Supplementary Material (ESI) for Lab on a Chip
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Theory of Spectral-Domain Doppler Optical Coherence Tomography

SDDOCT is a fusion of laser Doppler velocimetry and optical coherence tomography based on a Michelson interferometer as shown in Fig. 1. Four arms around a 50:50 beam splitter in the Michelson interferometer are assigned by (1) a low-coherence light source at the source arm, (2) a spectrometer with a line array of detectors and a diffraction grating at the detector arm, (3) an immobilized mirror at the reference arm, and (4) a two-axis scanner and a sample with moving scatterers at the sample arm. Reflected lights from the immobilized mirror and each scattering particle in the sample make a signal in the spectral-domain which is detected by the spectrometer.

In order to mathematically describe the principle of SDDOCT, let us consider a steady-state velocity field of moving scatterers, $\mathbf{V}(\mathbf{X}) = (v_X, v_Y, v_Z)$ as a function of position vector $\mathbf{X} = (X, Y, Z)$. The coordinates X, Y, and Z are attached on the microchannel as shown in Fig. 1, and the XZ-plane is the top surface while the Y-coordinate is the depthwise direction of the microchannel. Let us define another set of coordinates, x, y, z, attached on the sample arm. Then, the description of the velocity field is $\mathbf{V}(\mathbf{x}) = (v_x, v_y, v_z)$ as a function of position vector $\mathbf{x} = (x, y, z)$. Let us have the y-coordinate coincide with the incident light to the microchannel. In order to measure v_Y with SDDOCT, we keep the incident light aligned to the Y-direction during two-axis scanning of the light in the x- and z-directions. Once a line field of $v_y(y)$ at a fixed position of (x, z) is measured, the scanner moves the light to another position of (x, z) to get a three-dimensional velocity field of $v_y(x, y, z)$. We, hereafter, describe how the line field is measured.

The instantaneous positions of moving scatterers in the y-coordinate are described as $y = y_0 + v_y(y_0)t$ for a sufficiently short time t where y_0 denotes initial positions. Now let us consider an input analytic signal $U_{in}(\omega,t)$ to the interferometer:

$$U_{in}(\omega,t) = s(\omega)\exp[-i(\omega t - \varphi)], \tag{1}$$

where $s(\omega)$ is the amplitude spectrum of the light source, ω is frequency, and φ is phase accumulated throughout the interferometer. Since the interferometer only measures the relative phase between two optical paths, the phase of input analytic signal U_{in} is chosen as a reference and the input analytic signal is written as $U_{in}(\omega, t)=s(\omega)\exp(-i\omega t)$. Then, output analytic signal U_{out} is the sum of analytic signals at the reference $U_r(\omega, t)$ and sample arms $U_s(\omega, t)$.

In order to mathematically represent $U_r(\omega, t)$ and $U_s(\omega, t)$, let us consider the time-space diagram in Fig. 2. We chose two representative scattering particles which were located at y_0^1 and y_0^2 initially and moved with velocities of $v_y(y_0^1)$ and $v_y(y_0^2)$, respectively. The time-space diagram depicts interactions between the moving scatterers and light wave in the sample arm and between the immobilized mirror and light wave in the reference

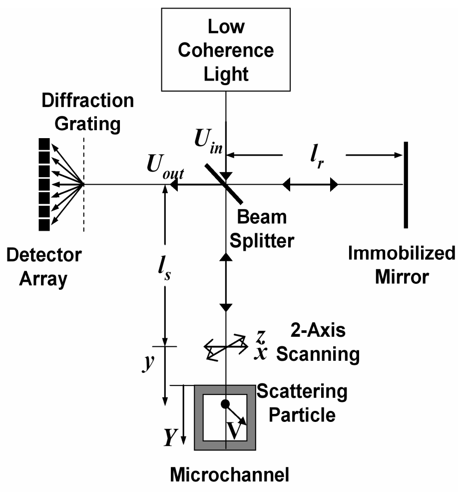

Fig. 1 Michelson interferometer for spectral-domain Doppler optical coherence tomography.

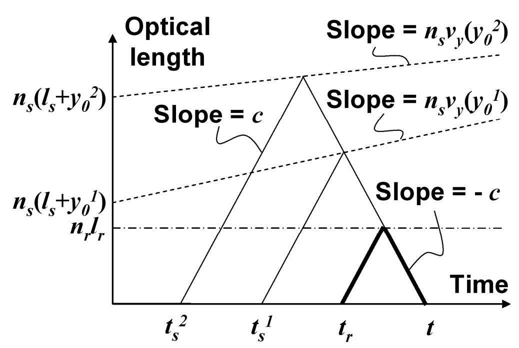

Fig. 2 Time-space diagram showing the trajectories of the scattering particles (dotted lines), travel of the light wave in the sample (solid lines) and reference arms (bold line), and the position of the immobilized mirror (dash dot line).

arm. The departure times of light from the beam splitter to each scatterer is denoted by t_s^1 and t_s^2: t_r is the departure time of light from the beam splitter to the immobilized mirror, n_s and n_r are refractive indices of the sample and reference arms, respectively, l_r is the physical length of the reference arm, l_s is the physical length between the beam splitter and the origin of the *y*-coodinate, and *c* is the speed of light in free space. Using the time-space diagram, we can trace back the light that has returned to the beam splitter at a certain time *t* and set up the relationship between the departure and arrival times with a negligible dispersion:

$$t_s(y_0,t) = \frac{1-n_s v_y/c}{1+n_s v_y/c}t - \frac{2n_s(l_s+y_0)/c}{1+n_s v_y/c}, \tag{2}$$

$$t_r(t) = t - 2n_r l_r/c, \tag{3}$$

where the factor of 2 is included to take account of double path. Therefore, the $U_r(\omega, t)$ and $U_s(\omega, t)$ can be represented as:

$$U_r(\omega,t) = \sqrt{\frac{1}{4}}U_{in}(\omega,t_r) = \sqrt{\frac{1}{4}}s(\omega)\exp(-i\omega t)\exp(i\frac{\omega}{c}2n_r l_r), \tag{4}$$

$$\begin{aligned} U_s(\omega,t) &= \sqrt{\frac{1}{4}}\int_0^\infty a(y_0)U_{in}(\omega,t_s)dy_0 \\ &= \sqrt{\frac{1}{4}}s(\omega)\exp(-i\omega t)\int_0^\infty a(y_0)\exp\left[-i\omega\left\{\left(\frac{1-n_s v_y/c}{1+n_s v_y/c}-1\right)t - \frac{2n_s(l_s+y_0)/c}{1+n_s v_y/c}\right\}\right]dy_0 \\ &\equiv \sqrt{\frac{1}{4}}s(\omega)\exp(-i\omega t)H(\omega,t), \end{aligned} \tag{5}$$

where $a(y_0)$ is the initial distribution of backscattering amplitude. If we have two infinitesimal scatterers as in Fig. 2, $a(y_0)$ is a linear combination of two delta functions with two constants *p* and *q*: $p\delta(y_0-y_0^1) + q\delta(y_0-y_0^2)$. We assumed a perfect reflection at the immobilized mirror in Eq. (4). The coefficient of $\sqrt{1/4}$ is added because of the 50:50 beam splitter. The accumulated phases due to the path length delays and/or Doppler effect of the reference and sample arms are $\exp(i\omega/c2n_r l_r)$ in Eq. (4) and $H(\omega,t)$ in Eq. (5), respectively, where $H(\omega,t)$ is a frequency response function of a sample. The frequency response function provides the input analytic signal with time delay and compression factors. The time delay factor comes from the path length delay and the compression factor from the Doppler effect. In another point of view, the frequency response function represents instantaneous phase accumulation by the multiple optical paths within the sample and, therefore, is a sum of many elementary waves reflected from moving scatterers with different initial depths of $l_s + y_0$. Since

$n_s v_y/c$ << 1, we use the approximation $(1 + n_s v_y/c)^{-1} \approx 1 - n_s v_y/c$ repeatedly to get a simple expression for $H(\omega,t)$:

$$H(\omega,t) \approx \int_0^\infty a(y_0)\exp\left[i\frac{\omega}{c}2n_s(y_0 + v_y t + l_s)\right]dy_0. \tag{6}$$

Now we adjust the physical length of the reference arm l_r to satisfy $n_r l_r = n_s l_s$. This is equivalent to locating a virtual image of the immobilized mirror at the origin of the y-coordinate in the sample arm. Then, the intensity as a function of time and wavenumber in free space k (= ω/c), which is recorded by the spectrometer, can be formulated as:

$$\begin{aligned} I(k,t) &= \frac{1}{\tau}\int_{t-\tau/2}^{t+\tau/2} U_{out}(k,t)U_{out}^*(k,t)dt \\ &= \frac{1}{4}S(k) + \frac{1}{2}S(k)\int_0^\infty a(y_0)\mathrm{sinc}(kn_s v_y \tau)\cos(2kn_s(y_0 + v_y t))dy_0 \\ &+ \frac{1}{4}S(k)\int_0^\infty\int_0^\infty a(y_0)a(y_0')\mathrm{sinc}[kn_s(v_y - v_y')\tau]\exp[i2kn_s(y_0 - y_0' + (v_y - v_y')t)]dy_0 dy_0', \end{aligned} \tag{7}$$

where τ is the integration time of the spectrometer, $S(k)$ is the intensity spectrum of the light source, and * denotes the complex conjugate. The first term is referred to as the reference-intensity term. Since we assume a perfect reflection at the immobilized mirror of the reference arm, we get 25% of the source power. This term can be measured by blocking the sample arm. The third term is referred to as the sample-intensity term because it contains the interference among the elementary waves reflected from different sample depths. The second term is our target signal and is referred to as the cross-interference term. The larger y_0 we have, the higher the encoding frequency in the k-domain. Since we have a finite number of detectors within a line array in the spectrometer, the maximum detectable frequency is limited by the Nyquist sampling criterion. Therefore, we have to minimize y_0 by adjusting the origin of the y-coordinate (i.e., adjusting the length of the reference arm l_r). On the other hand, if we have the origin inside the sample in order to minimize y_0, either side around the origin has the same encoding frequency and leads to ambiguity. Therefore, we put the origin just above the top surface of the sample as in Fig. 1.

Suppose that the light source has a Gaussian power spectral density given by

$$S(k) = P_0\exp\left[-4\ln 2\frac{(k-k_0)^2}{\Delta k^2}\right], \tag{8}$$

where k_0 is the center wavenumber, Δk is the full-width-half-maximum (FWHM) spectral width in wavenumber, and P_0 is the maximum power at the center wavelength. Since $|y_0| << |v_y\tau|$ and, therefore, $|\Delta k y_0| << |\Delta k v_y \tau|$, the phase of $kv_y\tau$ approximates to $k_0 v_y \tau$. Then, we can rewrite Eq. (7) as:

$$\begin{aligned} I(k,t) &= \frac{1}{4}S(k) + \frac{1}{2}S(k)\int_0^\infty a(y_0)\mathrm{sinc}(k_0 n_s v_y \tau)\cos(2kn_s y_0 + 2k_0 n_s v_y t))dy_0 \\ &+ \frac{1}{4}S(k)\int_0^\infty\int_0^\infty a(y_0)a(y_0')\mathrm{sinc}[k_0 n_s(v_y - v_y')\tau]\exp[i2kn_s(y_0 - y_0') + i2k_0 n_s(v_y - v_y')t)]dy_0 dy_0'. \end{aligned} \tag{9}$$

In order to decode the backscattering amplitude $a(y_0)$ from Eq. (9), we introduce an even function $\tilde{b}(y_0)$:

$$\tilde{b}(y_0) = \begin{cases} b(y_0) \\ b(-y_0) \end{cases} = \begin{cases} a(y_0)\mathrm{sinc}(k_0 n_s v_y(y_0)\tau) & if \quad y_0 \geq 0 \\ a(-y_0)\mathrm{sinc}(k_0 n_s v_y(-y_0)\tau) & if \quad y_0 < 0. \end{cases} \tag{10}$$

Note that $a(y_0) = 0$ for any y_0 less than 0 because we put the origin of the y-coordinate just above the top surface of the sample. If we replace $a(y_0)\mathrm{sinc}(k_0 n_s v_y \tau)$ in the cross-interference term with the even function

$\tilde{b}(y_0)$ and take inverse Fourier transform from the k- to $2n_s y_0$-domain (i.e., optical double path length domain which will be denoted as η_0-domain), we get:

$$\begin{aligned} \Im^{-1}[I(k,t)] &= \frac{1}{4}\Im^{-1}[S(k)] \\ &+ \frac{1}{8n_s}\Im^{-1}[S(k)] \otimes \left[\tilde{b}\left(\frac{\eta_0}{2n_s}\right)\exp(i2k_0 n_s v_y t)\right] \\ &+ \text{sample - intensity term,} \end{aligned} \tag{11}$$

where $\Im^{-1}$ and $\otimes$ denote inverse Fourier transform and convolution operator defined in the η_0-domain:

$$\Im^{-1}(F(k)) = \frac{1}{2\pi}\int_{-\infty}^{\infty} F(k)\exp[-ik\eta_0]dk, \tag{12}$$

$$(f \otimes g)(\eta_0) = \int_{-\infty}^{\infty} f(\eta_0')g(\eta_0' + \eta_0)d\eta_0'. \tag{13}$$

The second term in Eq. (11) is a complex signal. The magnitude of the complex signal gives a structural image and the phase, a velocity image. The inverse Fourier transform of $S(k)$ with a broad bandwidth gives a narrow Gaussian distribution where the FWHM is $8\ln2/\Delta k$ in the η_0-domain. If we have a stationary mirror as a sample, the structural image is the convolution of delta function and $\Im^{-1}[S(k)]$ with a FWHM depth resolution of $4\ln2/n_s\Delta k$ in the y_0-domain. If the mirror is moving with v_y, a motion artifact comes in because of the finite integration time τ and degrades the spatial resoultion. In fact, the degradation can be explained by the convolution of the stationary image with a rect function, that is the inverse Fourier transform of the sinc function. In order to get the line field of $v_y(y_0)$, we need two consecutive exposures of the spectrometer at time t and $t + T$ at a fixed position of (x, z). This gives two complex signals of $\Im^{-1}[I(k, t)]$ and $\Im^{-1}[I(k, t + T)]$. The ensemble average of the phase difference can be related to the line field of velocity:

$$\overline{\Delta\phi}(y_0) = 2k_0 n_s v_y(y_0)T. \tag{13}$$

Since the ensemble average of the phase difference ranges from $-\pi$ to π, the detectable velocity range of v_y is from $-\lambda_0/4n_sT$ to $\lambda_0/4n_sT$ where λ_0 is the center wavelength. Any velocity outside this range will cause an aliasing effect. A phase unwrapping technique using flow continuity can further increase this limitation by a factor of 4. Therefore, the time interval T should fall in the range of $\tau < T < \lambda_0/n_s v_y^{max}$ where v_y^{max} is the maximum velocity.

In general, the contribution of the third term in Eq. (11) is negliglble because the intensity of the sample-intensity term is much weaker than that of the cross-interference term. Recall that we assumed a perfect reflection at the immobilized mirror and the cross-interference term is weighted by the strong reference amplitude (= 1). In addition, the third term has a maximum at $y_0 = 0$ and decreases rapidly as $|y_0|$ increases for a fluid seeded with highly scattering particles. Hence, the side lobes of the third term are too weak to disturb the cross-interference term even with a small separation between the origin of the y-coordinate and the top surface of the sample.