

Bi-Level Optimization for Multi-Wavelength Fluorescence Spectroscopy: Automatic Detection of Tumor Margins in Neurosurgery

The development of intraoperative optical imaging is crucial for improving surgical precision in brain tumor resection [1]. **Fluorescence spectroscopy** enables real-time tissue characterization, but requires intelligent post-processing to distinguish between healthy and tumor tissue [2].

Medical and Scientific Context

High-grade gliomas demand complete surgical resection, yet precise identification of tumor margins remains challenging since healthy and diseased tissue may appear visually identical. Current clinical standards (5-ALA-induced PpIX fluorescence) suffer from limited sensitivity [4]. Recent studies demonstrate that **spectral complexity of fluorescence** is highly relevant for tumor identification [6], and **multi-wavelength excitation** [5, 3] further improves tumor detection capability by leveraging complementary spectral information across different wavelengths.

The core challenge: how to automatically optimize **excitation wavelengths** to maximize discrimination between healthy and tumor tissue without manual parameter tuning?

Proposed Approach and expected deliverables

Keywords: Bi-level optimization · Multi-wavelength fluorescence · Tumor margin detection · Inverse problems · Neuro-oncology

Mathematical Framework and Problem Formulation

Inverse Problems and Regularization

At each excitation wavelength λ_j , fluorescence spectral measurements $\mathbf{y}_j$ satisfy a **diffusion approximation radiative transfer model** :

$$\mathbf{y}_j = \mathbf{A}(\lambda_j)\mathbf{x} + \boldsymbol{\epsilon}_j$$

where $\mathbf{A}(\lambda_j) \in \mathbb{R}^{m \times n}$ is a wavelength-dependent optical transfer matrix, $\mathbf{x} \in \mathbb{R}^n$ represents tissue optical properties (fluorophore concentrations), and $\boldsymbol{\epsilon}_j$ is noise.

Spectral reconstruction constitutes an **ill-posed inverse problem** that requires regularization to stabilize the solution :

$$\min_{\mathbf{x}} \sum_{j=1}^p \frac{1}{2} \|\mathbf{A}(\lambda_j)\mathbf{x} - \mathbf{y}_j\|_2^2 + \lambda_{\text{reg}} \mathcal{R}(\mathbf{x})$$

where $\mathcal{R}$ can be an **L_2 norm (Tikhonov)**, an **L_1 norm (sparsity)**, or a **total variation (TV)** depending on structural assumptions.

Bi-Level Optimization: Automatic Wavelength Selection

Rather than fix wavelengths empirically, we formulate a **nested optimization problem** :

Lower Level: For fixed wavelengths $\boldsymbol{\lambda}$ and weights $\boldsymbol{\gamma}$, solve :

$$\mathbf{x}^*(\boldsymbol{\lambda}, \boldsymbol{\gamma}) = \arg \min_{\mathbf{x}} \sum_j \gamma_j \|\mathbf{A}(\lambda_j)\mathbf{x} - \mathbf{y}_j\|_2^2 + \lambda_{\text{reg}}(\boldsymbol{\gamma}) \|\mathbf{D}\mathbf{x}\|_2^2$$

Upper Level: Optimize parameters to maximize clinical discriminant power :

$$\max_{\boldsymbol{\lambda}, \boldsymbol{\gamma}} \mathcal{J}(\mathbf{x}^*) = \max_{\boldsymbol{\lambda}, \boldsymbol{\gamma}} \text{SNR}_{\text{diagnostic}} = \frac{\|f_{\text{tumor}}(\mathbf{x}^*) - f_{\text{healthy}}(\mathbf{x}^*)\|_2}{\sigma_{\text{noise}}}$$

where $f_{\text{tumor}}(\mathbf{x}^*)$ and $f_{\text{healthy}}(\mathbf{x}^*)$ denote respectively **the characteristic spectral index extracted from the tumor region and the healthy region**, computed from the reconstructed optical properties $\mathbf{x}^*$.

Project Objectives

1. Formulate spectral reconstruction as a rigorous bi-level optimization problem with convergence analysis.
2. Develop algorithms combining implicit differentiation (upper level) and proximal methods (lower level) in Python/PyTorch.
3. Validate numerically using synthetic fluorescence data, comparing against classical methods.
4. Perform experimental validation on optical phantoms simulating brain tissue heterogeneity.

Expected Deliverables

- Open-source code on Gitlab with documentation and tutorials
- Dataset of synthetic and experimental validation results
- Master's thesis presentation and defense

Research Environment & Supervisors

Supervisors: Jérémy Cohen (CR CNRS, Researcher, CREATIS - Bi-level optimization expertise) and Arthur Gautheron (UCBL, Associate Professor, CREATIS - Fluorescence spectroscopy expertise).

Environment: Internship at CREATIS - INSA LYON, Léonard de Vinci Building, 21 Avenue Jean Capelle, 69621 Villeurbanne Cedex

Resources: Optical phantoms and imaging equipment, GPU computing, multidisciplinary team (mathematicians, physicists, engineers). Access to Python scientific ecosystem and collaboration with CREATIS experimental platforms.

Candidate Profile

Required: Master's degree (M2) in Applied Mathematics, Signal Processing, or Computer Science. Proficiency in Python (NumPy, SciPy), convex optimization, differential calculus.

Preferred: PyTorch/TensorFlow experience, proximal algorithms, signal processing background, Git/GitHub, biomedical imaging interest.

Application Details

Duration: 6 months - start between February and April 2027

Compensation: CREATIS research allocation (~500–700 €/month)

Status: Full-time Master's internship

To apply, send to both supervisors:

- CV (2 pages max) + motivation letter (1 page)
- Transcripts
- Optional: description of a previous project (provide a link to the code if possible)

Contacts:

- Jérémy Cohen: jeremy.cohen@creatis.insa-lyon.fr
- Arthur Gautheron: arthur.gautheron@creatis.insa-lyon.fr

Deadline: November 30th, 2026 (or until position filled)

References

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