

Contents

Abstract	i
Zusammenfassung	iii
Acknowledgements	v
List of Symbols	xiii
List of Abbreviations	xvii
List of Figures	xxiii
List of Tables	xxxii
1 Introduction	1
1.1 Objective and outline of this thesis	3
2 State of the Art	7
2.1 Infections on Implant Surfaces	7
2.2 Current Implant Infection Detection	11
2.3 Inflammatory Markers	13
2.4 Heat Flux as an Infectious Marker	16
2.5 Measurement of Metabolic Changes and Heat Flow of Biological Samples	18
2.6 Fluid Dynamic Aspect	21
2.7 Approach of this Thesis	23
3 Theory	25
3.1 Fluid Dynamics	26
3.1.1 Navier-Stokes Equations	26
3.1.1.1 Fluid Flow in Cylinders	26
3.1.2 Reynolds Number Re	28
3.1.3 Prandtl Number	28
3.1.4 Womersley Number	29
3.1.5 Hydrodynamic Entry Length	29
3.2 Heat Transfer	30
3.2.1 In Solids	30
3.2.2 In Fluids	30
3.2.3 Bioheat Transfer	31

3.2.4	Conduction	32
3.2.5	Convection	32
3.2.6	Thermal Entry Length	33
3.3	Theory for Aortic System and Microfluidic Chip	34
3.3.1	Flow in Aortic Channel	34
3.3.2	Convective Flow Regimes in Cylinders	35
3.3.2.1	Convective Flow in Cylinder $z > L_h, L_{th}$: Fully Developed Flow	35
3.3.2.2	Convective Flow in Cylinder $z > L_h$ and $z <$ L_{th} : Partly Developed Flow	36
3.3.2.3	Convective Flow in Cylinder $z < L_h$ and $z <$ L_{th} : Undeveloped Flow	36
3.3.2.4	Flow in Cylinder Turbulent Transitional regime $2300 < Re < 8000$	36
3.3.3	Flow in Microfluidic Chip	37
3.4	Thermal Lumped Element Model	39
3.4.1	Lumped Element Model of Microfluidic Chips	40
3.4.1.1	One Level Microfluidic Chip	40
3.4.1.2	Double Channel Microfluidic Chip	42
3.5	Finite Element Model Simulation Setup	44
3.5.1	COMSOL Fluid Dynamics	44
3.5.2	COMSOL Thermodynamics	46
4	Fabrication and Methods	49
4.1	Microfluidic Chip Fabrication	49
4.1.1	One Level Microfluidic Chip Fabrication	50
4.1.1.1	Lithography Steps	50
4.1.1.2	Soft Lithography Steps	54
4.1.2	Double Channel Microfluidic Chip Fabrication	56
4.2	Experimental Setup	58
4.2.1	Exothermic Chemical Reaction Calibration Setup	58
4.2.2	Microfluidic Bacterial Experimental Setup	60
4.2.2.1	Thermally Stable Environment	61
4.2.2.2	Thermally not Stabilized Environment	63
4.3	Microcalorimetric Experiments	64
4.3.1	Methyl Paraben Experiment	64
4.3.2	Immune Cell Experiment	65
4.4	Biological Protocols	66
4.4.1	Bacterial Protocols: <i>Escherichia Coli</i> and <i>Enterococcus Faecalis</i>	66
4.4.1.1	Bacterial Vaccine Protocol	67
4.5	Immune Cell: THP-1	69
4.5.1	THP-1 Monocyte Stimulation	70
4.5.2	Macrophage Removal	72
4.5.3	Preparation for FACS	73

4.5.4	Microfluidic Chip Preparation	75
5	Experimental Determination of Heat Originating from Cells	77
5.1	Microfluidic Chip Heat Transfer Efficiency Determination . .	79
5.1.1	Microcalorimetric Reference Measurement	79
5.1.2	One Channel Level Microfluidic Chip	81
5.1.2.1	One Channel Level Microfluidic Chip Chemical Calibration	82
5.1.2.2	Comparison Between Microcalorimetric Experiments and Microfluidic Exothermic Chip Experiments	86
5.1.2.3	One Channel Level Microfluidic Chip Bacterial Experiment	88
5.1.2.4	Extraction of Bacterial Thermal Values . . .	93
5.2	Double Channel Microfluidic Chip	100
5.3	Thermally Fluctuating Environment	105
5.4	Immune Cell Experiments	112
5.4.1	FACS Experiments	112
5.4.2	Immune Cell Microcalorimetric Experiments	119
5.4.2.1	Scraped Immune Cell Microcalorimetric Experiment	119
5.4.2.2	Accutase Immune Cell Microcalorimetric Experiment	121
5.4.3	Immune Cells as a Heat Source	123
6	FEM Simulations	125
6.1	Fluid and Thermodynamic Investigations of Aortic Vascular Graft	127
6.1.1	Fluid Dynamic Simulation Results	128
6.1.1.1	Constant Velocity $u = 0, v_z = v_{avg}$	129
6.1.1.2	Pulsatile Velocity $v_z = v_{avg} + u$	132
6.2	Thermodynamic Aspect of Aortic Blood Flow	135
6.2.1	Parametric Sweep of Heat Transfer Efficiency	136
6.2.2	Parametric Sweep Determining the Heat Flux Sensor Measurement Threshold	138
6.3	Implementation of Sensor Mesh in the Implant	141
7	Conclusions and Outlook	143
A	Appendix - Fluid Dynamics Theory	149
A.1	Fluid Dynamic Parameters of Water and Blood	149
A.2	Viscous Dissipation	152
A.3	Different Cylinder Flow Regions with Varying Radii	154
A.4	Determination of the Heat Transfer Coefficient in Laminar Flow	155
A.4.1	Average Velocity v_m	155

Contents

A.4.2	Average Temperature T_m	156
A.4.3	Determining the Heat Transfer Coefficient	157
A.5	COMSOL Partial Differential Equation	159
B	Appendix - Lumped Element Model Parameters	161
B.1	One Level Microfluidic Chip	161
B.2	Double Channel Microfluidic Chip	163
C	Appendix - Datasheet	165
C.1	greenTEG gSKIN Heat Flux	165
D	Appendix - Experimental System	167
D.1	Pictures of thermally stabilized and thermally not stabilized systems	167
E	Appendix - Microfluidic Chip Experiment	169
E.1	Comparison Between Inlet and Outlet Bacterial Growth	169
E.2	Determination of the OD to bacteria/mL Conversion	171
E.3	Error Propagation	172
E.4	Parameter Overview over Microfluidic Chip	174
E.5	Sensitivity, Resolution and the Limit of Detection	175
F	Appendix - COMSOL Simulations	177
F.1	Fluid Dynamic Simulations of the Aorta	177
F.1.1	Constant Velocity Fitting Parameters a and c	177
F.1.2	Full Flow Profiles	178
F.1.3	Extracted Percentage Differences Between Pulsatile and Stationary Flow	180
F.1.4	Radius Variation	182
F.2	Thermodynamic Simulations of the Aorta	183
F.2.1	Thermodynamic Material Properties for the Vascular Graft	183
F.2.2	Extracted Heat Transfer Efficiency for the Vascular Graft	184
F.2.3	Bacterial Populations and their Thermal Power Density	185
F.2.4	Increase in Infectious Thermal Power Densities	186
F.2.5	Calculation of Distance Between Sensor and Infection	187
F.2.6	Temperature Increase at the Implant	188
F.2.7	Calculation of Mesh of Sensors	189
	Bibliography	191
	Publications	209
	Curriculum Vitae	211