

# Contents

<b>Agradecimientos</b>	<b>iii</b>
<b>Acronyms</b>	<b>v</b>
<b>Sumari</b>	<b>xiii</b>
<b>Resumen</b>	<b>xv</b>
<b>Abstract</b>	<b>xvii</b>
<b>1 Introduction</b>	<b>1</b>
1.1 Motivation . . . . .	3
1.2 Objectives . . . . .	4
1.3 Structure of the thesis . . . . .	4
<b>2 State of the art</b>	<b>7</b>
2.1 Atrial Fibrillation . . . . .	7
2.1.1 Atrial electrophysiology and mechanisms of atrial fibrillation . . . . .	9
2.1.2 Classification of atrial fibrillation . . . . .	11
2.2 Measurement of the electric activity of the heart . . . . .	13
2.2.1 Intracardiac electrogram . . . . .	13
2.2.1.1 Electrophysiology evaluation . . . . .	15
2.2.2 The surface electrocardiogram . . . . .	16
2.2.2.1 The cardiac cycle. Formation of the ECG signal	18
2.2.3 Types of electrodes . . . . .	19
2.2.3.1 Electric characteristics . . . . .	19
2.2.3.2 Body-Surface biopotential electrodes . . . . .	19
2.2.3.3 Intratissue electrodes . . . . .	20
2.2.3.4 Catheters . . . . .	21
2.3 Characterization of atrial fibrillation . . . . .	22
2.3.1 Non-invasive characterization . . . . .	22

2.3.1.1	Techniques for atrial activity analysis from the electrocardiogram . . . . .	23
2.3.1.2	Techniques for non-invasive characterization of ventricular activity . . . . .	31
2.3.2	Invasive characterization . . . . .	34
2.3.2.1	Techniques for atrial activity analysis from the study of intra-atrial electrogram . . . . .	34
2.3.2.2	Characterization of the atrial activity from the intra-atrial electrogram . . . . .	35
2.4	Therapeutic options . . . . .	39
2.4.1	Rhythm and rate control strategies . . . . .	40
2.4.2	Ventricular rate control . . . . .	41
2.4.3	Restoration of sinus rhythm . . . . .	41
2.4.3.1	Pharmacologic cardioversion . . . . .	42
2.4.3.2	Nonpharmacological therapy for atrial fibrillation . . . . .	42
2.4.4	Anaesthetics in cardioversion therapies . . . . .	46
2.5	Autonomous nervous system and atrial fibrillation . . . . .	47
2.5.1	Atrio-ventricular conduction . . . . .	48
2.5.2	Ventricular response in atrial fibrillation . . . . .	48
2.5.3	Heart rate variability in atrial fibrillation . . . . .	49
2.5.4	Circadian rhythms . . . . .	50
<b>3</b>	<b>Database</b>	<b>53</b>
3.1	Electrocardiogram recordings . . . . .	53
3.2	Electrogram recordings . . . . .	54
3.3	Patients characteristics . . . . .	55
<b>4</b>	<b>Propofol Effects in Atrial Fibrillation Dominant Frequency</b>	<b>57</b>
4.1	Introduction . . . . .	58
4.2	Materials . . . . .	59
4.3	Methods . . . . .	59
4.3.1	Preprocessing process . . . . .	59
4.3.1.1	Traditional filtering . . . . .	59
4.3.1.2	Principal Component Analysis . . . . .	60
4.3.1.3	Partial Least Squares . . . . .	60
4.3.2	Parameter estimation . . . . .	61
4.3.3	Statistical analysis . . . . .	62
4.4	Results . . . . .	62
4.4.1	Results from the whole atrium . . . . .	62
4.4.2	Results from the different atrial regions . . . . .	64
4.5	Discussions and conclusions . . . . .	66

<b>5 Propofol Effects on Atrial Fibrillation Organization</b>	<b>69</b>
5.1 Introduction . . . . .	69
5.2 Materials . . . . .	70
5.3 Methods . . . . .	70
5.3.1 Signal preprocessing . . . . .	71
5.3.2 Interelectrode assessment . . . . .	71
5.3.2.1 Cross correlation analysis . . . . .	71
5.3.2.2 Coherence Spectrum . . . . .	72
5.3.3 Intraelectrode assessment: Entropy measurements . . . . .	73
5.3.3.1 Sample Entropy. Multiscale Analysis . . . . .	73
5.3.3.2 Shannon Entropy . . . . .	74
5.3.3.3 Statistical Analysis . . . . .	75
5.4 Results . . . . .	75
5.4.1 Inter-electrodes results . . . . .	75
5.4.1.1 Cross-correlation results . . . . .	75
5.4.1.2 Coherence spectrum results . . . . .	75
5.4.2 Entropy Results . . . . .	75
5.4.2.1 Multiscale Entropy . . . . .	75
5.4.2.2 Shannon Entropy . . . . .	78
5.5 Discussion and Conclusions . . . . .	80
<b>6 Time Delays between Atrial Activations in Adjacent Dipoles</b>	<b>81</b>
6.1 Introduction . . . . .	82
6.2 Materials . . . . .	83
6.3 Methods . . . . .	83
6.3.1 Detection of Activation Times . . . . .	83
6.3.2 Synchronization Index . . . . .	84
6.3.3 Delay Index . . . . .	85
6.3.4 Statistical analysis . . . . .	86
6.4 Results . . . . .	86
6.4.1 Synchronization index results . . . . .	86
6.4.2 Delay index results . . . . .	87
6.4.3 Results in AF paroxysmal and persistent patients . . . . .	88
6.5 Discussion and conclusions . . . . .	89
<b>7 Atrio-Ventricular Conduction under Anaesthetic Infusion</b>	<b>93</b>
7.1 Introduction . . . . .	94
7.2 Materials . . . . .	94
7.3 Methods . . . . .	95
7.3.1 RR interval analysis . . . . .	95
7.3.2 Histogram analysis . . . . .	95
7.3.3 Atrial and ventricular rates . . . . .	96
7.3.4 Statistics . . . . .	97
7.4 Results . . . . .	97

7.4.1	Results from RR intervals . . . . .	97
7.4.2	Results from the histogram analysis . . . . .	97
7.4.3	Results from atrial and ventricular activity . . . . .	98
7.4.3.1	Relation between mean atrial and ventricular activity . . . . .	98
7.4.3.2	Atrial activity impulses within RR impulses . . . . .	100
7.4.4	Results in paroxysmal and persistent atrial fibrillation . . . . .	100
7.4.4.1	Results from RR intervals . . . . .	100
7.4.4.2	Results from the histogram analysis . . . . .	100
7.4.4.3	Results from atrial and ventricular activity . . . . .	101
7.5	Discussion and conclusions . . . . .	102
<b>8</b>	<b>Conclusion</b>	<b>107</b>
8.1	Discussion . . . . .	107
8.1.1	Atrial rate during the propofol effect . . . . .	108
8.1.2	Propofol effect on the atrial organization . . . . .	108
8.1.3	Ventricular rate during the propofol effects . . . . .	110
8.1.4	Limitations . . . . .	111
8.2	Conclusion . . . . .	112
8.3	Guides for future work . . . . .	113
8.3.1	Analysis of the atrial and ventricular signals during AF .	113
8.3.2	Comparison of different drugs effect in AF . . . . .	114
8.3.3	Clinical applications . . . . .	115
8.3.4	Transfer of technology . . . . .	116
<b>9</b>	<b>Contributions</b>	<b>117</b>
9.1	Publications . . . . .	117
9.2	Framework of the dissertation . . . . .	118
9.2.1	Research projects . . . . .	118
9.2.2	International research stages . . . . .	119
9.2.3	Collaborations . . . . .	119
<b>A</b>	<b>Principal component analysis</b>	<b>121</b>
<b>B</b>	<b>Partial Least Squares</b>	<b>125</b>