New Simple Phenomenological Model for Laser Doppler Measurements of Blood Flow in Tissue

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Abstract: Laser Doppler flowmetry (LDF) for measurements of tissue blood flow is well-known today. The basic theory of forming the registered optical signal in LDF is the model developed by R.Bonner and R. Nossal. However, claiming to be a detailed and comprehensive analysis of the interaction of light with tissues, it does not describe many phenomena. Multiple simplifications and assumptions in the model diminish the efforts on the analysis of peculiarities of light scattering inside the tissue, resulting in a very approximate output. In this our study, a qualitatively similar result was obtained with the use of more simple and general approach. It was shown, that the power spectra of analyzed signals in the form of the exponential decay, similar to a fractal noise (*1/f* noise), is a consequence mainly of the Maxwell's distribution of moving particles' velocities. Moreover, in contrast to the classic model, our model shows that the first moment of the frequency is linearly proportional not only to the velocity of red blood cells, but also is inversely proportional to the wavelength of illuminating radiation, that is more physically grounded.

1 INTRODUCTION

Optical noninvasive diagnostic technique – the laser Doppler flowmetry (**LDF**) – to measure a tissue blood flow is well-known today. Physically based on the light-beating spectroscopy (Cummins et al., 1970) and the Doppler effect at light scattering on moving red blood cells (**RBCs**) (Nilsson et al., 1980), the method has already proved its usefulness in a number of medical disciplines (Rajan et al., 2009), (Roustit et al., 2012). However, in spite of more than 40-year history, LDF is not used daily in a clinical practice. It has a variety of implementations in different research, but its practical applications, without which a practicing clinician cannot work, are not known. Large low-frequency fluctuations (**LFF**) in the output signal and a high dispersion of the result often lead to an inability of the personal diagnostic conclusion. Only at scientific studies in groups of patients, when data are averaged, there are steadily observed significant differences in groups. As a result, in most clinical studies pulsations are usually smoothed by data processing, and only the mean blood flow is analyzed (Mizeva et al., 2016).

For this empirical simplification, perhaps, partial soundness exists in the theory. For example, recently it was shown, that variable hyperemia in tissues can be a noise source for the laser Doppler flowmeter (Lapitan et al., 2016). So, a theoretical description of the input signal formation in LDF is very important. The basic theory in LDF is the well-known model developed by R.Bonner and R.Nossal (Bonner and Nossal, 1981) (**B&N model**). Since its introduction, the model became the most used and, practically, the almost single-used theory of LDF. Although, there are a number of numerical methods, authors only talking here about the rigorous analytical description of the input optical signal. Apart from the B&N model, there are not any other widespread analytical approach to derive the power spectrum density of the measured optical signal and its relationship to the RBCs' velocity or to the blood flow (velocity multiplied by amount of moving RBCs).

However, the B&N model doesn't describe the LFF of the incoming optical signal. The model was formulated at the assumption, that amplitudes of all

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scattered fields are stationary. Therefore, assuming all LFF to be artefacts, a standard flowmeter usually cuts them off by means of a conventional filtration. Thus, LFF must not pass directly to the output of the flowmeter (Koelink et al., 1994). Nevertheless, a different LFF are often observed in experiments. Moreover, the existence of optical field fluctuations in a tissue microvasculature at external illumination is now well confirmed in experiments with the use not only the LDF technique, but also a thermometry (Padtaev et al., 2015), a photoplethysmography (Mizeva et al., 2015), and other methods. So, today there is a necessity to revise the classic B&N model.

In this study, we tried to make the first step in the direction. We tried to obtain the similar result, but by different way. Our hypothesis was: since the B&N model was developed at a very large number of simplification, the similar result can be obtained from the most general assumptions (from the first principles) without profound analysis of the light scattering in tissues.

2 MAIN APPROACH AND THE OUTPUT OF THE B&N MODEL

Bonner and Nossal assumed, first of all, that the tissue matrix surrounding RBCs is a strong diffuser of light and, therefore, all RBCs are irradiated with equal intensity from all directions, i.e. there is a pure 4π illumination. Then, they supposed that the Doppler shift principally arises at scattering of light on moving RBCs only, not on fluctuating vessel's walls, for example. Among other simplifications, we can also mark a number of the most important ones: intensity of the scattered radiation is independent on blood volume; multiple scattering is insignificant and is dominated by a single scattering. Although, the multiple scattering is analyzed in their article, the main result - the exponential power spectrum, similar to the fractal noise (Fig.1), was obtained by taking into account of a single scattering only.

At all these assumptions, it was shown, that the first moment of the light beating frequency spectrum is linear proportional to the root mean square (**r.m.s.**) velocity of moving RBCs:

$$\langle\omega\rangle = \int_{-\infty}^{+\infty} |\omega| P(\omega) d\omega = \frac{\sqrt{\langle V^2 \rangle}\beta}{\sqrt{12\psi a}} f(\overline{m}) \ , \qquad (1)$$

where: ω is the angular frequency, $P(\omega)$ is a power spectrum of the photocurrent, V - velocity of moving RBCs, β is a factor which primary depends on the optical coherence of optical signals at the detector surface ($0<\beta<1$), ψ is the empirical coefficient determining the shape of RBCs, a is the radius of an average spherical scatterer (erythrocytes) inside the tissue, $\overline{m}$ is the average number of photon scattering events on moving RBCs, function $f(\overline{m})$ linearly depends on the blood volume for $\overline{m} \ll 1$, and varies as the square root of the blood volume for $\overline{m} \gg 1$.

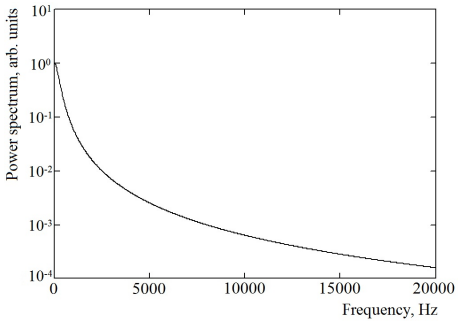

Figure 1: The typical power spectrum $P(\omega)$ of the laser Doppler signal described by the B&N model.

Surprisingly, in (1) there is not any dependence on the wavelength λ_0 of probing radiation, i.e. the waveband of the phenomenon doesn't matter...

3 BACKGROUND OF THE FIRST PRINCIPLES

Since almost all modern diagnostic optics and electronic devices are constructed nowadays as analog-to-digital measuring systems, in most cases an analyzed signal is a voltage $u(t)$ as a function of time. Often $u(t)$ is formed at the input of measuring converter, for example, at the input of the analog-to-digital converter, as a voltage drop on the measuring resistance R_m due to a photocurrent flow through the R_m. This photocurrent $i(t)$, in its turn, is proportional to the squared modulus of the optical field $|E(t)|^2$ incident on a photodetector due to a quadraticity nature of the photodetection:

$$i(t) \sim \frac{\eta A |E(t)|^2}{2Z_e}, \qquad (2)$$

where η is a conversion factor of the photodetector (A/W); A is a surface area of the photodetector (m^2); $E(t)$ is the electric field of radiation (V/m); Z_e is the wave impedance of the medium (Ohm).

The spectrum (spectral density) of the measured signal $u(t)=R_m \cdot i(t)$ is determined from (2) by the spectral density of the intensity $|E(t)|^2$, which can be

calculated using the direct Fourier transform:

$$G_E(\omega) = \int_{-\infty}^{+\infty} |\mathrm{E(t)}|^2 e^{-j\omega t} dt \quad , \qquad (3)$$

where $G(\omega)$ is a spectral density and ω is the angular frequency of the $|E(t)|^2$ fluctuations.

If heterodyne mixing of two harmonic waves on a photodetector is considered, then:

$$E(t) = E_0 e^{j\omega_0 t} + E_1 e^{j\omega_1 t}, \quad (4)$$

where ω_0 and ω_1 are frequencies of the waves, E_0 and E_1 are amplitudes of their fields. In this case, the photocurrent classically can be computed as:

$$i(t) \sim |\mathrm{E(t)}|^2 == E_0^2 + E_1^2 + 2E_0E_1\cos(\omega_1 - \omega_0)t \,. \quad (5)$$

Besides of the constant component with the amplitude $A_0=E_0^2+E_1^2$, this mixed signal has the LFF with the amplitude of fluctuations $A_1=2E_0E_1$ at the difference frequency $\omega_d=(\omega_1-\omega_0)$, which are formed due to the beating effect of two fields. Thus, the spectral density of $|E(t)|^2$ will have the form:

$$G_E(\omega) = (E_0^2 + E_1^2)\delta(\omega) + 2E_0E_1\delta(\omega - \omega_d)\,, \quad (6)$$

where $\delta(x)$ is the delta function. In the case of light scattering on a stationary tissue matrix and on the moving RBCs, ω_d represents the Doppler frequency shift. This $G_E(\omega)$ is a discrete (a line) spectrum of two lines:

$$\begin{aligned} G_{E0}(\omega) &= (E_0^2 + E_1^2)\delta(\omega) \\ G_{E1}(\omega) &= 2E_0E_1\delta(\omega - \omega_d) \end{aligned} \qquad (7)$$

with amplitudes of lines A_0 and A_1, which are determined by integration of (7) over ω. This well-known result was obtained at the assumption of a coherence (inphase) of the registered fields. The less the coherence degree of fields the less the beating amplitudes are observed. As to LDF, the light scattering in tissues is a random process over its volume. So, the phase shift of all mixed waves will be partially random, and (6) should be rewritten taking into account the coherence coefficient $\xi_{0,1}$ of these two waves (Born and Wolf, 1964):

$$|\mathrm{E(t)}|^2 = E_0^2 + E_1^2 + 2\xi_{0,1}E_0E_1\cos\omega_d t\,, \quad (8)$$

where $0 \le \xi_{0,1} \le 1$. Similarly, if the sum of three or even more fields with frequencies ω_0; ω_1; ... ω_n is considered, where each frequency $\omega_k=\omega_0+\omega_{dk}$ (k=1, 2, 3 … n), then:

$$\begin{aligned} |\mathrm{E(t)}|^2 = \sum_{k=0}^{n} E_k^2 + 2E_0\sum_{k=1}^{n}\xi_{0,k}E_k\cos(\omega_0 - \omega_k)t + \\ + 2\sum_{j=1}^{n-1}E_j\sum_{k=j+1}^{n}\xi_{j,k}E_k\cos(\omega_j - \omega_k)t \end{aligned} \qquad (9)$$

Without the loss of generality, we may accept for further analysis $\xi_{0,k}=const=\xi$. Since for LDF all E_k at k>0 are the field amplitudes scattered by RBCs, then coefficients of their mutual coherence $\xi_{m,k}$ at $m\neq0$ are $\xi_{m,k}<<\xi_{0,k}$ because the correlation between reference and scattered fields always is higher than the correlation between two randomly scattered fields. It is obvious, also, that $E_k<<E_0$ at $k\neq0$ because a fraction of RBCs in tissues is much less than a fraction of the tissue matrix. Thus, with a high degree of accuracy we may retain only first two sums in the equation (9). It yields:

$$|\mathrm{E(t)}|^2 = \sum_{k=0}^{n} E_k^2 + 2\xi E_0\sum_{k=1}^{n}E_k\cos\omega_{dk}t\,. \quad (10)$$

In analogy with (3)-(8), the spectral density of the registered signal (10) will consist of a series of "k" lines, which spectral amplitudes A_k at frequencies $\omega=\omega_{dk}$ for $k>0$ are:

$$A_k = 2\xi E_0 E_k \qquad . \qquad (11)$$

Equations (10)-(11) allow one to obtain the spectral density of the registered signal if all A_k are known.

4 EVALUATION OF SPECTRAL AMPLITUDES

Analytical estimation of the amplitudes A_k is always preferable. For this purpose, the improved two-flux Kubelka-Munk model is a good tool (Lapitan et al., 2016). To obtain the general qualitative result, the homogenous tissue model in the form of a semi-infinite turbid medium filled with blood can be used. The absorption coefficient μ_a as well as the average density μ_ρ of scattering inhomogeneities inside the tissue can be written as follows:

$$\mu_a = \mu_{at} + \mu_{ab}C_b\,; \quad \mu_\rho = \mu_{\rho t} + \mu_{\rho b}C_b\,, \qquad (12)$$

where μ_{at} and μ_{ab} are absorption coefficients of a bloodless tissue and a blood, $\mu_{\rho t}$ and $\mu_{\rho b}$ are the average density of scatterers inside the bloodless tissue and the blood respectively, C_b is a relative fraction (C_b=0…1) of the blood in tissues. In (12) it is assumed, that the volume of blood in tissues is much less than the volume of the tissue matrix.

For LDF it is sufficient to consider only the single scattering approximation (**SSA**). The intensity of a backscattered flux for SSA and for the semi-infinite turbid medium can be written as follows (Dmitriev et al., 2004):

$$I_{BS} = \frac{F_0 R\cdot\exp(-\mu_a/\mu_\rho)}{1-(1-R)\cdot\exp(-2\mu_a/\mu_\rho)}\,, \qquad (13)$$

where R is a reflection Fresnel coefficient on borders of inhomogeneities inside the medium, F_0 – incident flux. Since C_b<1 and usually $|\mu_a/\mu_\rho|$<<1, together with (12) the equation (13) can be expanded in a Taylor series by μ_a/μ_ρ and C_b. After

transformations, living only two first terms, one will have:

$$I_{BS} = Y\left[1 + Z\left(\frac{\mu_{at}\mu_{\rho b}}{\mu_{\rho t}^2} - \frac{\mu_{ab}}{\mu_{\rho t}}\right)C_b\right], \quad (14)$$

where: $Z = (2 - W)/W$;

$W = 1 - (1 - R)\cdot\exp(-2\mu_{at}/\mu_{\rho t})$ and

$Y = F_0 R\cdot\exp(-\mu_{at}/\mu_{\rho t})/W$.

The total backscattered radiation incident on a photodetector is the mixed radiation:

$$I_{BS} = I_0 + I_d, \quad (15)$$

where I_0 is the intensity of the scattered flux without Doppler shift and I_d is the intensity of the Doppler-shifted flux scattered on moving RBCs. For SSA, I_0 can be determined from (14) at $C_b \neq 0$, $\mu_{ab} \neq 0$, $\mu_{\rho b} = 0$:

$$I_0 = I_{BS}(\mu_{\rho b} = 0) = Y\left[1 + Z\left(-\frac{\mu_{ab}}{\mu_{\rho t}}\right)C_b\right]. \quad (16)$$

Then, I_d can be determined as follows:

$$I_d = I_{BS}(\mu_{\rho b} \neq 0) - I_0 = YZ\frac{\mu_{at}\mu_{\rho b}}{\mu_{\rho t}^2}C_b. \quad (17)$$

If different groups of RBCs have different speeds V_k (k =1, 2...n), then for each k-th fraction C_{bk} of RBCs its Doppler-shifted flux can be written as:

$$I_{dk} = YZ\frac{\mu_{at}\mu_{\rho b}}{\mu_{\rho t}^2}C_{bk}. \quad (18)$$

Note, that $I_d = \sum_{k=1}^{n} I_{dk}$, as well as $C_b = \sum_{k=1}^{n} C_{bk}$ are conditions closing the distribution. If the discrete velocity distribution of RBCs is proposed, then all fluctuation amplitudes A_k at frequencies ω_{dk} can be computed easily with the use of (10)-(18):

$$A_k \sim 2\xi\sqrt{Y\left[1 - Z\frac{\mu_{ab}}{\mu_{\rho t}}C_b\right]}\sqrt{YZ\frac{\mu_{at}\mu_{\rho b}}{\mu_{\rho t}^2}C_{bk}}. \quad (19)$$

From (19) it follows exactly, that A_k depend on ω_{dk} like the distribution of $\sqrt{C_{bk}}$, because other multipliers in (19) are independent on ω_{dk}.

5 EVALUATION OF CONTINUOUS SPECTRA

Usually in LDF, a continuous distribution of RBCs' velocities such as Maxwell's distribution is used:

$$dF(V) = \frac{\sqrt{2}V^2}{\sigma_V^3\sqrt{\pi}}\cdot\exp(-V^2/2\sigma_V^2)dV, \quad (20)$$

where V is the RBCs velocity, σ_V is r.m.s. deviation of V. The density of this distribution has the form:

$$f(V) = \frac{\sqrt{2}V^2}{\sigma_V^3\sqrt{\pi}}\cdot\exp(-V^2/2\sigma_V^2). \quad (21)$$

It also can be expressed with the use of the most probable value V_m of the velocity:

$$V_m = \sqrt{2}\sigma_V, \quad (22)$$

or with the use of the most expected mean value of the velocity $\langle V\rangle$:

$$\langle V\rangle = \frac{2\sqrt{2}\sigma_V}{\sqrt{\pi}} = \frac{2V_m}{\sqrt{\pi}}. \quad (23)$$

However, we need to have the Doppler-shift frequency distribution for RBCs, not the distribution of their velocities. To obtain one it is necessary to substitute in (20) a value of ω_{dk} instead of V. In the case of SSA, we can use the well-known expression:

$$V = \frac{\lambda_0}{4\pi}\omega_d, \quad (24)$$

It should be also taking into consideration that:

$$dV = \frac{\lambda_0}{4\pi}d\omega_d. \quad (25)$$

As a result, omitting the index "d" and taking into account (23), the distribution density of the Doppler frequency shift will get the form:

$$f(\omega) = \frac{\lambda_0^3\omega^2}{2\pi^5\langle V\rangle^3}\cdot\exp(-\lambda_0^2\omega^2/4\pi^3\langle V\rangle^2). \quad (26)$$

Each specific C_{bk}^* for the frequency interval $\Delta\omega_k$ is determined then from (26) by the integration:

$$C_{bk}^* = C_b\int_{\Delta\omega_k} f(\omega)d\omega \quad (27)$$

If the density function $f(\omega)$ for C_{bk} is known, then it is possible to compute the distribution density for $\sqrt{C_{bk}}$ - the function $f'(\omega)$ (see Appendix A):

$$f'(\omega) = \frac{\lambda_0^3\omega^5}{\pi^5\langle V\rangle^3}\cdot\exp(-\lambda_0^2\omega^4/4\pi^3\langle V\rangle^2). \quad (28)$$

Thus, the dependence of spectral amplitudes A_k on the frequency ω in the case of a continuous speed distribution gives the spectral density $G(\omega)$:

$$G(\omega) \sim \frac{\lambda_0^3\omega^5}{\pi^5\langle V\rangle^3}\cdot\exp(-\lambda_0^2\omega^4/4\pi^3\langle V\rangle^2). \quad (29)$$

We should understand (29) in such a way, that it reflects qualitatively a spectrum of the photocurrent LFFs (*ac* part of $i(t)$). The function $f'(\omega)$, which determines $G(\omega)$ (29), is shown in Figure 2. There is a series of curves for different $\langle V\rangle$ in the typical range of practical relevance of $\langle V\rangle$=0,02...1,5 mm/s at λ_0=810 nm. In addition, the approximating exponential function (black dotted line) as well as

1/ω function (black solid line) are presented.

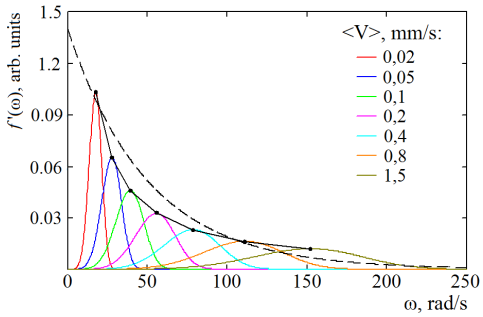

Figure 2: Distribution density $f'(\omega)$ for $\sqrt{C_{bk}}$ as a function of the mean velocity <*V*> of RBCs (colored curves), approximating exponential function (black dotted line) and approximated 1/ω function (black solid line).

Approximating exponential function for (28) is:

$$f_a'(\omega) = 0{,}14\exp(-0{,}02\omega)\ . \qquad (30)$$

It should be specially noted, that in the known B&N model the photocurrent spectrum (29) was not considered. All classic approaches considered the autocorrelation function for the photocurrent:

$$P(\omega) = \int_{-\infty}^{+\infty} \langle i(t)i(t+\tau)\rangle e^{-j\omega\tau} d\tau\ , \qquad (31)$$

which is of the order of the squared photocurrent $i^2(t)$ and reflects its power spectrum. To register $i^2(t)$, the quadratic converter in the instrument is required. To compute $P(\omega)$ in our approach, it is necessary to take into consideration, that:

$$i^2(t) \sim 4\xi^2 E_0^2 \left(\sum_{k=1}^{n} E_k \cos\omega_{dk} t \right)^2 . \qquad (32)$$

As a result, we will have three terms for $i^2(t)$ due to the strict phase synchronism of all components:

$$\Sigma_1 = \sum_{k=1}^{n} E_k^2 \cos^2 \omega_{dk} t = \frac{1}{2} \sum_{k=1}^{n} E_k^2 \left(1 + \cos 2\omega_{dk} t\right), \qquad (33a)$$

$$\Sigma_2 = \sum_{k=1}^{n} E_k \sum_{m=k+1}^{n-1} E_m \cos(\omega_{dk} - \omega_{dm})t\ , \qquad (33b)$$

$$\Sigma_3 = \sum_{k=1}^{n} E_k \sum_{m=k+1}^{n-1} E_m \cos(\omega_{dk} + \omega_{dm})t\ . \qquad (33c)$$

In this case, $P(\omega)$ will be determined by the distribution of C_{bk} (26), because each E_k and E_m includes $\sqrt{C_{bk}}$, and when multiplying they will give C_{bk}. Herewith, the cosines of close frequencies in (33b) in the limit to the continuous spectrum will be approximately equal to 1. The cosines of close frequencies in (33c) will give the doubled frequency and will become comparable with terms in (33a), allowing us to summarize them. The remaining components will be significantly less than the enhanced sum (33a), so for a qualitative analysis they can be neglected without the loss of the accuracy. Thus, the amplitude-frequency properties of $i^2(t)$ are mainly defined by Maxwell's frequency distribution (26), but with twice-shifted frequencies upwards due to squared cosines.

The distribution density $f(\omega)$ for C_{bk}, which determines $P(\omega)$, is shown in Figure 3. For $P(\omega)$ the approximating exponential function is:

$$f_a''(\omega) = 0{,}0007 \cdot \exp(-0{,}0002\omega)\ . \qquad (34)$$

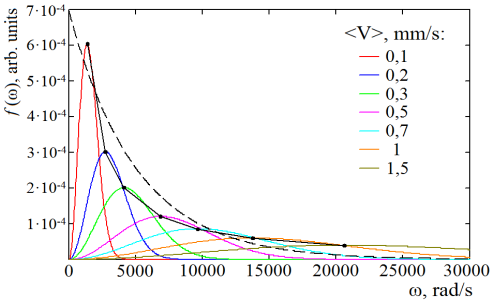

Figure 3: Distribution density $f(\omega)$ for C_{bk} as a function of the mean velocity <*V*> of RBCs (colored curves), approximating exponential function (black dotted line) and approximated *1/ω* function (black solid line).

6 DISCUSSION AND CONCLUSIONS

In this study, we have attempted to propose a new approach in LDF theory. From "first principles" of the classic spectral analysis, using the simplest SSA to determine the intensity of backscattered radiation, as well as with the use of the Maxwell's velocity distribution for moving RBCs, we have obtained the similar result as it was presented by Bonner and Nossal. For example, we have obtained the same order of the waveband of the summarized power spectrum $P(\omega)$ for the squared photocurrent $i^2(t)$ (Figure 3), but in a more simple way. What also is interesting in our result - the approximation function for $P(\omega)$ has the exponent power of $0{,}0002\omega$, exactly as it was stated in the end of the article (Koelink et al., 1994). Moreover, unlike the B&N model, we have obtained the spectral density of the photocurrent $G(\omega)$, as well. It has the main spectral region in a low-frequency waveband (Figure 2), exactly where the LFF of the LDF signal are often observed. Is there in other publications such spectra? We have found the same spectra in the article on a portable Laser Doppler Flowmeter (Hu et al., 2013). It contains the spectrum of the

same order of the waveband. Determining the spectrum, authors used *i(t)*, so our theoretical result is in a good correlation with their experimental one.

And, at last, in contrast to the B&N equation (1), in our output the weighted beating frequency <ω>, which is defined as the first moment of $P(\omega)$, can be analytically derived from (24) as: $\langle\omega\rangle = 4\pi\langle V\rangle/\lambda_0$. We see the linear relationship between <ω> and <V>, like in the B&N model, but we also see the inverse proportionality to the λ_0. The absence of one in (1) looks not physically explained. Moreover, in (1) the inverse proportionality of <ω> to the average radius of scatterers "a" without taking into account any light diffraction looks not quite justified, as well. What if in the limit $a \to 0$?

Thus, we see several advantages in our approach. It is a qualitative approach, an approximation only, but it allows to understand better several features of the input signal spectral properties in LDF. For example, it assists to understand better, that the power spectrum in the exponential form, similar to a fractal noise, is the consequence mainly of the Maxwell's distribution, not of the specialties of light scattering in tissues. Additionally, at SSA the linear proportionality between <ω> and <V> is a trivial consequence of the Doppler effect, (24) not more.

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APPENDIX A

According to Kolmogorov's axiomatic, a random variable is a measurable function on the probability space (Ω, $\mathcal{F}$,$\mathbb{P}$) (Shiryaev, 1996). Let a real random variable $\xi(\omega)$ has the probability density $p_\xi(x)$. Let a continuous function of this random variable $\eta(\omega) = f(\xi(\omega))$ has a probability density $p_\eta(x)$. We are going to prove, that

$$p_\eta(x) = \frac{d}{dx}\left(\int\limits_{\{t: f(t) \le x\}} p_\xi(t)\,dt \right).$$

The definition of a distribution function $F_\eta(x)$ of $\eta(\omega)$ is: $F_\eta(x) = \mathbb{P}\{\omega : \eta(\omega) \le x\}$. Substituting the definition of $\eta(\omega)$, we obtain $F_\eta(x) = \mathbb{P}\{\omega : f(\xi(\omega)) \le x\}$. Probability in the right hand side can be rewritten as an integral of p_ξ over a set of points in which $f(\cdot)$ is not greater than x: $F_\eta(x) = \int\limits_{\{t: f(t) \le x\}} p_\xi(t)\,dt$. To find the density $p_\eta(x)$ it remains to differentiate $F_\eta(x)$:

$$p_\eta(x) = \frac{d}{dx} F_\eta(x) = \frac{d}{dx}\left(\int\limits_{\{t: f(t) \le x\}} p_\xi(t)\,dt \right).*$$

* Note: The existence of the density $p_\eta(x)$ is not guaranteed for all $\xi(\omega)$ and $f(\cdot)$. Here, we don't study conditions under which the density of $\eta(\omega)$ exists, but we require its existence.