Tissue structural organization: Measurement, Interpretation, and Modeling

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ABSTRACT

Analysis of the first and second order statistical properties of light is a powerful means of establishing the properties of a medium with which the light has interacted. In turn, the first second order statistical properties of the medium dictate the manner in which light interacts with the medium. The former is the inverse problem and the latter is the forward problem. Towards an understanding of the propagation of light through complex structures, such as biological tissue, one might choose to explore either the inverse or the forward problem. Fundamental to the problem, however, is a physical parametric model that relates the two halves; a model that allows prediction of the measured effect or prediction of the parameters based on measurements. This is the objective of our study. As a means of characterizing the first and second order properties of tissue, we discuss measurements with differential interference contrast microscopy using a phase-stepping approach. First and second order properties are characterized respectively in terms of scatter phase functions and spatial power spectral densities. Results are shown for representative tissue.

Keywords: DIC, Monte Carlo, turbulent medium

1. INTRODUCTION

The propagation of light in complex, strongly-scattering random media is an important problem in diagnostic imaging and remote sensing [1-5]. Specific applications include laser communication through the atmosphere [1, 2], imaging in biological media and (underwater) littoral environments [3-5], and imaging in extreme environments such as turbulent combustion.

Due to the complexity of the interaction in strongly scattering media (such as biological tissue), physical optics (PO) methods of analysis are infeasible. In such cases, researchers have relied almost exclusively upon Monte Carlo (MC) methods based on radiative transfer theory [6-8]. Such methods employ an effective medium concept that views the medium as having certain scatter and absorption characteristics that are otherwise uniformly distributed. In other words, the medium is viewed as being homogeneous. Objects embedded within the medium (about which information may be desired) are viewed as having different scatter and absorption properties, but are otherwise assumed homogeneous as well. While this has been successful in mimicking empirical results, the method conveys no information about the actual light-matter interaction.

In a recent series of publications, we have introduced a copula-based algorithm for generating arbitrarily correlated field realizations [9]; introduced a Monte Carlo-based ray trace concept for describing propagation (including diffraction effects) in paraxial systems [10]; and a Greens function concept for propagation of coherence in high NA systems [11]. What remains is the development of structured stochastic models of the propagation medium. This is the objective here.

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2. MODEL

Ideally one would like to independently specify the first and second order properties of a scattering medium. Thus the model could describe empirically observed scatter properties. A common model employed for describing propagation through atmospheric turbulence is that of a weak phase screen [1]. To demonstrate why such a model may not be appropriate for describing propagation through biological tissues for example, we briefly describe such an approach.

2.1 Gaussian random phase screens

Current theory for scattering from a phase screen begins with the transmittance characterization

$$T(x,y) = \exp\left[i\phi(x,y)\right], \tag{1}$$

where it is assumed that $\phi(x,y)$ is a Gaussian random process (GRP). Under the assumption that ϕ is at least a wide-sense stationary process, we're lead to the following expression for the second moment of the field transmitted by the screen:

$$\Gamma(x,y;x',y') = E\left\{T(x,y)T^{*}(x',y')\right\} = \Gamma(s) = \exp\left\{-\sigma_{\phi}^{2}\left[1-\rho(s)\right]\right\}, \tag{2}$$

where

$$s = \sqrt{(x-x')^{2}+(y-y')^{2}}\ . \tag{3}$$

To generate random realizations of these phase screens, one can make use of the power spectral domain (PSD) algorithm [12], which allows us to independently specify the proper first and second order properties.

The problem with this approach becomes apparent if one considers the ray deflection angle that is generated. The angular deviation of a ray transmitted through a phase screen is a function of the local phase derivative. In the small angle approximation this angular deviation, say in the *x*-direction, θ_x, is

$$\theta_x \approx \frac{1}{k}\frac{\partial\phi(x,y)}{\partial x}. \tag{4}$$

From this expression, it's clear that the ray deviation is also distributed Gaussian. So how do we resolve this with the observation that the angular scatter from biological tissues, for example, is decidedly non-Gaussian? This leads to the idea of a random scatter screen.

2.2 Random scatter screens

Rather than attempting to simulate the phase effect of a scattering medium on the wavefield, we envision simulating the angular deviation itself. There are two general approaches one might take to accomplish this. The first is to generate a random realization of a real physical screen with prescribed first order (local slope) and second order statistics. In this case, the resulting angular deviation would be described in terms of Snell's law. The second approach is to generate a realization of a random scatter *rule*. Consider the illustration shown in Fig. 1.

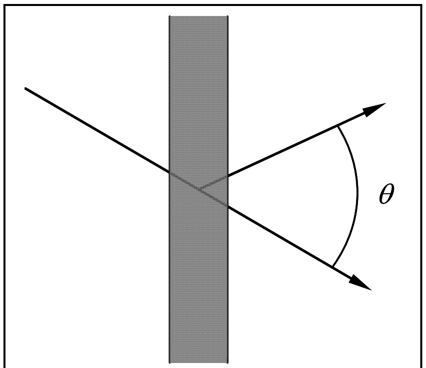

Fig. 1 Illustration of scattering screen

For a ray incident from an arbitrary direction, we directly randomize the scatter direction θ. This is a bit simpler that generating random realizations of a physical dielectric screen and then having to compute the angular deviations. It has the further advantage that specification of scatter into the back hemisphere is completely straightforward.

Specification of particular instantiations of scatter directions is not something new; it is the basis of all Monte Carlo codes for propagation through strongly scattering media. What is new, is the requirement that the angular deviations for closely-spaced incident rays be correlated. In other words, the scattering rule must describe a scattering screen with correlated local structure;

parallel, closely spaced incident rays must be deflected in a similar (correlated) fashion. For completeness, however, we briefly review the idea of generating random realizations of angular ray deviations.

To begin, we assume that the angular ray deviation in the polar and azimuthal directions is statistically independent.

$$p(\phi,\theta) = p_\Phi(\phi)\, p_\Theta(\theta) \tag{5}$$

Further, we assume that the azimuthal distribution is uniform over the $(0, 2\pi)$ interval,

$$p_\Phi(\phi) = \frac{1}{2\pi}\,. \tag{6}$$

Although there are many analytic and numerical polar angle distribution functions that could be used, we illustrate the technique with a particular analytic description, the so-called Henyey-Greenstein phase function [13],

$$P_\Theta(\theta) = P_{HG}(\theta) = \frac{1}{2}\frac{1-g^2}{\left(1-2g\cos\theta+g^2\right)^{3/2}}\,, \tag{7a}$$

where g is the asymmetry parameter defined as

$$g = E\{\cos\theta\} = \int_0^{2\pi} d\phi\, p_\Phi(\phi) \int_0^{\pi} d\theta\, p_\Theta(\theta)\cos\theta\sin\theta\,. \tag{7b}$$

It is well known that a pair of random instantiations of θ and ϕ can be generated from a pair of uniformly distributed deviates, r_1 and r_2 with use of the following formulas:

$$\phi = 2\pi r_1$$
$$\cos\theta = \frac{1}{2g}\left[1+g^2-\left(\frac{1-g^2}{1-g+2gr_2}\right)^2\right] \tag{8}$$

Now envision a scatter screen as an $N\times N$ array of instantiations of θ and ϕ. If the underlying arrays of uniformly distributed deviates, r_1 and r_2, are uncorrelated, so too will be the array of θ and ϕ instantiations. We can develop a degree of local correlation using a variation on the PSD method [12]. Say we wish the local spatial correlation function to be Γ. By the Wiener-Khinchin theorem, this correlation function is related to the PSD through a Fourier transform;

$$S = F[\Gamma]\,. \tag{9}$$

We can generate an array of Gaussian random samples with the prescribed local correlation by use of the formula

$$y_1 = \mathrm{Re}\left\{F^{-1}\left[\exp(i2\pi u_1)\, S^{1/2}\right]\right\}, \tag{10}$$

where u_1 is an $N\times N$ array of independent samples from a uniform distribution. Transformation of these Gaussian realizations via the cumulative distribution function [14] yields an array of locally correlated uniformly distributed samples, r_1. A repeat of the above algorithm using another set of uniform deviates, u_2 provides another array, r_2. Equations 8 subsequently provide the required instantiations of polar and azimuthal deviates, θ and ϕ.

As an example, say we wish to generate a 256×256 array of θ and ϕ instantiations that exhibit a Gaussian autocorrelation function, although many other forms are possible, such as fractal spatial behaviors, Lorentzian, etc. [12]. Further suppose that we desire a $1/e$ correlation length of 5 pixels and an asymmetry parameter, $g = 0.9$. The required

PSD S is easily calculated. The resulting realizations of θ and ϕ are shown in Fig. 2, and their first order statistics are shown in Fig. 3. The second order statistics are quite similar. That for the azimuthal angle is shown in Fig. 4a. Since the PSD has a "speckled" appearance, an azimuthal integration was performed to facilitate comparison with the specified PSD (Fig. 4b).

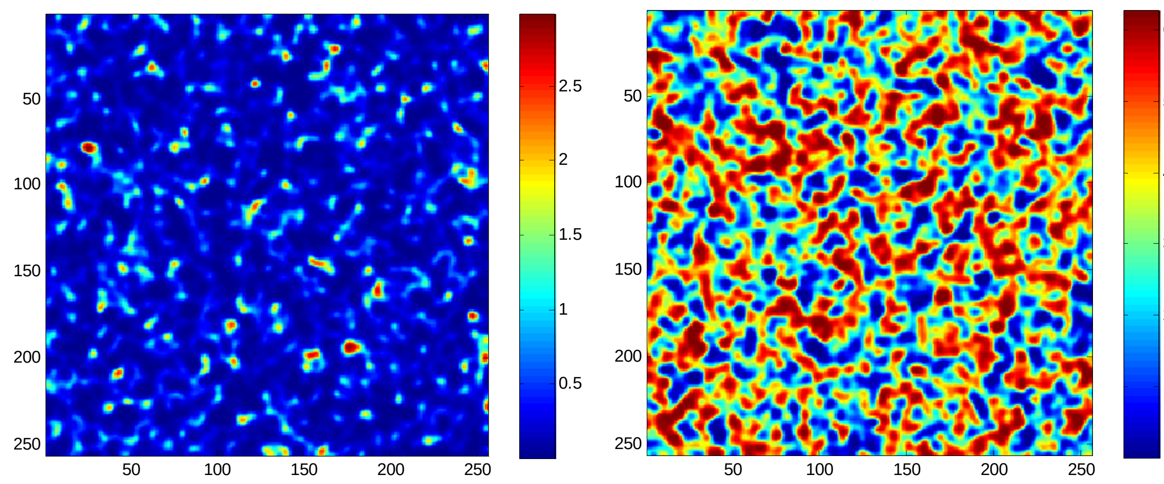

Fig 2 Random realizations of polar angle θ (left) and azimuthal angle ϕ (right)

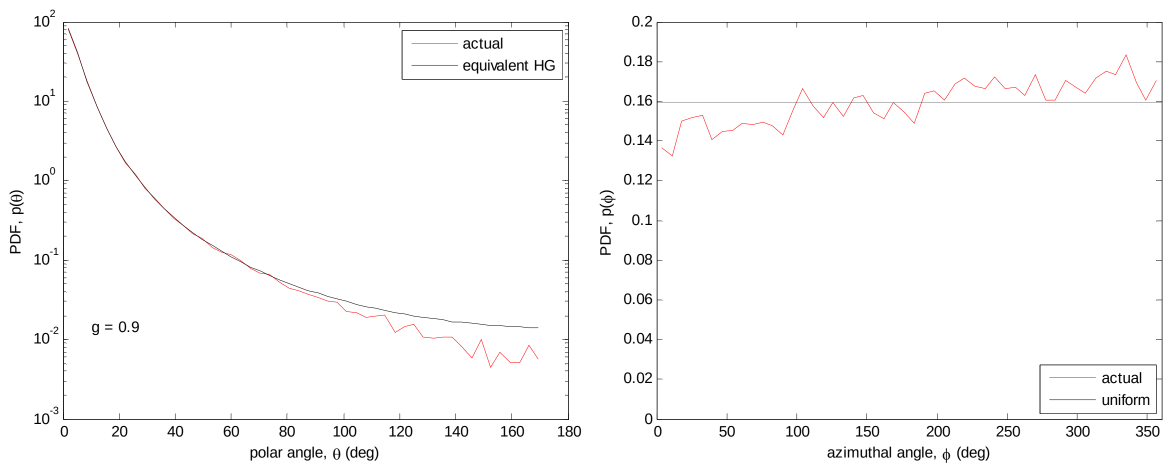

Fig. 3 First order statistics for polar angle (left) and azimuthal angle (right)

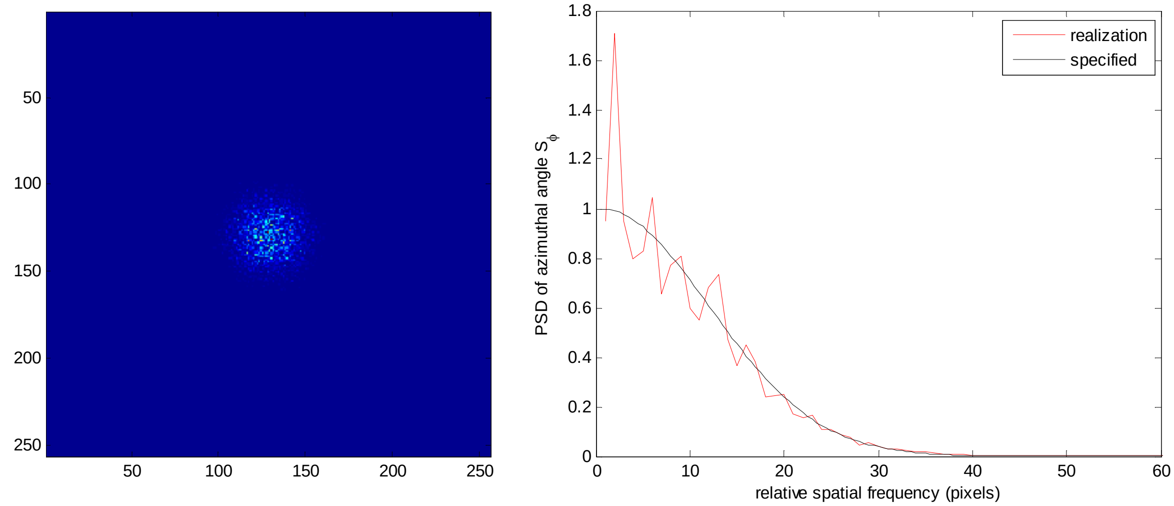

Fig. 4 PSD of azimuthal angle realization (left) and angular integration of PSD (right)

3. TISSUE CHARACTERIZATION

From the preceding, it's clear that we must characterize the medium in terms of an asymmetry parameter and a spatial autocorrelation function. Differential interference contrast imaging (DIC) [15] provides a means of doing so.

DIC microscopy yields an image of the form

$$I_D(x,y) = I_o(x,y)\left\{1+\cos\left[s\frac{\partial\phi(x,y)}{\partial x}+\Psi\right]\right\}, \tag{10}$$

where s is the amount of shear (here assumed to be in the x-direction), and ψ is the bias (which is an adjustable setting on the second Wollaston prism). Recall from the previous discussion that the ray deflection angle is dictated by the local phase gradient;

$$\text{ray deflection, } \theta_x = \sin^{-1}\left[\frac{1}{k}\frac{\partial\phi(x,y)}{\partial x}\right]. \tag{11}$$

From this expression we see that by recovering the local phase gradient, one can determine the ray direction, and subsequently the complete first and second order statistics of the ray deflection angle, i.e., g and Γ. To accomplish this phase gradient recovery we are led to a phase stepping concept, such as the Carré method [16].

The model for the Carré method is

$$I_i = a + b\cos(\phi+\alpha_i) \tag{12}$$

If one chooses the phase steps

$$\alpha_i = -3\alpha/2,\, -\alpha/2,\, \alpha/2,\, 3\alpha/2, \tag{13}$$

where α generally is not known, but the phase steps are constant and equally spaced, then α and the angle ϕ can be recovered from the expressions

$$\tan\left(\frac{\alpha}{2}\right) = \sqrt{\frac{3(I_2 - I_3) - (I_1 - I_4)}{(I_2 - I_3) + (I_1 - I_4)}}$$

$$\tan\phi = \tan\left(\frac{\alpha}{2}\right)\frac{(I_1 - I_4) + (I_2 - I_3)}{(I_2 + I_3) - (I_1 + I_4)} \tag{14}$$

This procedure is obviously predicated on knowledge of the image shear and the bias increments incurred by successive turns of the bias setting knob on the Wollaston prism [17].

4. DISCUSSION AND CONCLUSIONS

We have presented an algorithm for creating a scatter screen model that is capable of matching the empirically observed characteristics of a structured scattering medium. Our example of this approach used a Gaussian correlation function for the second order spatial structure and a Henyey-Greenstein phase function model for the first order ray direction. Many other second order characterizations are possible, such as fractal, Lorentzian, etc. Other first order properties are possible as well, such as Mie, Rayleigh, or isotropic phase functions. Even tabulated phase functions, as observed in other propagation media, e.g. ocean water [18], are easily accommodated. Moreover, this algorithm lends itself to straightforward generalization using the concept of a copula [19] to generate a general phase matrix capable of describing polarization effects, correlated azimuthal and polar ray directions, or an ensemble of temporally evolving scattering screens [9].

Conceptually, the idea of a scatter screen is a phenomenological model rather than a physical one such as the phase screen. This approach allows separate specification of the first and second order statistics of scatter. The re-mapping of the first order statistics, for the phase screen model for example (see Eq. 1), would clearly affect the second order statistics as well. Independent specification of the first and second order properties should provide the capability of modeling scatter in a wide range of propagation media. The medium characterization that we've chosen is essentially that of the atmospheric propagation community [1], and follows many of the ideas suggested by Schmitt and Kumar [20].

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