Measuring Light Absorption and Fluorescence of Pulsating Human Blood through Thumb Webbing

W.G. Paseman, Katherine Paseman and Sabrina Paseman
Blossom Diagnostics

Abstract

This paper describes the way the light is absorbed and emitted by the tissues around the thumb webbing. The paper starts by describing the Medical Spectral Window and how it amplifies unwanted illumination artifacts. The paper then describes how this amplification aids in taking fluorescence measurements. Next we report the sampling and integration periods used in our various approaches to date. Finally, we refer to papers describing some more advanced methods of fluorescence and absorption measurement.

Introduction

A “Complete Blood Count” or CBC is one of the key tools used by physicians. Two principle components include: Hematocrit, which measures the fraction of the sample that consists of red blood cells and Hemoglobin, which measure the amount of hemoglobin in the red cells present. Although limited, these two tests are very useful, especially in diagnosing anemia.

Hemoglobin Color Scale

Measuring Hemoglobin by observing how blood reflects and transmits light is a well developed idea.

In the late 90's, the ‘Hemoglobin Color Scale’ (HCS) [5] illustrated the difficulties inherent in a colorimetric approach. HCS consisted of putting blood on paper and comparing it to a color card. Unfortunately, results differed substantially between lab and field testing [6]. HCS’s inventors listed what they viewed as the key issues in moving HCS from the lab to the field [7].

1. Inadequate or excessive blood
2. Reading the results too soon or too late (beyond the limit of two minutes)
3. Poor lighting
4. Holding the scale at the wrong angle

According to HCS’s inventors, after eliminating these mistakes: “The accuracy improved dramatically when the tests were repeated under supervision and these faults were avoided: 95% of readings were within 1 g/dl of the reference measurements, and 97% within 1.5 g/dl. Anaemia screening showed 96% sensitivity and 86% specificity. Clinical judgement of pallor was frequently wrong, whereas the scale gave the correct diagnosis in more than 97% of

cases."

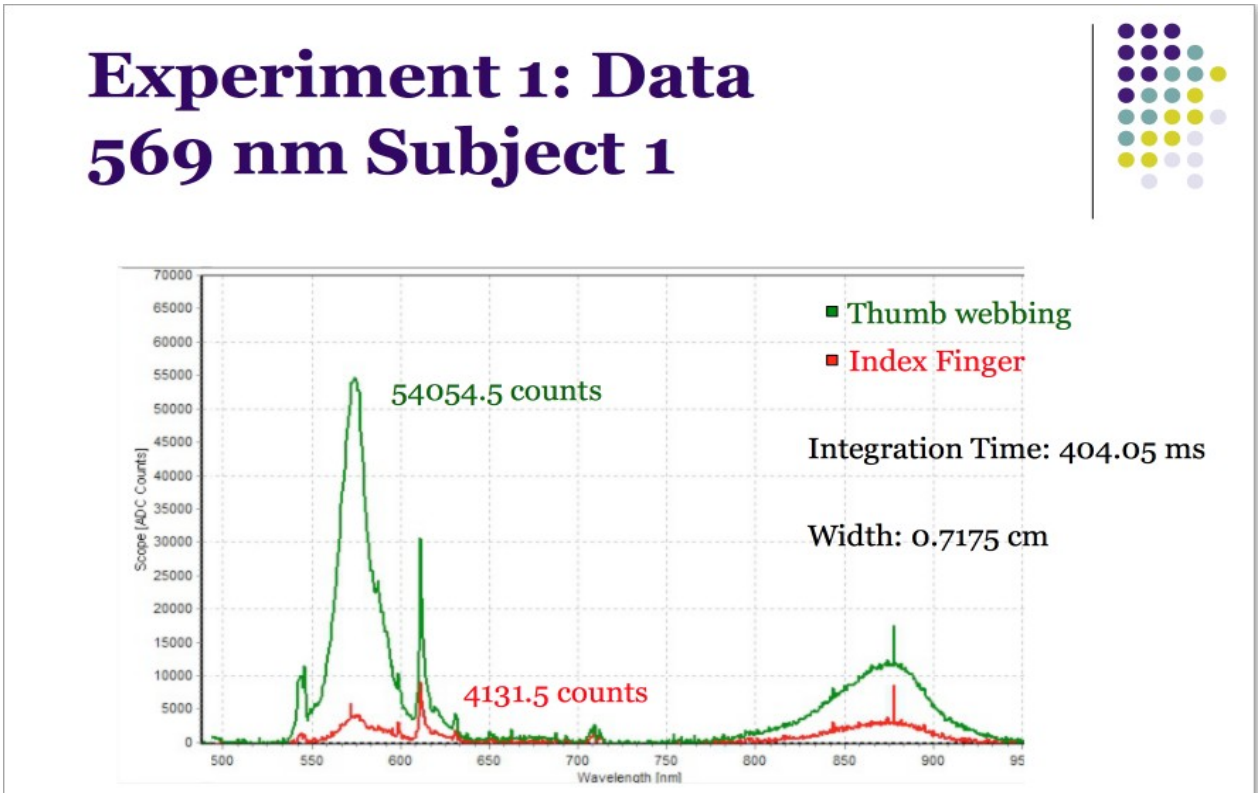
One can forgive Device builders for being heartened by this analysis since it implies that issues 1 and 2 can be addressed by a non-invasive approach and issues 3 and 4 can be addressed by using a mechanical vs manual approach.

Medical Spectal Window

In first approximation, light is absorbed/fluoresced in thumb webbing as it is through a finger. That is, within certain limits, there is a sharp transmission cutoff below 600 nm and above 1300 nm. [Tabulated Molar Extinction Coefficient for Hemoglobin in Water 2001]. This region is called the "Medical Spectral Window" and many non-invasive devices utilize it to optically measure blood properties. E.g. [Masimo US7377794] page 57 lists the 8 frequencies used by their Rainbow 7 Sensor as 610nm, 620nm, 630nm, 660nm, 700nm, 730nm, 805nm, and 905nm.

Artifact Amplification

Those attempting to interrogate blood outside the is range must be very careful. E.g. John Allen [John Allen 2007] reported that Samsung's device [Yoon et. Al. 2005] , [Jeong et. Al. 2002] has the best reported correlation co-efficient for Hemoglobin measurement. However Katherine Paseman [Katherine Paseman March 2013] duplicated Samsung's setup using their reported light emitter (Epitex L2*570/660/805/940/975-35Q96-I) and a low end Avaspec 211C spectrometer instead of a photodiode. As summarized in the slide below, she discovered that most of the reported 569 nm light (one of blood's isosbestic points) gathered by the device's photodiode actually came from an LED artifact at 875 nm. In fact, the 569 LED's strong 569 peak had been completely absorbed by the finger's blood, but the 875 nm artifact was strongly transmitted, since blood is relatively transparent to light at 800-900nm.



Artifact Amplification implies Differential Attenuation

The fact that blood differentially attenuates light can be leveraged in fluorescence measurement. Both Lead poisoning and Iron Deficiency Anemia are characterized by Zinc replacing the Iron in Blood's protoporphyrin ring [Hematofluorometer 1977]. Zinc protoporphyrin fluoresces. It excites at 425 nm and emits at 586, 594 and above. As such, a great deal of 426 nm energy can be transmitted in a Transmissive Geometry and the sensing device will not be

'blinded' since the overwhelming majority of the exciting energy is absorbed but the fluorescent products are not. [Sabrina Paseman 2008]

Targeting Thumb Webbing vs. a Finger aids Amplification below 600 nm

Differential Attenuation is fine and good, but SOME transmission is necessary so that fluorescent effects can be calibrated. The Beer-Lambert law determines Io (output light transmission) as a function of the parameters listed below.

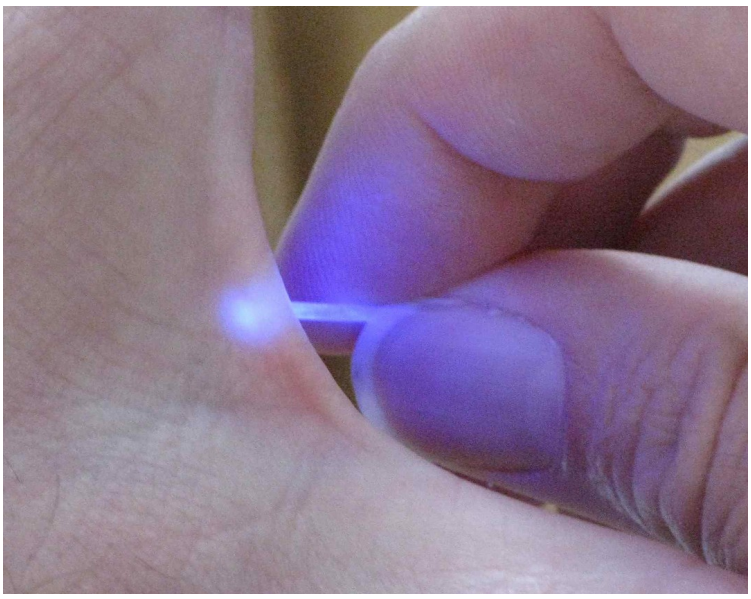
$$I_o = I_i \, 10^{-2.303 \, \text{epsilon(lambda)} \, c \, t \, / (64{,}500 \text{ g Hb/mole})}$$

- Io - output light intensity (To the photodiode or Spectrometer)
- Ii - input light intensity from the light source.
- epsilon(lambda) – extinction coefficient. A function of wavelength from [Tabulated Molar Extinction Coefficient for Hemoglobin in Water 2001]
- c – g/liter (A typical value of c for whole blood is 150 g Hb/liter.)
- t – cm

Notes:

- Thickness is in the exponent, and thumb webbing is roughly 5 times thinner than a finger. This means that theoretically, the signal is 10**5 or so stronger if you transmit through the thumb webbing. (Note however, [Katherine Paseman March 2013]'s slide indicates only a 54054/4131 = 13 x amplification for a 569 nm input wavelength)
- Blood is most opaque at 425 nm. (From the [Tabulated Molar Extinction Coefficient for Hemoglobin in Water 2001]).

How does all this net out in the fluorescence realm? Below shows a light fiber carrying 426 nm shining through Sabrina's Thumb webbing.



Sample Rate/Integration Time

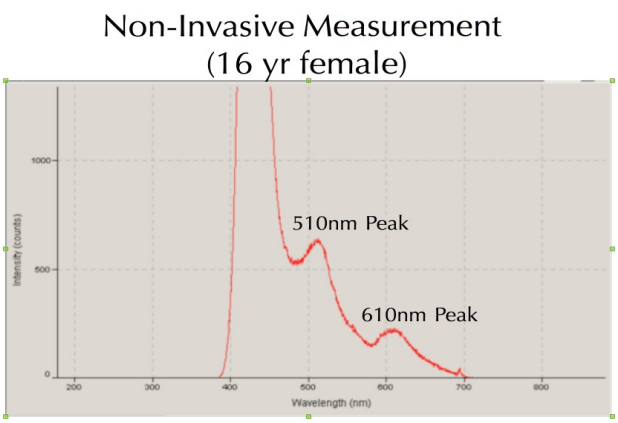
Sample rate depends on several factors.

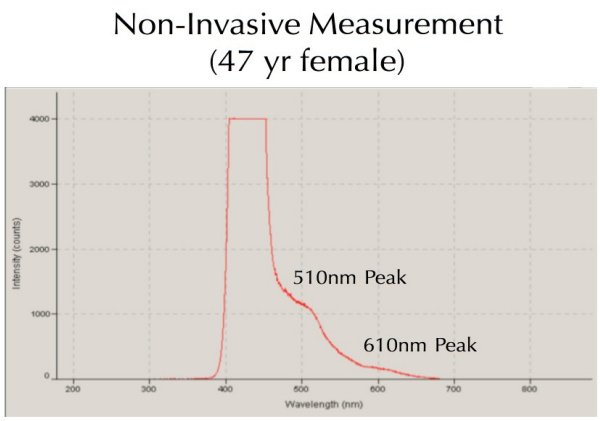
Traditional pulse oximeters sample internally around 500 samples per second [TI 2010] to 1000 samples per second [FreeScale 2012]. Here, no data is stored, and the metrics (Heart Rate, SPO2) are calculated on the device and reported to an attached LCD display.

To examine data from multiple channels post hoc, there are two options: Spool the data internal to the device and download the data at a later time, or internally average the readings and report at a lower samples per second rate. (75 samples per second for each of 5 LEDs in the case of [Katherine Paseman December 2013]).

However these devices use a photodiode, not a spectrometer as the receiver. [Katherine Paseman December 2013] used a spectrometer requiring 404 ms integration time for her data.

[Sabrina Paseman 2008] used a shorter integration time for her data on an Oceanoptics USB 2000+ (below).





Newer Methods

[ZnPP2016] combines several illuminators which may require less integration time for light fluorescence measurements.

[Katherine Paseman 2014] describes elements of an analytical method which relates Hgb/Hct measurements to light absorption measurements (optical density).

Bibliography

- [ZnPP 2016] Georg Hennig1, Christian Homann1, Ilknur Teksan, Uwe Hasbargen, Stephan Hasmueller, Lesca M. Holdt, Nadia Khaled, Ronald Sroka, Thomas Stauch, Herbert Stepp1, Michael Vogeser & Gary M. Brittenham; Non-invasive detection of iron deficiency by fluorescence measurement of erythrocyte zinc protoporphyrin in the lip; NATURE COMMUNICATIONS | 7:10776 | DOI: 10.1038/ncomms10776
- [Katherine Paseman 2014] Paseman, Katherine. c <> 35H: A New Model Relating Hemoglobin, Hematocrit, and Optical Density INTEL STS 2014 Semifinalists Paper
- [Katherine Paseman December 2013] Paseman, Katherine, Hemometer, meet HemoGlobe
- [Katherine Paseman March 2013] Paseman, Katherine. Improving Non-Invasive Blood Analysis by Expanding the Medical Spectral Window. Baltimore Science Fair 2013 (video)
- [Sabrina Paseman 2008] Paseman, Sabrina. The Ferrometer: A Device to Detect Iron Deficient Anemia via Non-Invasive Optical Measurement of Zinc Protoporphyrin. Issue brief no. SO499. Los Angeles: University of Southern California, 2008.
- [FreeScale 2012] Santiago Lopez Pulse Oximeter Fundamentals and Design
- [TI 2010] Vishal Markandey Pulse Oximeter Implementation on the TMS320C5515 DSP Medical Development Kit (MDK)
- [Masimo US7377794] "Multiple Wavelength Sensor Interconnect" – p57 lists Masimo's wavelengths
- [John Allen 2007] Photoplethysmography and its application in clinical physiological measurement Physiol. Meas. 28 (2007) R1–R39 doi:10.1088/0967-3334/28/3/R01
- [Yoon et. Al. 2005] Yoon, Gilwon, Ph.D, et al. "Development of a Compact Home Health Monitor for Telemedicine." TELEMEDICINE AND e-HEALTH 11.6 (2005): 660-67. - Their device has the best reported correlation co-efficient for Hemoglobin measurement according to John Allen (above).
- [Jeong et. Al. 2002] Jeong, Kye Jin, Su-Jin Kim, and Kun Kook Park. "Noninvasive Total Hemoglobin Measurement." Journal of Biomedical Optics 7.1 (2002): 45-50.
- [Tabulated Molar Extinction Coefficient for Hemoglobin in Water 2001] – This OMLC Website has Tabulated Molar Extinction Coefficient for Hemoglobin in Water as well as co-efficients for water and fat and a section on Hemoglobin. data: water, fat, Hgb
- [Hematofluorometer 1977] William E. Bumberg, Josef Elsinger, Angelo A. Lamola, and David M. Zuckerman; The Hematofluorometer; 70-274(1977) CLINICALCHEMISTRY.Vol. 23, No. 2