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Principal-component-analysis-based estimation of blood flow velocities using optical coherence tomography intensity signals

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Abstract

The intensity signal in optical coherence tomography contains information about the translational velocity of scatterers, and can be used to quantify blood flow. We apply principal component analysis to efficiently extract this information. We also study use of nonuniform temporal sampling of the intensity signal to increase the range of quantifiable flow velocities. We demonstrate this technique in simulation, phantom and *in vivo* blood flow measurements, and highlight its potential to enable three-dimensional wide-field mapping of blood flow using OCT.

Recent advances in optical coherence tomography (OCT) [1,2] instrumentation and technique have enabled wide-field imaging of microvascular networks in animal models of disease [3–8]. In cancer, stroke, and many other diseases with vascular involvement, it would be invaluable to additionally measure the blood flow velocity within each vessel in the network. However, mapping three-dimensional blood flow over a wide field and within a time consistent with practical experimentation and animal sedation limits presents significant challenges. Namely, current techniques require a large number of measurements from each spatial location to accurately determine flow. In this work, we introduce a flow velocity measurement algorithm that operates over a wide dynamic range from a minimal number of measurements. This is achieved by combining three features novel to OCT-based flow measurement: statistical estimation using principal component analysis; inclusion of a stochastic signal model; and support for measurements sampled nonuniformly in time. We show through simulations, measurements in phantoms, and preliminary *in vivo* imaging in the mouse ear that these features in combination allow highly efficient measurement of flow velocity over several orders of magnitude.

Conventional Doppler techniques for flow velocity measurement rely on the phase of the OCT signal [9–11]. These techniques have proven accurate when applied to a sufficiently large measurement set acquired at timing intervals matched to the flow velocity. If applied to a more limited set of measurements or over a broad range of velocities, challenges associated with phase wrapping, limited signal-to-noise, phase decorrelation, bulk motion, and environmental instability frustrate reliable flow measurement. Many of these challenges are eliminated or reduced by discarding the phase of the OCT signal, and instead estimating flow from fluctuations in the OCT intensity signal. To date, this has been demonstrated by extracting statistical properties such as autocorrelation width and power spectral density [12,13]. While these approaches are intuitive and straightforward to implement, they are also statistically inefficient because they do not incorporate known information about the signal generation process into the estimation of velocity [14], and do not support measurements at arbitrary time spacing.

We treat flow measurement from OCT intensity signals as a stochastic process estimation problem. We assume a specific continuous-time stochastic model of the OCT signal intensity $I(t)$ that is parameterized by the velocity of the scatterers, v . Our goal is to estimate, i.e., statistically infer, the value of that velocity parameter given a discrete set of N measurements $(I_1, I_2, \dots, I_N)$ acquired at known but arbitrarily spaced times $(t_1, t_2, \dots, t_N)$. In this work, we first describe our construction of a stochastic OCT signal model and, second, we describe our algorithm for statistical estimation. The models and methods described in this work are applicable to both time and Fourier domain OCT imaging.

We modified a Monte Carlo stochastic model of the complex OCT signal from translating scatters used to analyze noise in Doppler OCT [15]. In this model, we assume that, at time t , the OCT beam is incident on M scatterers, each with a complex scattering coefficient, a_k , where $k = 1 \dots M$. Let the amplitude of the OCT field profile at the k th scatterer be E_k . A Gaussian beam profile is used throughout this work. The intensity signal is given as the coherent sum of backreflections from the scatterers:

$$I(t) \propto \sum_{k=1}^M |E_k^2 a_k^t|. \quad (1)$$

For particles moving with a fixed velocity, we denote the time required for a new particle to enter the beam profile as δt . The backscattering array at a future time $(t + m\delta t)$ is related to that at time t by shifting the array by m positions:

$$a_k^{t+m\delta t} = a_{k-m}^t, \quad m < k \leq N, \quad (2)$$

and generating new random values in $a_k^{t+m\delta t}$ for $1 \leq k \leq m$. Here N is the number of particles in the imaging region. Note that the value of δt relative to the beam width, defines the flow velocity being simulated. Exemplary intensity signals generated by this model are illustrated in Fig. 1(a). We note that this mode will be less accurate when flow velocities vary significantly within a voxel.

We take as a generalized starting point this stochastic model and a measured signal vector, which we assume to be a realization of this model at a specific velocity. Our goal is to statistically infer the velocity value from the measured signal vector, i.e., to select the velocity for which the model generates signals that are statistically most similar to the measured signal vector. To this end, we first used the model to generate a library of intensity signals containing 5×10^4 signal vectors at each of 170 logarithmically spaced velocities spanning a range from 0.1 to 10,000 $\mu\text{m/s}$. To more accurately match modeled and measured optical frequency domain imaging (OFDI) signals, a multiplicative random noise was added to the model, yielding a signal-to-noise ratio (SNR) of 10 dB.

We next transformed each signal in the library using principal component analysis (PCA). Using eigenvalue decomposition, we generated the principal components of the library signals as an $N \times N$ transformation matrix ($\mathbf{T}$) [16], where N is the number of samples in the signal. With this matrix, we generated the transformed signal library $U = \mathbf{T}\mathbf{I}$, where $\mathbf{I}$ represents the original signal. We also transformed the measured signal vector under test using the same matrix. From the library of transformed simulated signals, we derived at each velocity the probability distribution function (pdf) of each of the N elements of the transformed signal vectors. PCA transforms the original time measurement (where velocity is encoded in element-to-element correlations but each taken separately follows a standard speckle intensity distribution) to an uncorrelated data series (where velocity is encoded directly in the distribution of individual elements). Finally, to estimate the velocity of a

given measured signal, we first transformed that signal using the transformation matrix $\mathbf{T}$, and then performed statistical comparison of resultant data and the multidimensional pdfs for each velocity. Specifically, we calculated the product of each pdf indexed by the elements of the transformed measured signal. The velocity was estimated as that for which this product, i.e., the likelihood, is maximized.

To validate the algorithm, we first tested its performance on simulated OCT intensity signals spanning the same velocity range as the model. The signals for testing were generated in the same manner as for the library creation. This entire process of library creation, transformation, and pdf generation was performed for two different timing patterns: (i) a uniform sampling defined by $(t_{i+1} - t_i) = 300 \mu\text{s}$ and (ii) a nonuniform power-scaled pattern given by $(t_{i+1} - t_i) = 20 \times (1:15)^i \mu\text{s}$. Each signal was transformed using the PCA transformation matrix associated with either the uniform or nonuniform timing pattern. The maximum likelihood velocity was calculated for a test set of signals (separate from those used to generate the library). For baseline comparison, we also analyzed the signals for uniform sampling using standard autocorrelation techniques [Fig. 1(b)]. Here, quantifiable velocity was obtained by calibrating the width of the autocorrelation function to the velocity using a large training set. The estimated velocities using the PCA approach for uniform sampling are presented in Fig. 1(c). Note that the autocorrelation technique features a larger variance in its estimation relative to the PCA approach. The improved performance can be attributed to the inclusion of signal properties into the flow estimation procedure in the PCA method.

By using nonuniform sampling, we can measure signal dynamics across a broader time scale. This was confirmed by applying the PCA algorithm to nonuniformly spaced samples as defined previously [Fig. 1(d)]. In comparing Fig. 1(c) and 1(d), we see that accuracy in the “sweet spot” of nonuniform sampling, e.g., $\sim 20 \text{ mm/s}$, is sacrificed to broaden the measurement range. Here, the ability of the PCA algorithm to operate on arbitrary sampling patterns allows one to compromise between the range over which the instrument operates and the accuracy of measurements within that range.

To provide experimental validation, we applied the PCA approach to measured OFDI data from a rubber scattering phantom translated at speeds of 1 to 1000 mm/s using a calibrated motor. In this work, we have opted to use a solid phantom to test our methods over a large range of velocities to avoid problems of Brownian motion and pulsating flow associated with the flow phantoms. The M -mode signal was collected using instrumentation discussed in [3]. The performance of the PCA-based velocity estimation method was tested using 32-point signals with both the uniform and nonuniform sampling patterns described previously. The principal components, transformation matrix $\mathbf{T}$, and probability distributions of the transformed signals were obtained using the simulations. Next we obtain the transformed measured signal vectors. Finally, maximum likelihood velocity estimates were obtained using the library probability distributions. The mean estimated velocities and their variance are denoted by red points in Figs. 1(c) and 1(d) for uniform and nonuniform sampling patterns, respectively. We can see that our experimental data closely matches the simulation results, demonstrating the accuracy of both our model to measured OCT signals and PCA-derived flow estimates to true translational velocities.

Finally, the PCA-based method was used to estimate in a preliminary manner *in vivo* blood flow rates in a mouse ear. We obtained 2500 successive A-lines at a rate of 50 KHz at each of 150 transverse locations. We estimated the Doppler shift at each point by measuring average phase difference over all 2500 measurements [17]. The angle of the vessel relative to the imaging beam ($\sim 69^\circ$) was calculated by the geometry of the imaging setup and the assumptions that all vessels within the thin ear tissue are parallel to the surface of the ear and

normal to the image plane. Figure 2(a) shows a representative B-scan frame with color-coded Doppler shift data. Blood vessels corresponding to the regions with large Doppler shifts are shown in red.

Figures 2(b) and 2(c) show two exemplary intravascular intensity signals. We used 32 of the 2500 temporal measured samples for testing the PCA-based method. These 32 samples were nonuniformly spaced in time (using the same pattern as used for simulations and the rubber phantom experiment with the total measurement time corresponding to 2500 A-lines at 50 KHz). PCA-based and Doppler-based average estimates of velocity were compared in 10 vessels identified by the Doppler datasets (Table 1). The averages were obtained using the pixels that were distinctly present in the vessel in the Doppler data. For large vessels, this excludes the regions dominated by strong scattering from superficial blood. There is a high correlation between the estimates of both methods, with a correlation coefficient of over 85%. We note that the Doppler estimates used here as a gold standard suffer from errors due to imprecise knowledge of beam angle and vessel orientation.

In conclusion, we have demonstrated an efficient method to obtain flow velocities from the OCT intensity signal. The method has the advantage of being insensitive to the orientation of the blood vessel under consideration, of operating over wide ranges of flow, and supporting arbitrary measurement timing. Although the quantification using intensity requires the knowledge of system parameters, such as beam diameter, this information is readily available. Additionally, the intensity-based technique is less sensitive to bulk motion than the phase-based technique. In computational overhead, the PCA-based technique requires approximately twice the number of floating-point operations as a standard autocorrelation technique (not including the initial training process). We note that the Doppler estimates used here as a gold standard suffer from errors due to imprecise knowledge of beam angle and vessel orientation. Such errors can result in bias between PCA and Doppler results. Processing approaches such as this may lay the foundation for wide-field mapping of three-dimensional blood flow using OCT. Future works will focus on the development of imaging microscopes for efficiently realizing arbitrary sampling in three-dimensional imaging.

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Fig. 1.

(Color online) (a) Simulated OFDI intensity signals are shown for different scatterer velocities. (b) Estimation using autocorrelation with a uniform sampling pattern ($N=32$). The dark curve presents the median estimate, and the yellow shaded band shows the 10%–90% interval about the median. (c) Estimation using the PCA method for a uniform sampling pattern ($N=32$). The median and the 10%–90% interval of estimated velocities of a translating rubber phantom using the PCA method are presented in red points. (d) Same as in (c), but with the nonuniform sampling pattern ($N=32$).

Fig. 2. (Color online) (a) Doppler OFDI B-scan of a mouse ear. The horizontal and vertical bars represent 500 and 20 μm , respectively. (b) and (c) Measured intensity signal from within a relatively slow-flowing and a fast-flowing blood vessel, respectively. Also shown by the bold red curve is the subsampled 32-point signal vector used as input in the PCA method.

Table 1*In Vivo* Flow Estimates [mm/s]

Doppler	2.40 ¹	1.37 ²	12.3 ³	5.84 ⁴	2.00 ⁵
PCA	3.30	2.30	8.00	8.28	2.63
Doppler	3.02 ⁶	14.2 ⁷	3.44 ⁸	0.74 ⁹	11.1 ¹⁰
PCA	5.58	17.6	8.11	2.61	18.2