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Machine learning optimization of supercontinuum properties towards multiphoton microscopy

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Abstract: We numerically study how the suitable adjustment of femtosecond pulse patterns in combination with machine learning can be leveraged to maximize the output spectral intensities and temporal waveforms at wavelengths relevant for multi-photon imaging.

1. Introduction

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. MPE microscopy relies on multi-photon absorption (MPA), enabling the use of different imaging modalities that strongly depend on the properties of both the selected fluorophore and the laser excitation (e.g., wavelength, pulse duration, peak power) [1]. However, versatile and tunable laser excitation for MPA is still a challenge, limited by e.g. the narrow bandwidth of laser gain medium or by the achievable tunability of parametric conversion. As an alternative, supercontinuum (SC) generation has been implemented for multi-photon imaging, as it can provide broadband excitation covering numerous fluorophore MPA peaks and enables multiplexed spectroscopy without wavelength scanning or filtering the excitation light [2].

Here, we report on the use machine learning 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. Specifically, we numerically explore how the use of reconfigurable (femtosecond) pulse patterns can be readily leveraged to suitably control the propagation dynamics in a highly-nonlinear fiber (HNLF), so that to maximize typical MPA excitations at selected wavelengths, and in a versatile manner for imaging applications.

2. Method and result

In our simulations, we consider multiple excitation pulse patterns whose customization and shaping has been previously reported experimentally via the use of a cascade system of Mach-Zehnder (IMZ) interferometers on chip [3,4]: This integrated system allows the generation of a maximum of 256 pulses, individually separated by 1 ps as shown in Fig. 1. In particular, we study the case of an initial pulse of 100 fs such that the pulse pattern at the chip output is obtained by adjusting the transmission ratios of the 8 IMZs before amplification and injection into a HNLF fiber.

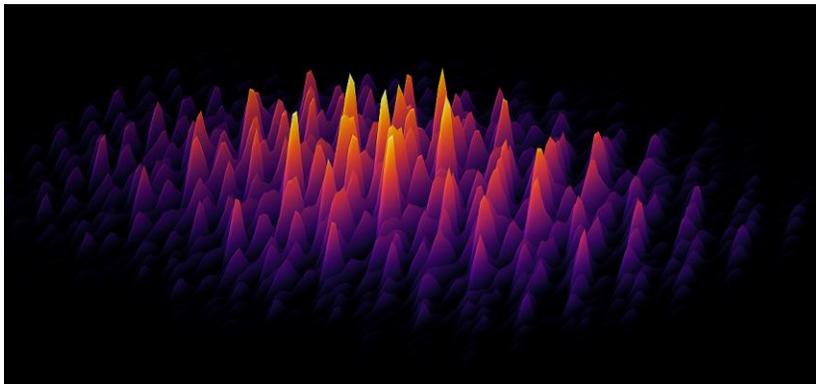


Fig. 1. Measured FROG (Frequency-Resolved Optical Gating) trace of a typical multiple pulse pattern generated by the on-chip IMZ cascade system.

HNLF propagation is simulated using split-step Fourier method to solve the general nonlinear Schrödinger equation [5]. After HNLF propagation and SC spectral broadening, the output spectrum is filtered at selected wavelengths and machine learning techniques, in particular a genetic algorithm (GA), is used to iteratively maximize MPA signals as shown in Eq. (1):

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

In this example, 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 machine learning optimization, we can efficiently probe the input parameter space and rapidly enhance the desired MPE signal when compared to random simulations, as seen in Fig. 1(a).

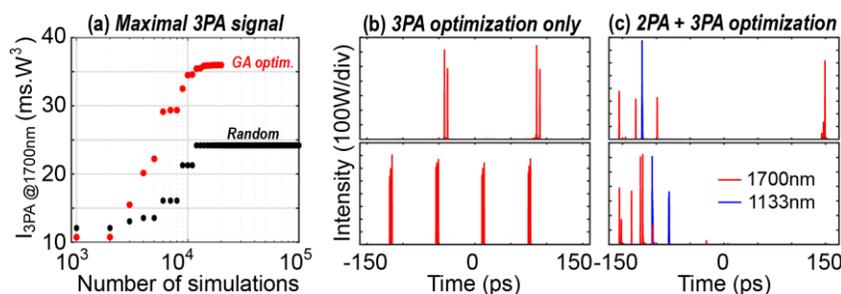


Fig2. (a) Evolution of maximal 3PA signal at 1700 nm obtained from Monte-Carlo (random) simulations or via GA optimization. Examples of temporal waveforms obtained after spectral filtering for (b) 3PA optimization or (c) conjoint 2PA and 3PA optimization.

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 as seen in 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 and ensure efficiency in versatile experimental optimization for MPE microscopy. In particular, we anticipate that this flexibility in terms of pulse shaping will allow for tailoring the intensities and delays of 2PA and 3PA signals and pave the way towards further MPE microscopy improvements in terms of spatial sectioning, optical toxicity and wavelength selectivity.

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