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Non-Rayleigh ultrasonic characterization of tissue scattering microstructure via a multibandwidth probing technique

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NON-RAYLEIGH ULTRASONIC CHARACTERIZATION OF TISSUE SCATTERING
MICROSTRUCTURE VIA A MULTIBANDWIDTH PROBING TECHNIQUE

by

María Helguera

A dissertation submitted in partial fulfillment of the
requirements for the degree of Ph.D.
in the Chester F. Carlson Center for Imaging Science
of the College of Science
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Abstract

Recent studies on the statistics of the envelope of the ultrasound echo signal from a random scattering medium suggest that the statistical moments of the signal may carry quantitative information about the scattering microstructure.

A mathematical model for the backscattered signal is developed borrowing from linear systems theory and assuming narrow bandwidth conditions.

Several microstructures, including sponges of different pore size as well as pig liver, human breast tissue, and human skeletal muscle, are probed experimentally with multiple bandwidth pulses with center frequency matched to the transducer center frequency. Variations of the second normalized intensity moment with the cell volume are considered and exploited experimentally for structure characterization.

The concept of effective cell volume and its relationship to the system point spread function is established. The influence of the imaging system point spread function on the statistical moments is considered.

To estimate an effective scatterer number and scatterer number density for every sample, higher order and fractional moments are calculated and fitted to theoretical Non-Rayleigh distributions: K, Generalized K, and Rice.

Information on interscatterer spacing is obtained from the autocorrelation of the second normalized intensity moment.

To analyze the sample structure, phantoms were created from histology sections and the same experimental and analysis procedures were followed. The concept of effective cell surface and its relationship to the system point spread function is established.

The experimental results indicate that non-Rayleigh statistical analysis of speckle prove to be useful in characterizing both normal, and abnormal tissue.
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1 Introduction

Speckle, as a physical phenomenon, can be observed in many different imaging modalities: optics, radar, sonar, etc. including ultrasonic medical imaging\(^1\). The interaction of an acoustic wave with an inhomogeneous medium, such as tissue, results in backscattered echo signals which exhibit random fluctuations. Even though these echo signals are considered to degrade an image (clutter, speckle) they contain information regarding the physical properties as well as the spatial structure of the medium. Since backscattered echo signals are random in nature, stochastic models should be constructed for describing them and deriving parameter estimation techniques. First-order statistics of the complex amplitude, intensity and phase of speckle can be derived from the basic idea of a random walk in the complex plane\(^2\). Understanding the relationship between the statistics of the echo signal, statistics of the scattering microstructure and the imaging system dependent parameters such as resolution cell volume, is fundamental in developing tissue characterization techniques.

In the last few years there has been a renewed interest in comprehending the relationship between the various different moments of the ultrasound echo signal and the scattering microstructure. Especially interesting is the situation where deviation from Gaussian statistics on the rf signal\(^3\)\(^4\), Rayleigh statistics on the amplitude\(^5\) or the negative exponential statistics on the intensity signal can be observed\(^6\)\(^7\) (Appendix A). The moments estimated from the three different signals (rf, amplitude, intensity) essentially carry the same information. However, there is a more complete understanding for the intensity moments\(^8\).
In the non-Rayleigh regime where deviations from fully developed speckle exist, the intensity moments estimated from the echo signal depend on several factors: (a) the number density of the scatterers in the medium and the resolution cell volume of the imaging system. More precisely, on the product of the two that yields the number of scatterers in the resolution cell 5, (b) the statistical distribution of the scattering cross-sections which themselves may show a frequency dependence, (c) the presence of any unresolved subresolution periodic or nearly periodic structure in the sonicated medium 9 and its relationship to the dominant frequency in the interrogating pulse 10.

The purpose of this work is to experimentally examine the implications of the factors mentioned above for structure characterization. First, we need to understand how the estimated normalized intensity moments depend on the resolution cell volume, and devise a method to remove its influence 11, 12. Only then can the moments be considered to depend on the scattering microstructure alone. Instead of using the entire bandwidth of the transducer, as is the case with impulse excitation, we probe the microstructure with a series of pulses of different bandwidths but same center frequency $f_0$, matched to that of the transducer, and examine the behavior of the intensity moments as a function of bandwidth.

Numerous studies have demonstrated that quantitative analysis of the echo signal may represent a promising means of characterizing the pathologic state of certain tissues. Histology is considered to be the gold standard when it comes to tissue pathology. The overall objective of this work is to develop and evaluate a bridge of understanding between tissue histology and quantitative analysis of the echo signal. This objective will be met through the following specific steps:

In chapter 2 we will introduce the concept of random walk and will generalize the concept in terms of ultrasonic signals under narrow band assumptions. We will define the
concept of resolution cell volume and its relationship to the system point spread function will be established. Variations of the second normalized intensity moment with the resolution cell volume are considered theoretically at this point, and will be exploited experimentally for structure characterization in chapter 5. A new method to evaluate the interscatterer distance will be introduced based on the autocorrelation of the second normalized intensity moment.

In medical ultrasound, considerations of three non-Rayleigh probability distributions for the amplitude signal have been reported in the literature: Rice, K, Generalized K. In chapter 3 we will review these three models and their normalized moments will be derived. We have extended the theory and will introduce moments of fractional order.

In chapter 4 the experimental setup as well as the experimental procedures will be introduced. A description of the different scattering microstructures is included. The scattering structures are: a set of artificial sponges of different pore size, fresh pig liver tissue, fresh human breast tissue, both normal and abnormal, and fresh human skeletal muscle. The analysis and discussion of the quantitative experimental results is presented in chapter 5.

To correlate experimental results with histology, a new technique was adapted to create 2-dimensional phantoms from the histology sections of the liver tissue samples analyzed. In order to compare 3-dimensional data to 2-dimensional data, the concept of resolution cell surface will be introduced in chapter 6. Results for a liver tissue phantom are included in this chapter as well.

Finally, in chapter 7 discussion and conclusions will be presented. Two appendices are found at the end of this paper; Appendix A presents the case for a Gaussian process and the derivation of the probability density functions for the amplitude and intensity signals. In
Appendix B, experimental results including histology images, speckle images, and plots of the normalized intensity moments for all samples can be found.
2 Theory

2.1 Random walk

When the number of randomly positioned scatterers is large enough the statistical properties of the signal approach those of a Gaussian distribution, this means that both the real and imaginary parts of the scattered signal are zero-mean, jointly Gaussian independent random variables and the magnitude of the backscattered signal follows a Rayleigh distribution. However, if the number of scatterers in a resolution cell is small enough, the backscattered signals will deviate from Gaussian.

In what follows, we will assume: (a) the randomly distributed scatterers give rise to all echoes. The probability that any scatterer is at one position is the same as the probability at any other position. (b) Multiple scattering is negligible. (c) Over the surface of the transducer the waves scattered by each particle are spherically symmetric, i.e. the scatterers are sufficiently far from the transducer.

The theoretical framework for studying the non-Gaussian behavior of scattered waves was laid down by Jakeman. We present here the results for the second normalized intensity moments derived by applying random walk concepts under the narrow bandwidth assumption with emphasis on the resolution cell volume definition.

Consider a narrow bandwidth signal driving the transducer as the real part of $p(t) = A(t)e^{j2\pi f_0 t}$ where $f_0$ is the center frequency and $A(t)$ is the pulse envelope (e.g. a Hanning window). The transmit/receive frequency response of the transducer is $h(f)$. $h(f)$
is typically a Gaussian shaped function centered at some resonant frequency \( f_0 \). It is important to note that in our experiments the center frequency of the drive signal is matched to the center frequency of the transducer, but its bandwidth \( \Delta f \) is gradually increased without exceeding the transducer's bandwidth.

If \( \overline{A}'(f) \) and \( \overline{A}(t) \) are Fourier transform pairs, the received pulse \( A(t)e^{j2\pi ft} \) has the same center frequency \( f_0 \) but its envelope \( A(t) \) will now be different from \( \overline{A}(t) \) due to the bandpass filtering by the finite bandwidth frequency response of the transducer. If we assume that the drive signal bandwidth \( \Delta f \) is very small compared to the bandwidth of the transducer frequency response \( h(f) \), then \( A(t)=\overline{A}(t) \).

The combined transmit/receive transducer beam profile \( B(r) \) is assumed to be circularly symmetric, where \( r \) is the perpendicular distance from the transducer beam axis which is assumed to be along the \( z \) axis (Fig. 2.1.1). The medium is considered to be nonattenuating and uniform except for small size scatterers (impedance discontinuities) distributed randomly in a three dimensional space. The location of the \( n^{th} \) scatterer in the beam can be represented by \( (r_n, z_n) \) and the two way travel time is \( t_n = 2\sqrt{r_n^2 + z_n^2}/c \) where \( c \) is the speed of ultrasound in the medium.
The echo signal from the $n^{th}$ scatterer is given by:

$$s_n(t) = F^{-1}[\overline{A'}(f - f_0)\overline{b'}(f)a'_n(f)\overline{b'}(r_n,z_n,f)e^{-j2\pi r_0 t}] = a_n B(r_n,z_0) A(t-t_n)e^{j2\pi r_0 t\over T_0}$$ (2.1)

Where $F^{-1}$ stands for inverse Fourier transform, $a'_n(f)$ is the frequency dependent backscatter coefficient of the $n^{th}$ scatterer, and $b'(r_n,z_n,f)$ is the two way propagation transfer function of the transducer (diffraction filter). The approximation in Eq. (2.1) follows from the assumption that the bandwidth $Af$ of the drive signal, i.e. $\overline{A'}(f-f_0)$ is "small enough" ($Af \leq 1$ MHz). The validity of the previous statement was examined through simulations. The spectrum of the pulse is the Fourier transform of $p(t) = \overline{A}(t)e^{j2\pi f_0 t}$ given by

$$P(f) = \frac{T_0}{2} \frac{\sin(\pi(f-f_0)T_0)}{\pi(f-f_0)T_0[1 - ((f-f_0)T_0)^2]}$$

Where $T_0$ is the length of the envelope $\overline{A}(t)$ and $f_0$ is the center frequency.
The scattering function is $I_r(f) = k f^n$, where $k$ and $n$ are dependent on the geometry and size of the scatterer. According to Narayana, liver, spleen, and brain have scattering functions with scattering order $n$ in the range $1 < n < 4$. Scattering orders from 1 to 3 were utilized in the simulations whose results are shown in Fig. 2.1.2 for the case $\Delta f = 1$ MHz (other bandwidths: 0.8, 0.6, 0.4, and 0.2 MHz are not shown for the sake of space). However, Fig. 2.1.3 shows a summary of the effects of scattering order on the central frequency of the pulse for all the cases considered. Fig. 2.1.4 shows the effect of scattering order on the bandwidth of the spectrum of the pulse.

![Figure 2.1.2 Effect of scattering order n on the spectrum of the signal. $\Delta f=1$ MHz, $f_0=3.5$ MHz.](image)
As can be seen from the previous results, the effects of scattering on bandwidth change and upshift of central frequency are negligible.

To study the effects of diffraction on the pulse, simulations were performed based on the impulse response given by $^{11}$
\[ h(z,R,t) = \begin{cases} \frac{c}{\pi} \cos^{-1} \frac{R^2 + c^2t^2 - z^2 - a^2}{2R(c^2t^2 - z^2)^{1/2}}, & \sqrt{z^2 + (a - R)^2}/c < t < \sqrt{z^2 + (a + R)^2}/c \\ \sqrt[0, t > \sqrt{z^2 + (a + R)^2}/c \end{cases} \]

Here, \( z \) corresponds to the focal point (60 mm), \( R \) is off axis distance (from 0.1 to 6 mm), \( a \) is the radius of the transducer (6.8 mm), \( c \) is the speed of sound in the medium (1.5 mm/\mu s). Figure 2.1.5 shows the effect of diffraction on the bandwidth of the pulse, Fig. 2.1.6 shows the effect of diffraction on the central frequency, and Fig. 2.1.7 shows the effect of diffraction on the amplitude of the pulse.

As can be seen from the following results, the effects on bandwidth and center frequency are negligible. At those distances off axis where diffraction effects are noticeable the amplitude of the signal has dropped so much that we will consider the approximation in Eq. (2.1) to be valid.
Figure 2.1.5 Effect of diffraction on the bandwidth (BW) of the signal, $f_0=3.5\text{MHz}$, $z=6\text{ cm}$, $R$ is off axis distance.

Figure 2.1.6 Effect of diffraction on the center frequency of the signal, $f_0=3.5\text{MHz}$, $z=6\text{ cm}$, $R$ is off axis distance.
The echo signal at any time \( t \) from a volume distribution of scatterers (\( M \) being the number of scatterers in a volume \( V_T \) that is formed by considering a cylinder of diameter equal to 20 dB beamwidth and length equal to 20 dB pulse width) is given by:

\[
s(t) = e^{j2\pi f_0 t} \sum_{n=1}^{M} a_n B(r_n, z_0) A(t - t_n) e^{-j2\pi f_0 t_n} = e^{j2\pi f_0 t} \sum_{n=1}^{M} E_n e^{\phi_n} \tag{2.2}
\]

where

\[
t_n = 2\sqrt{r_n^2 + z_n^2/c} \quad E_n = a_n B(r_n, z_0) A(t - t_n) \quad \phi_n = -2\pi f_0 t_n
\]

The problem can now be stated in the context of random walk as described by Jakeman. Eq. (2.2) can be considered as a vector sum of \( M \) phasors in the complex plane. The \( M \) phasors that make significant contributions to the signal at time \( t \) will generally have random amplitudes \( E_n \) and random phase \( \phi_n \). A given scatterer with some \( r_n \) and \( z_n \) will make a significant contribution to the signal at time \( t \) with phasor amplitude \( B_n \) only if both
B(r_n, z_0) and A(t-t_n) are not significantly small, i.e. the scatterer must be located well within the volume V_r centered at some depth z=c/2t as shown in Fig. 2.1.1.

The phasor amplitudes E_n also depend on the scattering microstructure through the scattering cross-section terms a_n which we assume to be statistically independent. If the interscatterer spacing in the microstructure is such that the phases \phi_n due to time delays t_n are independent and uniformly distributed between 0 and 2\pi, i.e. the surface is rough compared to a wavelength, then following Jakeman we can write the second normalized moment of the intensity distribution I(t)=|s(t)|^2 as

\[ \frac{\langle I^2 \rangle}{\langle I \rangle^2} = \frac{2\langle M(M-1) \rangle}{\langle M \rangle^2} + \frac{\langle E^4 \rangle}{\langle M \rangle \langle E^2 \rangle^2} \] (2.3)

where \langle \ldots \rangle stands for ensemble average. If M, in a given sonicated volume V_r is Poisson distributed and \langle M \rangle is large \textsuperscript{10} then \langle M(M-1) \rangle=\langle M^2 \rangle=\langle M \rangle^2 If we assume that a_n, B(r_n,z_0) and A(t-t_n) are statistically independent we have

\[ 2 \frac{\langle M^2 \rangle}{\langle M \rangle^2} + \frac{\langle a^4 \rangle / \langle B^4 \rangle / \langle A^4 \rangle}{\langle M \rangle \langle a^2 \rangle / \langle B^2 \rangle / \langle A^2 \rangle} \] (2.4)

Assuming ergodicity we can now replace the ensemble average over the terms A and B by its spatial average over the volume V_r as:
\[
\frac{\langle B^4 \rangle \langle A^4 \rangle}{\langle B^2 \rangle^2 \langle A^2 \rangle^2} = \frac{1}{V_T} \frac{\langle \langle B^4 \rangle \rangle \langle \langle A^4 \rangle \rangle}{\langle \langle B^2 \rangle \rangle \langle \langle A^2 \rangle \rangle} = \frac{V_T}{V_E}
\]

(2.5)

where \(\langle \ldots \rangle\) stands for integration over the volume \(V_T\). The effective volume \(V_E\) results from the volume integration

\[
V_E = \frac{c\int 2\pi B^2(r)dr \int A^2(t)dt}{2\int 2\pi B^2(r)dr \int A^2(t)dt} = \frac{c\int \int g(r,t)2\pi rdrdt}{2\int \int g^2(r,t)2\pi rdrdt}
\]

(2.6)

where \(g(r,t)\) is the experimental intensity point spread function (PSF) to be defined in the next section. If we use \(\langle M \rangle/V_T = \langle N \rangle\) as the volume scatterer number density, then Eq. (2.3) becomes:

\[
\frac{\langle I^2 \rangle}{\langle I \rangle^2} = 2 + \frac{\langle a^4 \rangle}{\langle a^2 \rangle^2 \langle N \rangle V_E} \approx 2 + \frac{1}{M_{\text{eff}}}
\]

(2.7)

Eq. (2.7) predicts that the slope of the \((I^2)/(I)\) vs \(V_E^{-1}\) plot should depend only on the scattering microstructure (i.e. \(\langle a^4 \rangle/\langle a^2 \rangle^2 \langle N \rangle\)) and hence can serve as a useful parameter.\(^\text{21, 22}\)

The intercept when \(V_E \to \infty\) or \(\Delta f \to 0\) is the well known high density limiting value 2, when the speckle becomes a fully developed speckle (Gaussian limit).

This number can go below 2 if a substantial unresolved coherent component is present in the backscattered signal.\(^\text{23}\) In Eq. (2.2) it was assumed that the random positions of the scatterers introduce path differences that exceed the dominant wavelength \(\lambda_0 = c/f_0\) of the pulse, so that \(\phi_n = 2\pi f_0 t_n\) can be regarded as being uniformly distributed.
between 0 and $2\pi$. However, when there is subresolution periodicity in the interscatterer spacing, constructive interference effects\(^7\) can ensue whenever the periodic spacing becomes half-integer multiple of the dominant wavelength $\lambda_0$. In the random walk context, this amounts to adding a constant phasor to the complex signal $s(t)\(^{24}\).

The slope estimate can be roughly seen as the inverse of the “effective scatterer number density” evaluated at the frequency $f_0$.

Deviations from the linear behavior predicted by Eq. (2.7) can be explained by either the violation of the narrow band assumption or by the fact that when varying the volume of the resolution cell more or less frequencies are allowed into the spectrum of the pulse and scattering may vary accordingly. As will be seen in the next chapter, the probability density function of the amplitude is dependent on frequency through the $M$ parameter, which is closely related to $M_{\text{eff}}$ in Eq. (2.7). $M_{\text{eff}}$ has embedded in it the frequency dependent scattering cross-section.

### 2.2 Resolution cell volume

To visualize the PSF, consider a wire target at depth $z_0$ in Eq. (2.1). By scanning in the direction perpendicular to the wire and taking the square of the echo envelope, we obtain the intensity point spread function $g(r,t)$ as

$$g(r, t) = \left[ F^{-1} \left[ \mathbf{A}'(f - f_0) b'(f) b'(r, z_0, f) \right] \right]^2 = |B(r, z_0) A(t)|^2 \quad (2.8)$$

where $t = 2\sqrt{r^2 + z_0^2}/c$. The approximation follows the narrow bandwidth arguments presented earlier. Strictly speaking, what we measure with the wire targets is the projection of the radially symmetric three-dimensional PSF. We will take it to represent a two dimensional radial slice of the PSF due to small differences in practice.

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Mathematically, the extreme right-hand side of Eq. (2.6) is a functional of the positive function \( g(r,t) \), which we will consider to be the experimental intensity PSF of the imaging system. This functional possesses the properties required to define a three-dimensional volume. We will refer to it as the "effective volume" \( V_e \). Note that the term \( V_e \) that appears in Eq. (2.7) and is defined by Eq. (2.6) results from expressing \( g(r,t) \) as a product of two separable functions \( B(r) \) and \( A(t) \). \( A(t) \) is the filtered version of the drive signal envelope \( \overline{A}(t) \) and hence takes into account the frequency response of the transducer. We assume that \( B(r) \) (diffraction term) depends on the center frequency \( f_0 \) of the pulse but not on \( \Delta f \). Eq. (2.7) then predicts that the normalized second moment should increase linearly with the drive pulse bandwidth \( \Delta f \), when \( f_0 \) is held fixed.

The envelope detected images of the point spread function (PSF), obtained from the experimental procedure described in the experimental chapter, are shown in Fig. 2.2.1 for the five different bandwidths considered in this project. 120 scans were performed per bandwidth. In the figures, the vertical axis corresponds to the number of points per scan in the \( z \) direction (depth) and the horizontal axis corresponds to the number of scans. In other words, the vertical axis is a collection of profiles of the pulse width and the horizontal axis is a collection of profiles of the beam width.
Figure 2.2.1 Envelope detected image of the point spread function at different bandwidths. Focal zone, $f_0 = 3.5$ MHz. 120 scans in horizontal axis correspond to 6 mm.

To calculate the resolution cell volume, profiles were obtained from the PSF for both the beam width $B^2(r)$, and the pulse width $A(t)$. Note from figure 2.2.1 that the function $B^2(r)$ has circular symmetry, therefore the point spread function is three-dimensional. The beam width profiles are shown in figure 2.2.2.
Integration of the PSF $g(r,t) = \left| F^{-1}[\bar{A}'(f-f_0)h'(f)b'(r,z_0,f)] \right|^2$ can be performed because under the narrow bandwidth assumption, it represents the product of two separable functions. The variable $t$ in this case encodes the depth $z$.

The volume expression is repeated here for convenience:

$$V_C = \frac{c \left[ \int 2\pi r B^2(r) dr \int A^2(t) dt \right]^2}{2 \left[ \int 2\pi r B^4(r) dr \int A^4(t) dt \right]} = \frac{c \left[ \int \int g(r,t) 2\pi r dr dt \right]^2}{2 \left[ \int \int g^2(r,t) 2\pi r dr dt \right]}$$

Note that, as explained before, $A(t)$ is the filtered version of the drive signal envelope $\bar{A}(t)$ and hence takes into account the frequency response of the transducer. $c$ is the speed of sound in the material; in the present calculation it was taken to be 1500 m/s.

Integration was carried out in a discrete manner as follows:

For the beam width profile, the origin was chosen at the center of the plot (maximum value). Rings of width $\Delta r$ were calculated and their areas summed up:
\[
\sum_{k=0}^{60} B^2(r_k) 2\pi (\Delta r k) \Delta r = B^2(r_{k=0}) \pi (\Delta r)^2 + \sum_{k=1}^{60} B^2(r_k) 2\pi (\Delta r k) \Delta r
\]

\(\Delta r = 50 \times 10^{-6} \text{ m}\) is determined by the motor's step size used for the wire scanning.

For the pulse width, the area under the envelope was calculated as:

\[
\sum_{k=-n/2}^{n/2} p^2(k) \Delta t
\]

\(n\) corresponds to the total number of points per scan (depends on the width on the Hanning window). \(\Delta t = 40 \times 10^{-9} \text{ s}\) is determined by the digitizer's sampling period.

Dimensionally, Eq. (2.6) indeed describes a volume:

\[
V_E = \frac{c}{2} \left[ 2\pi r B^2(r) dr \int A^2(t) dt \right]^2 = \frac{m^2 \cdot s^2}{\pi^2 m^2 \cdot s^2} = m^3
\]

The experiments involve probing the microstructure with different bandwidth pulses. In each case the normalized intensity moments (left-hand side of Eq. (2.7)) are estimated from the echo signal. \(V_E\) is also determined from a separate calibration experiment.

### 2.3 Interscatterer distance

Up to now, we have reviewed in section 2.1 the random walk formulation and we have shown that the theory is applicable to the ultrasound signal. An expression for the second normalized intensity moment was derived as Eq. (2.7). It was noted in this expression that the only system dependent variable is the resolution cell volume and it can be exploited for tissue characterization. In Section 2.2 we have reviewed the concept of
resolution cell volume and we have seen that under the narrow band assumption the volume can be calculated as the product of two separable functions.

If there is spatial correlation due to underlying periodicity in the scattering structure, the limiting value of the second normalized intensity moment as \( V_R \rightarrow \infty \) can be lower than 2. This is manifest due to the constructive interference and coherent buildup of a constant phasor term in the random walk.

Landini and Ferrazani \(^{25}\) as well as Nicholas \(^{26}\) and Wear et al. \(^{27}\) have developed methods to study interscatterer spacing in the frequency domain. They analyze the distance between peaks of the power spectrum.

We have developed an experimental method to investigate the interscatterer spacing in the time domain. A frequency scan in steps of 0.1MHz is performed under the bandwidth of the transducer. One A-line of data is recorded per frequency step. The second normalized intensity moment is calculated per line, allowing us to obtain a collection of values for the second moment as a function of frequency. The autocorrelation of this function is then performed to evidence any periodicity in the scattering structure; the interscatterer distance is later calculated through \( c = 2d/t \). This method avoids the use of Fourier transforms and therefore the usual concerns about windowing and Gibbs phenomenon.

The relationship between the two methods (time and frequency) is given by the Moment Theorem \(^{28}\), which states that, the kth moment of a function \( f(x) \) is proportional to the kth derivative of its Fourier transform, evaluated at the origin:

\[
m_k = \int_{-\infty}^{\infty} \alpha^k f(\alpha) d\alpha = \frac{F^{(k)}(0)}{(-j2\pi)^k}
\]
In our case, the second moment of the intensity signal (second derivative of the intensity spectrum) detects the maxima in the spectrum. The distance between two major peaks corresponds to the interscatterer distance. Smaller peaks can be present between two major peaks; these are a consequence of interference.

3 Statistical models

A Gaussian random process is widely used when there is a large number of scatterers present in the resolution cell volume. A random-walk formulation can be stated and the central limit theorem invoked:

\[ s(t) = \sum_{n=1}^{N} a_n e^{i\phi_n} \]  \hspace{1cm} (3.1)

Where \( s(t) \) is the backscattered echo, \( a_n \) are the amplitudes of the echoes from the independent scatterers and \( \phi_n \) are the phases. \( N \) is the number of scatterers in the resolution cell.

In this case the statistics of the backscattered envelope (amplitude) will follow a Rayleigh distribution and the intensity will follow a negative exponential distribution.

A number of assumptions about the statistical properties of the phasors composing the sum are typically made. Namely:

- The amplitude \( a_n \) and phase \( \phi_n \) of the \( n \)-th elementary phasor are statistically independent of each other and of the amplitudes and phases of all other phasors.
- The amplitudes \( \{a_n\} \) are identically distributed for all \( n \).
- The phases \( \{\phi_n\} \) are all uniformly distributed on \((-\pi, \pi)\).
However, in real applications these assumptions don't necessarily hold. To begin with, the number of scatterers is always finite leading to deviations from normal behavior. Also, it is possible that biological changes arise in tissue in the presence of benign or malignant growth affecting the scattering cross-section of the scatterers\cite{30}. And last but not least, scatterers within the resolution cell volume may present some well organized periodic or quasi-periodic structure\cite{7,31}. The previous considerations lead to non-Rayleigh regimes. As a consequence, models that take into account low scatterer density and randomness of the scattering cross-section have been developed based on the K distribution\cite{8,9}, Rice distribution\cite{6} and Generalized K distribution\cite{9,32}.

### 3.1 The K-distribution

We must note that in Eq. (3.1), \(a\), \(\phi\), and \(N\) are all random variables. However, in ultrasonic imaging the number of scatterers in the resolution cell does not change during the imaging process, therefore \(N\) can be taken as a constant, perhaps as the average number of scatterers\cite{15}.

To obtain an expression for the probability density function of the envelope of \(s(t)\) we can rewrite Eq. (3.1) as

\[
s(t) = \sum_{n=1}^{N} a_n \cos \phi_n + i \sum_{n=1}^{N} a_n \sin \phi_n = X + iY = Ae^{i\theta}
\]

where \(X, Y\) are independent random variables, so \(<XY> = <X><Y>\).

The joint characteristic function is defined as

\[
\phi(u,v) = \int \int f(x,y)e^{i(ux+vy)} \, dx \, dy
\]

(3.3)
This can be rewritten in terms of scattering cross-sections and phases as

\[ \phi(u,v) = \int_{0}^{2\pi} \int_{0}^{\infty} f(a_n, \phi_n) e^{i(ux + vy)} da_n d\phi_n = E\left[ e^{i(ux + vy)} \right] = \langle e^{i(ux + vy)} \rangle \]  

(3.4)

where \( f(a_n, \phi_n) \) is the joint density function of the amplitude and phase of the echo from each scatterer.

Converting to polar coordinates \( u=\cos\alpha, v=\sin\alpha \) we can rewrite Eq. (3.4) as

\[ \phi(u,v) = \int_{0}^{2\pi} \int_{0}^{\infty} f(a_n, \phi_n) e^{i(\cos\alpha x + \sin\alpha y)} da_n d\phi_n \]  

(3.5)

Now, let

\[ x = \Re\{ae^{i\theta}\} = \frac{1}{\sqrt{N}} \sum_{n=1}^{N} a_n \cos \phi_n \]

and

\[ y = \Im\{ae^{i\theta}\} = \frac{1}{\sqrt{N}} \sum_{n=1}^{N} a_n \sin \phi_n \]

as done in the random walk formulation \(^{20}\). We can substitute these into

\[ e^{i(ux + vy)} = e^{i\left(\frac{1}{\sqrt{N}} \sum_{n=1}^{N} a_n \cos \phi_n + r \cos \alpha \right) \left(\frac{1}{\sqrt{N}} \sum_{n=1}^{N} a_n \sin \phi_n \right)} \]

(3.6)

Using the trigonometric identity \( \cos(a-b) = \cos a \cos b + \sin a \sin b \) we can rewrite Eq. (3.6) as

\[ e^{i(ux + vy)} = e^{\frac{i}{\sqrt{N}} \sum_{n=1}^{N} a_n r \cos(\alpha - \phi_n)} \]

(3.7)

Taking now the expected value, and using the fact that the amplitudes and phases are statistically independent we get
\[
\phi(u, v) = \frac{2\pi}{\sqrt{N}} \sum_{n=1}^{N} e^{i\alpha_n r \cos(\alpha - \phi_n)} J_n(r a_n) f(a_n) \, da_n \, d\phi_n
\]  

(3.8)

From tables, we find that

\[
\phi(u, v) = \prod_{n=1}^{N} J_0(r a_n) f(a_n) \, da_n
\]  

(3.9)

where \(J_0\) is a Bessel function of the first kind, order zero.

In Eq. (3.9) we can take the product outside the integral, and because the \(a_n\) are independent and identically distributed we get

\[
\phi(u, v) = \left[ \prod_{n=1}^{N} J_0(r a_n) f(a_n) \right]^{N} = \left( J_0(r a) \right)^{N}
\]  

(3.10)

Before finding the density function of the envelope and phase we must have a model for the statistical fluctuations of the scattering cross-section.

From Watson, p.420, the problem of random flights, we have that the probability that after \(n\) steps the distance from the starting point shall be less than \(r\) is given by

\[
P_n(r; a_1, ..., a_n) = r \int_0^r J_0(r t) \prod_{m=1}^{n} J_0(a_m t) \, dt
\]  

(3.11)

which corresponds to Eq. (3) in Jakeman and Pusey.

Eq. (3.11) cannot be solved analytically for an arbitrary \(f(a)\), therefore, Jakeman and Pusey propose

\[
f(a) = \frac{2b}{\Gamma(1+\nu)} \left( \frac{ba}{2} \right)^{\nu+1} K_\nu(ba) \quad \nu > 1
\]  

(3.12)
with moments

\[ \langle a^{2\pi} \rangle = \left( \frac{2}{b} \right)^{2\pi} \frac{n!}{\Gamma(1 + v)} \Gamma(n + v + 1) \]

where \( K \) is a modified Bessel function of second kind. The density \( f(a) \) thus expressed is a two-parameter distribution. \( b \) is inversely proportional to the mean and \( v \) represents the skewness of the distribution. When \( v \rightarrow -1 \), \( f(a) \rightarrow \text{lognormal} \), when \( v \rightarrow \infty \), \( f(a) \rightarrow \text{Rayleigh} \). This means that by changing \( v \) we can assign different distributions to the amplitude fluctuations.

An expression for the parameter \( b \) can be deduced from the moments

\[ \langle a^2 \rangle = \left( \frac{2}{b} \right)^2 \frac{1}{\Gamma(1 + v)} \Gamma(2 + v) \]

\[ b^2 = \frac{4(1 + v)}{\langle a^2 \rangle} \]

\[ b = 2 \left( \frac{1 + v}{\langle a^2 \rangle} \right)^{\frac{1}{2}} \]  \hspace{1cm} (3.13)

We now can go back and integrate Eq. (3.10) \textsuperscript{34}

\[ \int_0 \frac{J_0(ra)}{\Gamma(1 + v)} \left( \frac{ba}{2} \right)^{v+1} K_v(ba) da = \frac{2b}{\Gamma(1 + v)} \left( \frac{b}{2} \right)^{v+1} \int_0 J_0(ra)a^{v+1} K_v(ba) da \]

\[ = \frac{2b}{\Gamma(1 + v)} \left( \frac{b}{2} \right)^{v+1} \left( \frac{(2b)\Gamma(v + 1)}{(b^2 + r^2)^{v+1}} \right) = \left( \frac{b^2}{b^2 + r^2} \right)^{(v+1)} \]  \hspace{1cm} (3.14)
Therefore
\[
\phi(u, v) = \left( \frac{b^2}{b^2 + r^2} \right)^{N(v+1)}
\]  

(3.15)

Define now \( M = N(1+v) \). \( N \) is the number of scatterers in the resolution cell. \( M \) is the effective number of scatterer and is defined by the severity of the amplitude fluctuations in the cell volume.

The characteristic function obtained in Eq. (3.15) can be inverted using the Fourier transform to obtain the joint function of \( X \) and \( Y \) and to calculate the joint density function of the envelope and phase.

The characteristic function in general is given by
\[
\phi(u, v) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x)e^{j(ux+vy)}dxdy
\]

\( \phi(-u) \) will be the Fourier transform of \( f(x) \):
\[
f(x) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \phi(u)e^{-jux}du
\]

Therefore
\[
f(X, Y) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \left( \frac{b^2}{b^2 + r^2} \right)^{N(v+1)} e^{-j(ux+vy)}dudv
\]

If we substitute again for polar coordinates and the expressions for \( x \) and \( y \) given above we find that the joint density function for the envelope and phase is again a K-distribution.
From this expression the marginal probabilities can be evaluated.

According to Jakeman, it is more reasonable to expect a variety of phenomena to be characterized by the same underlying clustering process than by identical scattering factors.

In the case of multiscale media, \( N \) is identified with the number of correlation cells characterized by the largest scale size present, since only these will contribute independently to the scattered field. Within these large cells many smaller ones will contribute in a correlated way, i.e., we are talking about the modulation of small scale inhomogeneities by larger ones, leading to clustering effects. It is pertinent to note here that Jakeman assumes the number-fluctuation model for \( N \), where \( N \) corresponds to clustering. These big cells are the ones that contribute independently to the scattered field, as stated previously. On the contrary, Oliver \(^{35} \) introduces correlation between the \( \{a_n\} \) and \( N \) is interpreted as the number of small scale inhomogeneities and is taken to be large.

As can be seen from Eq. (3.16), the statistics of the probability density function are determined by \( M \). That is, \( M \) is a measure of number of scatterers as well as scattering cross-section \(^{21} \).

According to this formulation, the characteristics of tissue can be specified through the parameters \( M \) and \( b \) if enough samples of the envelope are available. We have for the moments of the distribution

\[
m_n = E[x^n] = \int_{-\infty}^{\infty} x^n f(x) dx
\]

\( f(A, \theta) = \frac{1}{2\pi} \frac{2b}{\Gamma(M)} \left( \frac{bA}{2} \right)^M K_{M-1}(ba) \) (3.16)
\[ m_n = \mathbb{E}[A^n] = \int_0^\infty (bA)^n \frac{2b}{\Gamma(M)} \left( \frac{bA}{2} \right)^M K_{M-1}(bA) dA \quad (3.17) \]

Using tables\(^{24}\) we get:

\[ m_n = \mathbb{E}[A^n] = \left( \frac{2}{b} \right)^n \frac{\Gamma(M + \frac{n}{2})}{\Gamma(M)} \Gamma\left( \frac{n}{2} + 1 \right) \quad (3.18) \]

From Eq. (3.18) we can now obtain an expression for the parameter \( b \):

\[ \mathbb{E}[A] = \langle A \rangle = \left( \frac{2}{b} \right)^n \frac{\Gamma(M + 1/2)}{\Gamma(M)} \Gamma(3/2) \]

or

\[ b = \frac{2}{\langle A \rangle} \frac{\Gamma(M + 1/2)}{\Gamma(M)} \Gamma(3/2) \quad (3.19) \]

Eq. (3.19) implies that information on the average scattering cross-section can be obtained from the average value of the envelope and the effective number \( M \).

From the normalized moments we know that

\[ r_{2m} = \frac{\mathbb{E}[A^{2m}]}{\left( \mathbb{E}[A^2] \right)^m} \quad (3.20) \]

Therefore, the second normalized moment given by
\[ r_4 = \frac{\mathbb{E}[A^4]}{\mathbb{E}[A^2]^2} \]

where

\[ \mathbb{E}[A^4] = \frac{\Gamma(M+2)}{\Gamma(M)} \Gamma(3) \left( \frac{2}{b} \right)^4 \]

and

\[ \mathbb{E}[A^2]^2 = \left( \frac{\Gamma(M+1)}{\Gamma(M)} \Gamma(2) \left( \frac{2}{b} \right)^2 \right)^2 \]

will be

\[ r_4 = 2 + \frac{2}{M} \quad (3.21) \]

Here the property \( \Gamma(n+1)=n! \) has been used.

Note that this result is in close agreement with the result derived in the previous chapter as Eq. (2.7). The second normalized moment is expected to behave linearly as a function of \( M \) in Eq. (3.21), or \( \frac{\langle a^4 \rangle}{\langle a^2 \rangle^2} \frac{1}{\langle N \rangle V_E} \) in Eq. (2.7). \( M \) represents the effective number of scatterers per resolution cell volume and has embedded in its definition the term \( <a^2>/<a^4> \) which is governed by the PDF of the scattering cross-sections (a K distribution in the present case). When \( M \) becomes large, the second normalized moment is 2, which
corresponds to the Rayleigh limit as demonstrated in the following paragraph. Deviations from that value will evidence whenever \( <N>, <a^2>/<a>^2 \) or \( V_E \) become sufficiently small. The first two depend on the scattering structure, only \( V_E \) is an imaging system dependent term and can be exploited in structure characterization.

For large values of \( M \), the marginal probability \( f(A) \) calculated from Eq. (3.16) will approach the Rayleigh distribution. This can be seen from the characteristic function given by Eq. (3.10) rewritten here as

\[
\phi_n(u, v) = \prod_{n=1}^{N} E \left[ J_0 \left( r \frac{a_n}{\sqrt{N}} \right) \right]
\]

\( J_0 \) is a Bessel function of the first kind, order zero. As \( N \) grows large, the argument of the Bessel function grows small. Therefore, we can approximate the Bessel function by the first two terms of its power series expansion as

\[
\phi_n(u, v) = \prod_{n=1}^{N} E \left[ 1 - \left( \frac{ra_n}{\sqrt{N}} \right)^2 \right]
\]

Performing the average over the amplitudes we get

\[
\phi_n(u, v) = \left[ 1 - \frac{a^2}{N} r^2 \right]^N
\]

If we take the limit when \( N \to \infty \) we get

\[
\phi_n(u, v) = e^{-r^2 a^2}
\]

Performing now an inverse Fourier transform we obtain the two-dimensional Gaussian joint probability density function.
3.2 Periodic scattering structures. Rice distribution

The statistics described up to here only consider the effect of a fixed number of randomly distributed scatterers with randomly varying scattering cross-sections. It does not account however, for some of the underlying properties of tissue, namely some periodic alignment of scatterers within the resolution cell volume. This periodicity will lead to a nonzero mean for the real part of the envelope. A model that includes these effects is a biased random walk:

\[
\mathbf{s}'(t) = s_0 + \sum_{n=1}^{N} a_n \cos \phi_n + i \sum_{n=1}^{N} a_n \sin \phi_n = X' + iY' \quad (3.22)
\]

Here \( s_0 \) accounts for an isolated strong scatterer (constant phasor).

To find the joint density function of the envelope and phase \( f(A,\theta) \) we need to take the inverse Fourier transform of the characteristic function.

The process is similar to the one followed above, with the exception that this time we have

\[
x = s_0 + \frac{1}{\sqrt{N}} \sum_{n=1}^{N} \alpha_n \cos \phi_n
\]

and

\[
y = \frac{1}{\sqrt{N}} \sum_{n=1}^{N} \alpha_n \sin \phi_n
\]
The joint characteristic function is given by

$$
\phi(u, v) = e^{j\mu_0} \left[ \frac{b^2}{b^2 + r^2} \right]^M
$$

So that

$$
f(A, \theta) = \frac{1}{(2\pi)^2} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \left( \frac{b^2}{b^2 + r^2} \right)^M e^{j\mu_0} e^{-j(ux + vy)} dudv
$$

Defining $(X' - s_0) = R \cos \beta$ and $Y' = \sin \beta$ and using trigonometric identity $\cos(a-b) = \cos a \cos b + \sin a \sin b$ we obtain

$$
f(A, \theta) = \frac{1}{(2\pi)^2} \int_{0}^{2\pi} \int_{0}^{\infty} \left( \frac{b^2}{b^2 + r^2} \right)^M e^{-jrR \cos(\alpha - \beta)} rdrd\alpha
$$

Using tables we obtain

$$
f(A, \theta) = \frac{1}{2\pi} \left( \frac{1}{R} \right) \frac{2b}{\Gamma(M)} \left[ \frac{bR}{2} \right]^M K_{M-1}(bR)
$$

(3.23)

Here $R = \left[ A^2 + s_0^2 + 2As_0 \cos \theta \right]^h$. From this last expression it can be seen that if $s_0 = 0$ then Eq. (3.23) will be the same as Eq. (3.16), i.e. a $K$-distribution. If one varies the
values for $M$ and $s_0$ in Eq. (3.23) different distributions can be obtained. According to Shankar, values for $M > 10$ will correspond to a Rayleigh distribution. This is true when phases are uniformly distributed, otherwise, as $M$ tends to infinity and $s_0$ is different from 0, a Rice distribution will be obtained.

A Rice distribution then, arises from the sum of a constant vector $s_0$ and a real, isotropic Gaussian random variable.

The moments for a Rice distribution, as derived by Denbigh and Jakeman and Tough, are given by

$$\langle A^m \rangle = n!(\sigma_d)^n \, _1F_1(-n;1;\gamma)$$

(3.24)

Where $m=2n$, $\sigma_d$ is the variance of the incoherent random Gaussian contribution, and $\gamma$ is the ratio of the constant phasor intensity to the variance of the random Gaussian component. $_1F_1$ is a confluent hypergeometric function given by

$$F(a;b;x) = 1 + \frac{a}{b}x + \frac{a(a+1)}{b(b+1)2!}x^2 + ...$$

3.3 Generalized K- distribution

To obtain the marginal probabilities Eq. (3.23) should be integrated:

$$f(A) = \frac{A}{2\pi \Gamma(M)} \frac{2b^2}{2^M} \int_0^{2\pi} \frac{1}{bR} (bR)^M K_{M-1}(bR) d\theta$$

(3.25)

Eq. (3.25) proves to be difficult (if not impossible) to integrate because of the angle dependency in the $R$ term. Therefore a different approach, presented by Barakat has been
followed to obtain the probability density function for the intensity signal. Barakat distinguishes two scattering regimes. In the strong scatterer regime, the probability density function of the phases is taken to be uniform, as was assumed in our previous derivations. In the weak scattering regime the distribution of the phases is nonuniform (Von Mises) and is given by:

\[
f(\theta) = \left[2\pi I_0(v)\right]^{-1} \exp(v \cos \theta) \quad -\pi < \theta < \pi
\]  

(3.26)

\[I_0(v)\] is the modified Bessel function of order zero, \(v\) is a real nonnegative constant. Note that when \(v=0\), \(I_0(0)=1\) and Eq. (3.26) becomes the uniform distribution. When the number of steps \(N\) in the biased random walk is fixed but arbitrary, Barakat derived and expression for the intensity probability density function:

\[
f(I\mid N) = \frac{1}{2} I_0^{-N}(v) I_0(v\sqrt{I^2 / a}) \int_0^\infty I_0^N(\alpha r) J_0(I\sqrt{2r}) r dr
\]  

(3.27)

If the number of steps \(N\) is now considered a discrete random variable governed by \(P(N)\) we would get

\[
f(I) = \sum_{N=0}^\infty f(I\mid N) P(N)
\]  

(3.28)

\(P(N)\) can be taken to be the Poisson distribution

\[
P(N) = \frac{\langle N \rangle^N e^{-N}}{N!}
\]

in which case “events” are uncorrelated, i.e., an event consists of the presence of a scatterer, or the negative-binomial distribution

\[
P(N) = \binom{N + M + 1}{N} \left(\frac{\langle N \rangle / M}{1 + \langle N \rangle / M}\right)^N \left(1 + \langle N \rangle / M\right)^{-N-M}
\]
where $M$ is real and nonnegative. In this case the events are correlated and will occur in "bunches". Fluctuations in the number of scattering centers will only be correlated over distances less than the maximum length scale in the medium. When $M$ tends to infinity, the negative binomial distribution tends to the Poisson distribution. The parameters $M$ and $v$ will be essential to our analysis as will be shown in the experimental results section of this report.

The PDF of the intensity can be obtained by summing the series in Eq. (3.28):

$$f(I) = \frac{1}{2} I_0^{-N}(v) I_0 \left( v I_0^{1/2} \right) \sum_{N=0}^{\infty} \left( \begin{array}{c} N+M+1 \end{array} \right) \frac{\langle N \rangle^N J_0^N (ar) (I_0^{1/2} r) r dr}{1 + \langle N \rangle^N \left( \begin{array}{c} M \end{array} \right)^{N+M}}$$

The sum can be worked out to be:

$$\phi(r) = \sum_{N=0}^{\infty} \left( \begin{array}{c} N+M+1 \end{array} \right) \frac{\langle N \rangle^N J_0^N (ar) (1 + \langle N \rangle)^{-M}}{M^N I_0^N (v)}$$

Using the binomial theorem to sum the series we finally get

$$\phi(r) = \left( 1 + \frac{\langle N \rangle}{M} \left[ 1 - \frac{J_0 (ar)}{I_0 (v)} \right] \right)^{-M}$$

(3.29)
The moments for the generalized K-distribution were derived by Barakat \(^{32}\) and are given by

\[
\langle I^m \rangle = \eta^{2m} \frac{\Gamma(M + m)\Gamma(1 + m)}{\Gamma(M)M^m} \left(1 + \frac{v^2}{4M}\right)^m \left[I_{2\,I - 1 + v^2/4M} \left(1 + \frac{v^2}{4M}\right)^{-1}\right]
\]

(3.30)

The hypergeometric function in the previous expression is a polynomial of degree 1 in \((v^2/4M)(1+v^2/4M)^{-1}\):

\[
F(a, b; c; x) = 1 + \frac{a \cdot b}{c} x + \frac{a(a + 1)b(b + 1)}{2!c(c + 1)} x^2 + ...
\]

\(\eta^{2m} = (\langle N \rangle)^{1/2}\) a) is a rescaling parameter. It will cancel out when the normalized moments are calculated.
3.4 Higher order and fractional order moments

Theoretical normalized moments of orders 2, 2.5, 3, 3.5, 4 were calculated for a Rayleigh distribution according to \(^{21}\):

\[
r_{2m\text{Rayleigh}} = \frac{E\{A^{2m}\}}{E\{A^2\}^m} = m!
\]

A Rice distribution corresponds to a concentrated component that has the statistics of the envelope of a constant amplitude sine wave, and a noise-like distributed component. The normalized moments were derived as follows:

The probability density function for the amplitude of the signal is given by \(^{6,10}\)

\[
f(A) = \left(\frac{2A}{\sigma_d}\right)^{A^2 + \sigma_c} e^{-\frac{A^2}{\sigma_d}} I_0 \left(2A \sqrt{\sigma_c} \sqrt{\sigma_d}\right)
\]

here \(I_0\) is a modified Bessel function of order zero. \(\sigma_c\) is the power associated with the concentrated component and \(\sigma_d\) is the power associated with the distributed component.

The moments are given by \(^6\)

\[
E\{A^m\} = \langle A^m \rangle = \sigma_d^{m/2} \Gamma\left(\frac{m}{2} + 1\right) F_1\left(-\frac{m}{2};1; -\gamma\right)
\]

where \(\gamma\) is the ratio of the constant phasor intensity to the variance of the incoherent random Gaussian contribution \(\sigma_d\). \(F_1\) is a confluent hypergeometric function given by

\[
F_1(-a,b;x) = 1 + \frac{a}{b} x + \frac{a(a+1)}{b(b+1)} \frac{x^2}{2!} + ...
\]
To calculate even order moments for the amplitude, let $m=2n$ in Eq. (3.31):

For $n=1$

$$\langle I \rangle = \langle A^2 \rangle = \sigma_d \Gamma(2)_{\frac{1}{2}}F_{1}(-1;1;\gamma) = \sigma_d \Gamma(2)(1+\gamma)$$

For $n=2$

$$\langle I^2 \rangle = \langle A^4 \rangle = \sigma_d^2 \Gamma(3)_{\frac{1}{2}}F_{1}(-2;1;\gamma) = \sigma_d^2 \Gamma(3)(1+2\gamma + \frac{1}{2}\gamma^2)$$

Therefore

$$r_{2\text{mRice}} = \frac{\sigma_d^2 \Gamma(3)(1+2\gamma + 1/2\gamma^2)}{\sigma_d^2 \Gamma(2)^{2}(1+\gamma)^{2}} = \frac{2+4\gamma + \gamma^2}{(1+\gamma)^2}$$

(3.32)

It should be noted that this expression is equivalent to that derived by Denbigh when using Laguerre polynomials. The advantage of our method is that amplitude moments of odd order can also be obtained, therefore allowing calculation of fractional intensity moments.

To calculate odd order moments for the amplitude, let $m=2n+1$ in Eq. (3.31):

Take $n=2$, $m=5$ into:

$$\langle A^5 \rangle = \sigma_d^5 \frac{1}{2} F_{1} \left( \frac{m}{2} + 1; \frac{m}{2}; -\gamma \right)$$

to get

$$\langle A^5 \rangle = \sigma_d^5 \frac{1}{2} F_{1} \left( \frac{7}{2}; \frac{5}{2}; -\gamma \right).$$

Keeping terms in the confluent hypergeometric function up to $O(x)$ we then obtain the fractional normalized intensity moment as

$$\frac{\langle A^5 \rangle}{\langle A^2 \rangle^{5/2}} = \frac{\langle I^{5/2} \rangle}{\langle I \rangle^{5/2}}$$

(3.33)
For \( n=3, \ m=7 \) we obtain \( \langle A^7 \rangle = \sigma_0^{7/2} \frac{\Gamma\left(\frac{9}{2}\right)}{\Gamma\left(\frac{7}{2}\right)} F_1\left(-\frac{7}{2}; 1; -\gamma\right) \). In this case, terms in the confluent hypergeometric function up to \( O(x^2) \) are kept to obtain the fractional normalized intensity moment as

\[
\frac{\langle A^7 \rangle}{\langle A^2 \rangle^{7/2}} = \frac{\langle I^{7/2} \rangle}{\langle I \rangle^{7/2}}
\] (3.34)

If \( \gamma \to 0 \) the second normalized moment for the Rice distribution \( \to 2 \) as for a Rayleigh distribution. If \( \gamma \to \infty \) the second normalized moment for the Rice distribution \( \to 1 \) which corresponds to the case when constructive interference effects at the central frequency contribute to a significant build up of the constant phasor intensity.

For a Generalized K-distribution the moments were derived following Barakat 23. The probability density function for the intensity signal in a weak scattering regime is given by

\[
f(I) = \frac{2M}{\Gamma(M)\eta^{M+1}} \left(\frac{M}{\eta^2 + \frac{I}{4M}}\right)^{M-\frac{1}{2}} I^{M-\frac{1}{2}} \times I_0\left(\frac{\sqrt{\pi}}{\eta^2}ight) K_{M-1} \left(\frac{2}{\eta} \left[1 + \frac{\eta^2}{4M}\right] IM\right)^{\frac{1}{2}}
\]  

(3.35)

It should be remembered here that \( \psi \) is a measure of deviation from the uniform distribution of the phases in the random walk. \( M \) is a parameter that measures clustering. As \( M \) tends to infinity the negative binomial distribution of the phasors in the random walk will tend towards a Poisson distribution.

The moments for the Generalized K distribution can be obtained by direct integration of Eq. (3.35):
\[ \langle T^l \rangle = \eta^{2l} \frac{\Gamma(M+1)\Gamma(1+l)}{\Gamma(M)M^l} \left( 1 + \frac{\nu^2}{4M} \right) \ {} _2F_1 \left[ 1; 1 - M, -l; 1 + \frac{\nu^2}{4M} \right] \]  

(3.36)

Here \( \ {} _2F_1(a, b, c; x) = 1 + \frac{a \cdot b}{c} x + \frac{a(a + 1)b(b + 1)}{c(c + 1) \cdot 2} x^2 + \ldots \) corresponds to a hypergeometric function.

This formulation was favored again because it allows us to obtain fractional normalized intensity moments.

If \( l = 1 \):

\[ \langle I \rangle = \eta^{2} \frac{\Gamma(M+1)\Gamma(2)}{\Gamma(M)M} \left( 1 + \frac{\nu^2}{4M} \right)^2 (1 + Mx) \]

where \( x = \left( \frac{\nu^2}{4M} \right)^{-1} \left( 1 + \frac{\nu^2}{4M} \right) \)

If \( l = 2 \):

\[ \langle I^2 \rangle = \eta^{4} \frac{\Gamma(M+2)\Gamma(3)}{\Gamma(M)M^2} \left( 1 + \frac{\nu^2}{4M} \right)^3 \left( 1 + (2 + M)x + \frac{M + M^2}{2} x^2 \right) \]

Therefore

\[ r_{2mGen K} = \frac{\langle I^2 \rangle}{\langle I \rangle^2} = \frac{2(M+1)}{M} \left( 1 + (2 + M)x + \frac{M + M^2/2}{(1 + Mx)^2} \right) \]  

(3.37)

When odd order moments for the amplitude are calculated, such as 3th and 5th, terms in the hypergeometric function up to \( O(x) \) and \( O(x^2) \), respectively, are kept.

Normalization is then performed as

\[ \frac{\langle I^{1/2} \rangle}{\langle I \rangle^{1/2}} = \frac{\langle A^1 \rangle}{\langle A^2 \rangle^{1/2}} \]
If in Eq. (3.36) we take \( v = 0 \), then \( x = \left( \frac{\nu^2}{4M \left( 1 + \frac{\nu^2}{4M} \right)} \right)^{-1} = 0 \), and the moments for a K distribution are obtained.

### 3.5 Summary

In summary, four statistical distributions will be considered for the analysis of the experimental data: Rayleigh, Rice, K, Generalized K. These four distributions are related to each other essentially through the parameters \( M \), \( v \), and \( \gamma \). The Rayleigh regime occurs when \( M \) tends to infinity, \( \gamma \) is zero, and \( v \) is zero. For this case, the second normalized moment will be equal to 2. The Rice regime occurs when \( M \) tends to infinity and \( \gamma \) is different from zero. The second normalized moment is lower than 2. The \( K \) regime, when clustering is present, occurs when \( M \) is finite and \( v \) is equal to zero. The second normalized moment is higher than 2. The Generalized \( K \) regime, whose second normalized moment can be both higher and lower than 2, occurs when \( M \) is finite and \( \nu \) is different from zero. In this case, clustering occurs and the phase distribution of the phasors in the random walk deviates from uniform.

Figure 3.5.1 presents in a graphic and schematic way the relationship among the different statistical distributions outlined in the above paragraph.
Figure 3.5.1 Relationship among statistical distributions.
4 Experimental Verification

4.1 Experimental setup

The setup used for the experiments is shown in the following figure:

![Flowchart of Experimental Setup](image)

Figure 4.1.1 Experimental Setup

The previous theory was verified by recording the echo signals from three 14 cm × 7 cm × 6 cm blocks of sponge structures immersed in water making sure there were no trapped air bubbles in the medium, samples from a freshly excised pig liver, samples from fresh human breast tissue (normal and abnormal), and samples from fresh human skeletal muscle. One sponge, referred to as sample 1, had larger mean pore size (diameter, \(d=2\) mm). The other two (sample 2, sample 3) had much smaller mean pore size (diameter, \(d=0.5\) mm), sample 2 had a more organized structure.

The 13-mm diameter circular disk, 3.5 MHz medium focus transducer has a focal length of 4.5 cm. Its 6 dB bandwidth was approximately 1.2 MHz. The sample surfaces were positioned at the focal zone of the transducer and held perpendicular to the beam axis.
The transducer was excited with programmable signals generated by a waveform generator (Analogic Corporation, Model 2020) as follows:

\[ p(t) = \overline{A}(t) \cos(2\pi f_0 t) = 0.5 \left[ 1 - \cos \left( \frac{2\pi t}{T} \right) \right] \cos(2\pi f_0 t); \quad 0 \leq t \leq T \quad (4.1) \]

\( \overline{A}(t) \) is a Hanning window whose pulse width is inversely proportional to the 6 dB bandwidth \( \Delta f \). \( f_0 \) was set at 3.5 MHz (the center frequency of the transducer). The 6 dB pulse bandwidth \( \Delta f \), measured on the power spectrum of the signals was varied between 0.2 MHz and 1.0 MHz in steps of 0.2 MHz by changing \( T \) from 1.98 \( \mu s \) to 9.89 \( \mu s \). 10 \( \mu s \) of echo signal, centered in the focal zone were recorded in each case at a sampling interval of 0.04 \( \mu s \) with an 8 bit digitizer (Analogic Corporation DATA 6500). For each of the 5 bandwidths and each sample, echo signals were recorded at 30 different locations on the sample obtained by translating the transducer in the plane perpendicular to the beam axis with a stepper motor, covering a 10 mm by 3 mm area. Each translation was 1 mm. For some of the tissue samples, two sets of measurements were obtained at different tissue orientations, 90° with respect of each other, but always perpendicular to the transducer.

The two dimensional PSF was also measured in separate experiments by placing and scanning a 0.25 mm nylon wire at 2.5 cm (focal zone) from the transducer. This entire two-dimensional function represents \( g(r,t) \) in Eq. (2.8).
4.2 Resolution cell volume

Numerical integration of Eq. (2.8) led to the results shown in Table 4.2.1. Fig. 4.2.1 shows, alternatively, the calibration curve used to convert data from bandwidth into volume, thus removing system effects:

<table>
<thead>
<tr>
<th>Bandwidth, $\Delta f$ (MHz)</th>
<th>Volume, $V_E$ (mm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>42.7</td>
</tr>
<tr>
<td>0.4</td>
<td>21.37</td>
</tr>
<tr>
<td>0.6</td>
<td>16.06</td>
</tr>
<tr>
<td>0.8</td>
<td>13.74</td>
</tr>
<tr>
<td>1.0</td>
<td>13.3</td>
</tr>
</tbody>
</table>

Table 4.2.1 Results from integration of Eq. 2.8
Figure 4.2.1 Inverse of resolution cell volume as a function of bandwidth, $f_0=3.5$ MHz, focal zone.

4.3 Scattering structures

4.3.1 Sponge structures

Three sponge structures of different pore sizes were analyzed. Sponge sample 1 has a larger pore size of diameter about 2 mm. Sponge sample 2 and sample 3 have smaller pore diameter of about 0.5 mm, however sample 2 presents a more organized spatial structure than sample 3. 30 scans in a raster mode were performed. In Appendix B the optical images of the sponge structures are referred to a ruler in which every division corresponds to 1 mm.
4.3.2 Liver tissue

Freshly excised pig liver tissue was obtained from the slaughterhouse and was analyzed within 24 hours of excision. Pig liver tissue, as well as human liver tissue is organized into innumerable hepatic lobules. These lobules appear as small polygonal units consisting of hepatic cells arranged in cords radiating around a central blood vessel. Connective tissue lies in between the lobules. The portal area is apparent when three or more lobules meet. These areas contain the interlobular bile ducts together with branches from the portal vein and the hepatic artery.\textsuperscript{37}

Two sets of data, 30 scans in raster mode each, were obtained from the tissue. One, labeled as Liver 1, corresponds to the largest surface of the tissue placed perpendicular to the beam axis, the other, labeled Liver 2, corresponds to the largest surface of the tissue placed parallel to the beam axis. In Appendix B histology images are included. The area corresponds to 1 cm\textsuperscript{2}.

4.3.3 Breast tissue

The mammary gland is a very complex structure consisting of several (= 20) irregular lobes radiating from the nipple. The lobes are separated by layers of dense connective tissue and surrounded by adipose tissue.\textsuperscript{38} Each lobe is subdivided into lobules of different sizes, of which the smallest consist of elongated tubules covered by alveoli. The backscattered echo signal from this diversity of structures is analyzed.

Nine samples of freshly excised breast tissue were obtained from the Pathology department of Highland Hospital in Rochester, NY. These samples were identified with
letters from a to i. Two measurements, of 30 scans each (when the size allowed it) in raster mode were recorded for normal tissue. One, labeled as horizontal scan, corresponds to the largest surface of the tissue placed perpendicular to the beam axis, the other, labeled vertical scan, corresponds to the largest surface of the tissue placed parallel to the beam axis. Five samples belong to normal tissue (breast_a, b, c, d, h). One measurement, of 30 scans in raster mode labeled as horizontal scan, was recorded for diseased tissue due to the size of the samples. These samples were named (breast_e, f, g, i). Results are shown in Appendix B. The histology images correspond to an area of 1 cm².

4.3.4 Skeletal muscle

The histological unit of skeletal muscle is a fiber, a long cylindrical multinucleate cell. Large numbers of parallel muscle fibers form the fascicles which are visible to the naked eye. The muscle fibers, the fascicles and the whole muscle are invested by connective tissue which serves to bind together the contractile units and groups of units and to integrate their action.

A sample of freshly excised human skeletal muscle from a thigh was analyzed. Two data sets of 30 scans in raster mode were obtained. One, labeled as sk_ah (horizontal scan), corresponds to the largest surface of the tissue placed perpendicular to the beam axis, the other, labeled as sk_av (vertical scan), corresponds to the largest surface of the tissue placed parallel to the beam axis. Results are shown in Appendix B. The histology image corresponds to an area of 1 cm².
4.4 Moments Analysis

Echo signals from different scattering structures immersed in water were recorded.

The recorded echo signal was assumed to be the real part of the complex signal. The imaginary part was calculated as the Hilbert transform of the real part. The intensity $I(t)$ was calculated as the sum of the squares of the real and imaginary parts. Normalized moments of second, 2.5, third, 3.5, and fourth order were calculated on the signal $I(t)$ for the different bandwidth cases under consideration, i.e., from effective volume $V_e \rightarrow 0$ to $V_e \rightarrow \infty$.

The experimental results are organized in Appendix B as follows: Histology (optical) images and ultrasound speckle images are first presented. A plot of the second normalized intensity moment, $<I^2>/\langle I \rangle^2$ (labeled Iratio), as a function of inverse resolution cell volume is introduced along with a least squares fit that provides information on the slope and the intercept of the plot. It should be noted that the experimental points in these plots correspond to the average of 30 scans; error bars are not included but are usually within 15% of the data values. The inverse slope is an estimate of the average of the scatterer number density. The intercept can be interpreted as a measure of deviation from the Rayleigh limit of 2.

Next, a surface plot of higher order normalized intensity moments, $<I^m>/\langle I \rangle^m$ (labeled Iratio), as function of bandwidth and moments order is introduced. The following set of plots shows the normalized intensity moments $<I^m>/\langle I \rangle^m$ (Iratio) as a function of moments order at different bandwidths and includes fits to theoretical probability density functions.
Finally, a plot of the effective number of scatterers (M) obtained from fitting experimental data to a Generalized K distribution as a function of resolution cell volume is presented.

This sequence of results is presented for both horizontal and vertical scans.

4.5 Periodic samples

The quasi-periodic alignment of scatterers in some of the samples was further studied by performing a frequency sweep in steps of 0.1MHz within the bandwidth of the transducer (from 1.5MHz to 5.5 MHz). One A-line of data was recorded, the second normalized intensity moment was calculated and the autocorrelation performed. This procedure allowed us to calculate interscatterer distances without the need of performing a Fourier transform. The quasi-periodic alignment of scatterers was made evident through this analysis.
5 Experimental results

5.1 Sponge structures

The process outlined in section 4.4 was followed to analyze data from the three sponge structures. First, the second normalized intensity moment in terms of bandwidth was obtained (Fig. 5.1.1).

Figure 5.1.1 Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs. bandwidth, $f_0=3.5$ MHz. Sponges.

Using the lookup table in Fig. 4.2, data were converted in terms of resolution cell volume (Fig. 5.1.2).
A least squares fit was applied to each set of data and a slope and intercept were obtained. These are summarized in Table 5.1.1.

<table>
<thead>
<tr>
<th>Sponge</th>
<th>Slope</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample1</td>
<td>40.27</td>
<td>1.29</td>
</tr>
<tr>
<td>Sample2</td>
<td>8.93</td>
<td>1.25</td>
</tr>
<tr>
<td>Sample3</td>
<td>5.45</td>
<td>1.52</td>
</tr>
</tbody>
</table>

Table 5.1.1 Least squares fit. Sponges.

The first thing to note from the results presented thus far is the difference in the slope estimates between sample1 and samples 2 and 3. Remember that sample2 and sample3 have similar size pores even though their spatial structures differ. Please refer to images in Appendix B. Sample1 has a much larger pore size. According to Eq. (2.7), the slope estimate should be inversely proportional to $<N>$, the scatterer number density. The quantitative estimates reflect this behavior. It should be noted though, that the slope value also depends on the scattering medium via the term $<a^4>/<a^2>^2$. We cannot separate this
term from \( <N> \). The combined term is also known in the literature as the effective scatterer number density \(^{21}\).

Note also that the intercept estimates all fall below the Rayleigh limit of 2, therefore, fits to non-Rayleigh statistical distributions were studied.

Results from these fits are shown in Appendix B. Let us note here that both sample2 and sample3 seem to be better described by a Rice distribution at all bandwidths under consideration. This is reasonable since the number of scatterers per resolution cell volume is large, and in particular, sample2 has a very organized structure that will be further analyzed in section 5.5. This regularity accounts for the buildup of the coherent term in the random walk. On the other hand, sample1 which has fewer scatterers per resolution cell volume, seems to be better described either by a K distribution or a Generalized K distribution.

An estimate of the effective number of scatterers for each sample, as obtained from a Generalized K distribution, is presented in Figure 5.1.3. It should be stressed here that the Generalized K distribution was used even though it was not always the best fit. The reason being that it is the only distribution that sweeps the whole "moments space" as shown in Figure 3.5.1, and provides an approximate estimate of \( M \) at every instance.

![Figure 5.1.3](image-url)  
Figure 5.1.3 Effective number of scatterers, \( M \), as a function of resolution cell volume. Sponges.
As expected, sponge sample 1 presents fewer scatterers per resolution cell volume than the other two sponge samples.

The spatial structure of sample 1 is very similar (dimensionally) to that of the liver tissue. It was used as a model before attempting real tissue. The success of our experimental procedure allowed us to continue our study.

### 5.2 Liver tissue

The process outlined in section 4.4 was followed to analyze data from freshly excised pig liver tissue. First, the second normalized intensity moment in terms of bandwidth was obtained (Fig. 5.2.1). The two sets of data, perpendicular to each other are included.

![Figure 5.2.1 Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs. bandwidth. Liver.](image)

Using the lookup table in Fig. 4.2, data were converted in terms of resolution cell volume (Fig. 5.2.2).
Figure 5.2.2 Second normalized intensity moment \(<I^2>/\langle I\rangle^2\) (Iratio) vs. inverse of resolution cell volume, \(f_0=3.5\) MHz. Liver.

A least squares fit was applied to each set of data and a slope and intercept were obtained. These are summarized in table 5.2.1.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Slope</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver1</td>
<td>34.44</td>
<td>0.87</td>
</tr>
<tr>
<td>Liver2</td>
<td>40.34</td>
<td>1.09</td>
</tr>
</tbody>
</table>

Table 5.2.1 Least squares fit. Liver.

It should be noted at this point, that the linear behavior predicted by Eq. (2.7) is not followed by the liver samples analyzed. This can be explained by the frequency dependency of scattering. Remember that the slope is an estimate of the average of the effective scatterer number density and it includes the term \(\langle a^4\rangle/\langle a^2\rangle^2\). It is possible that the deviation from linearity carries itself information about the scattering microstructure. Such analysis has not been attempted thus far. On the other hand, intercept values fall well below
the Rayleigh limit of 2. As a consequence, fits to non-Rayleigh statistical distributions were studied.

Results from these fits are shown in Appendix B. It's interesting to note that when the resolution cell volume increases (bandwidth = 0.2MHz) constructive interference of the echo signal contributes to the coherent buildup of the constant phasor in the random walk formulation, therefore a Rice distribution is a good statistical model. As the resolution cell is decreased, fewer scatterers are included and it seems that clustering occurs, therefore the intensity signal is better described by either a $K$ distribution or a Generalized $K$ distribution.

An estimate of the effective number of scatterers for each sample, as obtained from a Generalized $K$ distribution, is presented in figure 5.2.3. It should be stressed once more that the Generalized $K$ distribution was used even though it was not always the best fit.

![Figure 5.2.3 Effective number of scatterers, $M$, as a function of resolution cell volume. Liver.](image)

The fact that these estimates are very close for two different orientations of the tissue tells us that liver could be considered an isotropic structure. This regularity will further be analyzed in Section 5.5.
5.3 Breast tissue

5.3.1 Normal tissue

The process outlined in section 4.4 was followed to analyze data from five samples of normal breast tissue and four samples of diseased breast tissue. First, the second normalized intensity moment in terms of bandwidth was obtained. Figure 5.3.1 includes data for normal tissue, horizontal scan. Figure 5.3.2 includes data for normal tissue, vertical scan. Case by case data are included in Appendix B.

Figure 5.3.1 Second normalized intensity moment \( \langle I^2 \rangle / \langle I \rangle^2 \) (Iratio) vs. bandwidth, \( f_0 = 3.5 \text{MHz} \). Normal breast tissue, horizontal scan.
Figure 5.3.2 Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs. bandwidth, $f_0=3.5$ MHz. Normal breast tissue, vertical scan.

Using the lookup table in Fig. 4.2, data were converted in terms of resolution cell volume. Figure 5.3.3 shows horizontal scan, and Figure 5.3.4 vertical scan.

Figure 5.3.3 Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs. inverse of resolution cell volume, $f_0=3.5$ MHz. Normal breast tissue, horizontal scan.
Figure 5.3.4 Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs. inverse of resolution cell volume, $f_0=3.5\text{MHz}$. Normal breast tissue, vertical scan.

A least squares fit was applied to each set of data and a slope and intercept were obtained. Table 5.3.1 summarizes these results for horizontal scan and table 5.3.2 summarizes data for vertical scan.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Slope</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>b_ah</td>
<td>47.98</td>
<td>0.96</td>
</tr>
<tr>
<td>b_bh</td>
<td>14.41</td>
<td>2.12</td>
</tr>
<tr>
<td>b_ch</td>
<td>36.72</td>
<td>0.83</td>
</tr>
<tr>
<td>b_dh</td>
<td>13.65</td>
<td>1.27</td>
</tr>
<tr>
<td>b_hh</td>
<td>25.55</td>
<td>1.01</td>
</tr>
</tbody>
</table>

Table 5.3.1 Least squares fit. Normal breast tissue. Horizontal scan.
5.3.2 Diseased tissue

First, the second normalized intensity moment in terms of bandwidth was obtained. Figure 5.3.5 includes data for four samples of diseased tissue, horizontal scan. Unfortunately, the samples of diseased tissue made available to us were very thin, making it almost impossible to realize a vertical raster. Case by case data are included in Appendix B.

![Figure 5.3.5](image)

Figure 5.3.5 Second normalized intensity moment $\frac{\langle I^2 \rangle}{\langle I \rangle^2}$ (Iratio) vs. bandwidth, $f_0=3.5$MHz. Diseased breast tissue.
Using the lookup table in Fig. 4.2, data were converted in terms of resolution cell volume (Fig. 5.3.6).

Figure 5.3.6 Second normalized intensity moment \( \langle I^2\rangle/\langle I\rangle^2 \) (Iratio) vs. inverse of resolution cell volume, \( f_0=3.5\text{MHz} \). Diseased breast tissue.

A least squares fit was applied to each set of data and a slope and intercept were obtained. These are summarized in table 5.3.3.
Breast tissue is a very complicated composition of structures and it is difficult to differentiate between normal tissue and diseased tissue using ultrasonic techniques as can be seen from the results presented so far. In the group of diseased tissue, breast_g seems to consistently have a higher second normalized moment, and presents a higher slope than the other samples in that group. It is the only sample that belongs to a male patient.

Once again, deviations from linear behavior can be observed for some of the samples, as stated before it is possible that these deviations carry themselves information about the scattering microstructure. On the other hand, intercept values fall well below the Rayleigh limit of 2. As a consequence, fits to non-Rayleigh statistical distributions were studied. Results from these fits are shown in Appendix B.

Estimates of the effective number of scatterers for each sample, as obtained from a Generalized K distribution, are presented in Figure 5.3.7 for normal, horizontal scan, Figure 5.3.8 for normal, vertical scan, and Figure 5.3.9 for diseased, horizontal scan. It should be stressed once more that the Generalized K distribution was used even though it was not always the best fit.
Figure 5.3.7 Effective number of scatterers, $M$, as a function of resolution cell volume. Normal breast tissue, horizontal scan.

Figure 5.3.8 Effective number of scatterers, $M$, as a function of resolution cell volume. Normal breast tissue, vertical scan.

Figure 5.3.9 Effective number of scatterers, $M$, as a function of resolution cell volume. Diseased breast tissue, horizontal scan.
One could be tempted to say that diseased tissue follows a different pattern from that of normal tissue. Evidently, more samples are required to achieve such a conclusion with a degree of statistical significance. In Figure 5.3.9, breast_g is the only one that does not follow the pattern. That is the sample from a male patient.

Unlike Shankar et al. 39, we have proved that both normal and diseased tissue are better characterized by a non-Rayleigh distribution.

5.4 Skeletal muscle

The process outlined in section 4.4 was followed to analyze data from freshly excised skeletal muscle from a male's thigh. First, the second normalized intensity moment in terms of bandwidth was obtained (Fig. 5.4.1). The two sets of data, perpendicular to each other are included.

Figure 5.4.1 Second normalized intensity moment $<I^2>/<I^2>$ (Iratio) vs. bandwidth, $f_o=3.5$MHz. Skeletal muscle.

Using the lookup table in Fig. 4.2, data were converted in terms of resolution cell volume (Fig. 5.4.2).
A least squares fit was applied to each set of data and a slope and intercept were obtained. These are summarized in table 5.4.1.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Slope</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>sk_ah</td>
<td>18.93</td>
<td>1.73</td>
</tr>
<tr>
<td>sk_av</td>
<td>10.75</td>
<td>1.49</td>
</tr>
</tbody>
</table>

Table 5.4.1 Least squares fit. Skeletal muscle.

The intercept estimates fall below the Rayleigh limit of 2, therefore, fits to non-Rayleigh statistical distributions were studied.

Results from these are shown in Appendix B. Let us note here that sk_av seems to be better described by a Rice distribution while the resolution cell volume is large, whereas sk_ah seems to be better describe by either a K or Generalized K distribution. This is an understandable result since the structure presented to the transducer at both orientations differs. When the tissue is place horizontally, that is, with its largest surface perpendicular to the transducer beam, the fascicles, which are visible to the naked eye, are probably the
principal scatterers at the operating frequency. On the other hand, when the tissue is placed with its largest surface parallel to the transducer beam (vertical scan), a cross section of the fascicles is presented. The fascicles are formed by a collection of long fibers, therefore a higher density of scatterers will fall into the cell volume. These fibers, as well as the fascicles present a very regular structure which contributes to the coherent buildup of the constant phasor in the random walk formulation, therefore a Rice distribution is a good statistical model to describe the echo signal.

An estimate of the effective number of scatterers for each sample, as obtained from a Generalized K distribution is presented in figure 5.4.3.

Figure 5.4.3 Effective number of scatterers, \( M \), as a function of resolution cell volume. Skeletal muscle.

As can be seen from the last figure, the scatterer density is higher for the vertical scan.

The regularity of the scattering microstructure will be further analyzed in section 5.5.
5.5 *Interscatterer distance*

Some of the samples analyzed present a rather organized spatial structure. These were further investigated following the procedure outlined in section 2.3.

To test the experimental protocol and the validity of the analysis, a preliminary study was conducted on sponge sample2. Two measurements were recorded. One with the sponge undisturbed, and a second one with the sponge placed inside a press with an acoustic window under uniform compression.

Results of this procedure after autocorrelation of the second normalized intensity moment are shown in Figure 5.5.1 for sample2 and Figure 5.5.2 for sample2 compressed. Each frequency step corresponds to 0.1 MHz.

![Figure 5.5.1 Autocorrelation of second normalized intensity moment as a function of frequency bins. Sample2.](image-url)
To calculate the interscatterer distance it suffices to convert distance between two major frequency peaks. From \( c = \frac{2d}{t} \), taking \( c=1500 \text{ m/s} \), we get \( d=0.5 \text{ mm} \) for sample2 and \( d=0.3 \text{ mm} \) for sample2 compressed. These estimates are very close to the real values. Please refer to the optical image of sponge sample2 in Appendix B.

The success of this technique allowed us to investigate some of the other samples.

Results for liver tissue are shown in Figure 5.5.3.

---

Figure 5.5.2 Autocorrelation of second normalized intensity moment as a function of frequency bins. Sample2 compressed.

Figure 5.5.3 Autocorrelation of second normalized intensity moment as a function of frequency bins. Liver.
The calculated interlobular distance corresponds to $d=0.5$ mm. Once again, this measurement is very close to the real value. Please compare to the histology image presented in Appendix B. The field of view of the image is 1 cm$^2$.

Results for skeletal muscle, horizontal scan, are shown in Figure 5.5.4.

![Figure 5.5.4 Autocorrelation of second normalized intensity moment as a function of frequency bins. Skeletal muscle.](image)

The calculated interscatterer distance corresponds to $d=0.3$ mm. It is very possible that this distance corresponds to the thickness of a fascicle which was visible to the naked eye.

Some interesting results were obtained from breast tissue. Breast_e was a reasonably large sample although very thin. It was comprised of one half of normal tissue and the other of tumor. It wasn't large enough to perform separate raster readings tissue/tumor, but it was enough to perform 2 A-lines, one on each half. Results are shown in Figure 5.5.5 for the tissue half and Figure 5.5.6 for the tumor half.
Figure 5.5.5 Autocorrelation of second normalized intensity moment as a function of frequency bins. Breast tissue.

Figure 5.5.6 Autocorrelation of second normalized intensity moment as a function of frequency bins. Tumor in breast tissue.

The distance calculated between two major peaks in the tissue breast_e corresponds to 0.3 mm. In the tumor the interscatterer distance is not resolvable.

Breast_h and breast_i correspond to the same patient. Breast_h is normal tissue and breast_i is a tumor. Results for these samples are shown in figure 5.5.7 for tissue and figure 5.5.8 for tumor.
Figure 5.5.7 Autocorrelation of second normalized intensity moment as a function of frequency bins. Breast tissue.

Figure 5.5.8 Autocorrelation of second normalized intensity moment as a function of frequency bins. Tumor in breast tissue.

The distance between major peaks in tissue breast_h corresponds to .26 mm. It’s difficult to get a conclusion from breast_i since there are no noticeable peaks, but it would look like the interscatterer distance is not resolvable.

Further analysis can be implemented following Landini and Verrazzani. It is possible that the thickness of the main peak, as well as the decay of the envelope carry information regarding the regularity of the scattering microstructure.
6 Phantom

6.1 Theory and implementation

To study the correlation between experimental results presented in chapter 5 and histology, phantoms were prepared from the histology sections. Tissue samples were digitized using a microdensitometer with a field of view of 1 cm$^2$. Once digitized they were processed using ImLab software.

In this case we have to redefine the concept of resolution cell volume for one of resolution cell surface because the phantom structure patterns are deposited on a transparency. The following geometry is considered:

![Image of Transducer scanning geometry and the concept of resolution cell area.](image)

Figure 6.1.1 Transducer scanning geometry and the concept of resolution cell area.
The phantom is a two dimensional plane of scatterers, therefore we can define $M_a$ as the number of scatterers in an area $S_T$ delimited by a rectangle of length equal to 20 dB pulsewidth in the $z$ direction and 20 dB beamwidth in the scanning direction. Following the arguments presented in chapter 2 we can write Eq. (2.5) as

$$\frac{\langle B^4 \rangle / \langle A^4 \rangle}{\langle B^2 \rangle / \langle A^2 \rangle^2} = \frac{1}{S_T} \left[ \frac{\langle B^4 \rangle / \langle A^4 \rangle_s}{\langle B^2 \rangle / \langle A^2 \rangle_s^2} \right] = \frac{S_T}{S_E}$$

(6.1)

where $\langle \ldots \rangle_s$ stands for area average over the area $S_T$. The effective area $S_E$ results from the integration

$$S_E = \left[ 2 \int_{r=0}^{\infty} B^2(r)dr \int A^2(t)dt \right]^2$$

(6.2)

where $B(r)$ is the beam profile and $A(t)$ is the pulse shape.

Note that this area is numerically much smaller than the effective volume $V_E$, however it is still proportional to the pulsewidth or bandwidth. If we define $N_s = M_a / S_T$ as the number of scatterers per unit area we can rewrite the second normalized moment of the intensity distribution as

$$\frac{\langle I^2 \rangle}{\langle I \rangle^2} = 2 + \frac{\langle a^4 \rangle}{\langle a^2 \rangle^2} \frac{1}{N_s S_E}$$

(6.3)

We consider that the main scatterers at 3.5MHz correspond to the lobular structure in the liver and the strands in the sponge structures, therefore following the idea developed by Parker and Phillips we implemented some thin film phantoms to evaluate the correlation.
with histology sections of our liver samples. The first approach consisted of designing a pattern that resembles the lobular structure with equivalent dimensions as the real tissue and the big pore size sponge (Fig. 6.1.2). This pattern was printed on paper using a 720 x 360 dpi thermal ink jet printer and then transferred to a Kodak Ektaprint transparency using a Cannon copier. The thin film was placed in the water tank with the same experimental setup and the experimental moments were calculated. In Figure 6.1.3 we present a comparison of the second normalized moments of the intensity signal (Iratio) as a function of bandwidth among tissue, sponge and phantom.

Figure 6.1.2 Pattern created to simulate liver structure.
Figure 6.1.3 Comparison of $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) for some samples and phantom from Fig. 6.1.2.

After the simulation pattern was tested and verified, an attempt was done using a real histology section. Liver tissue was chosen because of its regular structure.

Once ultrasound measurements were recorded, tissue samples were fixed and taken to Highland Hospital where histology slides were prepared. Phantoms were produced using a CCD video camera module with a 1 cm$^2$ field of view. IMLAB software was used to digitize and perform some image processing along with PhotoShop. For example, in liver samples contrast was reversed to enhance the lobular pattern, a median filter was applied to smooth the interlobular appearance, and the edges were sharpened. See Figures 6.1.4 (liver tissue) and 6.1.5 (processed image). Images were printed on a transparency using a Hewlett-Packard color laser printer with a resolution of 300 dpi. Using the same experimental setup, data are collected and the moments calculated.
The second normalized intensity moment was calculated for the phantom (phliv) and compared to that of the liver tissue. Results are shown in Figure 6.1.6:
Figure 6.1.6 Second normalized intensity moment, $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio), as a function of bandwidth, $f_0=3.5\text{MHz}$. Phantom and liver tissue.

To remove system's effects, a conversion from bandwidth to area cell was performed using the following lookup table:

Figure 6.1.7 Inverse of resolution cell area as a function of bandwidth, $f_0=3.5\text{MHz}$, focal zone.

Figure 6.1.8 shows results for the liver phantom after conversion:
Figure 6.1.8 Second normalized moment, \(\frac{<\varepsilon^2>}{<\varepsilon>^2}\) (Iratio), as a function of inverse of resolution cell area. Phantom.

A least squares fit was applied and evaluation of the slope and intercept obtained. These results are also shown in Appendix B.

To estimate the effective number of scatterers (M) within the resolution cell area, fits to theoretical distributions Rice, K, and Generalized K were obtained. \(1/M\) results from the latter are shown in figure 6.1.9 as a function of bandwidth and are compared to results from tissue samples.

Figure 6.1.9 Inverse of effective number of scatterers as a function of bandwidth, \(f_0=3.5\text{MHz}\). Liver tissue and phantom.
Effective number of scatterers \((M)\) for the phantom, as calculated from the Generalized K distribution, are shown in terms of resolution cell area in Figure 6.1.10.

![Graph showing effective number of scatterers](image)

Figure 6.1.10 Effective number of scatterers, \(M\), as a function of resolution cell area. Phantom.

As can be seen from the closeness of the results shown, the phantom created from the lobular structure of the liver tissue seems to be a good model for the scattering structure. Remember that it was assumed that at the operating frequency, the main scattering structure was the lobular pattern reproduced in the phantom.

To test for the periodicity of the structure, and evaluate the interscatterer distance, a frequency sweep as described in section 2.3 was performed. Results of this procedure after autocorrelation of the second normalized intensity moment are shown in Figure 6.1.11. Each frequency step corresponds to 0.1 MHz.
Figure 6.1.11 Autocorrelation of second normalized intensity moment as a function of frequency bins. Liver phantom.

The interscatterer distance can be calculated from these data based on the distance between two major peaks. The speed of sound was taken to be 1500 m/s. From $c=2d/t$ we obtain $d=0.7$ mm which is pretty close to the real dimensions. Remember the value calculated for tissue in Section 5.5 was $d=0.5$ mm.

Histology is considered to be the gold standard when it comes to the tissue pathology. The histology sections taken through the region of interest of the tissue sample can provide partial information about the scattering microstructure.

The method presented in this chapter may prove to be helpful when correlating parameters extracted from the statistical analysis of the tissue and the tissue’s spatial structure obtained from histology.
7 Discussion and Conclusions

This study examined the possibility of probing a scattering microstructure with multiple bandwidth pulses with center frequency matched to that of the transducer. The linear variation of the second normalized intensity moment with the inverse of the resolution cell volume was derived theoretically and tested experimentally.

The concept of three dimensional imaging point spread function (PSF) and the associated resolution cell volume were defined. An unambiguous relationship between these two concepts was established through equations (2.6) and (2.8). The resolution cell volume was numerically calculated from the experimental PSF from the approximate form $B(t)A(t)$. The volume definition used by others \(^{21}\) is not the same as ours because it is bounded by time gate and not by pulse width, and has been defined in the context of analysis performed in the frequency domain. The concept of three dimensional PSF also defines some important length scales in the random walk problem. The statistics of the echo signal is mostly determined by the properties of the scattering microstructure and the degree of phase coherence on these length scales.

The method described in this paper performs first the estimation of two parameters, namely the slope and intercept from a series of narrow bandwidth probing of the microstructure. If we had employed a pulse excitation as the drive signal utilizing the full bandwidth of the transducer, we would have obtained a single point for each sample at approximately the highest value of $1/V_e$. Although it is possible to estimate the effective number of scatterers $M^6$ from such single data point, it may not prove to be sufficient to discriminate between many different classes of microstructures encountered in real life. In
our method, the slope depends on the effective scatterer number density and the intercept mostly depends on the regularity of the structure. It is the intercept value, which usually differs from the Rayleigh limit of 2, that led us to non-Rayleigh statistical analysis of the echo signal allowing us to calculate other parameters such as effective number of scatterers as well as deviations from the uniform distribution of the phases in the random walk. Our experimental results showed that both normal and abnormal tissue are better characterized by these models.

Shankar et al. proposed a method for identification of tumors in ultrasound B-scans of the breast. In their work they never considered the resolution cell volume of the insonifying system. It has been shown in our work that parameters such as effective number of scatterers $M$ (which they use for their characterization) vary with the resolution cell volume. Besides, their analysis was done on the B-scan images, not the rf signal, regardless of any non-linearities introduced by the imaging system. Another point of contention with their work is the claim that values of $M$ greater than 10 correspond to a Rayleigh distribution. This might be the case if the phasor phases in the random walk are distributed uniformly. However, for a quasi periodic structure, the value of $M$ could be higher than 10 while the phasor phases are not uniformly distributed, leading to a Rice distribution or Generalized K distribution.

On the other hand, Chen et al. have proposed a method to estimate the effective scatterer number density at different frequencies by calculating the statistical moments on the Fourier transform of the echo signal. Due to significant oscillations in the data points in the Fourier domain, they have to apply a polynomial fit to extract the effective number density at the center frequency of the transducer. They are able to calculate the effective scatterer number density on phantoms with well known size distribution and shape of
scatterers using Faran's method. The method is not applicable to real tissue because the scattering cross-section of the scatterers is not known and cannot be separated from \(<N>\), as was discussed in section 2.1, and is evident from equation (2.7). The inverse of our slope estimate represents a similar effective scatterer number density at the dominant frequency \(f_0\). Our spatial domain analysis circumvents some of the problems associated with frequency domain analysis due to time truncation. The same holds true for our analysis of interscatterer spacing.

The experimental method introduced in this work along with the non-Rayleigh statistical analysis of speckle patterns has proven to have potential for tissue characterization. As far as we know, this work has been the first attempt at correlating tissue histology and the quantitative analysis of the echo signal using thin phantoms.
8 Appendix A. Gaussian Process

When the number of phasors $N$ in the random walk formulation is large, the statistical properties of the signal approach those of a Gaussian distribution. According to the central limit theorem the real and imaginary parts of the scattered signal are zero-mean, jointly Gaussian, independent random variables. Therefore, their joint probability density function is

$$P_{r,i}(a_r, a_i) = \frac{1}{2\pi \sigma^2} \exp\left(-\frac{(a_r^2 + a_i^2)}{2\sigma^2}\right)$$

Where $a_r$ and $a_i$ are the real and imaginary part, respectively, of the amplitude field,

$$\sigma^2 = \lim_{N \to \infty} \frac{1}{N} \sum_{k=1}^{N} \frac{|a_k|^2}{2}.$$

The intensity signal is defined by $I = a_r^2 + a_i^2$, from where $a_r = \sqrt{I}\cos\theta$, $a_i = \sqrt{I}\sin\theta$, and $\theta = \tan^{-1}\frac{a_i}{a_r}$.

To find the statistics of the intensity and phase we need to transform $P(a_r, a_i)$ to $P(I, \theta)$ via

$$P_{I,\theta}(I, \theta) = P_{r,i}(a_r, a_i) \|J\| = P_{r,i}(\sqrt{I}\cos\theta, \sqrt{I}\sin\theta) \|J\|.$$ Here $J$ is the Jacobian of the transformation and is given by

$$\|J\| = \begin{vmatrix} \frac{\partial a_r}{\partial I} & \frac{\partial a_r}{\partial \theta} \\ \frac{\partial a_i}{\partial I} & \frac{\partial a_i}{\partial \theta} \end{vmatrix} = \begin{vmatrix} \frac{1}{2}I^{-1/2}\cos\theta & -I^{1/2}\sin\theta \\ \frac{1}{2}I^{-1/2}\sin\theta & I^{1/2}\cos\theta \end{vmatrix} = \frac{1}{2}.$$
Therefore:

\[ P_{I, \theta}(I, \theta) = \frac{1}{2\pi \sigma^2} \exp \left( -\frac{(I \cos^2 \theta + I \sin^2 \theta)}{2\sigma^2} \right) \cdot \frac{1}{2} \]

\[ \int \frac{1}{4\pi \sigma^2} \exp \left( -\frac{I}{2\sigma^2} \right) \quad \text{for } I > 0 \text{ and } -\pi \leq \theta < \pi \]

\[ P_{I, \theta}(I, \theta) = \frac{1}{4\pi \sigma^2} \]

\[ 0 \quad \text{otherwise} \]

From here we can find the marginal probability density function of the intensity as

\[ P_I(I) = \int_{-\pi}^{\pi} \frac{1}{4\pi \sigma^2} e^{-I/2\sigma^2} d\theta = \frac{1}{2\sigma^2} e^{-I/2\sigma^2} \quad \text{for } I \geq 0 \]

with \( <I> = 2\sigma^2 \) and \( \sigma^2 = <I>^2 \).

The marginal probability density function for the phase can be calculated from

\[ P_\theta(\theta) = \int_{0}^{\infty} \frac{1}{4\pi \sigma^2} e^{-I/2\sigma^2} dI = \frac{1}{2\pi} \quad \text{for } -\pi \leq \theta \leq \pi \]

Therefore, for a Gaussian process, the intensity will obey a negative exponential distribution and the phase will obey a uniform distribution.

To find the statistics for the amplitude, we use the fact that \( |A| = \sqrt{a_r^2 + a_i^2} \) so that \( a_r^2 = |A|^2 \cos^2 \theta \) and \( a_i^2 = |A|^2 \sin^2 \theta \). We need to transform \( P(a_r, a_i) \) to \( P(|A|, \theta) \) using

\[ P_{|A|, \theta} = P_{r,i}(|A| \cos \theta, |A| \sin \theta) |J|. \]

Once again \( J \) is the Jacobian of the transformation and is given by.

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\[
\begin{bmatrix}
\frac{\partial a_r}{\partial |A|} & \frac{\partial a_i}{\partial |A|} \\
\frac{\partial a_r}{\partial \theta} & \frac{\partial a_i}{\partial \theta}
\end{bmatrix} = \begin{bmatrix}
\cos \theta & -|A| \sin \theta \\
|A| \cos \theta & \sin \theta
\end{bmatrix} = |A|
\]

Therefore \( P_{|A|,\theta}(|A|,\theta) = \frac{1}{2\pi \sigma^2} \exp \left( -\left( \frac{|A|^2 \cos^2 \theta + |A|^2 \sin^2 \theta}{2 \sigma^2} \right) \right) |A| \)

\( P_{|A|,\theta} = \frac{|A|}{2\pi \sigma^2} e^{-|A|^2/2\sigma^2} \) for \(-\pi \leq \theta \leq \pi\) and \(|A| > 0\).

From here we can find the marginal probability density function of the amplitude as

\[
P_{|A|}(|A|) = \int_{-\pi}^{\pi} \frac{|A|}{2\pi \sigma^2} e^{-|A|^2/2\sigma^2} d\theta = \frac{|A|}{2\sigma^2} e^{-|A|^2/2\sigma^2},
\]

which corresponds to a Rayleigh distribution.
9 Appendix B. Experimental results

Breast tissue

Normal tissue:
- breast_ah
- breast_av
- breast_bh
- breast_bv
- breast_ch
- breast_cv
- breast_dh
- breast_dv
- breast_hh
- breast_hv

Diseased tissue:
- breast_eh
- breast_fh
- breast_gh
- breast_ih

Sponge:
- sample 1
- sample 2
- sample 3

Liver:
- Liver 1
- Liver 2

Skeletal muscle:
- sk_ah
- sk_av

Phantom:
- phanliv
Breast_a

Histology, FOV 1 cm².

Ultrasound image, \( f_0=3.5\text{MHz} \), \( \Delta f=1.0\text{MHz} \),
20 scans.

Horizontal scan: Breast_ah:

Second normalized intensity moment \( <I^2>/\langle I \rangle^2 \) (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 47.98, intercept: 0.96
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Vertical scan: Breast_av:

Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 26.50, intercept: 1.24

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.
Normalized intensity moments $\langle T^n \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.

Effective number of scatterers, $M$, as a function resolution cell volume.
Breast_b

Histology, FOV 1 cm². Ultrasound image, \( f_0 = 3.5 \text{MHz}, \Delta f = 1.0 \text{MHz}, \) 20 scans.

Horizontal scan: Breast_bh:

Second normalized intensity moment \( \langle I^2 \rangle / \langle I \rangle^2 \) (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 14.41, intercept: 2.12
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function of resolution cell volume.
Vertical scan: Breast bv:

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 23.68, intercept: 0.91

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.
Effective number of scatterers, $M$, as a function resolution cell volume.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Breast_c

Histology, FOV 1 cm². Ultrasound image, f₀=3.5MHz, Δf=1.0MHz, 20 scans.

**Horizontal scan: Breast_ch:**

![Graph](image)

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 36.72, intercept: 0.83
Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Vertical scan: Breast_cv:

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 19.14, intercept: 1.18

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.

Effective number of scatterers, $M$, as a function resolution cell volume.
Breast_d

Histology, FOV 1 cm². Ultrasound image, \( f_0=3.5\text{MHz} \), \( \Delta f=1.0\text{MHz} \), 20 scans.

**Horizontal scan: Breast_dh:**

![Graph](image)

Second normalized intensity moment \( \frac{<I^2>}{<I>^2} \) (Iratio) vs inverse of resolution cell volume. Least squares fit: slope: 13.65, intercept: 1.27
Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Vertical scan: Breast_dv:

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 9.34, intercept: 1.36

Normalized intensity moments $<r^m>/<r>^m$ (Iratio) as function of bandwidth (BW) and moment order.
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.

Effective number of scatterers, $M$, as a function resolution cell volume.
Breast_e

Histology, FOV 1 cm².

Ultrasound image, f₀=3.5MHz, Δf=1.0MHz, 40 scans.

Horizontal scan: Breast_eh:

Second normalized intensity moment $\frac{<I^2>}{<I>^2}$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 13.88, intercept: 1.28
Normalized intensity moments $<I^n>/<I>^m$ (Iratio) as a function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^n>/<I>^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Breast_f

Histology, FOV 1 cm².

Ultrasound image, f₀=3.5MHz, Δf=1.0MHz, 30 scans.

**Horizontal scan: Breast_fh:**

Second normalized intensity moment $\frac{<I^2>}{<I>^2}$ (Iratio) vs inverse of resolution cell volume.

Least squares fit: slope: 4.01, intercept: 2.24
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function of resolution cell volume.
Breast_g

Histology, FOV 1 cm².  Ultrasound image, $f_0=3.5$MHz, $\Delta f=1.0$MHz, 40 scans.

**Horizontal scan: Breast_gh:**

![Graph showing the relationship between $\frac{\langle I^2 \rangle}{\langle I \rangle^2}$ (Iratio) and $1/Ve (\text{mm}^3)$]

Second normalized intensity moment $\frac{\langle I^2 \rangle}{\langle I \rangle^2}$ (Iratio) vs inverse of resolution cell volume.

Least squares fit: slope: 24.96, intercept: 1.78
Normalized intensity moments $<I^m>/<\langle I\rangle^m$ (Iratio) as a function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^m>/<\langle I\rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Breast_h

Histology, FOV 1 cm².

Ultrasound image, \( f_0 = 3.5 \text{MHz}, \Delta f = 1.0 \text{MHz}, \)
30 scans.

**Horizontal scan: Breast_hh:**

![Graph](image)

Second normalized intensity moment \( \langle I^2 \rangle / \langle I \rangle^2 \) (Iratio) vs inverse of resolution cell volume.

Least squares fit: slope: 25.55, intercept: 1.01
Normalized intensity moments \( \langle I^m \rangle / \langle I \rangle^m \) (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments \( \langle I^m \rangle / \langle I \rangle^m \) (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Vertical scan: Breast Hv:

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 4.85, intercept: 1.82

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ ($I_{ratio}$) as a function of moment order at different bandwidths. Fits to different probability density functions.

Effective number of scatterers, $M$, as a function resolution cell volume.
Breast_i

Histology, FOV 1 cm².

Ultrasound image, f₀=3.5MHz, Δf=1.0MHz, 30 scans.

**Horizontal scan: Breast_ih:**

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 3.30, intercept: 2.40
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Sponge Sample 1

Optical image

Ultrasound image, $f_0=3.5$MHz, $\Delta f=1.0$MHz, 100 scans.

Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 40.27, intercept: 1.29
Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Sponge Sample 2

Optical image

Ultrasound image, $f_0=3.5$MHz, $\Delta f=1.0$MHz, 100 scans.

Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 8.93, intercept: 1.25
Normalized intensity moments $\langle T^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle T^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Sponge Sample 3

Optical image

Ultrasound image, $f_0=3.5$MHz, $\Delta f=1.0$MHz, 100 scans.

Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs inverse of resolution cell volume.

Least squares fit: slope: 5.45, intercept: 1.52
Normalized intensity moments $<I^m>/<I>$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^m>/<I>$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Liver

Histology, FOV 1 cm². Ultrasound image, $f_0$=3.5MHz, $\Delta f$=1.0MHz, 30 scans.

Horizontal scan: Liver 1:

Second normalized intensity moment $<I^2>/<I>^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 34.44, intercept: .87
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Vertical scan: Liver 2:

Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 40.34, intercept: 1.09.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as function of bandwidth (BW) and moment order.
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.

Effective number of scatterers, $M$, as a function resolution cell volume.
Skeletal muscle

Histology, FOV 1 cm².

Ultrasound image, $f_0=3.5$ MHz, $\Delta f=1.0$ MHz, 30 scans.

Horizontal scan: Sk_ah:

Second normalized intensity moment $<I^2>/<I>$ ($I$-ratio) vs inverse of resolution cell volume.
Least squares fit: slope: 18.93, intercept: 1.73
Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of bandwidth (BW) and moment order.

Normalized intensity moments $\langle I^m \rangle / \langle I \rangle^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell volume.
Vertical scan: Sk_av:

Second normalized intensity moment $<I^2>/<I>$ (Iratio) vs inverse of resolution cell volume.
Least squares fit: slope: 10.75, intercept: 1.49

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.
Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.

Effective number of scatterers, $M$, as a function resolution cell volume.
Liver Phantom: phliv

Histology, FOV 1 cm².

Processed image.

Second normalized intensity moment $\langle I^2 \rangle / \langle I \rangle^2$ (Iratio) vs inverse of resolution cell area.
Least squares fit: slope: 12.28, intercept: 1.34
Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as function of bandwidth (BW) and moment order.

Normalized intensity moments $<I^m>/<I>^m$ (Iratio) as a function of moment order at different bandwidths. Fits to different probability density functions.
Effective number of scatterers, $M$, as a function resolution cell area.
10 References


