

Post Doctoral position in LYON, France (12 months)

Supervising team: Christian JONIN, Cédric RAY, Pierre-François BREVET (Institut Lumière Matière), Bruno MONTCEL, Carole FRINDEL, David ROUSSEAU (CREATIS).
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Nonlinear fluorescence as a biomarker of glioma in brain biopsy Instrumentation, acquisition and machine learning

Domain and scientific context: Gliomas are the most frequent tumors of the central nervous system. They are infiltrative tumors with a solid tumoral compound and an infiltrative compound that is very difficult to identify. Their treatment is mainly based on resection as complete as possible. During surgery, the decision to continue or stop resection is a trade-off between the resection of a maximum of tumor cells and the preservation of functional areas. The gold standard is still an anatomopathological measurements for which a biopsy is removed from the brain to identify the tissue nature (tumor / healthy). This procedure takes some time but it is relevant for the surgical procedure to obtain faster information on the biopsy. A complementary approach by intraoperative 5-ALA PpIX fluorescence imaging improves the resection but still lack sensitivity. We demonstrated in previous studies and preliminary results that the PpIX fluorescence spectrum is more complex than expected in literature and that this spectral complexity contains relevant and complementary information to identify tumor margin during resection. This spectral complexity has to be studied under different hypothesis which lead to the proof of the existence of two close emission spectra (one peaking at 620 nm and the other at 634 nm) of the biopsy.

Key-words: Biomedical optics, machine learning, Histology, Cancer detection, Glioma.

Scientific objective: The project is focused on the investigation of the PpIX response on biopsy of gliomas by linear and nonlinear spectroscopy measurements. This approach will tackle the issue of obtaining a relevant biomarker on biopsy strongly correlated to histology, the current “gold standard” for pathological analysis. Hence, the goal will be to correlate the measured optical parameters with the anatomopathological results. The result expected is to get a new method to achieve an optical tumor diagnostic on biopsy during gliomas neurosurgical resection allowing to the surgeon an immediate diagnostic of the biopsy. The work will include some optical development together with the acquisition on biopsies and the data analysis through statistical machine learning approaches. The machine learning will be based on multiple emission spectrum under linear and nonlinear excitation. Both supervised approaches based on the anatomopathological and fully unsupervised methods will be tested.

Scientific comitee: Christian JONIN, Bruno MONTCEL, Carole FRINDEL

Main supervisor: Christian JONIN, project leader

Christian JONIN, 47 years old, is full CNRS researcher of Physics at the University Claude Bernard Lyon 1 since 2003 where is leading the group of Nonlinear Optics and Interfaces (currently 7 permanent staff). After a Ph.D. in Physics from the “Université Claude Bernard Lyon 1” obtained in 1997, he moved to the

California Institute of Technology before joining the University Jean Monnet in Saint-Etienne in 1999. He is author or co-author of more than 60 papers, book chapters, and 1 patent.

- Optical Second Harmonic Generation of Single Metallic Nanoparticles Embedded in a Homogeneous Medium, J. Butet, J. Duboisset, G. Bachelier, I. Russier-Antoine, E. Benichou, C. Jonin, P.F. Brevet, *Nano Lett.*, **10** (2010) 1717
- Nonlinear Mie Theory for Second Harmonic Generation in Metallic Nanoshells, J. Butet, I. Russier-Antoine, Ch. Jonin, N. Lascoux, E. Benichou, P.F. Brevet, *J. Opt. Soc. Am. B*, **29** (2012) 2213 (Selected in the Virtual Journal of Biomedical Optics, Vol. 7, Issue 10, 2012)
- Second Harmonic Generation Study of Myoglobin and Hemoglobin and their Protoporphyrin IX Chromophore at the Water/1,2-Dichloroethane Interface, J. Perrenoud-Rinuy, P.F. Brevet and H.H. Girault, *Phys. Chem. Chem. Phys.*, **4**, 4774 (2002)

Local collaboration network of the post-doc in Lyon: The post doc will be developed among the ONLI team (Non Linear Optics at Interfaces) of Institut Lumière Matière (ILM) lead by Pierre-François BREVET expert in Non-linear optics. The biomedical part will be headed by Bruno MONTCEL expert in biomedical optics applied to neurosurgery at CREATIS. The data analysis and machine learning part will be supervised by Carole FRINDEL and David ROUSSEAU at CREATIS.

Funding and salary: LABEX PRIMES with 2700 euros/month gross salary (~ 2050 € / month net salary).

Candidate background: The candidate will have a PhD in optics with an emphasis on information processing and with academic achievement in terms of publication in this domain. Skills in nonlinear optical processes and/or machine learning will be greatly appreciated. Also, experience with anatomopathological diagnosis database creation will be an advantage.

Skills developed during the post-doc: The candidate will develop advanced skills in nonlinear optics, signal processing, machine learning. The position also constitutes an opportunity to work in a highly interdisciplinary team oriented toward real world biomedical applications of high potential.

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Reference:

- Two-peaked 5-ALA-induced PpIX fluorescence emission spectrum distinguishes glioblastomas from low grade gliomas and infiltrative component of glioblastomas, B. Montcel, L. Mahieu-Williams, X. Armoiry, D. Meyronet, and J. Guyotat, *Biomedical Opt. Exp.* **4**, 548 (2013).