General equation for the differential pathlength factor of the frontal human head depending on wavelength and age

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Abstract. Continuous-wave near-infrared spectroscopy and near-infrared imaging enable the measurement of relative concentration changes in oxy- and deoxyhemoglobin and thus hemodynamics and oxygenation. The accuracy of determined changes depends mainly on the modeling of the light transport through the probed tissue. Due to the highly scattering nature of tissue, the light path is longer than the source–detector separation (d). This is incorporated in modeling by multiplying d by a differential pathlength factor (DPF) which depends on several factors such as wavelength, age of the subject, and type of tissue. In the present work, we derive a general DPF equation for the frontal human head, incorporating dependency on wavelength and age, based on published data. We validated the equation using different data sets of experimentally determined DPFs from six independent studies.

Keywords: continuous-wave near-infrared spectroscopy; differential pathlength factor.

1 Introduction

By shining near-infrared (~650 to 950 nm) light into tissue and measuring the diffuse reflected light at different wavelengths (λ), continuous-wave (CW) near-infrared spectroscopy (NIRS) and imaging (NIRI) enable the determination of concentration changes in oxy- and deoxyhemoglobin ([O₂Hb], [HHb]), which are related to changes in hemodynamics and oxygenation. NIRS refers to a measurement at a single position (i.e., one light-path), whereas NIRI measures simultaneously in different positions.

Light transportation through tissue is a complex process. In a first approximation, it can be modeled using the modified Lambert–Beer law given as

\[ I(λ) = I_0(λ)e^{-\mu_a(λ)d} DP\text{F}(λ) + G(λ), \]  \( (1) \)

where \( I(λ) \) is the measured wavelength-dependent diffuse reflected light intensity, \( I_0(λ) \) is the incident light intensity, \( \mu_a(λ) \) is the absorption coefficient of the probed tissue, \( d \) is the distance between the positions of incident and measured light, i.e., the source–detector separation, \( DP\text{F}(λ) \) the differential pathlength factor (DPF), and \( G(λ) \) is a wavelength-, medium-, and geometry-dependent constant. The term \( d DP\text{F}(λ) \) corresponds to the mean light propagation distance in the medium, i.e., the parameter \( DP\text{F}(λ) \) is a scaling factor that indicates how many times farther than \( d \) the detected light has traveled.

Based on the diffusion equation for modeling light transport through a homogeneous semi-infinite medium, it can be shown that the DPF depends on \( \mu_a(λ) \), the reduced scattering coefficient \( \mu_s(λ) \), and \( d \).

Consequently, \( DP\text{F}(λ) \) increases with \( \mu_s(λ) \) and decreases with \( \mu_a(λ) \). The dependence of DPF on the source-detector separation \( d \) is crucial to be considered for small \( d \) values, but for \( d > 2.5 \) cm, the DPF is virtually independent of \( d \).

Keywords: continuous-wave near-infrared spectroscopy; differential pathlength factor.
subject, the larger the DPF. Physiological reasons for the age dependence of the DPF can be attributed to different developmental or aging processes in the human brain, such as the change in intracranial volume (increase from birth to adolescence; decrease after ~50 years of age), myelination (exponential increase over the first 3 years of life; myelin: strong scatterer), gray matter (GM) and white matter (WM) properties (after adulthood onwards: reduction in GM volume and deterioration in WM microstructure), cerebrospinal fluid layer thickness (increase with advanced age), or cortical thickness, bone mineral content, and cortical bone density (decrease starting from adulthood on).

Duncan et al. measured the DPF of 283 subjects (137 male, 146 female, age: 1 day to 50 years) for four different wavelengths (690, 744, 807, and 832 nm) by a FD-NIRS system with a $d = 4.3$ cm. The optode was placed on the left frontal region (adults) and on the left or right frontotemporal region (on neonates). By using a least squares fitting method, they derived four equations that relate the DPF with age ($A$):

$$\text{DPF}(\lambda = 690 \text{ nm}, A) = 5.38 + 0.049 A^{0.877},$$  
$$\text{DPF}(\lambda = 744 \text{ nm}, A) = 5.11 + 0.106 A^{0.723},$$  
$$\text{DPF}(\lambda = 807 \text{ nm}, A) = 4.99 + 0.067 A^{0.814},$$  
$$\text{DPF}(\lambda = 832 \text{ nm}, A) = 4.67 + 0.062 A^{0.819}.$$

Since the CW-NIRS/NIRI devices also apply wavelengths other than those employed by Duncan et al., a general equation modeling the DPF as a variable depending simultaneously on age and wavelength would be desirable. Surprisingly, no such equation has been published to date to the best of our knowledge. The aim of the present work was (1) to derive such an equation and (2) to compare its predictions to various published values of measured DPF.

2 Derivation and Validation of the General Equation

2.1 Derivation: Nonlinear Least Squares Surface Fitting

The general equation relating the DPF with age and wavelength is based on Eqs. (3)-(6).

All data processing was performed using MATLAB (version 2008b, The MathWorks, Natick, Massachusetts). To derive the formula, the general mathematical type of surface equation was first determined. Therefore, the DPF ($A$) dependence was modeled as power law, $\text{DPF}(A) = \alpha + \beta A^\gamma$, according to Eqs. (3)-(6). The DPF($\lambda$) equation was modeled as a cubic function, $\text{DPF}(\lambda) = \delta \lambda^3 + \epsilon \lambda^2 + \zeta \lambda + \eta$, since this ensures that the function fits to all four wavelengths [see Fig. 1(c)]. A higher polynomial degree than three would cause overfitting since only four data points are available.

Thus, the surface to be fitted to the data was defined as

$$\text{DPF}(\lambda, A) = \alpha + \beta \lambda^\gamma + \delta \lambda^3 + \epsilon \lambda^2 + \zeta \lambda + \eta. \quad (7)$$

All values obtained by evaluating Eqs. (3)-(6) for $A = 0, 1, \ldots, 50$ were fitted by a robust nonlinear least squares fitting method based on minimizing the (constrained) sum of the absolute residuals [LAR] method and the Levenberg–Marquardt algorithm (LMA). The LAR method is a version of the least sum of squares residuals fitting method based on minimizing the (constrained) sum of the absolute residuals, in comparison to ordinary least squares (OLS) that minimize the sum of squared residuals. LAR has the advantage over OLS of being robust against deviations from the normality assumption of the data. LMA is a cross between the Gauss–Newton algorithm and the steepest descent method; it has the advantage of being robust and iteratively more efficient.

The following parameter values were obtained: $\alpha = 223.3$, $\beta = 0.05624$, $\gamma = 0.8493$, $\delta = -5.723 \times 10^{-7}$, $\epsilon = 0.001245$, and $\zeta = -0.9025$. The goodness-of-fit statistics obtained were: summed squared of residuals: 0.09668, R-square: 0.9983, adjusted R-square: 0.9983, and root mean squared error (RMSE): 0.0221. These values indicate an excellent fit of the surface to the empirical data. An illustration of the determined DPF($\lambda, A$) function can be seen in Fig. 1.

2.2 Validation of the General Equation

In order to validate the derived general DPF($\lambda, A$) Eq. (7), it was compared to (1) the results of Eqs. (3)-(6) and (2) five data sets of DPFs measured in independent studies. Due to the fact that the DPF depends on tissue type, only DPF measurements of the forehead (frontal or frontotemporal) were used for the validation to ensure a homogeneous sample. In addition, only DPF values where $d > 2.5$ cm holds were included since this ensures a value

![Fig. 1](image-url)
Table 1 lists the details of the six studies employed in our validation.

The comparison of the values obtained by the general DPF(\(\lambda, A\)) equation with the values obtained by Eqs. (1)–(6) revealed a good agreement: DPF(\(\lambda, A\)) versus Eq. (1), RMSE: 0.0320; versus Eq. (4), RMSE: 0.0545; versus Eq. (5), RMSE: 0.0311; versus Eq. (6), RMSE: 0.0348.

As expected, the comparison with the different data sets of measured DPFs also revealed a good agreement in general (see Fig. 1). If the predicted value was inside the standard deviation (SD) or quartiles (first to third) of the value measured, we defined this as a correct prediction. The predicted DPF values agree with the measured ones for the data set of Duncan et al.\(^26\) and Cooper et al.\(^27\) For the van der Zee et al.\(^6\) data set, the

![Fig. 2 Visualization of the derived DPF (\(\lambda, A\)) equation for the age values 0 to 50 years, and the wavelength values 690 to 832 nm. The surface is shown from two different perspectives.](https://www.spiedigitallibrary.org/journals/Journal-of-Biomedical-Optics/105004-3/105004-3.png)
predicted DPF for the adults agrees with the measured value. For the neonates, the predicted value was outside the SD range of the measured one. Since experimental data were not reported with SD values for the data set of Zhao et al., the agreement was only determined qualitatively. Two out of six values agreed. The agreement was greatest for the values from the frontotemporal region. Concerning the data set of Bonnéry et al., all four values agreed with the predicted ones.

For the Essenpreis et al. data set of adults, the predicted DPF values agree with the measured ones. For the data set of a neonate also reported by Essenpreis et al., the predicted values differed from the measured ones. However, it must be noted that these data sets originate only from one subject, making the decision of agreement difficult, especially in the region of approximately 800 to 840 nm where the measured and predicted values are close together and might coincide when more than one neonate had been measured and thus SD values were available.

In summary, excluding the data sets of Zhao et al. and the neonate data set of Essenpreis et al., all four values agreed with the predicted ones.

The discrepancy between the predicted and measured DPF values for the neonatal data sets of Van der Zee et al. and Essenpreis et al. are likely due to the fact that the neonates were measured post mortem. In addition, the neonate measured by Essenpreis et al. was kept at 4°C prior to the measurement. Both death and low temperature influence the optical properties of the tissue. Our derived DPF equation is valid only for living humans. It is known that the optical properties of tissue are different for the in vivo and post mortem case although a study in rats found only a small change in the DPF upon death. Besides death, the cooling of the body is likely to influence the PDF measurement since a change in temperature has an effect on the optical properties of tissue.

As previous studies have shown, the DPF does not depend on skin color. The dependence on gender is controversial. But as already shown by Zhao et al., the DPF depends clearly on the head region investigated. Therefore, to go one step further in the modeling of DPF values, it would be necessary to incorporate the dependency on the head region, i.e., composition of different tissue types, as a third variable, besides wavelength and age. It is known that variations in tissue type and the presence of the cerebral spinal fluid (CSF) have a significant effect on the light-propagation characteristics and thus the DPF. For example, Okada et al. concluded that for a source–detector distance of 5 cm, the mean light propagation distance in the medium, i.e., d DPF, is composed of 65% contribution from the scalp and skull, 35% from the CSF, and 5% from the data sets of Zhao et al. and the neonate data set of Essenpreis et al. where the validation was difficult since no SD values were given and only one subject was measured, respectively.

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GM. However, later works demonstrated that the light-piping
effect of the CSF is reduced due to the presence of scattering
structures, i.e., arachnoid trabeculae, within the CSF reducing
the influence of the CSF. To account for the mean path-
length in each tissue layer, the concept of the “partial differential
pathlength” (also termed “partial optical path length”), i.e.,
the mean pathlength of the light in a specific layer, the “partial
differential pathlength factor,” and the “partial pathlength factor,”
were introduced.

Since the basis of the equation derived in this work comprises
DPF values measured on the frontal and frontotemporal
region, this equation is only valid for this head region. Another
source of variation of the DPF is the intersubject variability
indicating that the DPF varies by individual subject due to anatomical
differences. These factors might explain not only the
discrepancy of the DPF prediction and the actual values as
Zee et al. versus Cooper et al.

Concerning the validity of the newly derived equation, we
recommend its usage for the age range of 0 to 70 years and
the wavelength range of 690 to 832 nm since it is derived from
and validated using values in these ranges. For <690 nm
the equation is probably not correct due to a decrease of the DPF
in this range. It should be safe for application to values ranging
from 832 nm to 950 nm because the wavelength dependence in
this region should continue according to the model.

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