Contents

Abstract . . . . . **iii**

Zusammenfassung . . . . . **v**

Resumen . . . . . **vii**

Resum . . . . . **ix**

Acknowledgments . . . . . **xi**

Abbreviations . . . . . **xvii**

1 Introduction **1**
1.1 Motivation 1
1.2 Objectives of the Thesis 2
1.3 Structure of the Thesis 3

I Fundamentals **5**

2 Medical Fundamentals **7**
2.1 Atrial Anatomy and Physiology 7
2.2 Atrial fibrillation 7
2.3 Anatomy of the human heart 7
2.4 Histology of the heart 10
2.5 Eletrophysiology of the heart 11

3 Computational modeling of cardiac electrophysiology **15**
3.1 Cardiac cell modeling 15
3.2 Tissue and organ modeling 16

4 Electro-anatomical mapping **19**
4.1 Intracardiac signals 19
4.2 Mapping catheters 19
4.3 Clinical maps 21

II Cellular level 23

5 Human atrial myocyte electrophysiology 25
5.1 Methods 25
5.2 Results 27
5.3 Discussion 30

6 Human atrial myofibroblast electrophysiology 31
6.1 Methods 31
6.2 Results 32
6.3 Discussion 33

7 Myofibroblast Ca^{2+} current and intracellular Ca^{2+} handling 37
7.1 Methods 37
7.2 Results 38
7.3 Discussion 40

III Tissue level 43

8 Myofibroblast infiltration 45
8.1 Methods 45
8.2 Results 47
8.3 Discussion 49

9 Fibrosis composition 51
9.1 Methods 52
9.2 Results 53
9.3 Discussion 55

10 Computational modeling of intracardiac signals 57
10.1 Methods 57
10.2 Results 59
10.3 Discussion 61

11 Fibrosis characterization using machine learning 63
11.1 Methods 63
11.2 Results 67
11.3 Discussion 71

12 Determination of wavefront direction using transfer entropy 73
12.1 Methods 73
12.2 Results 75
12.3 Discussion 77

IV Clinical applications 79

13 Clinical fibrosis maps 81
13.1 Methods 81
13.2 Results 82
13.3 Discussion 83

14 Direct Graph - Transfer Entropy flow maps 85
14.1 Methods 85
14.2 Results 86
14.3 Discussion 87

15 Conclusion 89

16 Outlook 91

References 93

List of Publications and Supervised Theses 103