

# Tissue entropy and Low Coherence Trans-illumination Interferometry

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## 1. HOW TO ASSESS THE ENTROPY OF TISSUES?

The relevance of any diagnostic technique, including the biomedical ones, resides in its capacity to provide specific information concerning the phenomenon under study. For example, in order to recognize certain types of tissues (those not possessing intrinsic luminescent characteristics) when performing fluorescence microscopy, extrinsic fluorophores are necessary. In this case, without the addition of such fluorophores, fluorescence microscopy yields no usable information. That is to say, fluorescence microscopy is irrelevant until extrinsic fluorophores, that bind to the tissue of interest, are utilized. The importance of this example is that every diagnostic technique should seek to maximize the return of useful information.

First, though, it is necessary to establish means to assess the amount of information that a certain technique may unveil. The mathematical formulation of information theory presents a firm foundation to achieve this task. In order to fathom the concept of information, probability theory is necessary, since both are closely interrelated. Our intuitive notion of information is as follows: events that are highly unlikely (i.e., less probable) to occur reveal much information, whereas events that arise frequently (i.e., highly probable) are less informative. Therefore, a method of diagnosis that seeks to maximize information, would theoretically focus on the assessment of physical phenomena that are less likely to occur. Speaking of entropy rather than information, we would say that diagnostic techniques that center their attention on characteristics that are less likely to arise, generate diagnoses with more informative content as compared to those approaches studying the complementary physical characteristics.

Taking this short intuitive discussion as background, we may reflect upon the phenomena that occur frequently in radiation-tissue interactions. Instantaneously scattering and absorption events come to mind. These two phenomena arise very frequently in tissue optics. To illustrate qualitatively how often these events occur, let us recall the penetration depth (i.e., expected length before scattering and/or absorption event) of laser “light” in the radiation window for diagnosis and therapy. When an Er:YAG laser ( $2.940\ \mu\text{m}$ ) is utilized, the radiation is able to penetrate solely  $1\ \mu\text{m}$  in tissue. Meanwhile, whenever near infrared radiation (Nd:YAG,  $1.064\ \mu\text{m}$ ) interacts with tissue, photons are capable of traversing nearly three orders of magnitude longer path: penetration depth is about  $1400\ \mu\text{m}$ , or  $1.4\ \text{mm}$ . These facts serve to emphasize that scattering and/or absorption are recurrent (highly likely) events in radiation-tissue interactions. Therefore, the information that they provide is limited.

The superiority of using pass-through photons, for performing biomedical diagnosis, stems from the fact that this radiation provides a bountiful source of information, not being utilized today. Perhaps the most difficult aspect, concerning the implementation of such a diagnostic technique (based on pass-through photons), is that transmitted radiation is difficult to separate. It is indispensable (both ballistic and forward-scattered radiation are transmitted, as shown in Figure 1) to identify a process for discriminating between scattered and ballistic radiation.

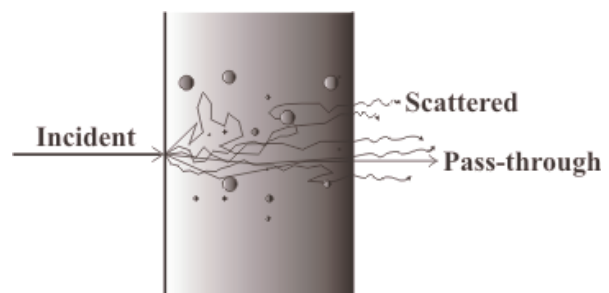
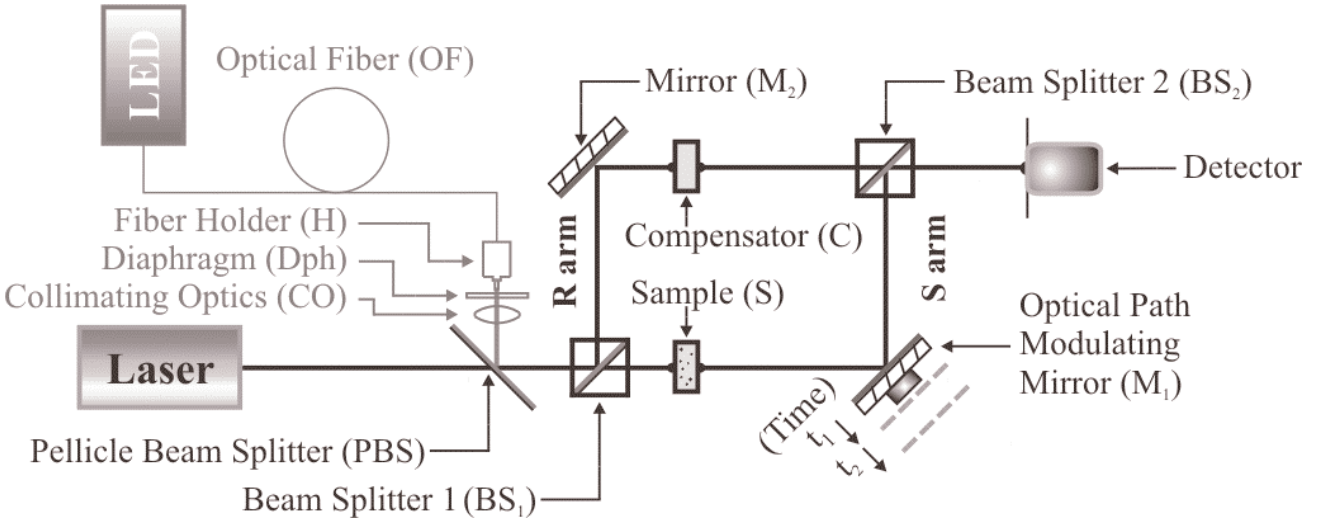


Fig. 1. Radiation-tissue interaction results in transmission of pass-through and scattered radiation.

We wish to complement the information currently available from the established (scattering- and/or absorption-based) diagnostic methods. Therefore, we propose a biomedical technique that focuses on the utilization of pass-through (trans-illuminating, or ballistic) photons to perform analysis. Pass-through photons are rare in radiation-tissue interactions (penetration depths ranging from 1-1400  $\mu\text{m}$ ). Hence, a diagnostic technique that utilizes such photons (that are less likely to be transmitted), as metric of analysis, would yield information that is complementary to the state-of-the-art scattering- and/or absorption-based methods in biomedical diagnosis. Furthermore, with this new approach, a better assessment of the entropy of tissues (applying the definition as it is used in information theory; i.e., the expected value of information) would result.

## 2. ISOLATION OF PASS-THROUGH PHOTONS: LOW-COHERENCE TRANS-ILLUMINATION INTERFEROMETRY

We have developed a mathematical model, considering a low-coherence trans-illumination interferometric setup, to separate pass-through from scattered radiation. This setup is depicted in Figure 2.



**Fig. 2.** Schematic layout of the low-coherence trans-illumination interferometer necessary to validate the mathematical model to account for the isolation of pass-through radiation. The sample arm is modulated ( $t_1$ ,  $t_2$ , etc) to generate an interferogram.

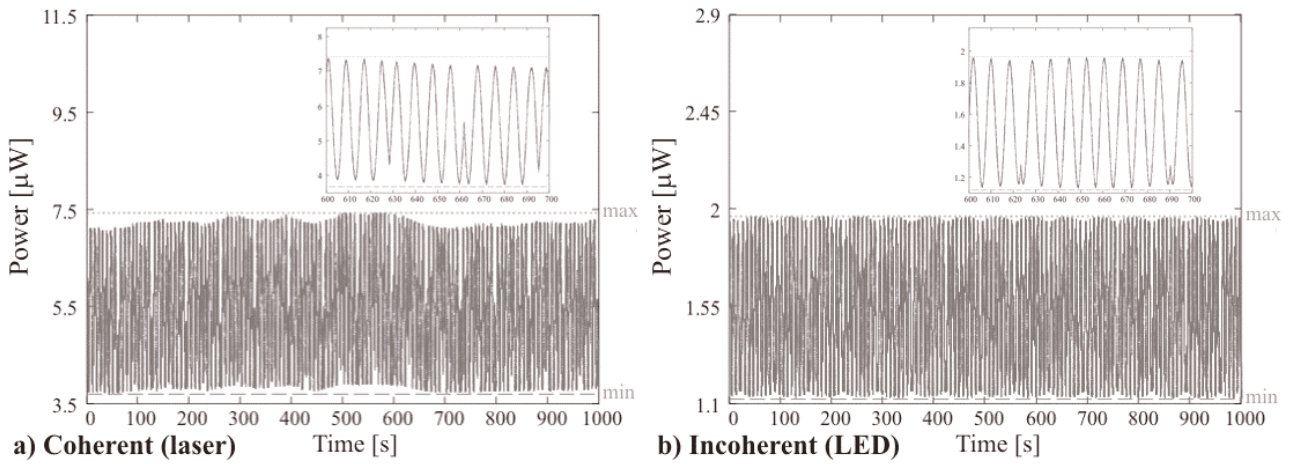
The interferometric setup serves to assure that only coherent radiation produces signal, thus eliminating noise introduced as scattered light. The hypothesis is that with insufficient temporal delay, the scattered photons retain a certain relation with the reference and pass-through photons. In mathematical terms, we can express these interactions by using the concepts of partial coherence theory.

$$\begin{aligned}
 P(t, T_{sc}) \propto & \langle \mathbf{E}_r^*(\tau) \mathbf{E}_r(\tau) \rangle + \langle \mathbf{E}_p^*(\tau+t) \mathbf{E}_p(\tau+t) \rangle + \langle \mathbf{E}_r^*(\tau) \mathbf{E}_p(\tau+t) \rangle + \langle \mathbf{E}_p^*(\tau+t) \mathbf{E}_r(\tau) \rangle \\
 & + \langle \mathbf{E}_r^*(\tau) \mathbf{E}_{sc}(\tau+t+T_{sc}) \rangle + \langle \mathbf{E}_{sc}^*(\tau+t+T_{sc}) \mathbf{E}_r(\tau) \rangle \\
 & + \langle \mathbf{E}_p^*(\tau+t) \mathbf{E}_{sc}(\tau+t+T_{sc}) \rangle + \langle \mathbf{E}_{sc}^*(\tau+t+T_{sc}) \mathbf{E}_p(\tau+t) \rangle + \langle \mathbf{E}_{sc}^*(\tau+t+T_{sc}) \mathbf{E}_{sc}(\tau+t+T_{sc}) \rangle
 \end{aligned} \quad [\text{W}] \quad (1)$$

Here,  $\mathbf{E}_r$  stands for the electric field in the reference arm, whereas  $\mathbf{E}_{sc}$  and  $\mathbf{E}_p$  represent the scattered and pass-through fields that emerge after having traversed the sample.  $\tau$  is the time delay taken as reference. The random time delay, introduced by the scattering centers to the impinging photons, is denoted by  $T_{sc}$ . In addition,  $t$  represents the modulation time necessary for the generation of the interferogram (refer to Fig. 2). Finally,  $P(t, T_{sc})$  is the detected power in the superposition plane. In all terms above,  $\langle \cdot \rangle$  denotes time averaging, an asterisk complex conjugation, and complex quantities are written in bold letters.

From Eq. (1) the representation of the expected detected signal, by partial coherence theory, follows. Moreover, the various interactions between pass-through, scattered, and reference photons are represented in this expression. The first four terms correspond to the relation between pass-through and reference photons. The first two terms in Eq. (1) are a non-stochastic DC component, whereas the next two terms constitute the expression of interference. This is the signal we are interested for performing ballistic diagnosis. The rest of the terms are all stochastic components and, as such, are functions of  $T_{sc}$ . The fifth and sixth components represent the stochastically varying function that results due to the scattered and reference photons interaction. The following two terms take into account the degree of similarity that the scattered and pass-through photons retain after traversing the tissue. Finally, the last term denotes the random offset introduced by the late arrival of the scattered photons. These latter interactions obscure the detected signal.

The importance of this analysis is that, a source with a reduced temporal coherence will serve to effectively separate pass-through from scattered photons. The verification of this proposal is quite straightforward with two radiation sources in an interferometer (see Fig. 2). First, a source with a significant coherence length is utilized. In this scenario, we expect to observe random fluctuations of the signal (as a function of time), as well as a random offset. Second, a reduced coherence source (such as an LED) is implemented. The expected outcome of this setup is a stable behavior with respect to time. We present the preliminary experimental results confirming theory in Figure 3.



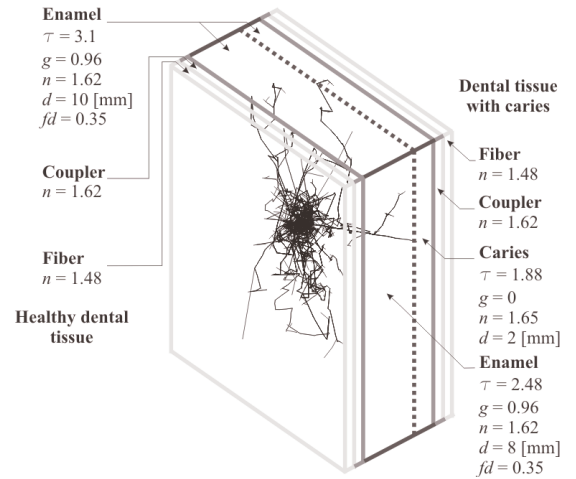
**Fig. 3.** a) The interferogram exhibits a stochastic behavior when the tissue (phantom) is irradiated with a laser source. b) The response of the tissue-trans-illumination system is stable when a broadband source (LED) is implemented. The inset above shows, in each case, the temporal response of the interferogram in more detail.

### 3. MONTE CARLO SIMULATION OF PHOTON TRANS-ILLUMINATION TIME OF FLIGHT

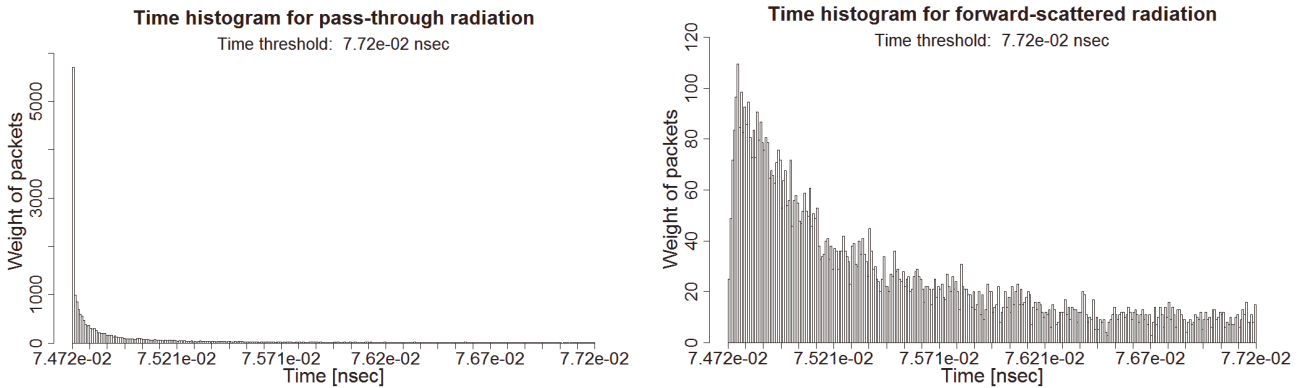
The experimental results shown in the previous section emphasize that the isolation of pass-through photons is feasible. Hence, the possibility of extracting the information that they provide is realizable. The results presented previously were obtained heuristically. More specifically, the low-coherence source was not optimized (i.e. calibrated) for the tissue (phantom) under study. Therefore, we complement these results by estimating (using a Monte Carlo, MC, simulation) the average photon migration time in tissue, with one or at most two scattering events. We assess the equation of transfer recursively, and determine the distribution function relating time of arrival of photons on the detector, versus tissue characteristics. The time delay measure serves to determine the optimal type of radiation source, and its coherence characteristics.

As accounted for in the previous section, the determination of radiation source depends closely on the tissue under test. More specifically, the coherence time of the source must be less than the expected time delay introduced by the scattering centers to the impinging photons. Therefore, we have determined theoretically the temporal behavior of different samples by using MC simulations. The information bestowed by such analysis is of paramount importance for the optimal implementation of our proposal, because specific coherence-related characteristics of the source are a direct consequence of the MC analysis. The determination of optimal source bandwidth, specifically, is central to the calibration procedure implicit in the proposed biomedical technique. Furthermore, this parameter is also obtainable from the MC analysis we have undertaken.

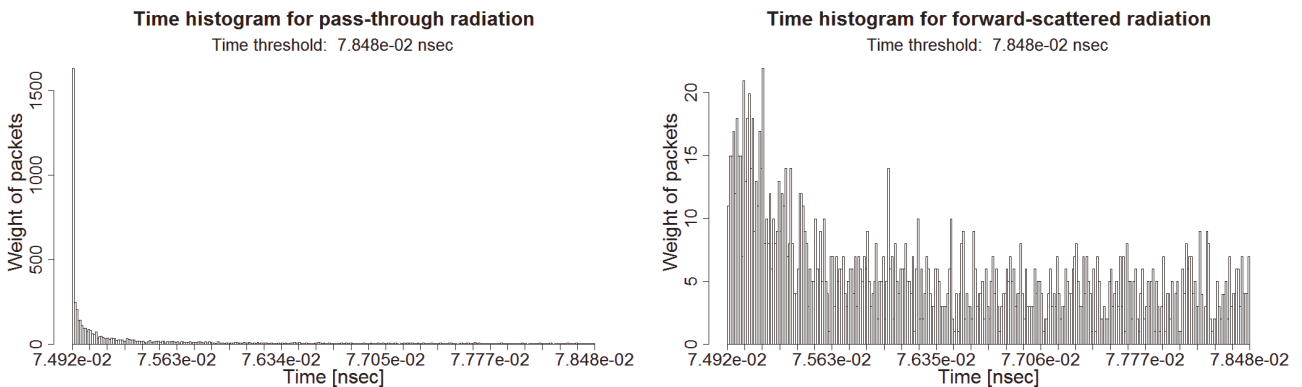
Hereafter, we depict two tissue models (a healthy dental tissue and one with caries), followed by the corresponding time-of-flight probability distribution functions, describing the samples. These measures were obtained by simulating 100,000 packets of photons.



**Fig. 4.** Dental models: ill tissue is composed of caries and enamel; healthy model only contains enamel.



**Fig. 5.** Temporal probability distributions for pass-through and scattered radiation for a healthy dental tissue.



**Fig. 6.** Temporal probability distributions for pass-through and scattered radiation for a dental tissue with caries.

Taking this information as starting point, we may determine signal-to-noise ratios and the most appropriate radiation (SLED, LED, or super continuum) source for trans-illumination interferometry. Therefore, in the near future, we will specify the optimal source bandwidth, in order to complement the current development of the technique. We expect that these efforts will eventually lead to a biomedical method that will bestow information not readily available these days.

## ABSTRACT

We have proposed an interferometric setup for performing biomedical diagnosis. In the present study, we extend the interferometric analysis to partially coherent (temporal) radiation. Temporal coherence limits the amount of delay permitted to the scattered photons, because incoherent photons do not produce interference. Thus, short coherence time differentiates between wanted pass-through and scattered radiation. The proposed as metric of discrimination is therefore coherence, tested in an interferometric setup.

We compare the detected signal in the radiometric trans-illumination experiment for two sources: a gas laser with high coherence, and an LED with low coherence. The detected signal is significantly improved when a low-coherent light source is utilized, allowing us to clearly separate pass-through photons from those that undergo multiple scattering. The preliminary experimental results confirm the feasibility of the concept, requiring precise matching of the source coherence with the scattering behavior of the tissue (phantom) under study.

We complement the experimental results with a stochastic Monte Carlo (MC) simulation to determine the average photon migration time in turbid media, in general, and a tissue, in particular. More specifically, we evaluate the time of flight necessary for the radiation to traverse the tissue under test, with one or at most two scattering events. The distribution functions, relating time of arrival of photons on the detector versus tissue characteristics, determine the signal-to-noise ratio for the interferometric measurements. The results of the MC simulation are useful to select an appropriate type of radiation source, and its coherence characteristics. Our initial expectation is that either super luminescent diodes (SLED) or light emitting diodes are adequate radiation sources for the trans-illumination experiment. Nonetheless, a super continuum source may represent a very flexible, although optional, luminous source.

**Key words:** Low coherence interferometry, Partial coherence, Trans-illumination, Scattering, Tissue optics, Information maximization, Entropy of tissues

## BRIEF BIOGRAPHY



Mr. Vacas-Jacques studies the third year of the Doctorate degree with specialization in Infrared Physics at CIO. He was granted an educational scholarship by SPIE for potential long-range contributions to optics and photonics (San Diego, USA; August 2007). He is part of the organizing committee for the AITA 2007 International Workshop. He is fluent in English, German, French, and Spanish.