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# Towards quantitative multispectral excitation fluorescence spectroscopy for intraoperative assistance in glioma resection in neurosurgery

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## Introduction

**Glioma** is a serious tumor in terms of malignancy and progression. It is the most common and aggressive primary brain tumor. The main therapy is surgery to completely remove the tumor. The healthy tissue and the tumor margin may look the same during surgery which is responsible for problems for delineating the boundaries of the lesion. The 5-ALA-induced protoporphyrin IX (PpIX) fluorescence microscopy technique is now the most effective clinical standard but still suffers from a lack of sensitivity [1].

Previously, we have demonstrated [2], [3] that the spectral complexity of the intraoperative fluorescence emission of PpIX is relevant to identify the tumor tissue and in particular the infiltrative component. We also performed a first clinical trial on 10 patients using a prototype intraoperative fluorescence spectroscopy validated by the ANSM. This study demonstrated the relevance of the two PpIX states as proposed new biomarkers to identify the tumor margin and its border with healthy tissue [3]. However, this work faces several obstacles related to the understanding and quantification of biomarkers.

In this work, we propose a novel approach to estimate the interest biomarkers contributions. In addition, we investigate the effect of internal reflectance on the estimation/prediction accuracy of optical properties. Finally we build a new experimental setup to get clinical data which can be processed using the combination of previous results.

## Methods

### Multiple Wavelength Excitation Fluorescence Spectroscopy

$$Ref(\lambda_e) = \alpha_{620} \cdot \eta_{620}(\lambda_e) \cdot S_{620}(\lambda) + \alpha_{634} \cdot \eta_{634}(\lambda_e) \cdot S_{634}(\lambda)$$

#### I- State of the Art Models (BF<sub>1</sub>, GB<sub>1</sub>)

$$m = Ref(405) + b(\lambda)$$

#### II- Baseline Free (BF<sub>2</sub>)

$$m = Ref(405)$$

$$m' = Ref(385)$$

Analytic Baseline

#### III- Gaussian Baseline (GB<sub>2</sub>)

$$m = Ref(405) + Ab(\lambda)$$

$$m' = Ref(385) + A'b(\lambda)$$

Analytic models suffer from lack of specificity when endogenous fluorophores emit near PpIX's fluorescence emission range

#### Our Method

#### IV- Estimated Baseline (EB)

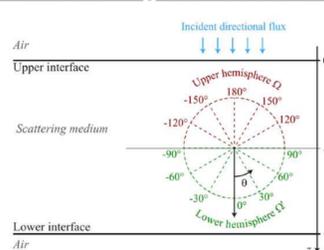
$$m = Ref(405) + b$$

$$m' = Ref(385) + \gamma b$$

Estimated Baseline

Non Linear Least-Square Regression with a closed form solution of EB model [4]

### Radiative Transfer Solving to improve light scattering corrections



$$\mu \frac{dL}{d\tau}(\tau, \mu) = -L(\tau, \mu) + \frac{1}{2} \int_{-1}^1 p_0(\mu, \mu') L(\tau, \mu') d\mu'$$

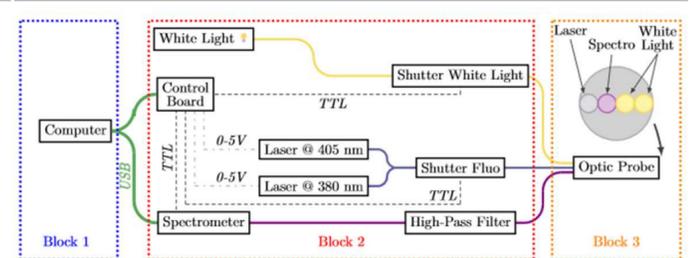
$L$  Radiance ( $Wm^{-2}sr^{-1}$ )  
 $\mu_a$  Absorption coefficient ( $cm^{-1}$ )  
 $\mu_s$  Reduced scattering coefficient ( $cm^{-1}$ )  
 $\mu$  cosine of the interest angle  $\theta$   
 $\tau$  Optical Thickness ( $\tau = (\mu_a + \mu_s)z$  where  $z$  is the depth of interest in cm)  
 $p_0$  Phase Function partially integrated

Solved using Discrete Ordinates Method [5]

$$r_{id} = \frac{\int_0^{\pi/2} L_0(\pi - \theta) R_{21}(\theta) \sin(2\theta) d\theta}{\int_0^{\pi/2} L_0(\pi - \theta) \sin(2\theta) d\theta}$$

$L_0$  Radiance at  $z=0$  ( $Wm^{-2}sr^{-1}$ )  
 $R_{21}$  Fresnel Reflectance at the medium interface  
 $\theta$  interest angle as defined above

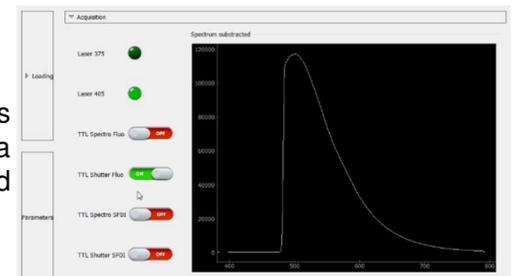
### Experimental Setup



Measurement of fluorescence at two wavelengths to determine sample's PpIX contributions

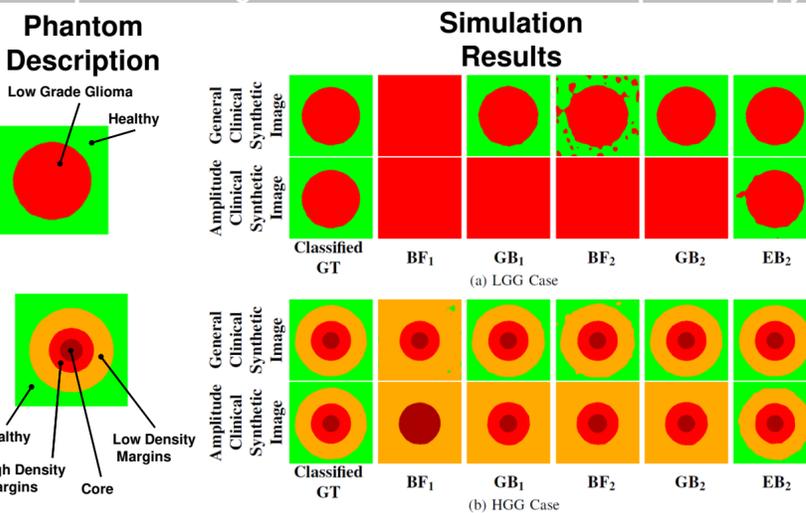
Measurement of Diffused Reflectance under white light illumination to extract sample's optical properties

Acquisition is done by a custom build software



## Results and Discussion

### Multiple Wavelength Excitation Fluorescence Spectroscopy

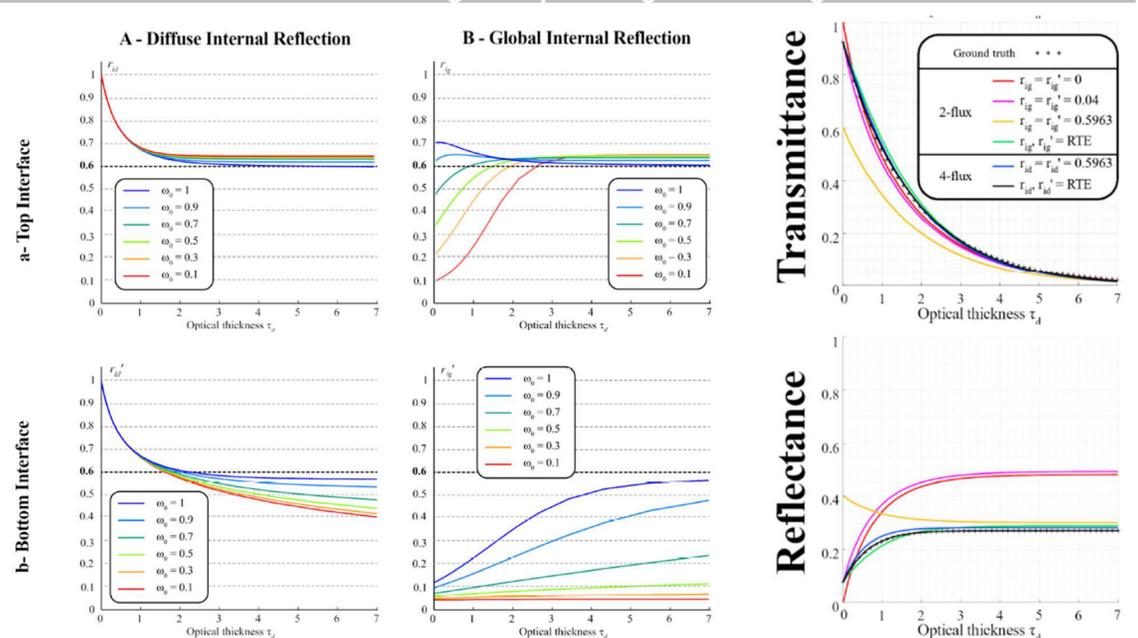


This new model keeps a specificity almost equal to that of the ground truth while the one of existing models drops to 0.

In addition, it is as accurate as existing models elsewhere.

This new model reveals the potential of multiple excitation wavelengths to increase the classification sensitivity of fluorescence measurements.

### Radiative Transfer Solving to improve light scattering corrections



Internal reflection equal to its Lambertian value can lead to significant errors (up to 100%) for 2-flux models when dealing with translucent materials.

Moreover, parameter extraction with the 2- and 4-flux models can be significantly improved using the internal coefficient calculated using the radiative transfer equation.

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## Perspectives

- Application of estimation model on clinical data acquired with the experimental setup
- Improve the measurement correction due to biological tissues with RTE Solving in Fluorescent cases

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 [5] Ishimaru A., Wave propagation and scattering in random media, vol 2, (1978)

