Optical imaging in medicine: II. Modelling and reconstruction

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Abstract. The desire for a diagnostic optical imaging modality has motivated the development of image reconstruction procedures involving solution of the inverse problem. This approach is based on the assumption that, given a set of measurements of transmitted light between pairs of points on the surface of an object, there exists a unique three-dimensional distribution of internal scatterers and absorbers which would yield that set. Thus imaging becomes a task of solving an inverse problem using an appropriate model of photon transport. In this paper we examine the models that have been developed for this task, and review current approaches to image reconstruction. Specifically, we consider models based on radiative transfer theory and its derivatives, which are either stochastic in nature (random walk, Monte Carlo, and Markov processes) or deterministic (partial differential equation models and their solutions). Image reconstruction algorithms are discussed which are based on either direct backprojection, perturbation methods, nonlinear optimization, or Jacobian calculation. Finally we discuss some of the fundamental problems that must be addressed before optical tomography can be considered to be an understood problem, and before its full potential can be realized.

1. Introduction

The clinical potential of optical transillumination has been known for many years (Jöbsis 1977), and stems from the fact that the relative attenuation of light in tissue at some near-infrared wavelengths is related to the global concentrations of certain metabolites in their oxygenated and deoxygenated states (Cope and Delpy 1988). Thus an optical imaging modality offers the promise of functional as well as structural information. Despite considerable recent interest in the problem (Chance and Alfano 1993, 1995), progress towards optical tomography has been inhibited by the lack of suitable instrumentation to acquire sufficient useful data in reasonable times, and an adequate theoretical treatment of the reconstruction problem. A companion paper by Hebden *et al* (1996) reviews the experimental techniques which have been proposed in order to acquire data suitable for imaging through tissues, and examines the relative effectiveness of some direct approaches to imaging. In this paper we examine recent approaches to image reconstruction based on solution of the inverse problem, and discuss some of the difficulties involved.

The fundamental problem is that biological tissue is a highly scattering medium, so the transport model deviates highly from the Radon transform. As a consequence, inversion schemes have depended on one of the following general approaches: (i) restriction of the domain of measurement to those observables that give rise to straight-line integrals of the

Radon transform type; (ii) development and inversions of a partial differential equation (PDE) of diffusion type; or (iii) restriction of the set of scattering directions to allow the problem to be modelled as a Markov random process with finite state space. In the first case, the source is assumed to be a δ-function in time, and it is argued that the first photons that arrive at the measurement site have undergone little or no scattering, so that rejecting photons that have pathlengths which exceed the source–detector distance leads to a Radon transform approximation. However, the number of undeviated photons quickly falls to zero as tissue thicknesses exceed a few millimetres. Meanwhile, the Markov random process transition probability recovery schemes are at present limited to noiseless data. Consequently, most practical approaches are of the second type. The severe ill posedness of inverse problems of diffusion type has to be offset against the favourable signal-to-noise ratio (SNR) of the data compared to the Radon transform approach, and the computationally efficient methods available for solution, as described below. It is possible that hybrid approaches, using less severe restrictions on the measurement domain, may hold the key to more accurate methods.

2. Models of photon transport

The history of the scientific study of optics is characterized by a discrepancy between the wave and particle interpretations of light. Although in principle Maxwell's equations can be solved for complex systems with spatially varying permittivity, in practice most models are based on a particle interpretation of light. Nevertheless, by interpreting photon density as proportional to the scalar field for energy radiance I, various differential and integro-differential equations can be established. In this paper we concentrate on methods that lead to a computation scheme for complex inhomogeneous geometries. (For a more complete treatment of theories and models for light transport, refer to the excellent review paper by Patterson *et al* (1992).) The most widely applied equation in optical imaging is the radiative transfer equation (RTE) (Chandrasekhar 1950, Ishimaru 1978):

$$\frac{1}{c}\frac{\partial I}{\partial t} + \hat{\boldsymbol{s}}\cdot\nabla I(\boldsymbol{r},t,\hat{\boldsymbol{s}}) + (\mu_a+\mu_s)I(\boldsymbol{r},t,\hat{\boldsymbol{s}}) = \mu_s\int_{4\pi} f(\hat{\boldsymbol{s}},\hat{\boldsymbol{s}}')I(\boldsymbol{r},t,\hat{\boldsymbol{s}}')\,\mathrm{d}^2\hat{\boldsymbol{s}}' + q(\boldsymbol{r},t,\hat{\boldsymbol{s}}) \tag{1}$$

which describes the change of the radiance $I(\boldsymbol{r},t,\hat{\boldsymbol{s}})$ at position $\boldsymbol{r}$ in direction $\hat{\boldsymbol{s}}$. The parameters μ_a and μ_s are the absorption and scattering coefficients respectively, c is the velocity of light in the medium, and the function $f(\hat{\boldsymbol{s}},\hat{\boldsymbol{s}}')$ is the scattering phase function characterizing the intensity of a wave incident in direction $\hat{\boldsymbol{s}}'$ scattered in direction $\hat{\boldsymbol{s}}$. The formulation of equation (1) ignores electromagnetic wave properties such as polarization, and particle properties such as inelastic collisions, but is generally sufficient to describe the interaction of electromagnetic radiation in tissue for many medical imaging modalities. Note that an equivalent form for particle radiation is the linear transport equation (Case and Zweifel 1967, Duderstadt and Hamilton 1976).

The RTE is a balance equation describing the change of energy radiance $I(\boldsymbol{r},t,\hat{\boldsymbol{s}})$ in time due to changes in energy flow: loss due to absorption and scattering, and gain due to scattering and radiation sources. I is defined so that the energy transfer per unit time by photons in a unit solid angle $\mathrm{d}^2\hat{\boldsymbol{s}}$ through an elemental area $\mathrm{d}a$ given by its unit normal $\hat{\boldsymbol{n}}$, at position r, is given by

$$I(\boldsymbol{r},t,\hat{\boldsymbol{s}})\hat{\boldsymbol{s}}\cdot\hat{\boldsymbol{n}}\,\mathrm{d}a\,\mathrm{d}^2\hat{\boldsymbol{s}}. \tag{2}$$

The exitance Γ through a unit area perpendicular to $\hat{\boldsymbol{n}}$ is obtained by integrating equation (2) over all angles:

$$\Gamma(\boldsymbol{r}, t) = \int_{4\pi} I(\boldsymbol{r}, t, \hat{\boldsymbol{s}})\hat{\boldsymbol{s}} \cdot \hat{\boldsymbol{n}}\, \mathrm{d}^2\hat{\boldsymbol{s}}. \tag{3}$$

Practical modelling schemes derived from the RTE proceed either stochastically or deterministically, and these approaches are considered separately in the following sections.

2.1. Stochastic models

Stochastic methods involve modelling individual photon interactions either explicitly (e.g. Monte Carlo), or implicitly, by deriving the probability density functions for photon transitions (e.g. random walk or Markov random field).

2.1.1. Monte Carlo methods. Monte Carlo methods have a long pedigree, especially in transport theory (Duderstadt and Hamilton 1976). The histories of individual photons are simulated as they undergo scattering and absorption events governed by local values of optical parameters. Photons are followed until absorbed (or have negligible contribution) or escape the surface, thus contributing to a measurement (Wilson and Adam 1983). Such methods offer great flexibility in modelling arbitrarily complex geometries and parameter distributions, but they are prohibitively costly in computational time. For tissue thicknesses of several centimetres, typical photon paths are several hundred interactions in length, and many millions of photons need to be followed to obtain useful statistics. When using Monte Carlo methods to estimate the signal it is advantageous to use a model with minimum variance, since then the confidence of the estimate is increased. Analogue Monte Carlo (AMC) models are those which model both scattering and absorption probabilistically, since (as the name implies) they are thought to be direct analogues of the real physical process. Unfortunately AMC methods have the worst statistics, precisely because their variance is highest, and require very lengthy computation times. Variance reduction Monte Carlo (VRMC) models have better statistics, but underestimate the variance, which is a disadvantage if one wishes to have realistic models of noise. Recently Arridge *et al* (1995) compared the statistics of Monte Carlo methods with the diffusion equation and demonstrated that the latter could model the noise characteristics of the former.

2.1.2. Random walk theory. Random walk theory (RWT) describes the statistical behaviour of random walks in space, constrained along the elements of a discrete lattice. Although working within a simple structure, such as a cubic lattice, severely restricts the number of directions in which motion is possible, a powerful description of photon migration is achieved using a relatively simple mathematical analysis (Bonner *et al* 1987, Gandjbakhche and Weiss 1995). When motion in a homogenous space occurs with each of the lattice directions having equal probability, RWT can be considered to be equivalent to a finite-difference approximation of the diffusion equation.

The application of RWT to the study of photon migration in tissue has been pioneered by investigators at the National Institutes of Health, USA, and at the Bar-Ilan University, Israel. Expressions for the time-dependent transmittance through homogenous scattering slabs have been derived by Gandjbakhche *et al* (1993) and were shown to be in general agreement with the results of Monte Carlo simulations and curves calculated from diffusion theory. This work has also provided a useful analysis of time-gating imaging methods. For example, an analytical description of the spatial distribution of photons as they cross the midplane of a finite slab which yielded a simple model for the dependency of spatial resolution on photon flight-time was developed by Gandjbakhche *et al* (1994). The predictions of this model have since been validated using experimental measurements (Hebden and Gandjbakhche 1995). Recently RWT has been used to study the perturbation in the time-dependent transmittance through scattering slabs produced by an embedded partial absorber (Gandjbakhche *et al* 1996). Resulting expressions were used to assess the affects of time resolution on the detectability of the absorber. This perturbation approach is analogous to the diffusion theory analysis of Arridge (1995).

2.1.3. The Markov random field method. Professor Grünbaum and coworkers at the University of California at Berkeley have developed a very different, completely general stochastic model based on transition probabilities (Patch 1994, Grünbaum 1992, Grünbaum and Zubelli 1992). The model can recover the internal transition probabilities in the time-independent case given exact values of the probabilities on the boundary of a domain. Thus the model expects noiseless data. Despite leading to an exact solution to the non-linear inverse problem it has never been applied to real data because of the difficulty in relating the essentially topologically invariant analysis to real conditions.

2.2. Deterministic models

The RTE is a deterministic equation and simpler deterministic models can be derived from it. The principle of expanding the density ϕ, source q, and phase function f in spherical harmonics and retaining only a limited number of terms is well established (Lewis 1950, Bremmer 1964). One of the best recent summaries on this topic has been provided by Kaltenbach and Kaschke (1993) who derive a hierarchy of equations, of which the simplest is the time-dependent diffusion equation:

$$\begin{aligned} &(1/c)\partial\Phi(\boldsymbol{r},t)/\partial t - \nabla\cdot\kappa(\boldsymbol{r})\,\nabla\Phi(\boldsymbol{r},t) + \mu_a(\boldsymbol{r})\Phi(\boldsymbol{r},t) = q_0(\boldsymbol{r},t) \\ &\boldsymbol{J}(\boldsymbol{r},t) = -\kappa(r)\,\nabla\Phi(\boldsymbol{r},t) \end{aligned} \tag{4}$$

where Φ is the photon density

$$\Phi(\boldsymbol{r},t) = \int_{4\pi} I(\boldsymbol{r},t,\hat{\boldsymbol{s}})\,\mathrm{d}^2\hat{\boldsymbol{s}} \tag{5}$$

and $\boldsymbol{J}$ is the photon current

$$\boldsymbol{J}(\boldsymbol{r},t) = \int_{4\pi} \hat{\boldsymbol{s}} I(\boldsymbol{r},t,\hat{\boldsymbol{s}})\,\mathrm{d}^2\hat{\boldsymbol{s}}. \tag{6}$$

Equation (6) uses only spherical harmonics to first order for the expansion of I and zeroth order for the expansion of $\boldsymbol{q}$, and also ignores temporal variation in $\boldsymbol{J}$. Incorporation of time dependence in $\boldsymbol{J}$ and anisotropy in the source leads to the P_1 approximations:

$$\begin{aligned} &(\partial/\partial t)\Phi(\boldsymbol{r},t) + \mu_a\Phi(\boldsymbol{r},t) + \nabla\cdot\boldsymbol{J}(\boldsymbol{r},t) = q_0 \\ &[3\kappa(\boldsymbol{r})/c](\partial/\partial t)\boldsymbol{J}(\boldsymbol{r},t) + \boldsymbol{J}(\boldsymbol{r},t) + \kappa(\boldsymbol{r})c\,\nabla\Phi(\boldsymbol{r},t) = \boldsymbol{q}_1 \end{aligned} \tag{7}$$

where q_0 and $\boldsymbol{q}_1$ are the first two terms of the expansion of the source function and describe the isotropic and dipole-like anisotropic component of the source, respectively. In the homogenous case, where $\nabla\kappa(\boldsymbol{r})$ is assumed to be negligible, a single scalar wavefunction results, which is the so-called diffusive-wave approximation (DWA):

$$\begin{aligned} &\frac{3\kappa}{c^2}\frac{\partial^2}{\partial t^2}\Phi(\boldsymbol{r},t) + \frac{1+3\kappa\mu_a}{c}\frac{\partial}{\partial t}\Phi(\boldsymbol{r},t) - \kappa\,\nabla^2\Phi(\boldsymbol{r},t) + \mu_a\Phi(\boldsymbol{r},t) = S^{(0)}(\boldsymbol{r},t) \\ &\qquad \text{with } S^{(0)}(\boldsymbol{r},t) = (1/c)\{q_0 + (3\kappa/c)\partial q_0/\partial t - \nabla\cdot\boldsymbol{q}_1\}. \end{aligned} \tag{8}$$

Continuing to higher-order terms in the spherical harmonic expansion leads to the P_N approximations. However, by far the most commonly used approximation is the diffusion equation (DE). Newcomers to the field often find this surprising. For example, it is immediately clear that the DE is causal (in opposition to the fundamental time reversibility of light propagation) and in violation of relativity (sources of photons give rise to photon densities instantaneously). Such factors lead to some difficulties in exact mathematical analysis of the inverse problem that are often glossed over. The DWA obviates many of these difficulties yet is not routinely used. This is because for the low modulation frequencies (<1 GHz) and high-scattering regimes encountered in tissue optics, the difference from the DE is negligible.

Frequency-domain partial differential equations (PDEs) are easily obtained by Fourier transforming the time-domain equations. Alternatively they can be derived from first principles by considering the solution to the RTE with an intensity modulated source. The frequency-domain analogy to equation 4 is given by

$$-\nabla \cdot \kappa(\boldsymbol{r})\, \nabla \hat{\Phi}(\boldsymbol{r}, \omega) + (\mu_a(\boldsymbol{r}) + \mathrm{i}\omega/c)\hat{\Phi}(\boldsymbol{r}, \omega) = \hat{Q}_0(\boldsymbol{r}, \omega) \tag{9}$$

where it is to be noted that the frequency is incorporated as a complex attenuation coefficient. Note also that equation (9) is *elliptic* whereas equation (4) is *parabolic*—a distinction which has considerable significance in regard to numerical solutions.

2.3. Solution methods for deterministic equations

2.3.1. Analytical methods. A general method for solving a PDE which involves a source condition is the application of Green functions. The Green function is the solution when the source is a δ-function, and the solution for any other source can be obtained by convolution. However, pulsed sources used in optical imaging are often sufficiently close approximations to δ-functions that the Green function itself is appropriate. Analytical solutions for the RTE are scarce and have been obtained for only very simple cases, for example one-dimensional geometries such as planetary atmospheres. Green functions for various homogeneous geometries (slabs, cylinders and spheres) have been published, for both the time and frequency domains (Patterson *et al* 1989, Arridge *et al* 1992a). Eason *et al* (1978) provide analytic forms with more complex source conditions including collimated and distributed sources. These can be used as the basis for validating other models. Recently the analytic form for the Green function of a sphere embedded in an infinite scattering domain was derived by drawing an electrostatics analogy and matching the gradient of Φ across the boundary between surfaces (den Outer *et al* 1993, Boas *et al* 1994, Feng *et al* 1995).

2.3.2. Finite-difference schemes. The finite-difference method (FDM) is a standard technique to solve a PDE. A regular grid is established in the problem domain and differential operators are replaced by discrete differences. Then the problem becomes one of sparse matrix algebra or (for explicit schemes) simply a local convolution. For elliptic equations (frequency-domain DE) the multi-grid scheme is optimal (Hackbush 1980) and has recently been applied in optical tomography (Pogue *et al* 1995). For parabolic equations (time-domain DE) the alternating direction implicit scheme is optimal (Ames 1977), provided that the grid is regularly spaced in each of the component x, y, z-directions. A group led by Professor Frank Natterer at Westfälische Wilhelms-Universität in Münster has developed very efficient schemes using this method. The FDM can also solve the transport equation, provided that the angular integral over scattering directions is discretized (Natterer 1995).

2.3.3. Finite-element methods. The finite-element method (FEM) is somewhat more versatile than the FDM, especially in regard to complex geometries and for modelling boundary effects. The key principle in the FEM as applied to photon transport problems is the reduction of the general problem to that of finding an approximate solution that lies in the vector space spanned by a finite number of basis functions. Then the forward problem is reduced to one of matrix algebra of a finite size for which efficient techniques have been developed. In principle this method can be applied to any PDE model of the transport process. An FEM for the transport equation is described by de Oliveira (1986) where the number of scattering directions was chosen to be 12. The basic application of the FEM to solving the diffusion equation has been described by Arridge *et al* (1993a), who includes a comparison with Monte Carlo and analytic methods. Its application to the inverse problem was first introduced by Schweiger *et al* (1993). Fast methods for deriving measurement operators are described by Arridge (1995), and boundary conditions for a diffuse source are discussed by Schweiger *et al* (1995).

3. Image reconstruction

The formation of an image representing one or more internal optical characteristics from a series of boundary measurements is an example of a so-called inverse problem. Specifically, it involves the recovery of the parameters of an appropriate model, such as described in section 2. The forward problem can be stated as follows:

Given a distribution of light sources $\{\boldsymbol{q}\}$ *on the boundary* $\partial\Omega$ *of an object* Ω*, and a distribution of tissue parameters* $\{\boldsymbol{p}\}$ *within* Ω*, find the resulting measurement set* $\{\boldsymbol{y}\}$ *on* $\partial\Omega$*.*

The solution to the forward problem can be expressed in the form of a general non-linear forward operator:

$$\boldsymbol{y} = F[\boldsymbol{p}(\boldsymbol{r})]. \tag{10}$$

Similarly, the inverse problem may be stated as follows:

Given a distribution of light sources $\{\boldsymbol{p}\}$ *and a distribution of measurements* $\{\boldsymbol{y}\}$ *on* $\partial\Omega$ *derive the tissue parameter distribution* $\{\boldsymbol{p}\}$ *within* Ω

and this can be represented by

$$\{\boldsymbol{p}\} = \boldsymbol{F}^{-1}[\{\boldsymbol{y}\}]. \tag{11}$$

3.1. Backprojection methods

Many medical imaging modalities are governed by the same physical process, represented by the RTE. For example, if μ_s and $\boldsymbol{q}$ are zero, and the system is assumed to be at steady state, then equation (1) in the steady state becomes the differential form of the Radon transform for x-ray CT:

$$\{\hat{\boldsymbol{s}} \cdot \nabla + \mu_a(\boldsymbol{r})\} I(\boldsymbol{r}, \hat{\boldsymbol{s}}) = 0 \Rightarrow I(\boldsymbol{b}, \hat{\boldsymbol{s}}) = I(\boldsymbol{a}, \hat{\boldsymbol{s}})\, \mathrm{e}^{-\int_0^1 \mu_a(\boldsymbol{a}+\lambda(\boldsymbol{b}-\boldsymbol{a}))\mathrm{d}\lambda}. \tag{12}$$

Similarly if μ_a and μ_s are zero and $\boldsymbol{q}$ is non-zero and isotropic, we obtain the Radon transform for SPECT:

$$\hat{\boldsymbol{s}} \cdot \nabla I(\boldsymbol{r}, \hat{\boldsymbol{s}}) = q(\boldsymbol{r}) \Rightarrow I(\boldsymbol{b}, \hat{\boldsymbol{s}}) = \int_0^1 q(\boldsymbol{a} + \lambda(\boldsymbol{b} - \boldsymbol{a}))\, \mathrm{d}\lambda. \tag{13}$$

If both μ_a and $\boldsymbol{q}$ are non-zero, then the problem becomes the attenuated Radon transform, with the exponential Radon transform representing the case where μ_a is non-zero and constant.

The Radon transform is invertible in closed form by a variety of methods, such as resampling in the Fourier domain, convolution backprojection, or backprojection convolution (Natterer 1986). Thus it is attractive to consider an equivalent form for optical CT. If an unscattered component of light could be isolated, a Radon transform in $(\mu_a + \mu_s)$ could be employed. For diffuse light it is commonly suggested (see the work reported by Chance and Alfano 1993, 1995) that the line integrals in equation (12) could be replaced by integrals over a volume weighted by the photon measurement density functions (see subsection 3.4), and that backprojection using the same weighting functions could replace the convolution filter in the inverse Radon transform. Various *ad hoc* backprojection methods have also been postulated and demonstrated (Benaron *et al* 1994). However, such formulations have not been proved to solve the inverse problem, and the generalization of these methods to complex shaped inhomogeneous objects should be treated with caution.

3.2. Perturbation methods

If we have an estimate $\hat{\boldsymbol{p}}$ that is close to the ideal solution, then its projection $\hat{\boldsymbol{y}} = \boldsymbol{F}[\hat{\boldsymbol{p}}]$ is close to $\boldsymbol{y}$. We can expand equation (10) in a Taylor series:

$$\boldsymbol{y} = \boldsymbol{F}[\hat{\boldsymbol{p}}] + \boldsymbol{F}'[\hat{\boldsymbol{p}}](\boldsymbol{p} - \hat{\boldsymbol{p}}) + (\boldsymbol{p} - \hat{\boldsymbol{p}})^T \boldsymbol{F}''[\hat{\boldsymbol{p}}](\boldsymbol{p} - \hat{\boldsymbol{p}}) + \cdots \tag{14}$$

where $\boldsymbol{F}'$ and $\boldsymbol{F}''$ are the first- and second-order Fréchet derivatives respectively. In the discrete case, these derivatives are over a finite number of dimensions and are represented by matrices $\boldsymbol{F}' \to \mathbf{J}$, the Jacobian and $\boldsymbol{F}'' \to \mathbf{H}$, the Hessian. Putting $\Delta\boldsymbol{y} = (\boldsymbol{y} - \hat{\boldsymbol{y}})$ and $\Delta\boldsymbol{p} = (\boldsymbol{p} - \hat{\boldsymbol{p}})$ leads to

$$\Delta\boldsymbol{y} = \mathbf{J}[\hat{\boldsymbol{p}}]\Delta\boldsymbol{p} + \Delta\boldsymbol{p}^T \mathbf{H}[\hat{\boldsymbol{p}}]\Delta\boldsymbol{p} + \cdots. \tag{15}$$

Neglecting terms after the first, linear term constitutes the perturbation approach and the problem reduces to inversion of the matrix representation of $\mathbf{J}$ at $\hat{\boldsymbol{p}}$. This is therefore a linear problem which may well be ill posed, and is amenable to standard matrix inversion methods. Its success is largely dependent on how closely the initial estimate is to the correct solution, and how little effect is played by higher-order terms in equation (15).

The majority of reported results use this approach. Without exception they require, either explicitly or implicitly, a *difference experiment* that measures $\Delta\boldsymbol{y}$ as the difference between two states. This approach provides a means of imaging which is sensitive to changes in optical properties, which may be particularly useful for functional imaging of the brain, for example. Graber *et al* (1993) derived $\mathbf{J}$ from a Monte Carlo model, and acquired the difference data explicitly by performing an experiment with and without embedded absorbers. Arridge *et al* (1991) performed a similar procedure with an analytical kernel and with experimental data derived by a differencing experiment. O'Leary *et al* (1995) also used an analytical kernel, but derived the difference data implicitly by using two sources and subtracting the measured values. The investigators made the assumption that the resulting difference is an approximation to that obtained in an actual difference experiment, which is reasonable given that the image was of a localized perturbation and the sources and detectors were relatively far away.

3.3. Nonlinear optimization methods

If equation (10) is recognized as a non-linear mapping from parameters $\boldsymbol{p}$ to measurements $\boldsymbol{y}$ then standard non-linear methods may be used. A seminal paper by Singer *et al* (1990) introduced this approach using a Markov random field model on a discrete lattice to recover absorption and directional scattering parameters. The approach employed by Arridge *et al* (1992b, 1993b) uses FEM for the forward model and a Newton–Raphson scheme to iteratively progress towards the minimization of a least-squared error norm. Levenburg–Marquardt conditioning, together with Tikhonov and Phillips–Twomey regularization, were used to control the stability of the solution. Recently the same method was applied by Jiang *et al* (1995) to frequency-domain data.

3.4. Jacobian calculation

The entries in the Jacobian represent the sensitivity of a particular measurement at a detector ξ_k, from a source ζ_j, to changes in the image parameters $\boldsymbol{p}(\boldsymbol{r}_i)$. This may be calculated in many ways. A general framework introducing the term 'Photon measurement density functions' was recently developed by Arridge (1995) and Arridge and Schweiger (1995).

Various methods exist to derive the basic perturbation equations. Arridge (1995) used a linear perturbation method to derive the change in intensity in the Fourier domain as

$$\begin{aligned}\Delta\hat{\Gamma}(\xi_k,\omega) \simeq &-\hat{G}^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,\omega)\alpha(\boldsymbol{r}_i)\hat{G}^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,\omega)\\ &-\nu(\boldsymbol{r}_i)\,\nabla_r\hat{G}^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,\omega)\cdot\nabla_r\hat{G}^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,\omega)\end{aligned} \tag{16}$$

and in the temporal domain as a convolution:

$$\begin{aligned}\Delta\Gamma(\xi_k,t) \simeq &-\int_0^t \mathrm{d}t'\,g^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,t')\alpha(\boldsymbol{r}_i)g^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,t-t')\\ &-\nu(\boldsymbol{r}_i)\,\nabla_r g^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,t')\cdot\nabla_r g^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,t-t')\end{aligned} \tag{17}$$

where $\alpha(\boldsymbol{r})$ refers to a change in absorption and $\nu(\boldsymbol{r})$ to a change in diffusion coefficient, $\hat{G}^{(\Phi)}(\boldsymbol{r}_2,\boldsymbol{r}_1,\omega)$ and $g^{(\Phi)}(\boldsymbol{r}_2,\boldsymbol{r}_1,\omega)$ are the Green functions for equations (9) and (4) respectively, and the superscript (Γ) implies taking the normal derivative. The first term in equation (17) was derived by Schotland *et al* (1993) by taking the first term in the Feynman path integral expression for the Hamiltonian operator. Feng *et al* (1995) derived the first term in equation (16) by taking the limiting value of the exact perturbed intensity of a spherical inhomogeneity as the radius of the inhomogeneity reduced to zero. O'Leary *et al* (1995) noted that if $\hat{G}^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,\omega)$ is considered as the unperturbed initial field of a wavelike equation then equation (16) is the Born approximation for a scattered wave. Sevick *et al* (1994) derived the first term in equation (16) using a Monte Carlo argument.

Alternatively, instead of considering changes in intensity, changes in some transformation of the intensity can be used to derive the Jacobian. For example, if we consider logarithmic intensity then $\mathrm{d}(\log\Gamma) = \mathrm{d}\Gamma/\Gamma$ so that the expressions in equations (16) and (17) are normalized by the Green function from ζ_j to ξ_k (Schweiger *et al* 1993, Schotland *et al* 1993, O'Leary *et al* 1995):

$$\begin{aligned}\Delta\log\hat{\Gamma}(\xi_k,\omega) \simeq &-\frac{1}{\hat{G}^{(\Gamma)}(\xi_k,\zeta_j,\omega)}(\hat{G}^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,\omega)\alpha(\boldsymbol{r}_i,\zeta_k,\omega)\\ &-\nu(\boldsymbol{r}_i)\,\nabla_r\hat{G}^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,\omega)\cdot\nabla_r\hat{G}^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,\omega))\end{aligned} \tag{18}$$

$$\begin{aligned}\Delta\log\Gamma(\xi_k,t) \simeq &-\frac{1}{g^{(\gamma)}(\xi_k,\zeta_j,t)}\int_0^t \mathrm{d}t'\,g^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,t')\alpha(\boldsymbol{r}_i)g^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,t-t')\\ &-\nu(\boldsymbol{r}_i)\nabla_r g^{(\Gamma)}(\xi_k,\boldsymbol{r}_i,t')\cdot\nabla_r g^{(\Phi)}(\boldsymbol{r}_i,\zeta_j,t-t').\end{aligned} \tag{19}$$

The first term in equation (19) is what Schotland *et al* (1993) termed the 'photon hitting density' (they consider the measurement to be Φ rather than Γ). Arridge *et al* (1992b) compared reconstruction from intensity and log intensity measurements and found the latter provided considerable improvement. This was later confirmed by O'Leary *et al* (1995), who pointed out that the logarithmic intensity is equivalent to the Rytov approximation whereas absolute intensity is the Born approximation. More generally we can consider the logarithmic transformation as one example of a *measurement operator* or postprocessing transformation on the obtained data $\Gamma(t)$. The general treatment of any kind of measurement operation is given by Arridge (1995), where it is proposed that the moments of $\Gamma(t)$ give an improvement to imaging algorithms because the sensitivity functions are maximized at interior points, rather than by boundary effects.

It may be noted that the Jacobian entries, involving the product (or convolution in the time domain) of Green functions, may also be considered as the interaction of the photon density generated from the source and an *adjoint* density generated from the measurement position. In a transport model this reciprocity principle derives directly from the temporal reversibility of this equation. In the diffusion approximation the adjoint formulation is less intuitive—it requires a measure flux to be used as an intensity source. The use of reciprocity relations makes the Jacobian calculation very fast (Arridge and Schweiger 1995).

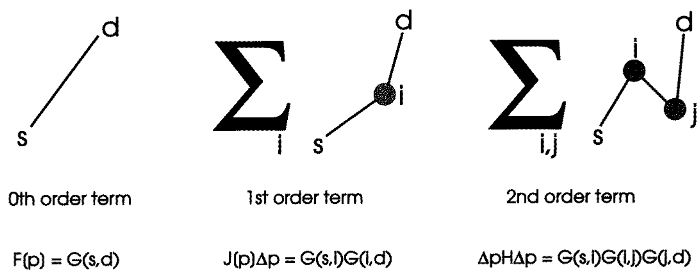

Figure 1. The successive terms in the Taylor series expansion of the forward problem are determined by the sum of Feynman type diagrams. The straight lines represent Green function propagators that are the solution to the diffusion equation in the appropriate geometry.

It may also be noted that Feynman diagrams allow computation of Hessian and higher-order terms in the Taylor series. This is illustrated schematically in figure 1. Usually classical optimization does not compute the Hessian but may approximate it via conjugate gradients, for example. Possibly an acceleration is available using Feynman terms $\hat{G}(\boldsymbol{r}_2, \boldsymbol{r}_1, \omega)\hat{G}(\boldsymbol{r}_3, \boldsymbol{r}_2, \omega)\ldots\hat{G}(\boldsymbol{r}_n, \boldsymbol{r}_{n-1}, \omega)$, but in practice it appears difficult to produce a computationally efficient scheme.

4. Discussion

The development of image reconstruction techniques for optical imaging through diffuse media is at a very preliminary stage. The most advanced work is largely being done using simulated data, which is useful for predicting which instrumentation is worth developing and what experiments to perform. However, the field will not attract significant attention until the predictions have been fully validated by experiment. Unfortunately, due to lack of appropriate instrumentation or of a sufficiently sophisticated model, most experimental data reported to date have involved geometries or conditions which are very simplistic compared to what would be encountered for a medical imaging system. We now enumerate some of the fundamental difficulties involved in optical tomography. Although these are often acknowledged, they remain largely unexplored, especially from an experimental viewpoint.

4.1. The intensity matching problem

In theory, the simplest type of data to model and therefore to reconstruct is intensities, either continuous wave, time dependent, or frequency domain. However, the comparison of measured intensities to a given model is complicated by the inherent unreliability of absolute intensity measurements. There are various potential causes of this, including fluctuation in the power source, unknown losses in fibre coupling, and unknown or variable detector gain. The problem may be obviated to some extent by employing a reference measurement so that the model is formulated in terms of relative intensity I/I_0. Similarly, using the logarithm of intensities is helpful. As illustrated in figure 2(a), reference intensity measurements are easily achieved for laboratory 'blob-in-a-fishtank' experiments, but for a general complex geometry encountered clinically such a measurement is not routinely available. The use of mean flight time or higher-order moments eliminates this problem and is the reasoning behind its advocation by Arridge (1995).

4.2. The boundary effect problem

Whereas the Green function formulation is exact for determination of the Jacobian, and is applicable to any geometry, the precise form of the Green functions cannot be found in general. However the attraction of this method has led some workers (O'Leary *et al* 1995) to propose experiments using 'embedded systems'. This involves immersing the object, the source, and the detectors in a tank of scattering liquid. The geometry is one we might call 'blob-in-an-infinite-fishtank', as illustrated in figure 2(b). Having essentially disposed of the boundaries, it is argued that the infinite-space Green functions can be employed to high approximation. However, the fact that experiments validate the method for small localized absorbing and scattering objects is not conclusive evidence that it can be applied to medical imaging situations, as represented by figure 2(c). The alternative is the application of numerical methods such as finite differences or finite elements which can handle arbitrarily complex geometries. Their perceived drawback is the high computational cost, although the advent of increasingly fast computers is rapidly diminishing this obstacle.

4.3. The 2D versus 3D problem

A disadvantage of some iterative approaches using numerical forward models is that they are modelled in two dimensions. Although the computational cost in 3D is significantly greater, to apply these methods to real data a 3D model is deemed necessary. Although this problem must be addressed it is perhaps naive to reject such methods on the grounds of current computational cost. Fortunately, improvements in computer performance and more detailed analysis of algorithms has led to a continual reduction in the overheads of these methods. Furthermore, it is well known that inverse methods are often improved as the problem increases in dimensionality, owing to fundamental mathematical properties of partial differential equations.

4.4. Initial estimate problem

Reconstruction procedures which localize perturbing regions generally depend on knowing the optical properties of the background material. Even more general iterative reconstruction

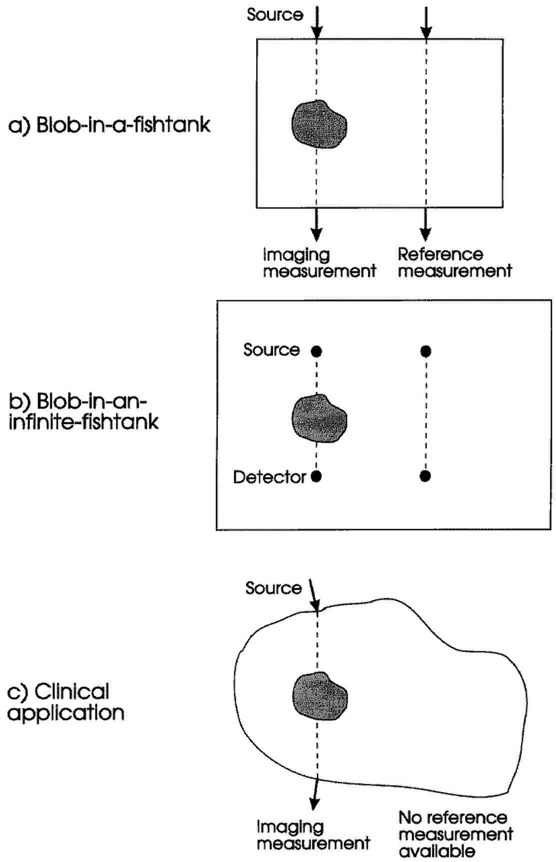

Figure 2. A comparison of common experimental configurations with the situation encountered for clinical applications. The latter involves a complex inhomogeneous region with an irregular boundary, and thus no reference measurement is available.

processes require some initial estimate of the object properties. Some experimenters avoid this problem by using embedded systems with liquids of pre-determined scatter and absorption coefficients. Experiments involving isolated embedded objects in homogenous media can also make use of measurements made sufficiently far away from the object to determine the background properties. For a realistic geometry it is necessary to acquire the initial guess by global fitting mechanisms. However, this problem may be at least partially alleviated by employing a 'coarse-to-fine' image recovery method, which starts with a random or uniform guess, and uses the result of an iteration with coarse resolution as the initial estimate for iterations at finer resolution.

5. Conclusions

Optical imaging in medicine presents some challenging problems for both experimental and theoretical work. To gain an appreciation for the tasks that lie ahead it is essential to consider the non-linear nature of the forward problem. A wide variety of methods have been proposed for both the forward and inverse problems, but experimental validation has been largely inadequate due to lack of appropriate instrumentation and/or the use of unrealistic physical conditions and geometries. Although there is clearly much work to do before the full potential of optical tomography can be realized, the benefits are significant enough to make the effort worthwhile.

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