Simulation on scattering features of biological tissue based on generated refractive-index model

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Abstract. Important information on morphology of biological tissue can be deduced from elastic scattering spectra, and their analyses are based on the known refractive-index model of tissue. In this paper, a new numerical refractive-index model is put forward, and its scattering properties are intensively studied. Spectral decomposition[1] is a widely used method to generate random medium in geology, but it is never used in biology. Biological tissue is different from geology in the sense of random medium. Autocorrelation function describe almost all of features in geology, but biological tissue is not as random as geology, its structure is regular in the sense of fractal geometry[2], and fractal dimension can be used to describe its regularity under random. Firstly scattering theories of this fractal media are reviewed. Secondly the detailed generation process of refractive-index is presented. Finally the scattering features are simulated in FDTD (Finite Difference Time Domain) Solutions software. From the simulation results, we find that autocorrelation length and fractal dimension controls scattering feature of biological tissue.

1. Introduction
Since J. M. Schmitt and G. Kumar[2] discuss the turbulent nature of biological tissue index, the fractal structure of biological tissue has been intensively studied[3,4,5]. Tissue images obtained by various imaging technology and tissue slice[6,7,8,9] are the most usually used and direct way to study biological tissue structures. And their results indeed shows that tissue structures ,such as vasoganglion under skin, membranes of organelles, texture of nucleus, are fractals[6,8,9]. Unfortunately the interaction between light and fractal structures is not studied enough.

J. M. Schmitt and G. Kumar[2] are pioneers of this topic. Based on their study of the mouse liver tissue image under phase-contrast microscopy, they found that the spectrum of tissue index variations possesses a power-law behavior over a range of scales. Inspired by the similar structure function of the classical Kolmogorov model of turbulence, they consider biological tissue index variation as a kind of turbulence too, and take it as the fundamental feature of biological tissue. Since then biological tissue can be called fractal random media.

M. Xu and R. R. Alfano[10] develop this theory. They start their study from the postulate that the biological tissue is a kind of continuous random media. Based on potential scattering theory and Born approximation, light scattering by continuous random media is modeled and studied. Their model shows that biological tissue is a complex of random media with different autocorrelation lengths of fractal distribution. In their theory, the scattering properties derived from this model, e.g. reduced scattering coefficient, the anisotropy factor, the phase function are studied.

Because of the complexity of biological tissue, all the research groups above use approximates in their work, and one thing more they ignore one nature of lights that lights are vectors with phases and polarization states in their theory. FDTD (Finite Difference Time Domain)[11] is a numerical method solving Maxwell’s equations, and a powerful tool to study scattering problems of structures. Applying
this method, there are two advantages. One is unlimited structures that can be studied, another is full vector scattering field you can get. Therefore, numerical simulation approach provides a novel and powerful way to study scattering problems.

2. Principle
The exact theory of the scattering by fractal structures is not available yet. But when the index variations of tissue is very weak, e.g. relative index \( m \approx 1.01 \sim 1.1 \), Born approximate and Rytov approximate etc. are valid, and for most cases in biological tissue, Born approximate is a reasonable assumption. So under these approximates a lot of useful deductions can be achieved, and these deductions are foundations of other researches.

2.1. Scattering theory of fractal medium
Potential scattering theory\[13\] declares that under Born approximate the scattering amplitude is derived from a special Fourier component of potential scattering of tissue. Martin Hunter\[14\] shows that the potential scattering of random media is the autocorrelation function of the media. For the simplification in math, biological tissue can be treated as an isotropy stationary random media, and its autocorrelation function can be the following form,

\[
C(r) = C_0 \times \exp\left(\frac{r}{l_c}\right) \tag{1}
\]

Where \( l_c \) is the autocorrelation length, \( C_0 \) is a constant, \( r \) is the distances between any two points. And \( l_c \) follows a fractal distribution\[10\],

\[
f(l_c) = \cos \tan t \times l_c^{3-D_f} \tag{2}
\]

Where \( D_f \) is fractal dimension. According to Wiener-Khinchin theorem, the power spectrum density of random media is the Fourier transformation of autocorrelation function. So, we get the power spectrum density\[10\],

\[
\hat{R}(k) = \frac{\epsilon^2 l_3}{\pi^2 (1 + k^2 l_3^2)^2} \times f(l) dl \tag{3}
\]

And the scattering intensity\[10\] is,

\[
|S(\theta)|^2 = \frac{\epsilon^2 \times \cos \tan t \times k^{D_f-1} x^{6-D_f}}{2\pi[1 + 2(1-\mu)x^2]^2} dx \tag{4}
\]

Where the \( \theta \) is the scattering angle , \( \mu = \cos(\theta) \) , \( \epsilon^2 = 4n_0^4 (m-1)^2 \) , \( k \) is the wave vector, \( l_{max} \) is the maximum autocorrelation length. From equation (4), we can get scattering intensity distribution as a function of either scattering angle \( \theta \) , or wave vector \( k \).Based on this, other scattering coefficients can be derived.

2.2. Spectral decomposition method
The FDTD method demands a exact refractive index distribution as an input, so we have to generate a special random media with a controlled statistic. Spectral decomposition method is widely used to generate random medium in geology\[1\], and this method has universality in generating a random media, so it can be used in biological. In general, spectral decomposition is based on Wiener-Khinchin theorem too, the only difference is that we multiply the power spectrum density by random phases. The process is demonstrated in the flow chart below,
Figure 1. Flow chart of spectral decomposition method.
Applying this method we get an exact refractive index distribution shown below.

Figure 2. A 2D random medium.
This 2D random medium with a mean refractive index value 1.03, $Df$ 6.32, $l_{max}$ 8.5um, standard deviation 0.01, and 100um×100um in area.
Figure 3. Power spectrum of refractive index variations

Figure 3 show the power spectrum of generated fractal random media. The power spectrum of refractive index variations is calculated using the algorithm mentioned in Ref.2. Applying least square fit to the experimental data, we get $Df = 6.32$, $l_{max} = 8.2 \mu m$, this fit our initial setup exactly.

3. FDTD Simulations

$Df$ and $l_{max}$, together with the mean value of refractive index $m_0$ and standard deviation $\sigma$ (these two combined as $\varepsilon^2$), we get four controllable input parameters. In most application, tissue is semi-infinite, and a limited range of scattering angle can be detected. So in this simulation, only backscattering properties are studied. We use multi-waves in the simulation, so we will get scattering amplitude as the function of scattering wavelength.

3.1. Simulation Setup

Using the method mentioned above, We generate a 3 dimension random media. It has a $Df = 5.2$, $l_{max} = 0.5 \mu m$, mean refractive index 1.05, standard deviation 0.01, and $5 \mu m \times 5 \mu m \times 5 \mu m$ in volume, 0.05$\mu m$ in step size. Then we put the generated media in the software FDTD Solutions 6.5.11 (lumerical) to run the simulation. In my simulation, we use the wavelength range 400nm~700nm, and set the periodic boundary conditions in the direction normal to wave vector and a absorbing boundary condition on other boundaries.

3.2. Simulations of bulk scattering

Figure 4 shows the parallel polarized part of scattering intensity as the function of wavelength. Based on the simulated data, we apply a least square fit in the log-log coordinates, and we get $Df = 5.4$, $l_{max} = 0.6 \mu m$, these results fit our initial setting roughly. Because of limited simulation area and accuracy, there is a little error between the two.
3.3. $Df$ and $l_{\text{max}}$

From equation 3, we know that $Df$ and $l_{\text{max}}$ control the shape of power spectrum density, and as the figure 2 shows, the curve of power spectrum density follows a line-curve-line pattern. So which parameter controls the position of the curve, which parameter controls the slope of line? We do the simulation below.

**Figure 4.** parallel polarized scattering intensity vs wavelength

**Figure 5.** Scan $Df$ or $l_{\text{max}}$ while keep the other unchanged
This figure shows the power spectrum changes while $Df$ or $l_{\text{max}}$ changes. The left one is the case that keep $l_{\text{max}}$ 1.5um, change $Df$ every time, and this shows that $Df$ changes the slope of oblique line only. The right one is the case that keep $Df$ 3.5, change $l_{\text{max}}$ every time, and this shows that $l_{\text{max}}$ change the position of curve only.

Ground on figure 5, we know that $l_{\text{max}}$ controls the position of curve, while $Df$ only affects the slope of the line. Further more, the slope of the oblique line changes when lower limit of autocorrelation length $l_{\text{min}}$ changes. All in all, $Df$ is more sensitive to small scale structures. Size-testing shows that the sensitive size range is from 1um to 0.01um. FDTD simulations support this proposition too.

4. Discussion
Based on my simulation, $Df$ and $l_{\text{max}}$ can be derived from the backscattering intensity spectrum. But as the equation 4 shows, $m_0$ and $\sigma$ are constants for either wavelength or scattering angle. So $m_0$ and $\sigma$ variations don’t change the shape of the scattering curve, and if you want to get them, you have to get the absolute quantity of scattering intensity. This is difficult for both experiments and practical applications. Fortunately tissues are more complex than fractal random media, as the nucleuses are the most import scattering centers for most kinds of surface tissues, large particles make a great contribution to the scattering pattern in small scattering angles, and $m_0$ coupled with $\sigma$ are parameters of particle scattering. So make use of nucleus scattering is a good way to solve this problem\[15\].

The backscattering spectrum of figure 3 obtains a fluctuation deflected from theory curve. An initial guess is that this fluctuation is caused by randomness of the input media, but when applying 35 times average, this fluctuation still exits, only smaller a little. So this fluctuation is an inherent property of scattering field, and the relation between the scattering field fluctuation and refractive index variation will tell us more information\[12\].

5. Conclusions
The numerical model of tissue generated by the spectral decomposition method performs good in the backscattering direction. Based on this model, we can derive $Df$ and $l_{\text{max}}$ from the backscattering spectrum detected in experiments or practical applications. while $Df$ means the overall complexity of refractive index variations, particularly $Df$ is sensitive to small structures ranging from 1um to 0.01um, and $l_{\text{max}}$ stands for maximum scale in biological tissue which is an important characteristic in tissue morphology.

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7