Blood oxygenation and flow measurements using a single 720-nm tunable V-cavity laser

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Abstract: We propose and demonstrate a single-laser-based sensing method for measuring both blood oxygenation and microvascular blood flow. Based on the optimal wavelength range found from theoretical analysis on differential absorption based blood oxygenation measurement, we designed and fabricated a 720-nm-band wavelength tunable V-cavity laser. Without any grating or bandgap engineering, the laser has a wavelength tuning range of 14.1 nm. By using the laser emitting at 710.3 nm and 724.4 nm to measure the oxygenation and blood flow, we experimentally demonstrate the proposed method.

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1. Introduction

The microcirculation plays an essential role in health care, and abnormalities in the microvascular function often occur at the preliminary stages of the microvascular diseases. Microvascular blood flow and tissue oxygenation are two critical parameters to assess the microvascular function and its abnormal changes. Their detection and monitoring can provide early disease diagnosis and prevention, such as hypertension, edema and hypoxemia [1–3].

To meet the demand of providing blood flow and tissue oxygenation assessment at microvascular level, various techniques have been developed in the last decades. For example, microvascular blood flow can be directly accessed using a laser Doppler flowmeter (LDF) [4, 5] and tissue oxygenation can be obtained using transmissive or reflective pulse oximeter [1–3, 6, 7]. However, most commercial LDFs and pulse oximeters have the limitation of single function. Besides, the conventional LDFs usually are desktop-sized pieces of equipment, weighing several kilograms and expensive, so they are not suitable as portable devices for daily health monitoring. Therefore, it is desirable to develop a portable instrument combining both functions.

There have been some reports on prototype instruments combining LDF and pulse oximeter. The instrument developed by Dougherty used two LDs to complete the both readings [8]. One LD at 810 nm is used to give a blood flow index and oxygenation information, and the other one at 670 nm to complete the estimation of oxygen saturation. Hongyuan Liu reported a white-LED based tissue oxygen monitor, and the oxygen monitor is used in conjunction with a laser Doppler monitor [1]. While there are still some other instruments combining LDF and pulse oximeter [9,10], all of the reported instruments need at least two light sources and often have various limitations, such as complicated control algorithm or high power consumption.

To our knowledge, there has not been a method for monitoring blood oxygenation (SpO2) and blood flow simultaneously by using a single light source. In this paper, we propose and investigate a single-laser-based sensing method for both blood oxygenation and microvascular blood flow measurements. Based on the optimal wavelength range found from theoretical analysis, we designed and fabricated a widely tunable semiconductor laser in the desired wavelength range around 720nm. Using the fabricated laser which is tunable over 14nm, we successfully demonstrated the single-laser based measurement of both blood oxygenation and blood flow. The development, preliminary calibration and evaluation of the proposed system are described, combining both functions. Since the 720-nm-band widely-tunable V-cavity laser has the features of compactness, fabrication simplicity and easy wavelength control, the technology has potential advantages of low cost, low power consumption, small size and easy control, which is suitable for wearable health monitoring devices.

2. Analysis of the SpO2 measurement method using a single tunable laser

In order to measure the blood oxygenation and blood flow simultaneously using a single tunable laser with limited tuning range, we need to find the wavelength range that is most sensitive to the blood oxygenation. Human tissue is a strongly scattering media. In reflectance oximeter, the detector mainly receives scattered light after a parabolic path in tissue and the photon migration in biological tissue can be considered as a diffusion process [11]. Therefore, light propagation in homogeneous biological tissue can be described by photon diffusion equation [12]:

$$\frac{1}{V} \frac{\partial}{\partial t} \phi(r,t) - D \nabla^2 \phi(r,t) + \mu_t \phi(r,t) = S(r,t)$$  (1)
where $\phi(r,t)$ is the effective photon density at the position $r$ at time $t$. $S(r,t)$ represents the light source. $D$ represents diffusion coefficient. $\mu_a$ is absorption coefficient and $v$ is the speed of light in the tissue.

The diffusion coefficient $D$ for photon migration can be expressed as

$$D = \frac{1}{3[\mu_a + (1 - g)\mu_s]}$$  \hspace{1cm} (2)$$

where $g$ is the mean cosine of the scattering angle and $\mu_s$ represents scattering coefficient.

Taking into account Eq. (1) and the real boundary condition in biological tissue, Patterson et al deduced the expression of detected light intensity $\varphi(\rho, t)$,

$$\varphi(\rho, t) = (4\pi Dv)^{-3/2} z_0^{-5/2} \exp(-\mu_s vt) \exp\left(-\frac{\rho^2 + z_0^2}{4Dvt}\right)$$  \hspace{1cm} (3)$$

where $z_0$ is the effective transmission depth which can be expressed as $[(1 - g)\mu_s]^{-1}$ and $\rho$ is the source-detector separation.

Since $\rho^2 \gg z_0^2$ in reflectance oximeter, we also note that

$$\frac{\partial}{\partial t} \ln \varphi(\rho, t) = -\frac{5}{2t} - \mu_s v + \frac{\rho^2}{4Dvt}$$  \hspace{1cm} (4)$$

When time is long enough, the change rate of reflected light intensity $W$ is

$$W = \lim_{t \to \infty} \frac{\partial}{\partial t} \ln \varphi(\rho, t) = \lim_{\varphi \to \varphi} \frac{1}{\varphi} \frac{\partial \varphi(\rho, t)}{\partial t} = -\mu_a v$$  \hspace{1cm} (5)$$

In the near infrared region, the absorption caused by such substance as water, cytopigment, etc. is much smaller than that caused by oxyhemoglobin ($HbO_2$) and deoxyhemoglobin (Hb). Based on Beer-Lambert’s law, the absorption coefficient $\mu_a$ can be expressed as:

$$\mu_a = e_{Ib} C_{Ib} + e_{HbO_2} C_{HbO_2}$$  \hspace{1cm} (6)$$

where $e_{Ib}$ and $e_{HbO_2}$ are the molar absorptivities of Hb and HbO2, respectively. $C_{Ib}$ and $C_{HbO_2}$ are the concentrations of Hb and HbO2, respectively. Then, taking into account Eqs. (5) and (6), we can get

$$W = -(e_{Ib} C_{Ib} + e_{HbO_2} C_{HbO_2}) v$$  \hspace{1cm} (7)$$

When illuminating the tissue with light of two wavelengths $\lambda_1$ and $\lambda_2$, we can deduce

$$\frac{W_{\lambda_1}}{W_{\lambda_2}} = \left(\frac{e_{Ib}^{\lambda_1} C_{Ib} + e_{HbO_2}^{\lambda_1} C_{HbO_2}}{e_{Ib}^{\lambda_2} C_{Ib} + e_{HbO_2}^{\lambda_2} C_{HbO_2}}\right) v_{\lambda_1}$$  \hspace{1cm} (8)$$

In our study, since the difference between $\lambda_1$ and $\lambda_2$ is small (~14 nm), we can assume

$$v_{\lambda_1} = v_{\lambda_2}$$  \hspace{1cm} (9)$$

As for pulse oximeters, the reflectance light consists of a constant (DC) component and a pulsating (AC) component. The AC component is the result of the absorption by the
fluctuating volume of arterial blood, while the DC component is the result of the absorption by the body tissue and veins. Therefore, the signal from detector consists of a direct current ($I_{DC}$) and an alternating current ($I_{AC}$) and the change rate of reflectance light intensity can be expressed equally as

$$W = \frac{I_{AC}}{I_{DC}}$$

(10)

Then we can obtain the expression of oxygen saturation $SpO_2$

$$SpO_2 = \frac{C_{\text{HbO}_2}}{C_{\text{HbO}_2} + C_{\text{Hb}}} = \frac{\epsilon_{\lambda_1}^{\text{abs}} - \epsilon_{\lambda_2}^{\text{abs}} \ast R}{(\epsilon_{\lambda_1}^{\text{abs}} - \epsilon_{\lambda_2}^{\text{abs}}) - (\epsilon_{\lambda_1}^{\text{abs}} - \epsilon_{\lambda_2}^{\text{abs}}) \ast R}$$

(11)

where $R$ is the ratio of the signals $I_{AC}$ and $I_{DC}$ for wavelength $\lambda_1$ and $\lambda_2$, which has the expression:

$$R = \frac{I_{\lambda_1}^{AC} / I_{\lambda_1}^{DC}}{I_{\lambda_2}^{AC} / I_{\lambda_2}^{DC}}$$

(12)

According to Eq. (11), we know that the sensitivity and accuracy of the sensor is determined by the variation of the parameter $R$, not $W$. That is to say, the lower the slope of the function curve of Eq. (11), the higher accuracy the sensor has. Therefore, in order to increase the sensitivity and accuracy of the sensor, the changes in $R$ value should be as large as possible when the actual saturation $SpO_2$ changes. Considering the fact that it is difficult to obtain reliable human calibration data at saturations less than 70% [13], we assume the $SpO_2$ value in Eq. (11) changes from 70% to 100%. We can then obtain the ratio difference $\Delta R = R_{70\%} - R_{100\%}$ based on Eq. (11), where $R_{70\%}$ and $R_{100\%}$ are the ratios for $\lambda_1$ and $\lambda_2$ at 70% and 100% oxygen levels, respectively. Since we want to measure the $SpO_2$ by using a single widely tunable laser, the required tuning range is $\Delta \lambda = \lambda_2 - \lambda_1$. We have previously analyzed the feasibility using a tunable V-cavity laser with a conservatively estimated wavelength tuning range of 8 nm [14]. Here, we assume that the wavelength tuning range of the lasers could reach 8 nm, 11 nm and 14 nm, respectively, and calculate the corresponding $\Delta R$ value based on Eq. (11). Figure 1(a) shows the ratio difference $\Delta R$ as a function of the starting wavelength $\lambda_1$. We can see that the largest $\Delta R$ is obtained when the $\lambda_1$ value is between 700 nm to 720 nm. The $\Delta R$ value can reach approximately 0.26, 0.2 and 0.15 for a wavelength tuning range of 14 nm, 11 nm, and 8 nm, respectively.

![Fig. 1. (a) The ratio difference $\Delta R$ as a function of $\lambda_1$ for a wavelength tuning range of 8, 11 and 14 nm and (b) $SpO_2$ as a function of the ratio $R$ for different dual-wavelength combinations.](image-url)
To compare the variation $\Delta R$ with other pulse oximeters, Table 1 lists the $\Delta R$ values of six dual-wavelength combinations used by various groups, which range from 0.089 to 0.863. The tunable laser we fabricated for this study has a tuning range of about 14 nm starting at about 710 nm (see Sec. 3). The corresponding $\Delta R$ value is calculated to be 0.26, which is within the reported range. This confirms the feasibility of monitoring oxygen saturation using a single tunable laser with wavelength variation from 710 nm to 724 nm. However, according to Eqs. (11) and (12), the lower $\Delta R$ inevitably leads to an accuracy decrease. Figure 1(b) shows the calculated curves of the SpO2 versus the ratio R for the six dual-wavelength combinations in Table 1. We can find that the ratio R value of our method increases from 0.84 to 1.1 as the oxygen saturation falls from 100% to 70% and the R value of commercial oximeter increases from 0.263 to 1.126. Therefore, the commercial pulse oximeter has the highest accuracy (2%) and the accuracy of the proposed system in this paper is 3.3%. Although the accuracy of the single-laser-based method is not as good as a commercial oximeter at this time, the advantage of our technology is the use of only a single light source, instead of at least two light sources. Additionally, the technology can realize the measurement of blood flow simultaneously. Compared with conventional LDFs, the V-cavity-laser-based technology has potential advantages of low power consumption, small size, and low cost.

| Reference                     | $\lambda_1$ (nm) | $\lambda_2$ (nm) | $\Delta R$ | Accuracy | Source Type |
|-------------------------------|------------------|------------------|------------|----------|-------------|
| Tomoyuki Yokota et al., 2016  | 609              | 517              | 0.089      | -        | Two PLEDs   |
| Nitzan et al., 2000 [16]      | 767              | 811              | 0.258      | 3.0%     | Two LEDs    |
| This paper                    | 710              | 724              | 0.26       | 3.3%     | One LD      |
| SM Lopez Silva et al., 2003   | 750              | 850              | 0.335      | 3.1%     | Two LDs     |
| Tommasi et al., 2006 [18]     | 750              | 810              | 0.34       | -        | Two LDs     |
| Commercial Pulse Oximeter     | 660              | 940              | 0.863      | 2.0%     | Two LEDs    |

Fig. 2. (a) Optical microscope image of the laser, and (b) measured single-mode spectrum.

3. Experiments

3.1 Tunable laser fabrication and characterization

In order to realize the method for monitoring blood oxygenation and blood flow simultaneously using a single tunable laser source, we designed and fabricated a 720-nm-band widely tunable V-cavity laser (VCL) based on AlGaAs multiple quantum well (MQW). The layer structure consists of 0.2 $\mu$m Zn-doped GaAs cap, 1 $\mu$m Zn-doped Al$_{0.2}$Ga$_{0.8}$As cladding, three repeats of 4 nm undoped Al$_{0.18}$Ga$_{0.82}$As quantum well and 10 nm
Al$_{0.45}$Ga$_{0.55}$As barrier, 1.4 μm Si-doped Al$_{0.8}$Ga$_{0.2}$As cladding, and 0.5 μm Si-doped GaAs buffer on S-doped GaAs substrate. The center wavelength of the measured photoluminescence peak is about 720 nm.

The operation principle of the VCL has been described in detail in [19]. The VCL comprises a fixed gain or short cavity and a channel selector or long cavity with different optical path lengths, which are coupled by a reflective 2 × 2 half-wave coupler. Figure 2(a) shows the top-view microscope photograph of the V-cavity laser fabricated in AlGaAs/GaAs system. The length of the short cavity is designed to be 182 μm and the length of the long cavity is 5% longer to employ the Vernier effect to increase the wavelength tuning range. Deeply etched facets are used to form the cavity mirrors so that the length of the two cavities and of the half-wave coupler can be controlled accurately. Three electrodes have been deposited on the respective cavities of the VCL. The half-wave coupler electrode and the short cavity electrode are used to inject a constant current to provide an optical gain, and the long cavity electrode is used for wavelength tuning.

| Range | Current (mA) | Number of channels | Wavelength (nm) |
|-------|--------------|-------------------|-----------------|
|       | Coupler | Short-cavity | Long-cavity |
| 1     | 34.7    | 9.8             | 8.6 → 25.8     | 22 | 710.3 → 717.4 |
| 2     | 36.4    | 33.6            | 23.4 → 34.6    | 20 | 717.8 → 724.4 |

Since the VCL does not involve any grating or epitaxial regrowth, the fabrication process is similar to that of a Fabry-Perot (FP) laser with the addition of a deep etching step for the reflection facets, which has been described in [20]. The chip size is only about 250 μm × 200 μm.

The fabricated VCL chip was mounted on an aluminum nitride (AlN) carrier with a thermal-electric cooler (TEC) controlled at 20 °C. The VCL reaches its threshold when the half-wave coupler electrode is biased at about 20 mA. When both of the short-cavity electrode and the half-wave coupler electrode are biased at 40 mA, the output power from the coupler side can reach about 10 mW. Figure 2(b) gives a typical single-mode lasing spectrum of the VCL, with a SMSR of 33 dB.

![Fig. 3. (a) Measured tuning curves in two ranges with different bias currents in the half-wave coupler electrode and the short-cavity electrode, and (b) overlapped 42-channel laser spectra.](image)

By adjusting the current in the long-cavity electrode, we can tune the lasing wavelength with high SMSR. Figure 3(a) shows the wavelength of the lasing mode as a function of the tuning current injected in the long-cavity electrode. When the tuning current in the long-cavity electrode increases, the lasing channels move toward longer wavelength. In each wavelength range, the currents on the half-wave electrode and short-cavity electrode are constant, as shown in Table 2. A total wavelength tuning range of 42 channels from 710.3 nm to 724.4 nm is obtained, with a uniform channel spacing of about 0.35 nm. Figure 3(b) shows...
the superimposed emission spectra of the 42-channel wavelength tuning, and the SMSRs are above 30dB for most of the channels.

### 3.2 System design

In order to directly apply the theoretical model described in Sec. 2, we developed an emission-detection system of the reflective oximeter and flowmeter by employing the fabricated VCL. We use the wavelength 724.4 nm of the VCL to give a blood flow index and oxygenation information, and the wavelength 710.3 nm to complete the estimation of oxygen saturation. In order to control the VCL easily, we only need to adjust the current in the long-cavity electrode to obtain the 14.1 nm wavelength tuning range. The currents in the coupler electrode and short-cavity electrode are 27 mA and 16 mA, respectively. The output power of the VCL is about 2 mW. When the current in the long-cavity electrode is set to 9 mA, the output wavelength of the VCL is 710.3 nm. When the current in the long-cavity electrode changes to 34 mA, the wavelength is switched to 724.4 nm.

![Diagram](image-url)

**Fig. 4.** (a) Schematic of the experimental set up and (b) oxygen saturation as a function of the R value. The dotted line is the nonlinear fitting of SpO2 versus R to the rational function.

Figure 4(a) shows the schematic of the measurement system. The signal generator generates the trigger signal for the laser diodes driver, and the wavelength of the laser is switched from 710.3 nm to 724.4 nm by the laser diodes driver at a repetition rate of 250 Hz. The output of VCL is coupled to a multimode fiber, which convey the radiation to a human finger. The backscattered radiation is detected by a silicon photodiode (PD), and the obtained signal from the PD passes through an analogue front end where the PPG signal is amplified. A data acquisition board (PCI-6251, National Instruments) is used to collect the PPG signal from the amplifier and the 250 Hz trigger signal from the signal generator. The sampling rate of the DAQ board is 50 kS/s per channel. Finally, the two collected signals are sent to a personal computer for filtering, processing, analysis and visualization.

### 3.3 Blood oxygenation measurement

The relationship between the parameter R obtained from the measurement and the oxygenation value SpO2 is given by the calibration curve. This curve is specific for each sensor configuration and emitter wavelength used [17]. To calibrate the proposed system, we measured the SpO2s of three volunteers for many times within a couple of days. The right index finger of each subject was attached to the reflective sensor of our system. A commercial pulse oximeter (Yuwell-YX301) [21] was attached to the left index finger to record the oxygenation at the same time. Low-level oxygenation was obtained by holding the breath. A total of 25 arterial samples of different oxygenation levels were measured.
Fig. 5. Performance of the single-laser-based reflective pulse oximeter system. (a) The PPG signals at wavelength 710.3 nm. (b) The PPG signals at wavelength 724.4 nm. Note that a partial enlarged view shows four cardiac cycles of the PPG signals. (c) The calculated R based on Eq. (12). (d) The blue line indicates the calculated SpO₂ based on Eq. (13), and the red line indicates the reference saturation obtained from the commercial co-oximeter.

Figure 4(b) shows the arterial oxygen saturation as a function of the R value for each sample. Note that each R value is the average of several cycles of PPG signal over a time interval of 5 s, and each corresponding SpO₂ value is the average of five recorded values obtained from commercial co-oximeter every 1 s over a time interval of 5 s. The relationship between the level of oxygen saturation measured by co-oximeter and the R value derived from the PPG signals was obtained through a nonlinear curve fitting to a rational function of the following form

\[
SpO_2 = \frac{120 \times R - 267}{83 \times R - 235}
\]  

Equation (13) allows us to compare the SpO₂ values from the proposed single-laser-based pulse oximeter system with respect to the reference saturations from the commercial co-oximeter. The standard deviation (SD) of the calibrating data is 3.2%. As described in [8,22], prolonged breath holding produces characteristically shaped oxygenation responses, so we tested the accuracy of the system by measuring the SpO₂ of a completely new subject. Figure 5(a) and 5(b) show the typical measured PPG signals of the proposed system during breath holding test at the wavelengths of 710.3 nm and 724.4 nm, respectively. The ratio R values calculated directly from the PPG signals based on Eq. (12) are shown in Fig. 5(c). Figure 5(d) shows the arterial blood oxygenation (blue line) derived from the corresponding ratio R based
on Eq. (13), with the reference data measured with the commercial co-oximeter (red line). For the convenience of comparison, each ratio R value is calculated by two cycles of PPG signal every 5 s, and the corresponding reference SpO₂ value from co-oximeter is recorded every 5 s. In Fig. 5(d), we can find that 20 seconds after the subject started holding his breath, the oxygen saturation was seen gradually decreasing but then rapidly increased to the prior level in about 15 seconds as soon as the breath was resumed. The standard deviation of the differences between the two SpO₂ data in Fig. 5(d) is 3.3%.

Since the range of SpO₂ values for calibrating is from 86% to 100% in this paper, the system does not have data support at low level SpO₂ below 86% and further calibration with a wider range of lower SpO₂ data remains to be carried out. Our work in this paper focuses mainly on the investigation and demonstration of the single-laser-based sensing method for measuring SpO₂ and blood flow. The preliminary calibration and evaluation of the proposed system has successfully demonstrated this technology.

### 3.4 Blood flow measurement

The laser Doppler flowmeter is a useful diagnostic technique for monitoring microvascular blood flow. The VCL at wavelength 724.4 nm was used to measure the blood flow simultaneously. Laser Doppler flowmeter is based on the principle that coherent light backscattered from the tissue is spectrally broadened by Doppler shifts produced by moving red blood cells. When the frequency-shifted signal interferes with the unshifted signal, a detectable beat signal is produced. Then, we can calculate the blood flow by integrating the products of the beat signal power spectrum and frequency [4,5]. Here, in order to test the dynamic response of microcirculation, we occlude the right upper arm with a pressurized cuff. Figure 6(a) shows the power spectra of the PPG signals from the fingertip. The upper spectrum was measured during normal perfusion and the lower during an occlusion. There is clearly a distinct difference in the two frequency spectra. Figure 6(b) and 6(c) shows the typical derived blood flow signal obtained simultaneously with the VCL system and a commercial LDF (PeriFlux 5000). The integration is performed from 5 Hz to 15 kHz, which is based on the Eq. (1) in [5]. It is clearly seen that there is a gradual drop in the flow signal when the pressure of the cuff increased gradually. The flow signal returned to the original level rapidly as soon as the pressure released completely. The signal curve from the VCL system agrees well with the one from the commercial LDF, which confirms that the blood flow has been successfully measured by the proposed system.
4. Conclusion

We have proposed and demonstrated a single tunable laser based sensing method for measuring both oxygenation and blood flow using a widely tunable V-cavity laser fabricated in-house. The wavelength band around 720nm is shown to have the highest sensitivity for a given tuning range for blood oxygen saturation measurement. A VCL in AlGaAs MQW system is fabricated, with a wavelength tuning range from 710.3 nm to 724.4 nm and SMSR above 30 dB, which is shown to be sufficient for the application. Future improvements in the tuning range and device packaging can further improve the performance. It is also possible to design and fabricate a V-cavity laser integrated with a photodiode, thus eliminating the fibers, which will simplify the system and improve the stability and accuracy of the method. Our experimental results demonstrate the validity of the single-laser-based reflective oximeter and blood flowmeter technique. The 720-nm band tunable VCL we present in this paper does not involve any grating or bandgap engineering and has a size of only 250 μm × 200 μm. The advantages of compactness, fabrication simplicity and easy wavelength control make the laser promising for multifunctional non-invasive health monitoring devices.

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Disclosures

The authors declare that there are no conflicts of interest related to this article.