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Statistical basis for the determination of optical pathlength in tissue

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Abstract. In this paper we show how to derive the mean and variance of the transilluminated signal obtained in models of light propagation in tissue, based both on a stochastic Monte Carlo method and on a deterministic diffusion approximation. The theoretical treatment of the Monte Carlo model applies only to integrated intensity measurements, whereas the diffusion approximation gives an estimator for the time-dependent case as well. We present results that show the accurate prediction of Monte Carlo statistics, and propose that the diffusion approximation is therefore a suitable mechanism for incorporating noise into modelling procedures.

1. Introduction

In the field of near-infrared spectroscopy and imaging, ultrashort light pulses and a fast optical detector are used to measure the time of flight of photons in tissue. Biological tissue is a highly light scattering medium, and the light that is detected in such studies has travelled considerably further through the tissues than the direct distance between the input and output optodes.

It is of great importance to have a reliable model that can predict the value of measurements for any given experimental situation. Models are either *stochastic*, such as Monte Carlo (Lux and Koblinger 1991, Wilson and Adam 1983, van der Zee and Delpy 1987, Flock *et al* 1989) or random walk (Bonner *et al* 1987) models that follow individual photon histories, or *deterministic*, based on a partial differential equation for photon density. Whereas the former are more directly related to the physics of the situation, the latter are preferable in the development of analytic methods. However stochastic models have an important property: they incorporate noise directly. Noise modelling is arguably equally as important as signal modelling, especially if trying to use the model as the basis for an *a posteriori* parameter fitting process, such as global optical property determination (Madsen *et al* 1991), or image reconstruction (Grünbaum *et al* 1991, Arridge *et al* 1991, Arridge 1993).

In this paper we show how to derive the statistical properties of the transilluminated signal based first on a stochastic model (Monte Carlo) and then on a deterministic model (the diffusion approximation). We show that the deterministic model predicts both the

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expectation value and variance of the stochastic model to high accuracy in the time-independent case, and for temporal moments. We conjecture that the deterministic model may also predict the fully time-dependent case.

2. Photon transport models

Both the Monte Carlo and the diffusion approaches may be derived from an integrodifferential equation description (Patterson *et al* 1991): the radiative transfer equation of atmospheric physics (Chandrasekhar 1950), or the linear transport equation of neutron transport theory (Case and Zweifel 1967). We write this as

$$\left\{\hat{s}\cdot\nabla + \mu_a(r) + \mu_s(r) + \frac{\partial}{c\partial t}\right\}\phi(r,\hat{s},t) = q(\hat{s},\hat{r},t) + \mu_s(r)\int (f(\hat{s}',\hat{s},r)\phi(r,\hat{s}',t))\,\mathrm{d}^2\hat{s}' \tag{1}$$

which describes the change of the radiance $\phi(r,\hat{s},t)$ at time t at position r into direction $\hat{s}$ within a domain Ω, bounded by a surface $\partial\Omega$. $q(r,\hat{s},t)$ is the source term, μ_a and μ_s are the absorption and scattering coefficients respectively (dimensions of inverse length), c is the speed of light, and $f(\hat{s}',\hat{s},r)$ is the scattering phase function characterizing the intensity of a wave incident in direction $\hat{s}'$ scattered into direction $\hat{s}$.

2.1. Monte Carlo approach

Monte Carlo methods proceed by defining regions of Ω that have particular values of μ_a, μ_s and possibly $f(\hat{s}',\hat{s},r)$. Individual photons are run through the model, undergoing scattering and absorption events according to the local values of parameters, until they either have negligible contribution, or escape the surface $\partial\Omega$, thus contributing to a measurement. Such measurements offer great flexibility in modelling arbitrarily complex geometries and parameter distributions, but they are prohibitively costly in computational time—typically photon paths are several hundred interactions in length, and many millions of photons needed to be followed to obtain sufficient statistics.

We have demonstrated (Hiroaka *et al* 1994) that a variety of Monte Carlo models are possible, all of which converge in the limit of large numbers of photons to an estimate of the signal with the same mean, but different variances. When using Monte Carlo models to estimate the signal it is advantageous to use one with minimum variance, since then the confidence of the estimate is increased. For example the *variance reduction Monte Carlo* (VRMC) models have good statistics, but when modelling noise we require an unbiased estimate of the true variance, and the VRMC would appear to produce underestimates. Therefore in this paper we will consider only *analogue Monte Carlo* (AMC) models, 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 these AMC methods have the worst statistics, precisely because their variance is highest, and require very lengthy computation times to provide reliable estimators.

2.2. Diffusion approximation

Expansion of the radiative transfer equation (RTE) in spherical harmonics and retention of k terms results in $(k+1)$ coupled linear partial differential equations (Bremmer 1964, Lewis 1950). If k is odd these reduce to a single $(k+1)$th-order equation. The simplest is the P_1 approximation, or diffusion equation, which is defined in terms of the isotropic photon density $\Phi(r,t) = \int \phi(r,\hat{s},t)\,d^2\hat{s}$ and corresponding source term $q_0(r,t) = \int q(r,\hat{s},t)\,d^2\hat{s}$:

$$\{\nabla \cdot \kappa(r)\nabla - \gamma(r) - \partial/\partial t\}\Phi(r,t) = -q_0(r,t) \tag{2}$$

where $\gamma(r) = \mu_a(r)c$ and $\kappa(r)$ is given by

$$\kappa(r) = c/3(\mu_a(r) + \mu_s'(r)) \tag{3}$$

where $\mu_s'(r) = (1-\bar{f})\mu_s(r)$ is the reduced scattering coefficient, and $\bar{f}$ is an *anisotropy factor* $(0 \leqslant \bar{f} \leqslant 1)$. The values of $\bar{f}$ for biological tissue are typically of the order of 0.9, indicating strongly forward-biased scattering. Use of the diffusion approximation (DA) is widespread, even though it is the simplest approximation to the more general RTE, and shows significant differences from higher-order approximations such as the diffusive wave approximation (DWA) (Kaltenbach and Kaschke 1993). Experimental and theoretical work has demonstrated the validity of this equation under conditions that are appropriate for the types of application we are considering where $\mu_a \ll \mu_s$ (Groenhuis *et al* 1983).

3. Statistical properties of Monte Carlo simulations

3.1. Definitions

The following assumptions are made with regard to Monte Carlo.

(i) Monte Carlo simulations assume that photons are ballistic particles; thus wave phenomena such as coherence and interference effects can be ignored.

(ii) Optical properties of the medium are defined only by (1) the absorption coefficient $\mu_a(r)$, (2) the scattering coefficient $\mu_s(r)$, and (3) the angular intensity distribution of a single scattering (i.e. the scattering phase function) $f(\hat{s}',\hat{s},r)$; therefore other effects such as fluorescence are ignored. Usually it is additionally assumed that the phase function is independent of both r and $\hat{s}$ (the absolute direction), and is a function only of $\theta = \cos^{-1}(\hat{s}'\cdot\hat{s})$, the relative angle of scattering.

(iii) The energy of photons is unchanged by scattering (i.e. the scattering is elastic).

(iv) When photons are absorbed, their energy is completely absorbed and does not influence the optical properties of the medium.

In AMC simulations, the weight of a photon is always unity and it continues its random walk until (i) it is absorbed or (ii) it leaves the region of interest with no possibility of return.

The probability that a photon travels distance l without scattering or absorption is $\exp(-\mu_t l)$ and the free pathlength (l) is calculated by

$$l = -(1/\mu_t)\ln(R_1) \tag{4}$$

where $\mu_t = \mu_s + \mu_a$ is the total attenuation coefficient and R_1 is a random number between zero and unity. After the photon travels distance l it can be scattered or absorbed. The probability of scattering at this point is μ_s/μ_t and the probability of absorption is μ_a/μ_t; therefore another random number R_2 is used to determine the interaction:

$$\begin{array}{ll} \text{if } R_2 < \dfrac{\mu_s}{\mu_t} & \text{then continue random walk} \\ \text{else} & \text{stop random walk} \end{array} \tag{5}$$

For the scattered photon, the scattering direction is chosen usually by using two other random numbers (R_3, R_4) distributed over the polar and azimuthal angles (θ, ϕ) with a probability density function defined by the phase function.

The accuracy of the simulation depends on the number of simulated photons. The theoretical basis to calculate mean and variance of the AMC simulation can be found in the book by Lux and Koblinger (1991).

3.2. *Statistics of integrated intensity*

A photon history can be expressed by a vector:

$$X(\zeta) = [\zeta, x_1, x_2, \ldots, x_n] \tag{6}$$

for a photon starting at ζ, where each element x_i is the subsequent location of the photon and is calculated by four random numbers as mentioned above (independent sets X_1, X_2 do not necessarily contain the same number of data elements). When an infinite number of histories are simulated, the result is a Green function. This can be expressed by the integral

$$G^{(MC)}(\xi, \zeta) = \frac{1}{\delta S(\xi)} \int_{\Xi(\zeta)} H(X, \xi) p(X) \, \mathrm{d}X \tag{7}$$

where $\delta S(\xi)$ is the area of the detector around the measurement position ξ, $\Xi(\zeta)$ is the domain of the integral for X (i.e. every possible history starting at ζ), $p(X)$ is the probability density function (PDF) of the histories and $\int p(X(\zeta)) \, \mathrm{d}X(\zeta) = 1$; $H(X, \xi)$ is a function to determine the value of the result. When considering integrated intensity and AMC it is given by

$$H(X, \xi) = \begin{cases} 1 & \text{when photon arrives in a small region } \delta S \text{ around } \xi \\ 0 & \text{otherwise.} \end{cases} \tag{8}$$

In the following we will make repeated use of the fact that H is idempotent:

$$\{H(X, \xi)\}^2 = H(X, \xi). \tag{9}$$

(7) indicates that the expectation value of the result for a single photon is the Green function, $\langle H \rangle(\xi) = G^{(MC)}(\xi, \zeta)$. The empirical mean of the simulation for N photons input, $\bar{H}$, is

$$\bar{H}(\xi) = \frac{1}{N} \sum_{i=1}^{N} H(X_i(\zeta), \xi) \tag{10}$$

where X_i is randomly chosen from $p(X)$. This empirical mean is an unbiased estimator of $G^{(MC)}(\xi, \zeta)$, because its expectation value is the Green function:

$$\begin{aligned} \langle \bar{H} \rangle(\xi) &= \int_{\Xi(\zeta)} \left\{ \frac{1}{N} \sum_{i=1}^{N} H(X_i, \xi) \right\} p(X) \, \mathrm{d}X \\ &= \frac{1}{N} \sum_{i=1}^{N} \int_{\Xi(\zeta)} H(X_i, \xi) p(X_i) \, \mathrm{d}X_i = G^{(MC)}(\xi, \zeta) \delta S(\xi) \end{aligned} \tag{11}$$

and the variance of the empirical mean for N photons input is σ_H^2/N, where the variance of the result for a single photon history (σ_H^2) is

$$\begin{aligned} \sigma_H^2(\xi, \zeta) = \mathrm{var}[\bar{H}](\xi) &= \int_{\Xi(\zeta)} \{H(X, \xi) - G^{(MC)}(\xi, \zeta)\delta S(\xi)\}^2 p(X) \, \mathrm{d}X \\ &= \int_{\Xi(\zeta)} H(X, \xi)^2 p(X) \, \mathrm{d}X - \{G^{(MC)}(\xi, \zeta)\delta S(\xi)\}^2. \end{aligned} \tag{12}$$

For the simulation of intensity, invoking (9), we find

$$\sigma_H^2 = G^{(MC)}(\xi,\zeta)\delta S(\xi) - \{G^{(MC)}(\xi,\zeta)\delta S(\xi)\}^2. \tag{13}$$

We may similarly consider the time-dependent behaviour as a Green function:

$$g^{(MC)}(\xi,\zeta,t) = \frac{1}{\delta S(\xi)\delta t}\int_{\Xi(\zeta)} h(X,\xi,t)p(X)\,\mathrm{d}X \tag{14}$$

where $h(X,\xi,t) = H(X,\xi)W(X,t)$ and $W(X,t)$ is a windowing function:

$$W(X,t) = \begin{cases} 1 & \text{when photon arrives in a small temporal interval } \delta t \text{ around } t \\ 0 & \text{otherwise} \end{cases} \tag{15}$$

$\langle h\rangle(\xi,t) = g^{(MC)}(\xi,\zeta,t)$ and

$$\sigma_H^2(\xi,\zeta,t) = g^{(MC)}(\xi,\zeta,t)\delta S(\xi)\delta t - \{g^{(MC)}(\xi,\zeta,t)\delta S(\xi)\delta t\}^2. \tag{16}$$

Other Monte Carlo models may also be analysed in this approach (Hiroaka *et al* 1994), but a full treatment is outside the scope of this paper.

4. Diffusion method

4.1. Definitions

We solve (2) in the domain Ω, with the output flux on $\partial\Omega$ given by

$$\Gamma(\xi,t) = -\kappa(\xi)(\partial/\partial n)\Phi(r,t)|_{\partial\Omega(\xi)} = -\kappa(\xi)\hat{n}(\xi)\cdot\nabla\Phi(r,t)|_{\partial\Omega(\xi)} \tag{17}$$

where ξ is a point on $\partial\Omega$ and $\hat{n}$ is the outward normal to $\partial\Omega$ at ξ.

The isotropic source term $q_0(r,t)$ in (2) represents the form of the input pulse as a function of space and time. In general, the solution for any input pulse can be derived by convolution of $q_0(r,t)$ with the Green function for (2) in the appropriate geometry. Then this solution can be substituted into (17) to obtain the flux intensity. We will represent the Green function for (2) as $g^{(\Phi)}(r,r',t-t')$, and the result of substituting this into (17) as $g^{(\Gamma)}(\xi,r',t-t')$ where ξ is a point on the boundary; in the Fourier domain we use $\hat{G}^{(\Phi)}(r,r',\omega)$, and $\hat{G}^{(\Gamma)}(r,r',\omega)$ respectively; the stationary case can be considered to be the frequency domain case at $\omega = 0$, and we have the result (Arridge *et al* 1992)

$$G^{(\Gamma)}(\xi,r') = \int_{-\infty}^{\infty} g^{(\Gamma)}(\xi,r',\tau)\,\mathrm{d}\tau \tag{18}$$

where $G^{(\Phi)}(r,r')$ is the Green function for the time-independent diffusion equation

$$\{\nabla\cdot\kappa(r)\nabla - \gamma(r)\}\Phi(r) = -q_0(r). \tag{19}$$

The time-dependent Green function $g^{(\Gamma)}(\xi,r',t-t')$ is commonly referred to as a *temporal point spread function* (TPSF) following Delpy *et al* (1988).

Our treatment considers $\{\Gamma(t)\}$ to be a non-stationary random process, and is based on a central conjecture.

Conjecture 1. The PDF $p(\xi,t)$ for a photon launched at ζ at time t' to leave the object in a small area δS around $\xi\in\partial\Omega$ in an interval $[t\to t+\delta t)$ is the Green function $g^{(\Gamma)}(\xi,\zeta,t-t')$.

This conjecture is tantamount to saying that the *a posteriori* frequency distribution in space and time is also the *a priori* PDF. Evidence for conjecture 1 comes from the fact that for a δ function input the integral over $\partial\Omega$ and all times of $g^{(\Gamma)}(\xi, \zeta, t-t')$ is equal to the integral through the volume of the photon density attenuated by γ:

$$\begin{aligned}\int_{\partial\Omega} \mathrm{d}^2S(\xi) \int_{-\infty}^{\infty} g^{(\Gamma)}(\xi, r', \tau)\,\mathrm{d}\tau &= \int_{\partial\Omega} G^{(\Gamma)}(\xi, r')\,\mathrm{d}^2S(\xi) \\ &= -\int_{\partial\Omega} \kappa(\xi)\nabla G^{(\Phi)}(\xi, r')\cdot \mathrm{d}S(\xi) = -\int_{\Omega} \nabla\cdot\kappa(r)\nabla G^{(\Phi)}(r, r')\,\mathrm{d}^3r \\ &= \int_{\Omega} [q_0(r') - \gamma(r)G^{(\Phi)}(r, r')]\,\mathrm{d}^3r. \end{aligned} \tag{20}$$

When absorption is zero, then the volume integral is unity, which we interpret as meaning that an entering photon has to leave somewhere unless it is absorbed.

4.2. Time-dependent case

Consider t, the time of arrival of a photon at ξ, to be a random variable distributed with probability density function $p(\xi, t)$. Consider $y(\xi, t)$ to be a binary function of t which is unity if a photon arrives at ξ at time t, and zero otherwise. By the central conjecture the probability of a photon arriving at (ξ, t) in a small area $\delta S(\xi)$, in a small interval δt, is given by

$$a = \alpha(t)\delta t = g^{(\Gamma)}(\xi, \zeta, t-t')\delta S(\xi)\delta t. \tag{21}$$

Assuming a binomial distribution, we derive the mean and the variance of these photons as

$$\begin{aligned}\langle y\rangle_N(\xi, t) &= Na \\ \mathrm{var}[y]_N(\xi, t) &= Na(1-a)\end{aligned} \tag{22}$$

where N is the number of input photons. This is the same result as (16) if we make the assumption that $g^{(MC)} = g^{(\Gamma)}$.

4.3. Statistics of integrated intensity

Consider the expectation value of y at point ξ:

$$\begin{aligned}\langle y\rangle(\xi) = E[y](\xi) &= \int_{-\infty}^{\infty} y(\xi, t)p(\xi, t)\delta S(\xi)\,\mathrm{d}t \\ &= \int_{-\infty}^{\infty} g^{(\Gamma)}(\xi, \zeta, \tau)\delta S(\xi)\,\mathrm{d}\tau = G^{(\Gamma)}(\xi, \zeta)\delta S(\xi).\end{aligned} \tag{23}$$

We interpret $\langle y\rangle(\xi)$ as the expected intensity $I(\xi, \zeta)$ received at ξ for one photon input into the system at position ζ and (23) implies that the solution given by the time-independent Green function gives precisely the mean of the statistically distributed data. This leads naturally to the following conjecture.

Conjecture 2. The PDF $p(\xi)$ for a photon launched at ζ to leave the object in a small area δS around $\xi \in \partial\Omega$ at any time is the time-independent Green function $G^{(\Gamma)}(\xi, \zeta)$.

Note that the quantity y plays the role of h in subsection 3.2. In that case the PDF was a function of a random variable X representing history, whilst here y is a function of the random variable t representing time. Beforehand we took the ensemble average to obtain a meaning to $\bar{h}$, then took the expectation value. Here we take the expectation value directly.

Monte Carlo. $H(\xi, \boldsymbol{X})$ and $W(\boldsymbol{X}, t)$ are functions of a vector random variable $\boldsymbol{X}$ with PDF $p(\boldsymbol{X})$

$$\text{sample mean } \bar{H}(\xi) = \frac{1}{N}\sum_i h(\xi, \boldsymbol{X}_i) \qquad \bar{h}(\xi, t) = \frac{1}{N}\sum_i H(\xi, \boldsymbol{X}_i)W(\boldsymbol{X}_i, t)$$

$$\text{expectation value } \langle H\rangle(\xi) = \int h(\xi, \boldsymbol{X})p(\boldsymbol{X})\,\mathrm{d}\boldsymbol{X} \qquad \langle h\rangle(\xi, t) = \int H(\xi, \boldsymbol{X})W(\boldsymbol{X}, t)\,\mathrm{d}\boldsymbol{X}.$$

Diffusion theory. $y(\xi, t)$ is a function of a scalar random variable t with PDF $p(\xi, t)$

$$\text{sample mean } \bar{y}(\xi) = \frac{1}{N}\sum y(\xi, t_i)$$

$$\text{expectation value } \langle y\rangle(\xi) = \int y(\xi, t)p(\xi, t)\,\mathrm{d}t.$$

In the Monte Carlo case a single sample of h represents the sampled measurement of integrated intensity at ξ for one photon input into the system, and in the diffusion case a single sample of y represents the same thing. In both cases, in the limit of large N, $\bar{H} \to \langle h\rangle$ and $\bar{y} \to \langle y\rangle$ are interpreted as the integrated intensity I received at ξ, which is also given by $G^{(\Gamma)}$; this supports our central conjecture. The difference is that in the diffusion case t is the random variable directly, whereas in the Monte Carlo case it is only derived from the length of $\boldsymbol{X}$. Also $p(\xi, t)$ is a *deterministically* generated PDF whereas $p(\boldsymbol{X})$ is essentially the result of a Markov chain.

We now consider the variance of intensity detected at ξ for a single input photon

$$\begin{aligned}\mathrm{var}[y](\xi) &= E[(y - \langle y\rangle(\xi))^2] = \int_{-\infty}^{\infty}\{y(\xi, t) - \langle y\rangle(\xi)\}^2 p(\xi, t)\,\mathrm{d}t \\ &= \int_{-\infty}^{\infty} g^{(\Gamma)}(\xi, \zeta, \tau)\delta S\,\mathrm{d}\tau - \langle y\rangle(\xi)^2 = G^{(\Gamma)}(\xi, \zeta)\delta S(\xi) - \{G^{(\Gamma)}(\xi, \zeta)\delta S(\xi)\}^2\end{aligned} \tag{24}$$

which is identical to (13) if we make the assumption that $G^{(MC)} = G^{(\Gamma)}$.

We are now in a position to ask from what population a sample of integrated intensity I is drawn. If one photon is input, the probability that it arrives at ξ is $\beta = G^{(\Gamma)}(\xi, \zeta)\delta S$ so that as N photons are input the signal detected at ξ will have mean and variance given by

$$\langle I\rangle_N(\xi, \zeta) = N\beta \tag{25}$$

$$\mathrm{var}[I]_N(\xi, \zeta) = N\beta(1 - \beta). \tag{26}$$

By the central limit theorem we can deduce that the intensity detected at ξ will be a sample of a random variable I distributed with Gaussian probability density $p(I)$ of mean and variance given by (25) and (26).

4.4. Statistics of mean time

Suppose we have a Monte Carlo trial of N photons. Consider the count of photons arriving at position ξ. In the following we will write $\alpha(t)$ for $g^{(\Gamma)}(\xi, \zeta, t - t')\delta S(\xi)$ (as defined in (21)), and β for $G^{(\Gamma)}(\xi, \zeta)\delta S(\xi)$. Let us consider that n photons are detected at ξ, with times of arrival $\{t_1, t_2, \ldots, t_n\}$. Let $T = \sum_1^n t_i$ be the integrated time of arrival, and $\langle t\rangle = T/n$ be the mean time. Let $p(T)$ be the PDF of T, and $p(\langle t\rangle)$ be the PDF of $\langle t\rangle$. Our goal is to find $p(\langle t\rangle)$.

Suppose $N = 1$. The probability that the photon arrives in an area δS around ξ is β. The *conditional probability* $a_1 = \Pr[T|1]$ of a photon arriving in interval $[t \to t+\delta t)$ given that it arrives in an area δS around ξ is therefore $\alpha(t)\delta t/\beta$, and the *conditional expectation* value of T is

$$\langle T_1\rangle = E[T|1] = \frac{1}{\beta}\int_{-\infty}^{\infty} t\alpha(t)\,\mathrm{d}t = \frac{1}{G^{(\Gamma)}(\xi,\zeta)}\int_{-\infty}^{\infty} \tau g^{(\Gamma)}(\xi,\zeta,\tau)\,\mathrm{d}\tau \qquad (27)$$

and the *conditional variance* is

$$\sigma_{T_1}^2 = \mathrm{var}[T|1] = \frac{1}{\beta}\int_{-\infty}^{\infty} t^2\alpha(t)\,\mathrm{d}t - \langle T_1\rangle^2 = \frac{1}{G^{(\Gamma)}(\xi,\zeta)}\int_{-\infty}^{\infty} \tau^2 g^{(\Gamma)}(\xi,\zeta,\tau)\,\mathrm{d}\tau - \langle T_1\rangle^2. \qquad (28)$$

We have previously shown (Arridge and Schweiger 1995) that the moments of $g^{(\Gamma)}(\xi,\zeta,\tau)$ can be efficiently calculated from its Fourier transform:

$$G^{(\Gamma,k)}(\xi,\zeta) = \int_{-\infty}^{\infty} \tau^k g^{(\Gamma)}(\xi,\zeta,\tau)\,\mathrm{d}\tau = (-\mathrm{i})^k \frac{\partial^{(k)}}{\partial\omega^{(k)}}\hat{G}^{(\Gamma)}(\xi,\zeta,\omega)|_{\omega=0} \qquad (29)$$

therefore we can write

$$\begin{aligned}\langle T_1\rangle &= G^{(\Gamma,1)}(\xi,\zeta)/G^{(\Gamma)}(\xi,\zeta)\\ \sigma_{T_1}^2 &= G^{(\Gamma,2)}(\xi,\zeta)/G^{(\Gamma)}(\xi,\zeta) - (G^{(\Gamma,1)}(\xi,\zeta)/G^{(\Gamma)}(\xi,\zeta))^2.\end{aligned} \qquad (30)$$

Now consider large N of which n photons are detected at ξ. The probability for this is represented by a binomial distribution

$$\begin{aligned}\Pr[n] &= B(\beta,N) = \binom{N}{n}\beta^n(1-\beta)^{(N-n)}\\ \langle n\rangle &= N\beta\\ \sigma_n^2 &= N\beta(1-\beta).\end{aligned} \qquad (31)$$

Now consider the *conditional probability* $\Pr[T|n]$ of an integrated time T occurring given that n photons were detected. Since the arrival of photons is uncorrelated, the conditional joint PDF of random variables $t_1, t_2, \ldots, t_n$ is just the product of individual probabilities

$$J(t_1,t_2,\ldots,t_n) = \prod_{i=1}^{n}\alpha(t_i)/\beta = \prod_{i=1}^{n} g^{(\Gamma)}(\xi,\zeta,t_i)/G^{(\Gamma)}(\xi,\zeta) \qquad (32)$$

and the conditional PDF for summed time T is given by the integral over the hyperplane $T = \sum_1^n t_i$:

$$\begin{aligned}p(T|n) &= \int_{T=\sum t_i} J(t_1,t_2,\ldots,t_n)\,\mathrm{d}^n t\\ &= \int_{-\infty}^{\infty}\mathrm{d}t_1\int_{-\infty}^{\infty}\mathrm{d}t_2\ldots\int_{-\infty}^{\infty}\mathrm{d}t_{n-1}\left[\alpha\left(T-\sum_{i=1}^{n-1}t_i\right)\Big/\beta\right]\prod_{i=1}^{n-1}\frac{\alpha(t_i)}{\beta}.\end{aligned} \qquad (33)$$

To find the unconditional PDF for T requires summation over each case

$$p(T) = \sum_{i=1}^{N} p(T|i)\Pr[i]. \qquad (34)$$

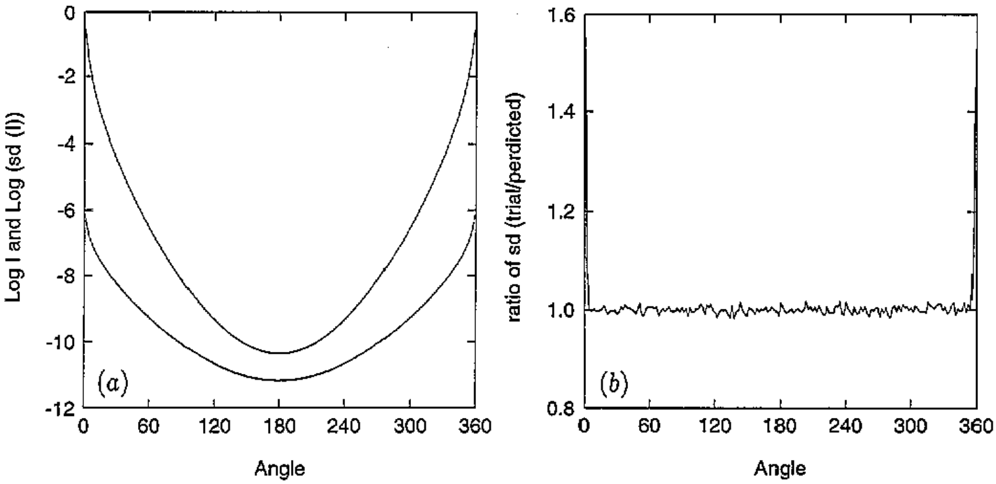

Figure 1. Results for a circle of radius 25 mm, $\mu_a = 0.025$ mm^{-1}, $\mu_s' = 2$ mm^{-1}: (*a*) mean (upper lines) and standard deviation (lower lines) of $\log I$ derived by adding noise to the TPSF (statistical trial—ST) and directly using (25) and (26) differences are not distinguishable; (*b*) the ratio of standard deviation derived from ST and directly using (26).

4.4.1. The limit of small N. If the number of received photons is small we consider the exact expression for $p(T)$ given in (34). By transformation of PDFs $p(\langle t\rangle) = np(T)$. It is trivial to show that

$$E[\langle t\rangle] = \int \langle t\rangle p(\langle t\rangle)\,\mathrm{d}\langle t\rangle = \langle T_1\rangle \tag{35}$$

(i.e. the mean of the population of means is the signal expectation value) and similarly

$$\sigma^2_{\langle t\rangle|n} = \sigma^2_{T_1}/n \tag{36}$$

(i.e. that the variance of the population of means is the signal variance over the sample size). We may then evaluate the unconditional variance

$$\sigma^2_{\langle t\rangle_N} = \frac{\sigma^2_{T_1}}{(1-(1-\beta)^N)}\sum_{n=1}^{N}\frac{1}{n}\binom{N}{n}\beta^n(1-\beta)^{(N-n)}. \tag{37}$$

Note that the denominator in (37) is the probability that any photons arrive. It is necessary to normalize by this value since if no photons arrive we have no sample of $\langle t\rangle$. Since β is very small, (37) will be dominated by the first term ($n = 1$) so that

$$\sigma^2_{\langle t\rangle_N} \approx \sigma^2_{T_1}(1 - N\beta). \tag{38}$$

In the case where N is large, but n is small (i.e. where $N\beta$ is small) the binomial distribution for n is well approximated by the Poisson distribution:

$$\begin{aligned} \Pr[n] &= [(N\beta)^n/n!]\mathrm{e}^{-N\beta} \\ \langle n\rangle &= N\beta \\ \sigma_n^2 &= N\beta. \end{aligned} \tag{39}$$

In this case

$$\sigma^2_{\langle t\rangle_N} = \frac{\sigma^2_{T_1}}{(\mathrm{e}^{N\beta}-1)}\sum_{n=1}^{N}\frac{1}{n}\frac{(N\beta)^n}{n!}. \tag{40}$$

Again, we expect that the first term will dominate giving the same approximation (38).

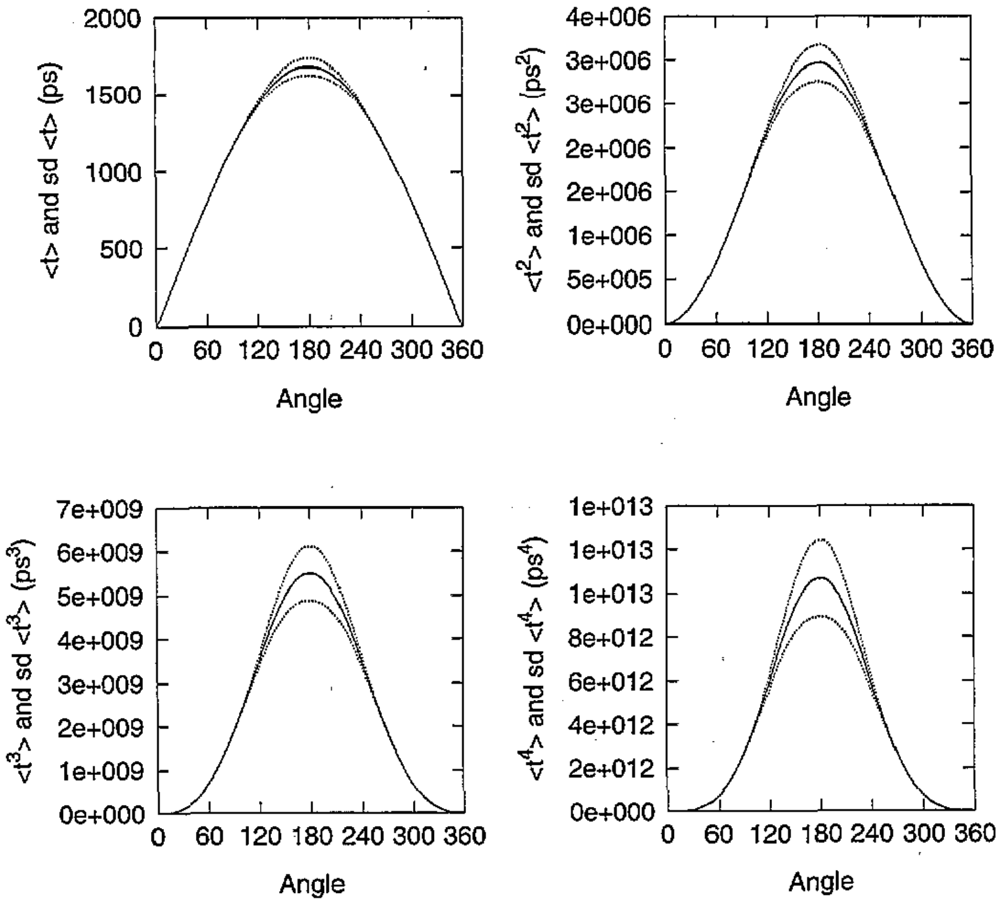

Figure 2. The first four temporal moments of the calculated TPSF (solid line) and bounds of $\pm$ one standard deviation derived from numerical integration of (50).

4.4.2. The limit of large N. For large N we may invoke the central limit theorem for the binomial distribution of n given in (31):

$$\Pr[n] \approx \left[1/\sqrt{2\pi N\beta(1-\beta)}\right] \exp[-\tfrac{1}{2}(n-N\beta)^2/N\beta(1-\beta)] \tag{41}$$

so that we may approximate the binomial in (37) (or the Poisson in (40)) by a normal distribution:

$$\sigma^2_{\langle t\rangle_N} = \frac{\sigma^2_{T_1}}{\sqrt{2\pi N\beta(1-\beta)}} \sum_1^N \frac{1}{n} \exp\left[-\frac{1}{2}\frac{(n-N\beta)^2}{N\beta(1-\beta)}\right]. \tag{42}$$

We may obtain an approximation by replacing the sum by an integral and using standard numerical integration methods:

$$\sigma^2_{\langle t\rangle_N} = \frac{\sigma^2_{T_1}}{\sqrt{2\pi N\beta(1-\beta)}} \int_1^N \frac{\mathrm{d}n}{n} \exp\left[-\frac{1}{2}\frac{(n-N\beta)^2}{N\beta(1-\beta)}\right]. \tag{43}$$

As a further simplification we note that

$$\lim_{a\to\infty} \frac{1}{\sqrt{2\pi}a} \exp\left[-\frac{1}{2}\frac{(x-b)^2}{a^2}\right] = \delta(x-b) \tag{44}$$

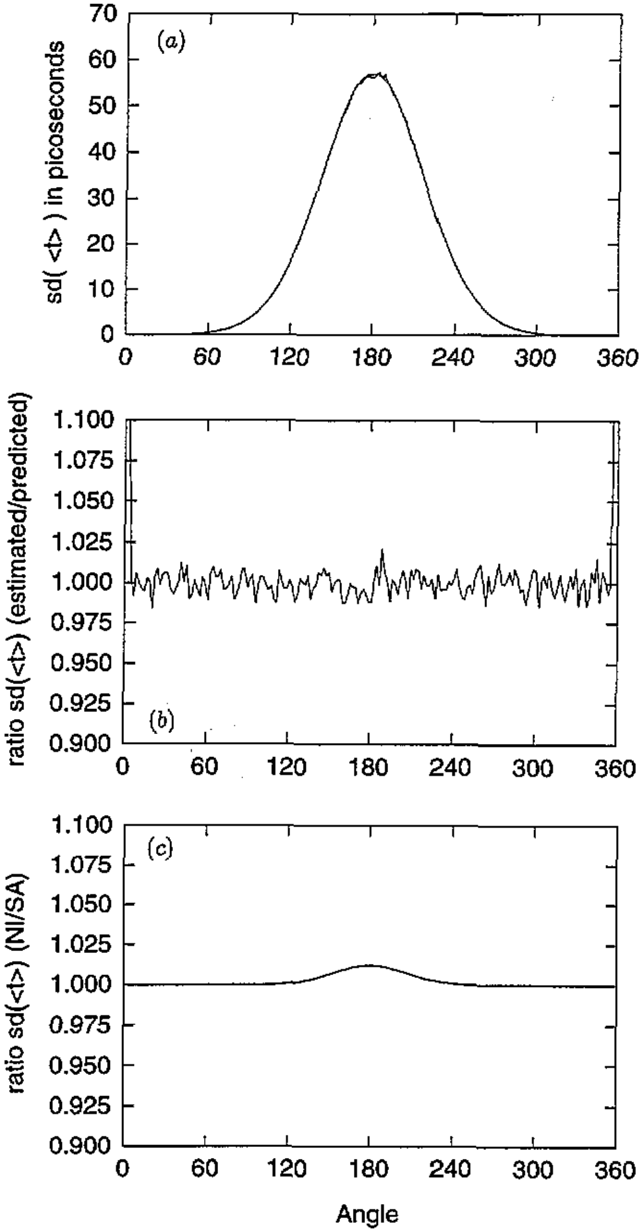

Figure 3. (a) The standard deviation of $\langle t \rangle$, estimated from trials (ST—solid line), and predicted by numerical integration (NI—dashed line) of (43) for 10^{12} photons input. (b) The ratio of ST/NI. (c) The ratio of NI over the simple approximation (SA) prediction of (46).

is a standard form for a δ function. Thus we can approximate (43) by

$$\lim_{N\to\infty} \sigma^2_{\langle t \rangle_N} = \sigma^2_{T_1} \int_1^N \frac{\mathrm{d}n}{n} \delta(n - N\beta) \tag{45}$$

so that the final result for the variance is approximated by

$$\sigma^2_{\langle t \rangle_N} \approx \sigma^2_{T_1} / N\beta. \tag{46}$$

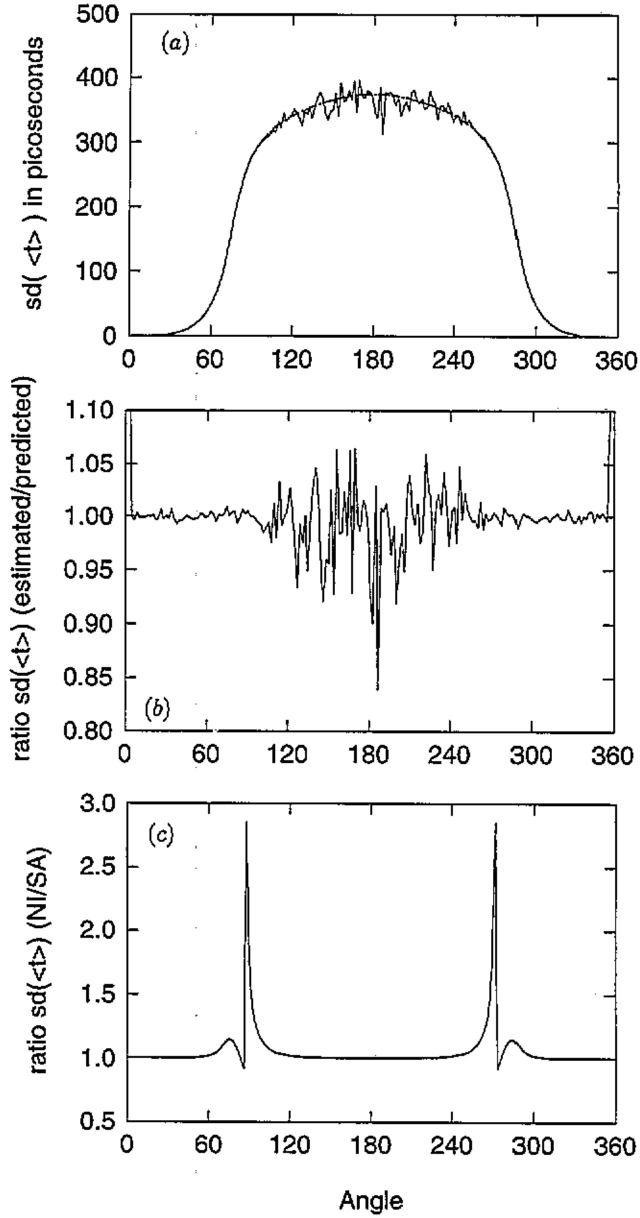

Figure 4. As figure 3 for 10^8 photons input. In (*c*) the simple approximation is given by (38) if $N\beta < 1$ (i.e. large angles) and by (46) if $N\beta > 1$ (i.e. small angles), with a crossover region where the approximation does not hold.

For this we note (i) that the standard deviation scales by $1/N^{1/2}$ as expected and (ii) the variance of the mean time is given by the ratio of the conditional variance of a single received photon, divided by the mean received intensity. Note the very different forms of these limiting expressions—(38) and (46).

4.5. Statistics of higher moments

We can repeat the above argument identically for the calculation of the variance of higher moments $\langle t^2 \rangle$, $\langle t^3 \rangle$ etc. All that is required is a method of determining the conditional means and variances:

$$\langle T_1^k \rangle = E[T^k|1] = \frac{1}{\beta} \int_1^N t^k \alpha(t)\, \mathrm{d}t \tag{47}$$

$$\sigma^2_{T_1^k} = \mathrm{var}[T^k|1] = \frac{1}{\beta} \int_{-\infty}^{\infty} t^{2k} \alpha(t)\, \mathrm{d}t - \langle T_1^k \rangle^2. \tag{48}$$

Using the same notation as (29) we can write

$$\begin{aligned} \langle T_1^k \rangle &= G^{(\Gamma,k)}(\xi,\zeta)/G^{(\Gamma)}(\xi,\zeta) \\ \sigma^2_{T_1^k} &= G^{(\Gamma,2k)}(\xi,\zeta)/G^{(\Gamma)}(\xi,\zeta) - (G^{(\Gamma,k)}(\xi,\zeta)/G^{(\Gamma)}(\xi,\zeta))^2. \end{aligned} \tag{49}$$

We will get as above

$$\sigma^2_{\langle t^k \rangle_N} = \frac{\sigma^2_{T_1^k}}{\sqrt{2\pi N\beta(1-\beta)}} \int_1^N \frac{\mathrm{d}n}{n} \exp\left\{ -\frac{1}{2} \left[\frac{(n-N\beta)^2}{N\beta(1-\beta)} \right] \right\} \tag{50}$$

with for large N

$$\sigma^2_{\langle t^k \rangle_N} \approx \sigma^2_{T_1^k}/N\beta. \tag{51}$$

5. Results

5.1. Diffusion-modelled noise

The diffusion equation was solved numerically using a finite-element method (FEM) described by Arridge *et al* (1993). The FEM program was run to produce TPSF data at all boundary elements of a circle of radius 25 mm, $\mu_a = 0.025\ \mathrm{mm}^{-1}$, $\mu_s' = 2\ \mathrm{mm}^{-1}$. The number of time samples was 800, with a time step Δt of 5 ps. For each angle, we generated a noisy TPSF in the following way.

```
repeat Ntrials times [
    for each angular position ξ_m [
        for each time step t_i    [
            1. generate a random number r drawn from a binomial distribution B(a, N),
            where a = Γ(ξ_m, t_i)δSΔt, and N is the number of photons.
            2. Γ'(i) = Γ(ξ_m, t_i) + r
        ]
        Form sample statistics {I_k(ξ_m), ⟨t⟩_k(ξ_m), ⟨t²⟩_k(ξ_m) ...} from Γ'(i), where k is
        the number of the trial
    ]
]
Form mean and standard deviation estimates of each statistic from the Ntrials samples
```

In the following results *Ntrials* $= 10\,000$ and δS was assumed to be unity. In figure 1(*a*) we show the mean and standard deviation of $\log I$, on a log scale, for $N = 10^{12}$ photons, calculated with this simulation and with the prediction of (25) and (26). To highlight any differences, we show also the ratio of the standard deviations in figure 1(*b*). Apart from the zero-angle point (i.e. where the source is) the two methods give almost identically the same result.

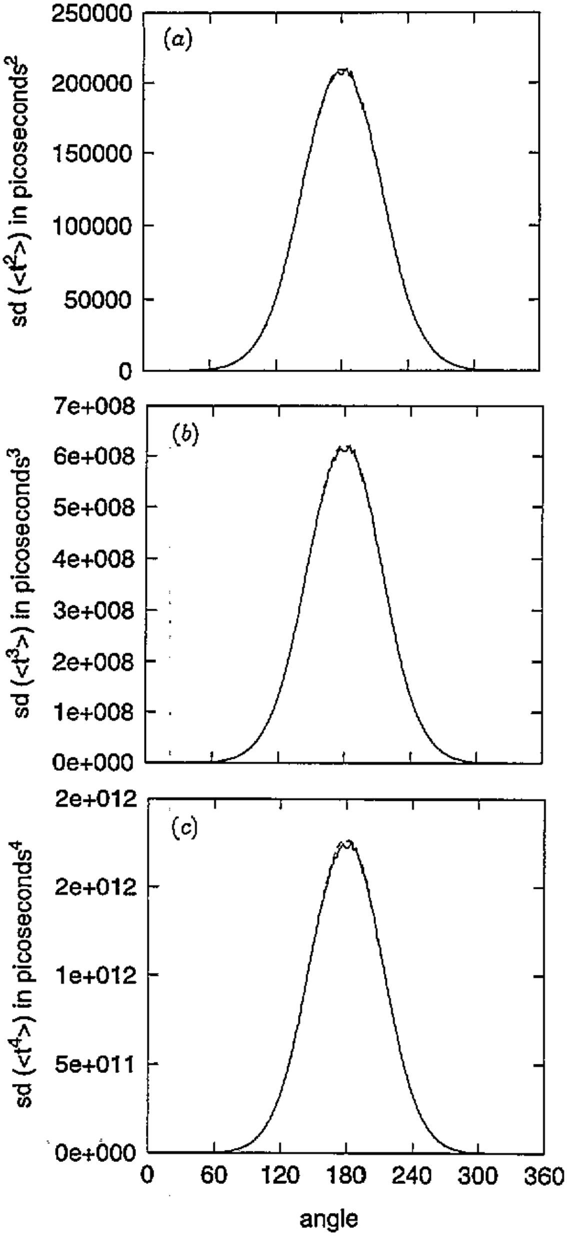

Figure 5. The standard deviation, estimated from trials (ST—solid line), and predicted by numerical integration (NI—dashed line) of (47) for 10^{12} photons input: (*a*) second moment; (*b*) third moment; (*c*) fourth moment.

In figure 2 we show the values of the temporal moment statistics with their standard deviations, as calculated from numerical integration of (50). In figure 3(*a*) we compare this estimate of standard deviation with the statistical trial. In figure 3(*b*) we show the ratio of these for the first moment (mean time) where again the agreement is excellent. In figure 3(*c*) we show the ratio of the two predictors (numerical integration of (43)/simple approximation by (46)). The result is better than 1% for this number of photons.

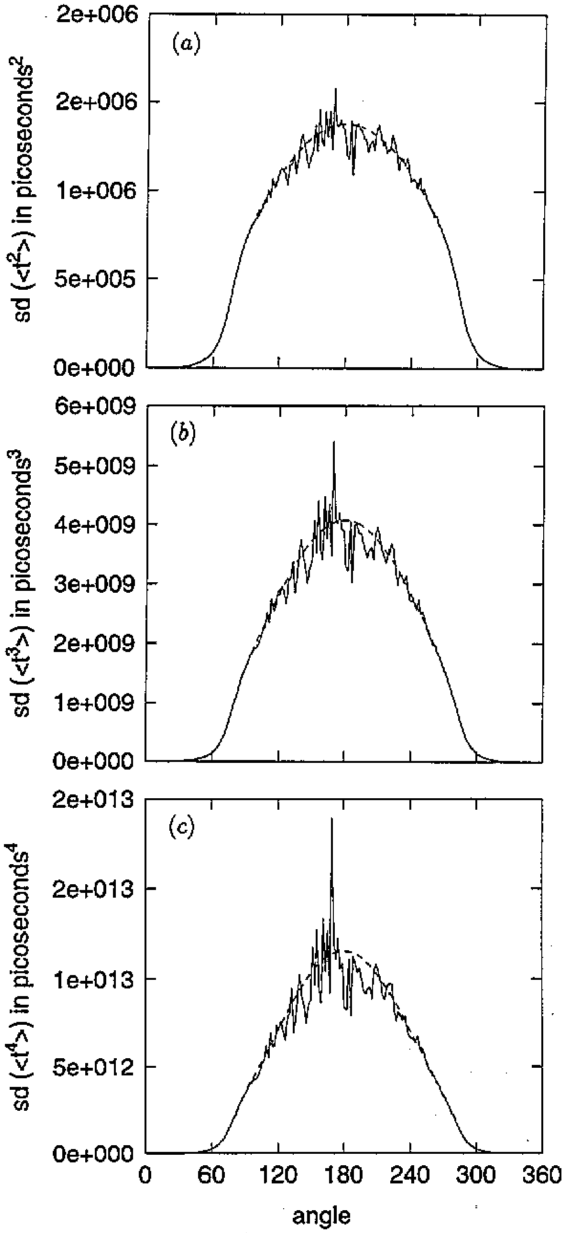

Figure 6. As figure 5 for 10^8 photons input.

In figure 4 we show the same results as figure 3 for 10^8 input photons. In this case the simple approximation is given by (38) if $N\beta < 1$ and by (46) if $N\beta > 1$. There is a crossover region where neither approximation applies.

In figure 5 we show the standard deviation of the second, third and fourth moments for 10^{12} photons. All are predicted with high accuracy. In figure 6 we show the same results for 10^8 photons.

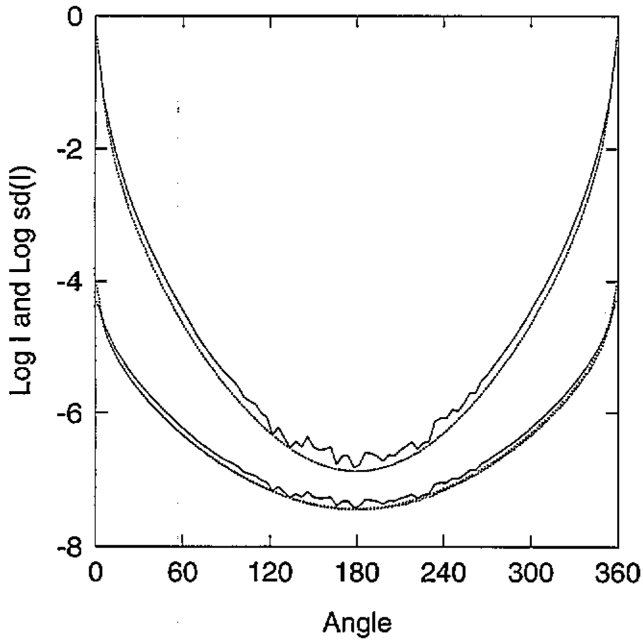

Figure 7. $\log I$ and log standard deviation of I, from AMC (solid), statistical trial (dashed) and predicted by (26) (dotted), for 10^8 photons in an infinite homogeneous cylinder of radius 15 mm, $\mu_a = 0.025\ \text{mm}^{-1}$, $\mu_s' = 2\ \text{mm}^{-1}$, with isotropic phase function.

5.2. Comparison with Monte Carlo

The AMC algorithm described in section 3 was run for an infinite homogeneous cylinder of radius 15 mm, $\mu_a = 0.025\ \text{mm}^{-1}$, $\mu_s' = 2\ \text{mm}^{-1}$, with isotropic phase function. 10^8 photons were simulated and binned into 4° intervals around the perimeter, with infinite bin length in the z direction giving $\delta S = r\Delta\theta = \pi/3$. Figure 7 shows the predicted standard deviation of intensity from (26) and the Monte Carlo estimated sample standard deviation on a log scale. Also shown in this figure is the result of a statistical trial of the form described in subsection 5.1. The agreement is excellent, although the prediction is slightly underreading the sample.

Figure 8(a) shows the predicted standard deviation for $\langle t\rangle$, with the estimator derived from (43), from the AMC and from the statistical trial. Again the agreement is excellent, although in this case the prediction appears slightly to overestimate the sample. Note that in the Monte Carlo case, the estimate of standard deviation is derived from just one sample, because at each angle only one estimate of $\langle t\rangle$ and $\langle t^2\rangle$ is available. We would expect such an estimator to be quite a poor one, especially in regions where the number of detected photons is low—for example at the 180° position, only 15 photons were collected. By contrast the statistical trial is derived from 10 000 sample estimates and is much closer to the theoretical value, as can be seen clearly in figure 8(a). Although the Monte Carlo's self-estimate of $\sigma_{\langle t\rangle}$ is poor, and may be biased, we believe the theoretical estimate to be correct and unbiased, as demonstrated in figure 8(b) wherein the $\langle t\rangle$ values are seen to be distributed about the theoretical value and well within the bounds of $\pm 3\sigma_{\langle t\rangle}$.

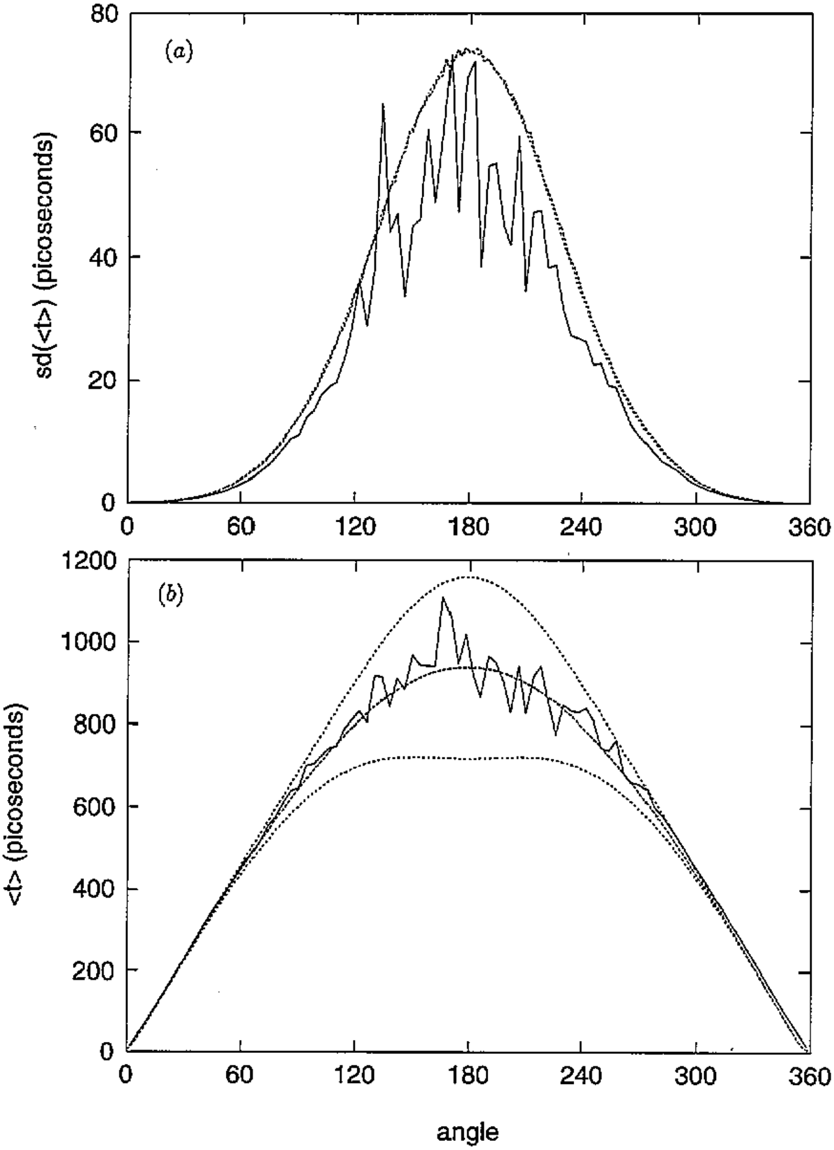

Figure 8. (*a*) The standard deviation of $\langle t\rangle$ from AMC (solid) statistical trial (dashed) and calculated by numerical integration of (43) (dotted), for 10^8 photons; (*b*) $\langle t\rangle$ from AMC (solid) and direct computation by FEM (dashed) with bounds of $\pm$ three standard deviations (dotted) as predicted by (43), for 10^8 photons.

5.3. *Extension to experimental conditions*

In an actual experiment, it is not usual to use exactly the same collection times at each measurement site. In fact, for positions close to the source it is usual to *attenuate* the intensity in order not to overload the detection device. In these circumstances it is not appropriate to use the expected number of photons $N\beta$. However we can recognize that $N\beta$ is just the mean number of *received* photons, and if large enough, is a good predictor of the expected value. Thus the formulae in (43) and (50) can still be used, provided that

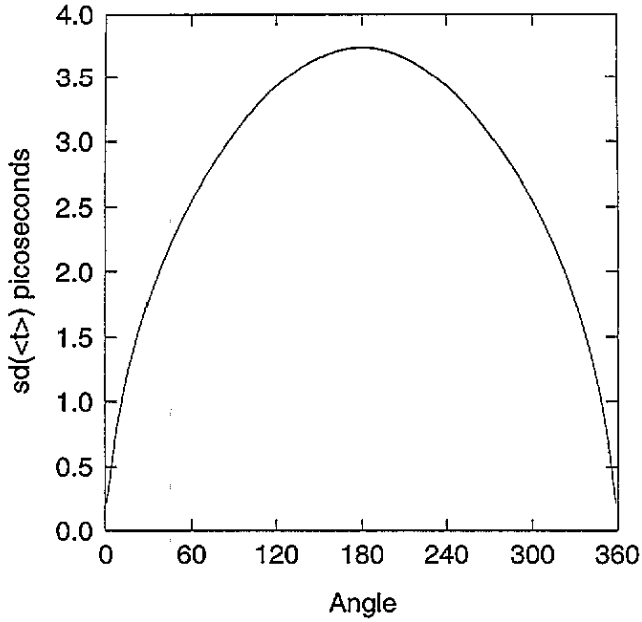

Figure 9. The prediction of the standard deviation of $\langle t \rangle$ for the circle of radius 25 mm, $\mu_a = 0.025\ \mathrm{mm}^{-1}$, $\mu_s' = 2\ \mathrm{mm}^{-1}$, assuming that 10^4 photons are collected at each detector.

the limits of integration are sufficiently large. Since in this case the photons are assumed to arrive with Poisson statistics, we simply use the mean as an estimator of the variance. Figure 9 shows the prediction of standard deviation of $\langle t \rangle$ for the same model as used in figure 3, but with the assumption of 10^4 photons detected at each measurement. The corresponding standard error of I would be 1%.

6. Conclusions

We have derived a method to predict the mean and variance of statistical measures derived from the temporal distribution of photon time of flight in tissue, by using a finite-element implementation of the diffusion approximation. We have concentrated on demonstrating the agreement with an AMC model. Although we demonstrated results using a simple geometry and homogeneous conditions, nothing in our theory was limited to such cases. We thus postulate that we may derive standard deviations of any measure for any geometry and distribution of optical parameters.

It is possible to extend the theory described here to other Monte Carlo algorithms although the extension to inhomogeneous conditions is much more complex. Since this is a large topic it will be the subject of a subsequent paper. However the main significance of our theory is to produce a predictor of noise in experiments, which is justified by the argument that AMC is the best description of the real physical process of light propagation. Thus we are now able to more realistically simulate experimental data, including noise, a factor of particular importance in testing parameter fitting algorithms and image reconstruction techniques.

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Appendix A. Alternative calculation of var[$\langle t\rangle$]

This appendix provides an alternative method for deriving the limiting form of var[$\langle t\rangle$] for large numbers of photons. For large enough N we can assume that sufficient photons n arrive that the central limit theorem applies so that T is drawn from a Gaussian distribution of mean $\langle T_n\rangle = n\langle T_1\rangle$ and variance $\sigma_{T_n}^2 = n\sigma_{T_1}^2$

$$p(T|n) = \left(1/\sqrt{2\pi n\sigma_{T_1}^2}\right)\exp[-\tfrac{1}{2}(T - n\langle T_1\rangle)^2/n\sigma_{T_1}^2]. \tag{A1}$$

To find the total PDF $p(T)$ we sum over all possible numbers of detected photons:

$$p(T) = \sum_{n=1}^{n=N}\left\{\frac{1}{\sqrt{2\pi n\sigma_{T_1}^2}}\exp\left[-\frac{1}{2}\frac{(T - n\langle T_1\rangle)^2}{n\sigma_{T_1}^2}\right]\binom{N}{n}\beta^n(1-\beta^{(N-n)})\right\}. \tag{A2}$$

To find $p(\langle t\rangle)$ we simply note that $\Pr(\langle t\rangle|n) = \Pr(T = n\langle t\rangle, n)$, i.e. that the conditional probability of the mean time being $\langle t\rangle$ given that n photons were detected is exactly the conditional probability of the integrated time being $n\langle t\rangle$. We may therefore put

$$p(\langle t\rangle) = \sum_{n=1}^{n=N}\left\{\frac{n^{1/2}}{\sqrt{2\pi\sigma_{T_1}^2}}\exp\left[-\frac{1}{2}\frac{(n\langle t\rangle - n\langle T_1\rangle)^2}{n\sigma_{T_1}^2}\right]\binom{N}{n}\beta^n(1-\beta^{(N-n)})\right\}. \tag{A3}$$

To obtain an analytic expression we substitute (41) into (A3) and make two further assumptions: (i) that the summation may be replaced by an integral, and (ii) that the limits of the integral are $[-\infty \to \infty]$. Both of these are certainly reasonable if we have assumed the central limit theorem, since N will be sufficiently large that the probability of $n = 1$, or $n = N$, is negligible. We now have the following:

$$p(\langle t\rangle) = \int_{-\infty}^{\infty}\mathrm{d}n\left\{\frac{n^{1/2}}{2\pi\sqrt{\sigma_{T_1}^2 N\beta(1-\beta)}}\exp -\frac{1}{2}\left[\frac{(n\langle t\rangle - n\langle T_1\rangle)^2}{n\sigma_{T_1}^2} + \frac{(n - N\beta)^2}{N\beta(1-\beta)}\right]\right\}. \tag{A4}$$

Rearranging

$$p(\langle t\rangle) = \frac{1}{2\pi\sqrt{\sigma_{T_1}^2 N\beta(1-\beta)}}\int_{-\infty}^{\infty}\mathrm{d}n\sqrt{n}\exp\left\{-\frac{1}{2}\left[\frac{n^2}{N\beta(1-\beta)} + n\left(\frac{(\langle t\rangle - \langle T_1\rangle)^2}{\sigma_{T_1}^2} - \frac{2}{(1-\beta)}\right) + \frac{N\beta}{(1-\beta)}\right]\right\}. \tag{A5}$$

We want to find the variance of $\langle t\rangle$ given by $E[\langle t\rangle^2] - (E[\langle t\rangle])^2$. We can see by inspection that $p(\langle t\rangle)$ is symmetric around $\langle T_1\rangle$ so that $E[\langle t\rangle] = \langle T_1\rangle$. To evaluate the variance, we can substitute $z = \langle t\rangle - \langle T_1\rangle$ to give

$$\sigma_{\langle t\rangle_N}^2 = \frac{1}{2\pi\sqrt{\sigma_{T_1}^2 N\beta(1-\beta)}}\int_{-\infty}^{\infty}z^2\,\mathrm{d}z\int_{-\infty}^{\infty}\mathrm{d}n\sqrt{n}\exp\left\{-\frac{1}{2}\left[\frac{n^2}{N\beta(1-\beta)} + n\left(\frac{z^2}{\sigma_{T_1}^2} - \frac{2}{(1-\beta)}\right) + \frac{N\beta}{(1-\beta)}\right]\right\}. \tag{A6}$$

By changing the order of integration we obtain

$$\sigma^2_{\langle t\rangle_N} = \frac{\sigma^2_{T_t}}{\sqrt{2\pi N\beta(1-\beta)}} \int_{-\infty}^{\infty} \frac{\mathrm{d}n}{n} \exp\left\{-\frac{1}{2}\left[\frac{(n-N\beta)^2}{N\beta(1-\beta)}\right]\right\} \tag{A7}$$

which is the same as given by (43), apart from the extreme ends of the integral, which we assume are negligible.

References

Arridge S R 1993 The forward and inverse problems in time-resolved infra-red imaging *Medical Optical Tomography: Functional Imaging and Monitoring* ed G Muller *et al* (Bellingham, WA: SPIE) pp 35–64

Arridge S R, Cope M and Delpy D T 1992 Theoretical basis for the determination of optical pathlengths in tissue: temporal and frequency analysis *Phys. Med. Biol.* **37** 1531–60

Arridge S R and Schweiger M 1995 Direct calculation of the moments of the distribution of photon time of flight in tissue, using a finite element method *Appl. Opt.* 34 2683–7

Arridge S R, Schweiger M, Hiraoka M and Delpy D T 1993 A finite element approach for modelling photon transport in tissue *Med. Phys.* **20** 299–309

Arridge S R, van der Zee P, Delpy D T and Cope M 1991 Reconstruction methods for infra-red absorption imaging *Proc. SPIE* **1431** 204–15

Bonner R F, Nossal R, Havlin R, Weiss G H 1987 Model for photon migration in turbid biological media *J. Opt. Soc.* 4 423–32

Bremmer H 1964 Random volume scattering *Radio Sci. J. Res.* **680** 967–81

Case M C and Zweifel P F 1967 *Linear Transport Theory* (New York: Addison-Wesley)

Chandrasekhar R 1950 *Radiation Transfer* (Oxford: Clarendon)

Delpy D T, Cope M, van der Zee P, Arridge S R, Wray S and Wyatt J 1988 Estimation of optical pathlength through tissue from direct time of flight measurement *Phys. Med. Biol.* **33** 1433–42

Flock S T, Patterson M S, Wilson B C and Wyman D R 1989 Monte Carlo modelling of light propagation in highly scattering tissues—I: model predictions and comparison with diffusion theory *IEEE Trans. Biomed. Eng.* **BME-36** 1162–8

Groenhuis R A J, Ferwada H A and Ten Bosch J J 1983 Scattering and absorption of turbid materials determined from reflection measurements (parts 1 and 2) *Appl. Opt.* **22** 2456–67

Grünbaum F A, Kohn P D, Latham G A, Singer J R and Zubelli J P 1991 Diffuse tomography *Proc. SPIE* **1431** 232–8

Hiraoka M, Arridge S R and Delpy D T 1994 A new Monte Carlo algorithm for the description of light transport in tissue *Proc. 7th Int. Workshop on Multiple Scattering Lidar Experiments (MUSCLE7) (Chiba, 1994)* (Chiba: Chiba University) pp 74–7

Kaltenbach J P and Kaschke M 1993 Frequency- and time-domain modelling of light transport in random media *Medical Optical Tomography: Functional Imaging and Modelling* ed G Muller *et al* (Bellingham, WA: SPIE) pp 65–86

Lewis H W 1950 Multiple scattering in an infinite medium *Phys. Rev.* **78** 526–9

Lux I and Koblinger L 1991 *Monte-Carlo Particle Transport Methods: Neutron and Photon Calculations* (Boston, MA: Chemical Rubber Company)

Madsen S J, Patterson M S, Wilson B C, Park Y D, Moulton J D, Jaques S L and Hefetz Y 1991 Time resolved diffuse relectance and transmittance studies in tissue simulating phantoms: a comparison between theory and experiment *Proc. SPIE* **1431** 42–51

Patterson M S, Wilson B C and Wyman D R 1991 The propagation of optical radiation in tissue 1: models of radiation transport and their application *Lasers Med. Sci.* **6** 155–68

van der Zee P and Delpy D T 1987 Simulation of the point-spread function for light in tissue *Adv. Exp. Med. Biol.* **215** 179–92

Wilson B C and Adam G 1983 A Monte-Carlo model for the absorption and flux distribution of light in tissue *Med. Phys.* **10** 824–30