Studies in Optical Tomography

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Introduction: Optical tomography (OT), as a potential diagnostic tool for detecting growths in translucent soft tissue, has been proposed and studied by several groups in recent years. Its principle is to use multiple light sources and detectors attached to the tissue surface to collect information on light attenuation, and to reconstruct the internal 3-D absorption and scattering distributions. Unusual growths inside the tissue may be discerned from the recovered optical densities because tumorous tissue has different scattering and absorption properties.

The current state of the art shows some promise for clinical applications [11]. Its non-invasiveness, low cost, non-ionizing nature, safety, and constant improvements in both algorithm [3][6][7][10][15] and instrumentation [13][19] make it well worth continued and focused efforts aimed at advancing to a higher level of technical maturity and human-machine friendliness.

Problem: Our goal is to develop algorithm to image the otherwise inaccessible scattering and absorption distribution inside the illuminated tissue. To provide the neccessary data, we also need to design suitable information collection strategies, and explore the underlying mathematics of our model for the scattering and absorption process. We also hope to delimit the circumstances in which this inverse problems is reasonably well-posed.

Previous Work: Experiments have shown that visible and near infrared light, though highly attentuated, can travel through soft biological tissues, e.g. human brain and breast. Upon the recognition that scattering is dominant in the tissue-type media, the following time-independent diffusion approximation for the *photon density* Ψ was derived from the general radiative transport equation [1][2][12][16]:

$$-\nabla \cdot (\mu_d \nabla \Psi) + \mu_a c \Psi = q_0 \tag{1}$$

where μ_d and μ_a denote the *diffusion* and *absorption* coefficients, while q_0 is the *source* distribution. μ_d relates to the *absorption coefficient* μ_a, *scattering coefficient* μ_s and the *anisotropy factor* $\bar{f}$ by

$$\mu_d = \frac{c}{3[\mu_a + (1-\bar{f})\mu_s]} \tag{2}$$

The anistropy factor arises because light is not scattered uniformly in all direction, but predominantly in the forward direction. From this time-independent diffusion equation one can develop a reconstruction approach for the unknown optical parameters based on steady state source to detector attenuations. The basic idea is to collect detector responses for a large number of detector positions for each of a large number of source positions.

Consideration of time variation adds an extra dimension to the problem and allows various image recovery methods to be derived based on the choice of measurements, i.e. time-varying photon density, time-integrated photon density and frequency domain modulation and detection. We will focus here, however, on the steady-state approach—in part because of its very much simpler instrumentation requirements.

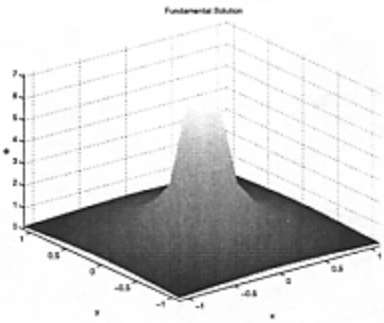
Much pioneering work has been done by Simon Arridge and his group [1]-[9] in this area. [4][8][9] provide theoretical framework for the inverse problem and the sensitivity issue is addressed. [3] develops a finite element approach to numerically solve the inverse problem. [20] presents a layered model for the adult head and their FEM simulation results. [5] summarizes existing inverse solvers and related regularization schemes. The most extensive survey on the development of optical tomography can be found in [11]. However, due to the mathematical difficulty in handling the severe ill-posed nature of the inverse problem, reconstruction algorithm remains inaccurate and computationally very expensive. So far no regularization scheme has been adapted to the 2-D or 3-D anatomical image data structure. The problem of experimental design waits for close investigation.

The model problem $\Delta \cdot \gamma \Delta u = 0$ has been intensively studied in the Electrical Impedence Tomography (EIT). John Sylvester gives rigorours accounts on the uniqueness of the inverse boundary problem [23][24]. Inverse reconstruction algorithms have been developed and applied in real practice. It is suggested that the studies of optical tomography will benefit from the preceeding development in EIT.

Difficulties/challenges: When compared with Computed Tomography, Magnetic Resonance Imaging, PET and ultrasound imaging, OT reconstruction encounters certain difficulties because photon density drops fast as light travels away from the source. This is characterized by the governing equation. In a homogeneous infinite medium, the fundamental solution to (1) is given by

$$\Psi(\rho) = \frac{A}{\rho} e^{-\frac{\mu_a}{\mu_d}\rho} \tag{3}$$

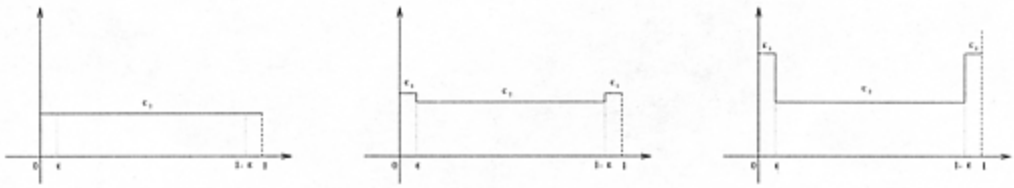
as a function of the distance ρ to a point source. Therefore in the near neighborhood of a point source, the photon density function drops at a rate proportional to ρ^{-1}. But away from the source the potential decays exponentially.



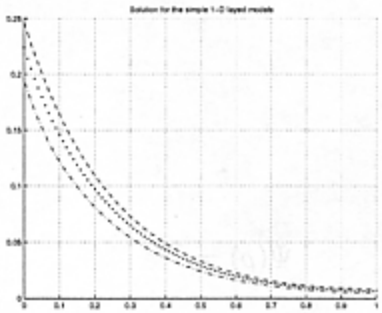
It becomes very difficult to recover any useful information about regions deep inside the object when $(\mu_a/\mu_d)^{-1}$ is much smaller than the thickness of the tissue. $(\mu_a/\mu_d)^{-1}$ called the *scale length*, is an important measure in considering the applicability of this particular imaging method.

This rapid attentuation of the light can make reconstruction problems ill-posed, and make it hard to obtain good signal-to-noise ratios in measurements.

As an example, consider three different simple, layered models in 1-D (modeling say homogeneous, breast, and head tissues), where $(\mu_a/\mu_d)^{-1}$ is in each case a piecewise constant function:



The following graph shows the dropoffs of the photon density away from the source when photon injection taking place at the left terminal and zero Neumann boundary condition being imposed at the right end:



Note that the differences in the optical parameter distribution have only a small effect on the photon density measurements conducted at the right end of the object. This implies that the reconstruction will tend to be sensitive to errors in measure-

ments. Consequently, regularization is of great significance in this inverse problem.

The physics of scattering and absorption bear a fair amount of similarity at the microscopic scale. Intuitively, a slab of material may be highly absorptive overall either because it just has a high coefficient of absorption, or because high scattering prevents the photons from leaving the volume as rapidly, thus increasing their chance of being absorbed. As we saw already, the distribution of photon flux is sensitive to the ratio $(\mu_a/\mu_d)^{-1}$, but not as sensitive to changes in the scattering and absorption that leave this ratio constant.

Separating the contributions to the light attenuation due to spatial variations in scattering and absorption properties is intrinsically difficult. This topic is given particular considerations in [21][22] and it has been suggested that investigation of the time resolved photon migration may lead to a resolution. However, this technique requires extremely sensible source and detector, causing excessive cost to the entire system. Whereas it is the recovery of the interior absorption density—based on the assumption that scattering is essentially uniform—lies at the core of the most recent competent results. The sensitivity of photon density on the *scale length* $(\mu_a/\mu_d)^{-1}$ suggests that we may focus on recovering the ratio rather than the two coefficients separately.

Reconstruction of the spatial distributions in scattering and absorption beneath the skin is made possible by the great freedom associated with the boundary conditions. Heuristically, the mapping from infinitely many feasible boundary functions, i.e.,

$$\mu_d \frac{\partial \Psi}{\partial \mathbf{n}} \mid_{\partial\Omega} = g$$

to the varying photon density functions Ψ measured on the boundary (Neumann-Dirichlet mapping), will assemble enough information for us to make dependable inferences, as long as the *scale length* $(\mu_a/\mu_d)^{-1}$ is not considerably oversize the thickness of the tissue. Yet what finite set of experiments and measurements lead us to a high resolution is unclear. In other word, we must study the choice of boundary conditions and how to conduct proper measurements. This will be embodied in the reconstruction algorithm. Optimal (or suboptimal) experimental design problem shall be treated as one of the main challenges and key ingredients in the study of OT. We are at present attacking this problem by qualitative perturbation analysis and entropy-based decision theory. Low frequency incoming pattern seems to improve the penetration depth. While high frequency input helps to sharpen the image in its trustworthy region.

Approach: In the first attempt to solve this inverse problem, we adopt the steady-state attenuation approach.

The physics of photon migration finds analogy in a resistive circuit model. The

underlying equation for the electrical potential in the steady state is the same as (1):

$$-\nabla \cdot (\sigma \nabla \Phi) + g\Phi = \frac{q}{\epsilon} \tag{4}$$

Here Φ is the scalar potential, σ and g are the *medium conductance* and the *leakage resistance* to ground. The right hand side represents the current source term. The correspondences between the optical parameters and the conductances of the circuit media are given by:

$$g = \mu_a c, \qquad \sigma = \mu_d = \frac{c}{3[\mu_a + (1 - \bar{f})\mu_s]}$$

and the inverse mapping

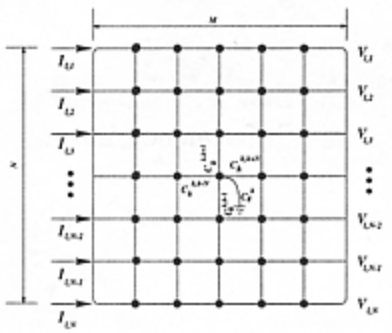
$$\mu_a = \frac{g}{c}, \quad \mu_s = \frac{c}{3\sigma(1 - \bar{f})} - \frac{g}{c(1 - \bar{f})}$$

Because of this analogy — and one-to-one mapping between the two sets of parameters — we can concentrate on the electrical model (4).

We can further approximate the continuous resistive model with a discrete network of resistors and use such a network for experimentation and simulation. It remains a matter of interest to find out how well a discrete network relates to the continuous medium, particularly under consideration of the complexity of the anatomical structures in most of the biological tissues.

We should also keep in mind that the network topology is not necessarily a regular lattice, but can be modeled or estimated, in one way or the other, to reflect the anotomical structure of the tissue. Regular tessellation is not ideal because it does not take into account local features. As a consequence, one need a fairly dense grid to capture the rapid changes and the ridge orientation. This will lead to too heavy a computational burden. The adaptibility of the network tolology to the underlying distribution is an unexplored field, and most likely, full of joyful challenges.

As an example, consider the simple 2-D network structure shown below:



Grid of Resistors

"Horizontal" resistors connect neighbouring nodes and each node is grounded by a "vertical" leakage conductor. The horizontal resistors model scattering, while the vertical conductors model absorption. Currents can be injected at the exposed nodes on the left boundary, while potentials can be measured at exposed nodes on the right boundary. Interior nodes are not accessible to either current injection or measurement of potential. The task is to recover the values of the vertical grounding conductors assuming that the horizontal conductors are all the same. Part of the problem is to determine a good source current injection and output potential measurement strategy.

If the grid has $N \times M$ nodes, then we have $N \times M$ unknown leakage conductances to ground. We can inject current at each of the N nodes on the left in turn, and each time read out N potentials on the right. So there are $N \times M$ unknowns and N^2 measurements. Clearly the aspect ratio of the rectangle controls how stably we can expect to recover the leakage conductances. If the rectangle is tall and skinny, then $M < N$ and we have an overdetermined system, if it instead is thick and flat then $M > N$ and we are dealing with an underdetermined system. From this crude analysis one might expect that the reconstruction problem may be well-posed for relatively "thin" objects, and ill-posed if light has to travel "too far" from source to detector.

The incoming currents $\vec{i}$ is linearly related to the potentials $\vec{v}$ by Ohm's rule:

$$G\vec{v} = \vec{i} \tag{5}$$

$\vec{i}$ and $\vec{v}$ are 1-D vectors (with NM components each) and G is the *forward conductance matrix* which encodes the unknown conductance parameters (see Appendix B for detailed formulation). G is symmetric, positive definite and sparse with only 5 nonzero diagonals. The discrete version (5) is an approximation of the diffusion equation (4).

The *forward problem* is to solve for the nodal potentials excited by a particular incoming current pattern when given the values of all the conductances. A well-known algorithm to obtain the solution of such a linear system is Cholesky Factorization which employs the particular matrix structure of G. It costs $O(N * (NM)^2)$ flops on a NxM rectangular grid. Because of the intensive use of the forward solver during inverse reconstruction, developing a faster algorithm is desired, especially when the grid size is large. One possible solution is parallel programming, i.e. implementing a parallel SOR (successive overrelaxation) solver with red-black ordering.

We note that while the above equation is linear in terms of the relationship between the injected currents $\vec{i}$ and the measured potential $\vec{v}$, $\vec{v}$ is nonlinear in terms of the unknown conductances. And it is the leakage conductances that we are interested in recovering.

When there is only one set of unknown parameters, i.e. the vertical conductances, nonlinearity and ill-posedness already generate tremendous difficulties in the inverse

reconstruction. Adding an extra set of unknowns, the horizontal conductances, does not drastically increase the complication and change our solution procedure. But the computational cost is greatly increased, and we expect the stability of the solution to be compromised.

In the case of biological tissues, consider the sensitivity of the light transportation to the perturbations in μ_a and μ_s we mutiply Eqn. (1) by $k = \bar{\mu}_s/c$:

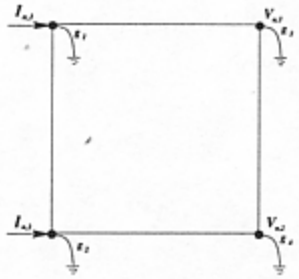
$$\nabla \cdot \frac{\bar{\mu}_s}{3[\mu_a + (1-\bar{f})\mu_s]} \nabla\Psi - \bar{\mu}_s \mu_a \Psi = \frac{q_0 \bar{\mu}_s}{c} \tag{6}$$

where $\bar{\mu}_s$ is the nominal scattering coefficient. Since $\mu_s >> \mu_a$, small deviations in either μ_a or μ_s from their norminal values are insignificant to $k\mu_d$ (the first coefficient in Eqn. (6)) which is predominated by $1/(3(1-\bar{f}))$. This convinces us to ignore variations in $k\mu_d$ (the horizontal conductance in the network case) at the early stage of algorithmic development.

Under the above simplification, we are capable of carrying on some rigorous mathematical analysis on the model problem (Eqn. (6)) with appropriate boundary condition and deriving a few nontrivial analytical solutions for certain nonhomogeneous absorption distribution (the horizontal conductance in the circuit network) with constant diffussion coefficient (or the leakage conductance). Comparison between the numerical reconstruction with the analytical solution can give one a general feeling of the system performance. But a prudent investigation of the sensitivities of different input/output patterns on each of the absorption and scattering coefficients is necessary in order to conceive a more sophisticated and accurate reconstruction algorithm.

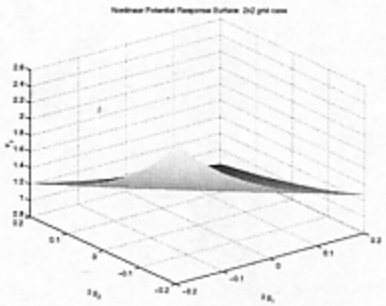
The recovery of the grounding conductance can be treated as a statistical parameter estimation problem. Parameters are chosen to minimize the misfit of the predictions and the observations. Since the dependency of the output potential on the grounding conductances is nonlinear, the approximate solution to this optimization problem is obtained recursively. At each intermediate step we acquire a linearized solution which is a better fit to our data.

The nonlinearity is studied by the expectation surface of each potential response. For the following $2 - by - 2$ rectangular grid,

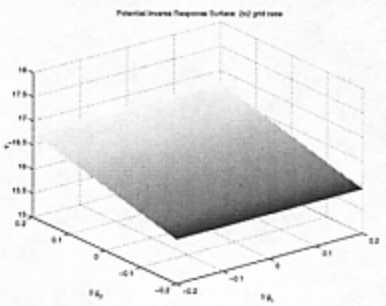


2x2 Grid of Resistors

we leave g_3 and g_4 fixed. When impulse current is applied at node 1, the expectation surface of the potential at node 3 is curved as a function of the perturbations in g_1 and g_2:



One of the significant improvement we have made so far is in reducing the nonlinearity via data transformation. The typical expectation surface of the new response variable, obtained by the transformation, has a very low degree of nonlinearity:



We have developed several iterative algorithms with high speed of convergence based on this technique and a novel linearization scheme.

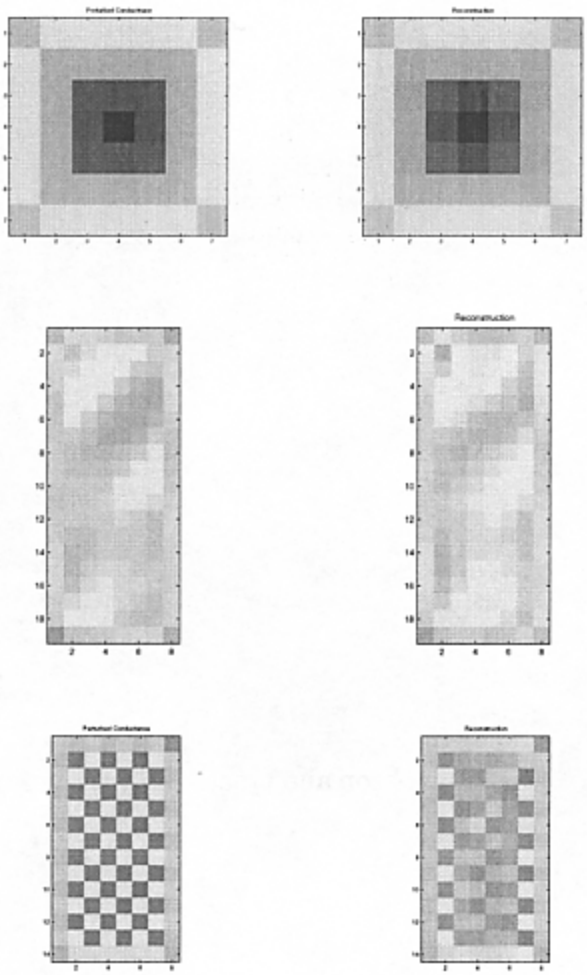
The regularized Newton-Raphson and Quasi-Newton iterative reconstructions have comparable performances, i.e. reconstruction errors and SNR. They differ in choosing iteration matrix. Newton-Raphson method compute the Jacobian and find a linear least-square solution at each step. Quasi-Newton method saves time on computation by efficiently updating its iteration matrix from the old one.

Various regularization strategies have been considered. Among them Tikhonov

regularization supplies analytical tools for convergence study and estimating the rate of convergence. Cubes, spheres and cylinders are among some simple geometric objects we have dealt with so far.

The generalized EM-algorithm is a Bayes approach capable of incorporating our prior knowledge about the tissue image of interest. The special handling of the multi-response variable is appealing because the parameters to be estimated are able to preserve their 2-D data structure and neighboring coherence. Regularization is natually performed in a 2-D random field with a prior information obtained from some other imaging modality, i.e. MRI. This general treatment of the nonlinear parameter estimation via data fitting and data modeling can also be easily adapted to variety of other inverse problems. But the computation involved in this formulation is more expensive than in the previous algorithms.

Here are some examples of our reconstruction:



Conclusion and Future Work:

Our algorithms are capable of recovering the overall pattern in the grounding conductance. Fast convergance is observed. As sensitivities suggest that the spatial resolution in the reconstruction degrades toward the center of the object.

Further study in recoverability of both absorption and scattering coefficients under appropriate experimental setup and network topology are desired, as well as the effective computational techniques. A reasonably good prior model will undoubtedly help improve the accuracy in the EM reconstruction. Only then performance of the regularized Newton-typed algorithm and Bayes-based algorithm can be made comparison.

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