

Novel Method for In Vivo Measurement of Hemoglobins



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INTRODUCTION

A novel and highly accurate method for measuring fractional concentrations of methemoglobin (MetHb) as well as oxyhemoglobin (O₂Hb) and deoxyhemoglobin (RHb) is presented. The fractional concentration of MetHb to total hemoglobin can increase rapidly from normal (< 2%) to more the 40% from exposure to certain chemicals and drugs, or as a response to cyanide poisoning treatment. High concentrations of MetHb can also be caused by genetic disorders. Such high concentrations can lead to tissue hypoxia, coma, and even death. Traditional methods for diagnosis of methemoglobinemia involve laboratory testing of blood samples because symptoms are vague and nonspecific [1]. The method developed in this research applies an innovative system and data analysis model to accurately measure methemoglobin fractional concentration in vivo.

BACKGROUND

Attenuation coefficients of hemoglobin moieties contain contributions from both absorption and scattering [2]. Oximetry applies spectrophotometric analysis that takes advantage of the differences between the attenuation coefficients of the Hb moieties. The concentration c_j of the Hb moiety j (j = RHb, O₂Hb, or MetHb) is found by inverting:

$$\mu_a(\lambda_i) = K \sum_j c_j \mu_a^j(\lambda_i) \quad (1)$$

where K is a calibration constant, $\mu_a^j(\lambda_i)$ is the absorption coefficient of the Hb moiety j at λ_i , and $\mu_a(\lambda_i)$ is the absorption coefficient of the system at λ_i . In theory, any measurements of optical transmission can be inverted to obtain the "apparent" absorption. In reality, the inversion process is complicated by scattering [3]. In pulse oximetry, two wavelengths (typically 660 nm and 940 nm) are used to deduce the oxygen saturation (SpO₂) using an experimental calibration [4]. In patients with high concentrations of MetHb or carboxyhemoglobin (COHb), pulse oximeters report unreliable SpO₂ values. Methylene blue (MB), an antidote for methemoglobinemia, may also interfere with oximetry measurements. The gold standard for MetHb concentration determination is co-oximetry, but co-oximeters requires hemolyzed blood.

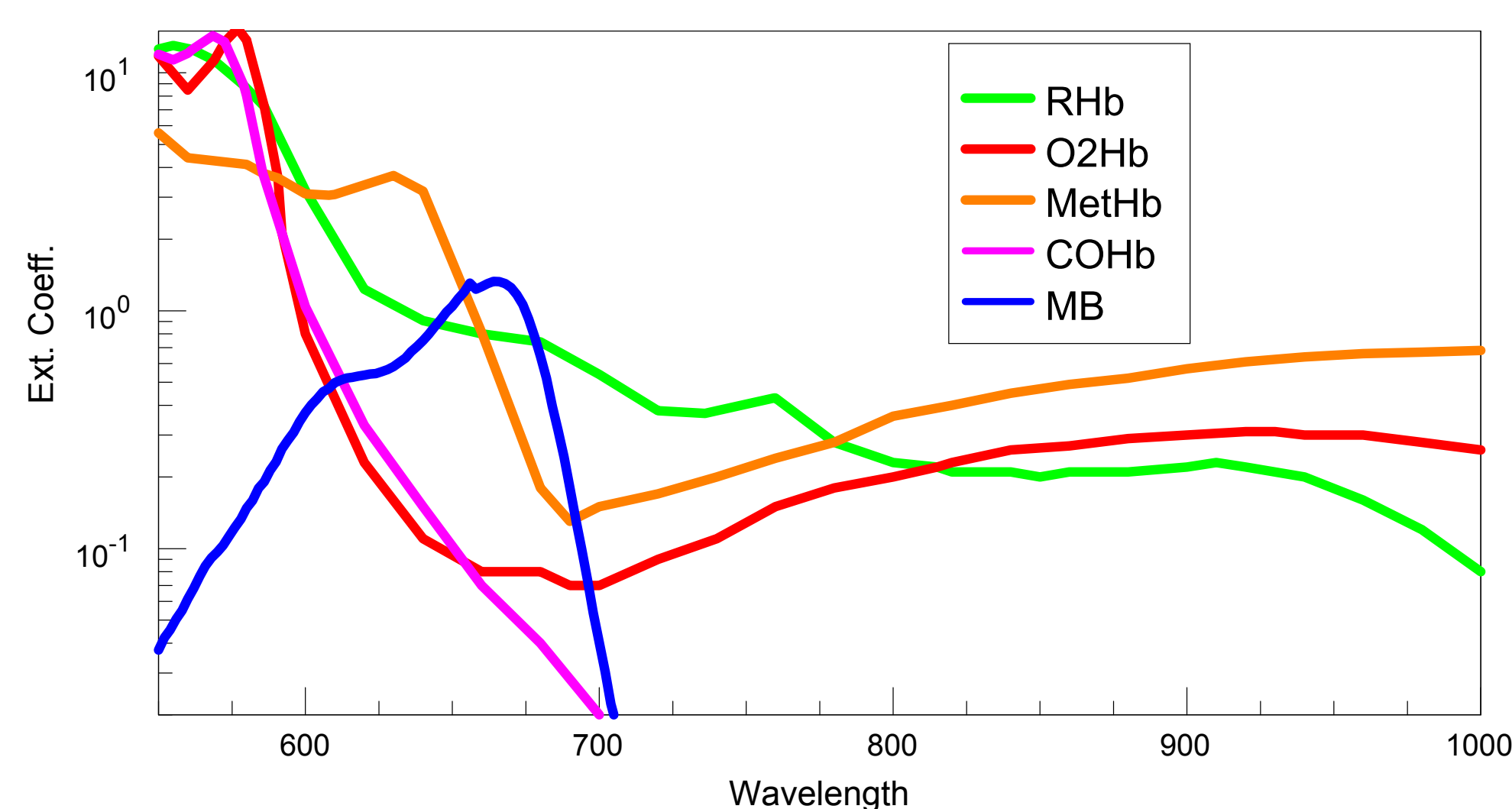


Fig. 1. Extinction coefficient spectra for RHb, O₂Hb, MetHb, COHb, and MB [2].

PROTOTYPE

A schematic diagram of the MetHb sensor head prototype is shown in Figure 2. The sensor head was designed to measure optical transmittance of in vitro (i.e. cuvette) or in vivo (i.e. finger or ear) samples by incorporating a spring-loading mechanism. Five T1 ¼ LEDs of wavelengths ranging from 660 nm to 940 nm and optical output powers ranging from 6 mW to 8 mW are mounted on a bulkhead with an interface to optical fibers. The optical fiber outputs meet at a point close to the fiber-sample interface, eliminating any differences in sample thickness for each wavelength. Input current for each LED is adjusted with a potentiometer to set the optical output power. The light transmitted through the sample is collected with an Advanced Photonix silicon detector/amplifier hybrid (application range 250 nm to 1100 nm) and sent to a data acquisition card with an A/D converter. LEDs are illuminated in a sequential pattern, with one LED ON at a time in 2 ms intervals.

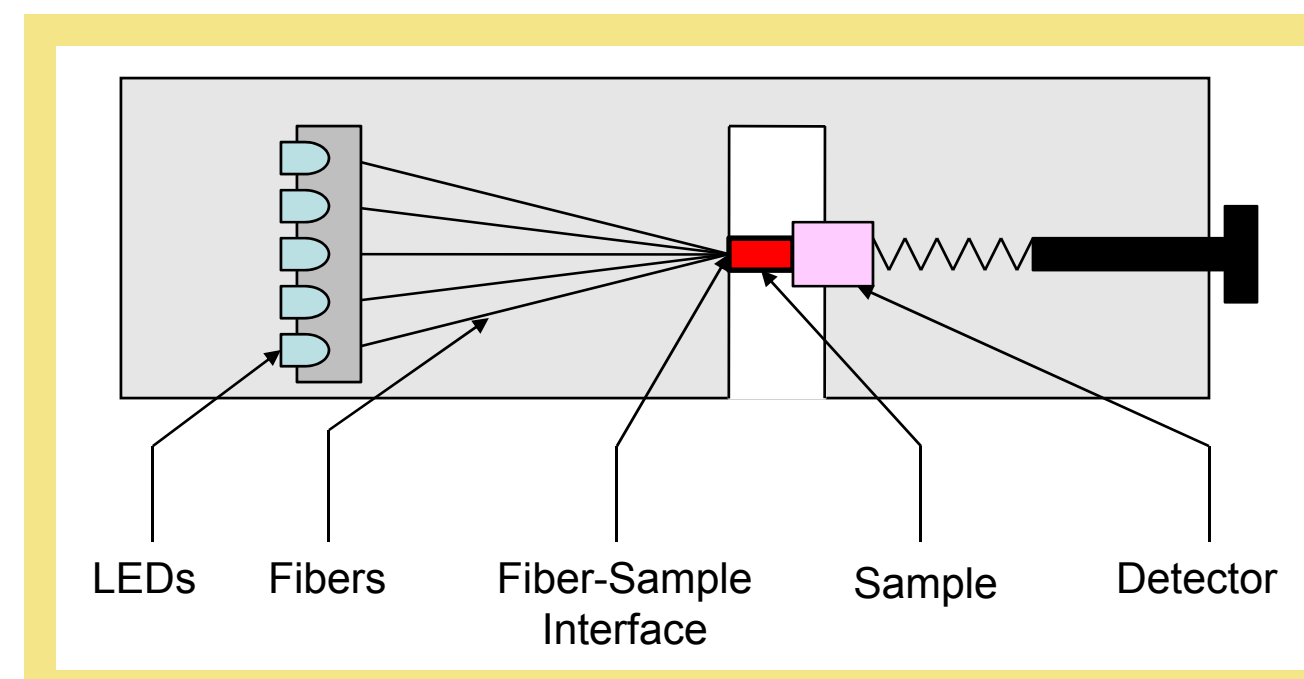


Fig. 2. Schematic diagram of the sensor head.



Fig. 3. Sensor head and power supply.

LABORATORY TEST RESULTS

A series of laboratory tests were performed to investigate the accuracy of the MetHb sensor. Figure 4 shows typical attenuation waveforms of five wavelengths measured at the tip of the left index finger of a 25-year-old, healthy Caucasian male. Measurement noise was reduced with electronic filters and data averaging algorithms. It is noted that the attenuation at the peak of the 660 nm cardiac pulse is about half of the attenuation at the peak of the 940 nm cardiac pulse. This corresponds to 98% SpO₂ on a standard calibrated pulse oximeter.

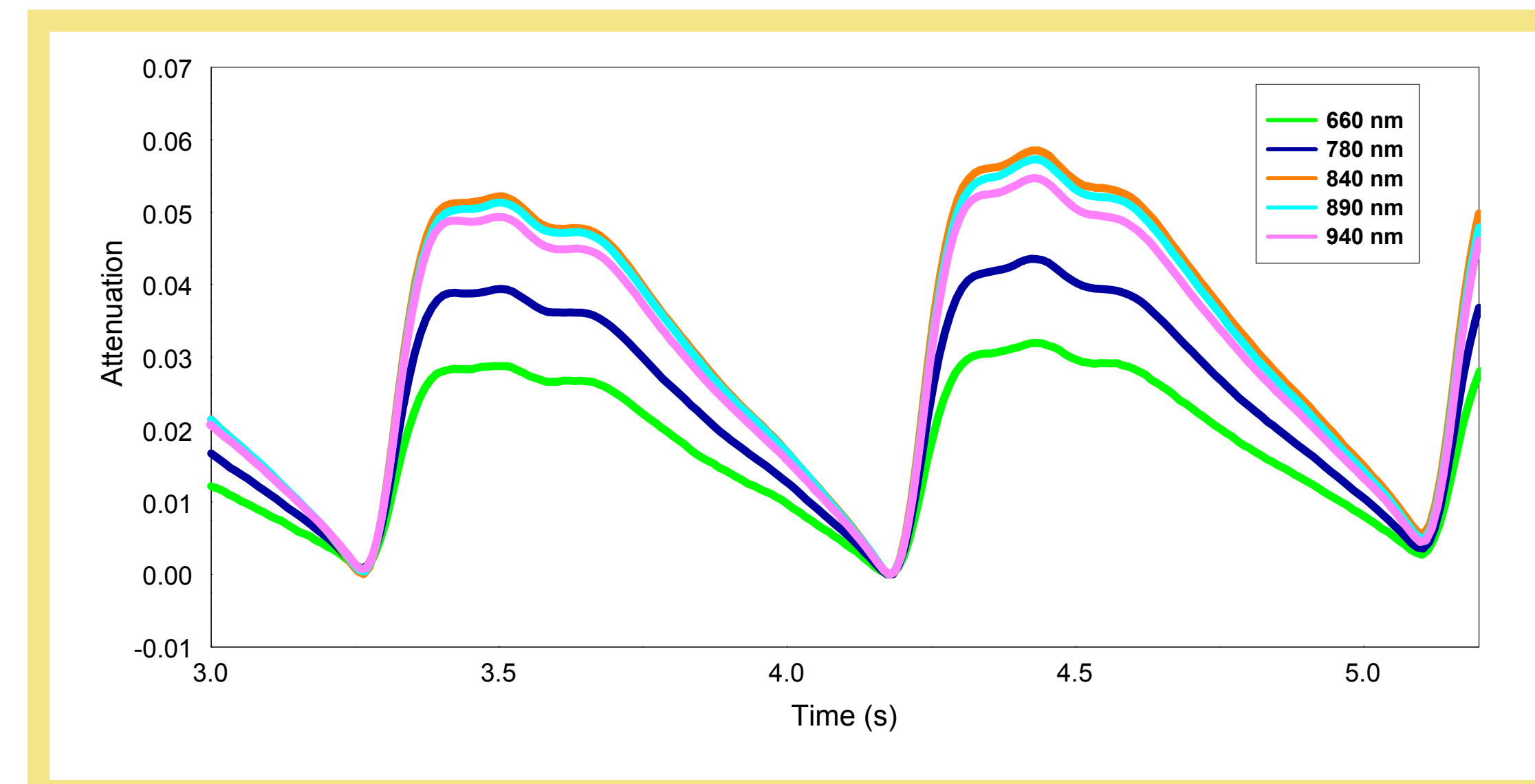


Fig. 4. Attenuation vs. time at five wavelengths.

DATA ANALYSIS

Test data obtained at five wavelengths were analyzed to compute the fractional concentrations of the hemoglobin moieties. Light attenuation for each pulse is calculated at each time point in the cardiac pulse by defining the incident light as the minimum signal for each pulse. The one-dimension diffusion approximation technique is used to determine the optical properties of the sample and account for multiple scattering. Spectral width of each LED is accounted for by defining a modified absorption coefficient (α_{jn}) for each LED 'n' as:

$$\alpha_{jn} = \int_{\Delta\lambda_n} I_n(\lambda) \mu_a^j(\lambda) d\lambda \quad (2)$$

where $I_n(\lambda)$ is the normalized LED intensity. To improve measurement accuracy, attenuation for each wavelength is integrated along each cardiac pulse with equal lower and upper time boundaries of integration for each wavelength. The lower and upper boundaries are defined as 100 ms before and 400 ms after the cardiac pulse peak, respectively. The fractional concentration c of each moiety j is found by inverting:

$$\mu_n = K \sum_j c_j \alpha_{jn} \quad (3)$$

which is a modified form of Eq. (1) where a_{jn} is substituted for $\mu_a^j(\lambda_i)$ and μ_n is the integrated attenuation for each LED. Eq. (3) is solved using either a linear least squares method or the singular value decomposition technique.

CONCLUSIONS

This novel hemoglobin sensor allows continuous measurement of various hemoglobin moieties noninvasively and in realtime while considering the effects of multiple scattering and LED spectral width. LEDs were chosen in the near-infrared region to reduce the effects of methylene blue and COHb. The design incorporates low-cost electronic components that will allow the future sensor to be inexpensive, compact, and portable. This system will be used in an animal to verify its performance.

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