Part III

Summary and Outlook

In the last part of this work we provide a **summary** of our main results. The major contributions of this work to the field of OT in general, and the importance of our findings for imaging of joints in particular, are discussed. We conclude this work, in Chapter 11, with an outlook towards possible extension of the presented studies. We describe a **time-dependent** forward model based on the ERT and a **stochastic optimization** method to reconstruct the optical parameters within the context of the MOBIIR scheme.

Chapter 10

Summary

In this work we presented and experimentally validated the first image reconstruction scheme in OT that is based on the ERT. This scheme overcomes limitations typically encountered by image reconstruction methods based on the diffusion equation. Diffusion-theory-based techniques have shown to be inadequate for imaging tissue that contains low-scattering regions [Dehghani99] [Riley00]. Important examples for such media are the brain, which contains and is surrounded by almost non-scattering CSF, and joints that are lubricated by the clear synovial fluid. As an example, we presented the first two-dimensional reconstruction of optical properties of a human PIP joint.

We approached the imaging problem in OT within a MOBIIR scheme. A MOBIIR scheme consists of two major parts. First, a forward model describes the light propagation in tissue for a given set of optical parameters inside the tissue and source positions on the tissue surface. Second, an inverse model reconstructs the spatial distribution of the optical parameters within the medium given the detector readings on the tissue boundary.

As forward model we employed a finite-difference discrete-ordinates method based on the ERT (see Chapter 2). The angular variable was replaced by discrete ordinates and the spatial derivatives were approximated by finite differences. We found that the number of ordinates had to be at least K = 8 for tissue-like media. Further refinement of the angular discretization did not lead to a significant change in the numerical result (see Figures 3.2 and 3.3). However, the radiance ψ strongly depended on the spatial discretization. Therefore, the step size (Δx, Δy) between adjacent grid points had to be at least $1/(5\mu_s')$ for an isotropically scattering medium (see Figure 3.4) and $1/\mu_s'$ for an anisotropically scattering medium (see Figure 3.5).

We estimated the accuracy of the numerical results obtained by our forward model. Calculated fluence profiles along the boundaries of tissue phantoms were compared with experimentally obtained data. The experimental data revealed good agreement with the calculated fluence ϕ (see Figure 4.4). We showed that different combinations of the parameters μ_s and g, which yield the same reduced scattering coefficient $\mu_s' = (1-g)\mu_s$, produced different fluence profiles on the boundaries. However, fluence profiles, which are solutions to the diffusion equation, are only functions of μ_s' and do not consider different values of μ_s and g. This example underscores further the need for a forward model based on the ERT. In addition, the forward model based on the ERT was also evaluated by using experimental data from a scattering phantom that contained a void-like ring. Good agreement between the experimental and numerical data was found (see Figure 4.8). Previous studies by Hielscher *et al* [Hielscher98] showed that diffusion-theory-based forward models do not correctly predict the fluence of scattering media containing void-like regions.

A major requirement for a clinical application, besides the correct modeling of light propagation in tissue, is a small processing time of the forward model to calculate the detector readings. A large number of repeated forward runs within the MOBIIR scheme is necessary for iteratively updating the optical parameters. Our forward model needed approximately 20-60 seconds of calculation time for tissue-like media on a 61×61 or 81×81

grid (see Section 2.4), because a computationally efficient successive overrelaxation method was used. Hence, the calculation time was sufficiently small and promised to generate cross-sectional images of the optical parameters within 30 - 300 minutes[1].

So far we discussed the major results of the forward model. Now, we summarize the results of the inverse problem, which introduced some unique features in OT, such as QN methods and the adjoint differentiation technique. In this work we viewed the inverse problem as an optimization problem. An objective function was defined as difference between predicted and measured detector readings. We implemented numerical optimization techniques to minimize the objective function, as described in Chapter 5. These optimization techniques employed the gradient of the objective function with respect to the optical parameters. The objective function depended approximately on 10^3 -10^5 variables, which leads to a severe computational burden in calculating the gradient by using divided differences (see page 83). Therefore, a computationally efficient gradient calculation was necessary. We employed the adjoint differentiation technique to our forward model to calculate the derivative of the objective function (see Chapter 6).

The adjoint differentiation technique is a particular numerical implementation of an adjoint model (see Equation 6.15). We described the differences and similarities of various numerical implementations of the adjoint model in OT, and showed how they are interconnected (see Figure 6.1). The adjoint differentiation technique was directly applied to the numerical code of the forward model. This technique had the advantage compared to other implementations of the adjoint model, that it did not need to solve the adjoint ERT. Instead, the adjoint differentiation approach computed the gradient of the objective function approximately in the same time as the forward model calculated the detector predictions. The small amount of computational operations was essential for subsequent use within the

[1]All estimates of processing time are based on the use of a single PENTIUM III XEON®processor.

optimization techniques to obtain cross-sectional images of the optical parameters in an acceptable amount of time.

The gradient of the objective function was employed within gradient-based optimization techniques. We utilized QN methods, such as the BFGS and lm-BFGS methods, to minimize the objective function. The BFGS method employed an approximation to the inverse Hessian matrix for calculating the search direction. The lm-BFGS method, which was derived from the BFGS method by replacing the approximated inverse Hessian with the identity matrix, overcame the need for storing the huge inverse Hessian matrix from the previous iteration step. Employing inexact line searches along the search direction we found the minimum of the objective function in less basic operations than the commonly applied CG method in OT. A basic operation accounts for either a forward calculation, e.g. determination of a value $\tilde{\varphi}$ of the objective function or a derivative calculation $\nabla_\mu \Phi$.

When optimization techniques were applied to practical situations in OT, we had to deal with noise-corrupted measurement data that altered the shape of the objective function. Furthermore, an initial guess of the optical parameters might be far from the solution and diminished the minimization process. Therefore, we studied the impact of noise and different initial guesses to the image reconstructions by using the BFGS, lm-BFGS, and CG methods (see Section 7.1). In general, the reconstruction results showed that the QN methods were superior to the CG technique in terms of calculation time. When no noise was present in the measurement data the BFGS and lm-BFGS needed fewer basic operations and found a smaller value $\tilde{\varphi}$ of the objective function than the CG method. The image accuracy, determined by the correlation coefficient and the deviation factor, was always higher in QN methods than that obtained by the CG method (see Table 7.1). At the presence of noise these advantages were partly diminished. For SNR smaller than 45 dB, the final value $\tilde{\varphi}$ of the objective function and the image accuracy were not significantly different for all three methods. Furthermore, when starting the reconstruction process from initial guess that was different than the optical parameters of the bulk medium, we found that the BFGS and lm-BFGS methods were approximately two times faster and yielded a smaller value $\tilde{\varphi}$ than the CG method. When we added noise to the measurement data and started from an initial guess of optical parameters different than the bulk medium, as encountered in a typical experimental situation, the QN methods still outperformed the CG method in computational speed (see Subsection 7.1.5). The QN methods were approximately 10 times faster than the CG method. However, the image accuracy of all three methods was not significantly different.

The QN methods sometimes failed at calculating a descent search direction, if the initial guess of the optical parameters was too far from the solution (see Subsection 5.2.5 and Figure 7.10). In those cases the approximated inverse Hessian was not positive definite. We enforced positive-definiteness by replacing the approximated inverse Hessian with the identity matrix.

The impact of different numbers D of source-detector pairs was studied in Section 7.2. We found that the image accuracy was increased when increasing the number D of sources and detectors until a certain limit (D $>$ 400 in Table 7.2) beyond which no enhancement was achieved. Therefore, the highest amount of sources and detectors available did not always achieve the highest image accuracy. Considering that the computational time for basic operations is directly proportional to the number of sources but independent of the number of detectors, we suggest using more detectors than sources for the image reconstruction.

So far we had performed numerical studies on the MOBIIR scheme based on the ERT. One of the specific aims of this work was to apply the MOBIIR scheme to biomedical problems that are connected to tissues with low-scattering regions. Therefore, we carried out experiments on tissue phantoms that contained void-like areas (see Section 8.2). One phantom contained a thin ring filled with clear water. This situation roughly mimics the CSF layer in the brain or the synovial fluid in a finger joint. Based on measurement data we performed reconstructions of the scattering coefficient and the absorption coefficient. The void-like ring could be clearly reconstructed. Previously, it was not possible to reconstruct low-scattering areas in tissue-like media, and thus these results account for the first reconstructions of void regions in OT.

As a first biomedical application of the transport-theory-based MOBIIR scheme we focused on the imaging of human finger joints for early diagnosis and monitoring of RA. RA is a severe inflammation of joints that has no cure. An early diagnosis has the potential to slow down the progression of the disease. Until now, no routine imaging technique existed for early diagnosis and monitoring of RA. OT is a potential candidate for imaging PIP joints, as RA changes the optical properties of joints. This has already been supported by earlier studies [Prapavat97].

In Section 9.2, we performed a numerical study on a finger joint model that constituted the optical parameters of the healthy or rheumatoid conditions of a PIP joint. We altered the optical parameters of the synovial fluid and the synovium according to *ex vivo* measurements of the optical parameters carried out previously by Prapavat *et al* [Prapavat97]. Reconstructed sagittal images of the optical parameters show that changes in the synovium and the synovial fluid can be detected. We took the ratio of the reconstructed images of the healthy and the rheumatoid conditions as a means of differentiating the inflamed from a healthy stage.

The final goal of this thesis was to provide a MOBIIR scheme that reconstructs the optical parameters of a human finger joint by using experimental data. A joint contains the almost non-scattering synovial fluid and requires a transport-theory-based forward model for light propagation. Until now, it was not possible to reconstruct the optical parameters of a joint, because existing forward models within a MOBIIR scheme failed to predict correctly the light propagation in void-like areas. Therefore, we carried out image reconstructions on a human finger joint. We provided for the first time sagittal images of the scattering and absorption coefficients that show the synovial fluid.