

Bio-Aerogel-Assisted Fluorescence Amplification for Biological Applications

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Detection of fluorescence signals from biological markers in tissues or cells is challenging due to the low quantity of molecules of interest, specific gene expression at the cellular level, or the limited number of cells expressing these markers within an organ or tissue. Enhancing signals from these weak emitters is essential to avoid background noise from post-electronic amplification. While costly and molecule-specific biochemical processes have been developed, an alternative, versatile physical mechanism involves the simultaneous action of stimulated emission and multiple scattering induced by nanoparticles suspended in the sample [1]. The role of stimulated amplification not only boosts fluorescence signals but also reduces their spectral width, thereby increasing the spectral density of simultaneously active probes.

However, suspending nanoparticles in a biologically compatible medium requires significant effort and preparation time for each measurement. Bio-aerogels present a unique opportunity due to their biocompatibility, intrinsic disorder, variable pore sizes (suitable for different objects, *e.g.*, cells), and ability to support nanoparticles. These aerogels prevent nanoparticle aggregation and partially shield against potential toxicity. The ease of fabrication and durability of aerogels provide a biosourced scaffold [2] that supports the 3D structure of nanoparticles and prevents detrimental aggregation in a biological buffer solution.

In parallel with experimental exploration, which involves material and optical expertise for sample preparation, a mathematical modeling of propagation and amplification properties in gain media (fluorophores) and disordered media (scatterers) is underway. Quantitative evaluation of fluorescence signal amplification under biocompatible conditions requires wave propagation modeling capable of reproducing the physics at multiple spatial and temporal scales and accounting for non-trivial geometric properties (shape and distribution of scatterers within the medium). Preliminary evaluation of a recently introduced family of high-order finite element solvers—suitable for modeling light-matter interactions at the nanometric scale [3,4] – confirms that high-fidelity simulations of stimulated emission amplification in the presence of multiple scattering are valuable for constructing a reliable system representation.

The advantages of our approach can be summarized as follows:

Substantial amplification of fluorescence through stimulated emission induced by multiple scattering.

Cost-effective, stable, and biocompatible support.

Increased flexibility in the choice and concentration of scatterers.

Absence of scatterer aggregation.

Mitigation or elimination of biocompatibility issues with scatterers.

Potential transfer to various other problems requiring the detection of weak signals (biocompatibility being a more stringent constraint than other applications).

References

- [1] S Bonnefond, A Reynaud, J Cazareth, S Abélanet, M Vassalli, F Brau and G L Lippi, *Nanomaterials* **13**, 2875 (2023)
- [2] T Budtova, *Cellulose* **26**, 81 (2019)
- [3] S Lanteri, C Scheid and J Viquerat, *SIAM J. Sci. Comp.* **39**, A831 (2017)
- [4] DIOGENeS: A DG-based software suite for nan-optics, <https://diogenes.inria.fr/>