

# Contents

|          |                                                                        |           |
|----------|------------------------------------------------------------------------|-----------|
| <b>1</b> | <b>Introduction</b>                                                    | <b>1</b>  |
| 1.1      | The Retina as a Model System . . . . .                                 | 1         |
| 1.2      | Functional Imaging of the Retina . . . . .                             | 2         |
| 1.3      | Phase Sensitive Imaging . . . . .                                      | 5         |
| 1.4      | Structure of this Thesis . . . . .                                     | 5         |
| <b>2</b> | <b>Theory</b>                                                          | <b>7</b>  |
| 2.1      | Fourier-Transformation in Signal Processing . . . . .                  | 7         |
| 2.2      | Fourier-Transformation in Optics . . . . .                             | 10        |
| 2.3      | Phase Detection, the Analytic Signal and the Hilbert-Transform . . . . | 11        |
| 2.4      | Optical Coherence Tomography . . . . .                                 | 13        |
| 2.4.1    | The OCT-Signal . . . . .                                               | 15        |
| 2.4.2    | Speckle Formation as a Hindrance for Phase Evaluation . . . .          | 17        |
| 2.4.3    | Full-Field Swept-Source OCT . . . . .                                  | 19        |
| 2.4.4    | Cause and Effects of Phase Errors . . . . .                            | 20        |
| 2.5      | The Nervous System . . . . .                                           | 25        |
| 2.5.1    | Membrane Potentials . . . . .                                          | 25        |
| 2.5.2    | Structure of Neurons . . . . .                                         | 28        |
| 2.6      | Anatomy of the Eye . . . . .                                           | 29        |
| 2.6.1    | The Retina . . . . .                                                   | 30        |
| 2.6.1.1  | Photometric Units . . . . .                                            | 32        |
| 2.6.1.2  | Photoreceptor Cells and Phototransduction . . . . .                    | 33        |
| 2.6.1.3  | Horizontal Cells . . . . .                                             | 37        |
| 2.6.1.4  | Bipolar Cells . . . . .                                                | 37        |
| 2.6.1.5  | Amacrine Cells . . . . .                                               | 39        |
| 2.6.1.6  | Ganglion Cells . . . . .                                               | 39        |
| <b>3</b> | <b>Full-Field Swept-Source OCT</b>                                     | <b>43</b> |
| 3.1      | Setup . . . . .                                                        | 43        |
| 3.1.1    | Mach-Zehnder-Based Setup . . . . .                                     | 43        |
| 3.1.2    | Michelson-Based Setup . . . . .                                        | 44        |
| 3.2      | Imaging Human Retina . . . . .                                         | 47        |
| 3.3      | Post-Processing . . . . .                                              | 47        |
| 3.3.1    | Reconstruction . . . . .                                               | 48        |

|          |                                                                                           |            |
|----------|-------------------------------------------------------------------------------------------|------------|
| 3.3.2    | Correction of Dispersion and Axial Motion . . . . .                                       | 49         |
| 3.3.3    | Correction of Aberrations . . . . .                                                       | 50         |
| 3.3.4    | Registration . . . . .                                                                    | 55         |
| 3.3.4.1  | Determination of the Movements . . . . .                                                  | 57         |
| 3.3.4.2  | Algorithmic Implementation . . . . .                                                      | 60         |
| 3.3.5    | Segmentation . . . . .                                                                    | 64         |
| 3.3.5.1  | Diffusion Maps . . . . .                                                                  | 67         |
| 3.3.5.2  | Clustering . . . . .                                                                      | 70         |
| 3.3.5.3  | Algorithmic Implementation . . . . .                                                      | 72         |
| 3.3.6    | Phase Evaluation . . . . .                                                                | 79         |
| 3.3.6.1  | Algorithmic Implementation . . . . .                                                      | 82         |
| <b>4</b> | <b>Results</b>                                                                            | <b>87</b>  |
| 4.1      | Intrinsic Optical Signal in the Photoreceptor Cells . . . . .                             | 88         |
| 4.1.1    | Signal Analysis . . . . .                                                                 | 89         |
| 4.1.1.1  | General Observation . . . . .                                                             | 89         |
| 4.1.1.2  | Reproducibility . . . . .                                                                 | 89         |
| 4.1.1.3  | Functional Imaging of Single Cones . . . . .                                              | 91         |
| 4.1.1.4  | Dependence on the Stimulation Strength . . . . .                                          | 93         |
| 4.1.1.5  | Depth-Dependence of Functional Changes in the Photoreceptor OS . . . . .                  | 97         |
| 4.1.1.6  | Reversibility . . . . .                                                                   | 98         |
| 4.2      | Intrinsic Optical Signals in the Inner Plexiform Layer . . . . .                          | 104        |
| 4.2.1    | Optimal Reference Layer . . . . .                                                         | 104        |
| 4.2.2    | Investigation of the Signal Dependency of Different IPL Levels . . . . .                  | 108        |
| 4.2.3    | Investigation of the Center-Surround Signal Transduction of the Receptive Field . . . . . | 110        |
| 4.2.4    | Frequency Dependence . . . . .                                                            | 113        |
| 4.2.5    | Functional Connection of the Photoreceptor Layer and the IPL . . . . .                    | 114        |
| <b>5</b> | <b>Discussion</b>                                                                         | <b>117</b> |
| 5.1      | Comparison of Contrast Mechanisms for Functional Retina Imaging . . . . .                 | 117        |
| 5.1.1    | Comparison of Different Phase-Sensitive OCT Techniques . . . . .                          | 118        |
| 5.1.2    | Comparison of the Functional Measurements . . . . .                                       | 122        |
| 5.2      | Origin of the Observed Phase Change . . . . .                                             | 125        |
| 5.2.1    | Photo Damage or Thermal Expansion . . . . .                                               | 125        |
| 5.2.2    | Neuro-Vascular Coupling and Increased Metabolic Demands . . . . .                         | 126        |
| 5.2.3    | Concentration Changes . . . . .                                                           | 127        |
| 5.2.4    | Causes for Osmotical Change . . . . .                                                     | 128        |
| 5.2.5    | Potential Changes . . . . .                                                               | 131        |
| 5.3      | Correlation of the Phase Changes . . . . .                                                | 131        |

|                                                                               |            |
|-------------------------------------------------------------------------------|------------|
| <b>6 Conclusion</b>                                                           | <b>133</b> |
| <b>7 Outlook and Future Work</b>                                              | <b>135</b> |
| 7.1 Further Developments of FF-SS-OCT . . . . .                               | 135        |
| 7.2 Exploration of Alternative Techniques for the Clinical Transfer . . . . . | 136        |
| 7.3 Functional Imaging of the Entire Retina . . . . .                         | 137        |
| 7.4 Investigating of the Molecular Origin . . . . .                           | 138        |
| 7.5 Clinical Studies . . . . .                                                | 139        |
| <b>Bibliography</b>                                                           | <b>139</b> |
| <b>Ciriculum Vitae</b>                                                        | <b>163</b> |
| <b>Danksagung</b>                                                             | <b>165</b> |