</b>
1.1. OBJECTIVES.....	4
1.2. STRUCTURE OF THE THESIS.....	5
<b>CHAPTER 2</b> .....	<b>7</b>
2.1. INTRODUCTION TO CARDIAC ELECTROPHYSIOLOGY .....	7
2.1.1. <i>The heart: Cardiac Anatomy and Physiology</i> .....	9
2.1.2. <i>Cardiac Physiology: The Specialized Conduction System</i> .....	14
2.1.3. <i>From Ionic Channel to Cardiac Action Potential</i> .....	18
2.1.4. <i>The Electromechanical Function. Excitation-contraction</i> <i>Coupling.</i>	27
2.1.5. <i>Normal and Abnormal Impulse Propagation</i> .....	31
2.1.6. <i>Basic Mechanisms of Arrhythmia. Reentry.</i> .....	37
2.1.7. <i>Atrial Fibrillation. Epidemiology and Treatment.</i> .....	42
2.1.8. <i>Theories and mechanisms. Heterogeneity.</i> .....	47
2.2. TECHNICAL BACKGROUND .....	50
2.2.1. <i>Registration Techniques</i> .....	52
2.2.2. <i>Principles of HH</i> .....	55
2.2.3. <i>Modelling cellular electrophysiology</i> .....	57
2.2.4. <i>Reentry dynamics: Functional and structural determinants</i> ...	59
2.2.5. <i>Ionic gradients and fibrillation dynamics.</i> .....	62
2.2.6. <i>Cardiac optical mapping advancements.</i> .....	66
<b>CHAPTER 3</b> .....	<b>72</b>
3 ATTRACTION OF ROTORS TO THE PULMONARY VEINS IN ATRIAL FIBRILLATION .....	73
3.1 Abstract.....	73
3.2 Introduction .....	74

3.3	<i>Methods</i> .....	76
3.3.1	Numerical models: anatomical descriptions .....	76
3.3.2	Ionic models .....	78
3.3.3	Simulations and Conditions.....	79
3.3.4	Rotors Initiation and Characterization .....	80
3.3.5	Data Analysis .....	83
3.3	<i>Results</i> .....	83
3.3.1	Ionic gradients and rotor attraction towards the PV .....	83
3.3.2	Heterogeneous excitability and rotor drift in the PV-LAJ.....	87
3.3.3	Pacing predictors of rotor drift in the PV-LAJ.....	92
3.3.4	The $I_{K1}$ and rotor drift direction.....	95
3.3.5	Comparative effects of ionic, passive and geometrical gradients on rotor drift.....	98
3.4	<i>Discussion</i> .....	102
3.4.1	Main findings.....	102
3.4.2	Mechanisms of AF and rotor dynamics .....	102
3.4.3	Substrate heterogeneity and rotor drift.....	103
3.4.4	$I_{K1}$ , $I_{Kr}$ and rotor dynamics during fibrillation .....	104
3.5	<i>Limitations</i> .....	106
3.6	<i>Conclusions</i> .....	107
<b>CHAPTER 4 .....</b>		<b>109</b>
4 SPECTRAL ANALYSIS-BASED RISK SCORE TO EARLY PREDICT MORTALITY AND CEREBRAL PERFORMANCE IN PATIENTS UNDERGOING THERAPEUTIC HYPOTHERMIA FOR VENTRICULAR FIBRILLATION AND COMATOSE STATUS.....		110
4.1.	<i>Abstract</i> .....	110
4.2	<i>Introduction</i> .....	111
4.3	<i>Methods</i> .....	112
4.3.1	Study Design.....	112
4.3.2	Hypothermia protocol in patients .....	113
4.3.3	VF Spectral Analyses .....	114
4.3.4	Outcomes .....	118
4.3.5	Follow-up .....	118
4.3.6	Statistical Analyses .....	119
4.4	<i>Results</i> .....	122
4.4.1	Outcomes .....	124
4.4.2	Prediction model .....	125
4.4.3	Risk score based on the predictive performance model .....	130
4.4.4	Contribution of spectral biomarkers to the predictive performance of the model .....	135
4.5	<i>Discussion</i> .....	136
4.6	<i>Limitations</i> .....	141

4.7	<i>Conclusion</i> .....	143
<b>CHAPTER 5 .....</b>		<b>145</b>
5 LOW-COST PANORAMIC IMAGING AND MAPPING OF COMPLEX CARDIAC ARRHYTHMIAS AND DRUG-ACTION IN TRANSLATIONAL ANIMAL MODELS.....		148
5.1.	<i>Abstract</i> .....	148
5.2	<i>Introduction</i> .....	148
5.3	<i>Materials and Methods</i> .....	152
5.3.1	Computer system .....	152
5.3.2	Software.....	153
5.3.3	Mechanical Framework.....	154
5.3.4	Electronics .....	154
5.3.5	Optical mapping systems: Optical Mapping System 1.....	154
5.3.6	Optical mapping systems: Optical Mapping System 2.....	155
5.3.7	Optical mapping systems: Optical Mapping System 3.....	156
5.3.7	Validation study in the Langendorff-perfused Rabbit Heart .....	156
5.3.7	Optical mapping in the rabbit heart .....	158
5.3.8	Optical mapping in the pig heart.....	158
5.4	<i>Results</i> .....	160
5.4.1	Optical mapping framework: Optical mapping system 1 .....	160
5.4.2	Optical mapping framework: Optical mapping system 2 .....	168
5.4.3	Optical mapping framework: Optical mapping system 3 .....	171
5.4.4	Validation study in the Langendorff-Perfused Rabbit Heart .....	174
5.5	<i>Discussion</i> .....	177
5.6	<i>Conclusion</i> .....	179
5.7	<i>Novel panoramic whole heart mapping for simultaneous non- overlapped parametric electrophysiological imaging: a platform for drug- testing, modelling and biomedical engineering applications</i> .....	180
<b>CHAPTER 6 .....</b>		<b>193</b>
6.1	<i>Conclusions</i> .....	193
6.2	<i>Future studies</i> .....	197
<b>CHAPTER 7 .....</b>		<b>199</b>
7.1.	CONTRIBUTIONS OF THIS THESIS.....	199
7.1.1.	<i>Journal papers</i> .....	199
7.1.4.	<i>Derived and related national conferences</i> .....	203
7.1.5.	<i>Registered intellectual property and patents</i> .....	204
7.1.6.	<i>Editorials and book chapters</i> .....	205
<b>REFERENCES .....</b>		<b>207</b>