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Smart Control of Supercontinuum Generation by Machine Learning Towards Multiphoton Microscopy Applications

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Multi-photon excitation (MPE) microscopy has played a significant role in biological imaging techniques since it allows to observe living tissues with further depth and excellent sectioning effect. Modalities of MPE depend on the properties of both the selected fluorophore and the laser excitation (e.g., wavelength, pulse duration, peak power). However, versatile and tunable laser excitation for MPE still constitutes a technical challenge, limited by e.g. the narrow bandwidth of laser gain medium or by the achievable tunability of parametric conversion [1]. As an alternative, supercontinuum (SC) generation has been implemented for multiphoton imaging, as it can provide broadband excitation covering numerous fluorophore multi-photon absorption peaks and can enable multiplexed spectroscopy without wavelength scanning or filtering the excitation light.

Here, we report on the use machine learning (ML) to optimize the spectro-temporal properties of SC generation to selectively enhance MPE signals compatible with a variety of fluorophores and excitation modalities for MPE microscopy. In particular, we numerically consider multiple pulse pattern excitation whose customization and shaping has been previously reported experimentally via the use of a cascade system of Mach-Zehnder interferometers (MZI) on chip [2,3]. This integrated system allows the generation of a maximum of 256 pulses, individually separated by 1 ps. The pulse pattern at the chip output is obtained by adjusting the transmission ratios of the 8 MZIs before amplification and injection into a highly nonlinear fiber. The SC output spectrum is filtered at selected wavelengths. Various ML techniques (e.g., a genetic algorithm (GA)) are used to iteratively maximize multiphoton absorption signals [4] as shown in Eq. (1):

$$I_{2PA} = \int |I_{1133}(t)|^2 dt \quad \text{and} \quad I_{3PA} = \int |I_{1700}(t)|^3 dt \quad (1)$$

We selected two particular wavelengths (1133 and 1700 nm) that can be respectively used for two-photon absorption (2PA) and three-photon absorption (3PA) towards the excitation of a fluorophore with an MPE at a central wavelength of 566 nm. Taking advantage of ML optimization, we can efficiently probe the input parameter space and rapidly enhance the desired MPE signal when compared to random simulations, Fig. 1(a). Besides MPA signal optimization, the use of reconfigurable input pulse patterns allows for versatile adjustment of the temporal output profile at selected wavelengths. This can be seen for instance in Fig. 1(b) for simple 3PA signals with either double or quadruple pulse bunching operation, or for conjoint 2PA and 3PA excitation with more complex interleaved optical waveforms, Fig. 1(c). Additional SC simulations also show the ability to successfully enhance MPE signals for different combinations of fluorophores and/or modalities. Altogether, we expect this approach to mitigate time-consuming adjustments, ensure efficiency in versatile experimental optimization for MPE microscopy, and pave the way towards further MPE microscopy improvements in terms of spatial sectioning, optical toxicity and wavelength selectivity.

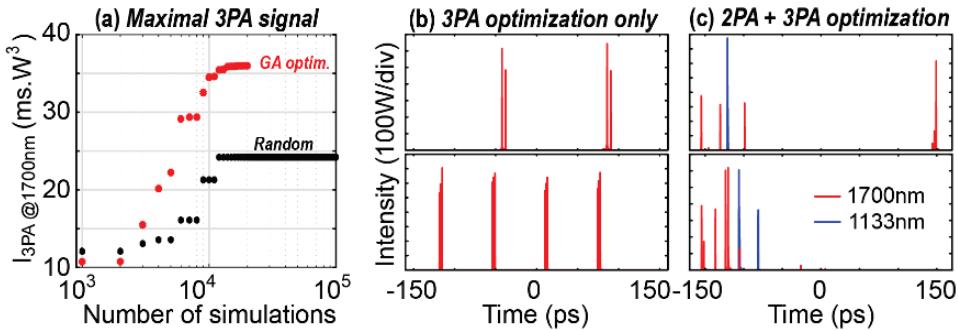


Fig. 1 (a) Evolution of maximal 3PA signal at 1700 nm obtained from Monte-Carlo (random) simulations or via GA optimization. Examples of temporal waveforms obtained after spectral filtering for (b) 3PA optimization or (c) conjoint 2PA and 3PA optimization.

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