Mid-infrared pulse laser for biological applications

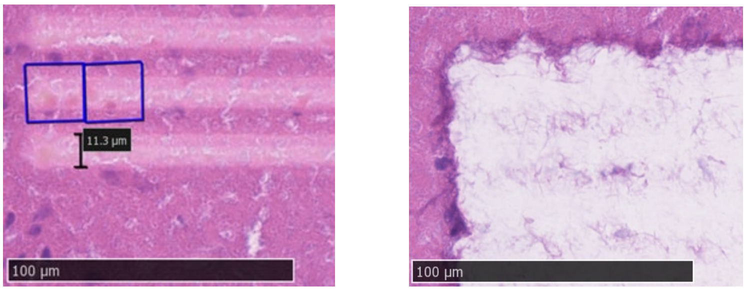
A system designed for generating ultrafast mid-infrared laser pulses, the wavelength at which water molecules absorb light resonantly.

Proposed use

Water is the most abundant molecule in biological tissue and absorbs light at 2.94 µm with very high efficiency (resonant absorption). The laser technology is tuned to this wavelength for highly efficient and localised absorption in any biological tissue at the laser focus. This absorption rapidly heats the sample in a very small region, causing rapid vaporisation and ultra precise tissue ablation, or removal.

As tissue absorbs the energy of the 10s – 100s picosecond pulses at the mid-infrared wavelength faster than the thermal and acoustic diffusion time of tissue, the technology, as shown below, enables highly precise ablation of tissue in the focus region *whilst* simultaneously minimising damage to the surrounding tissue. This collateral-free damage ablation is a key advantage of our technology, and when compared to commonly used existing laser technology the differences are stark (see images below).

Applying more precise laser ablation of tissue to ionisation mass spectrometry imaging, preliminary experiments have demonstrated higher resolution imaging of tissue at the single-cell level. This capability would potentially improve diagnostic capabilities through access to higher resolution imaging.



More precise ablation of tissue (left) as compared to standard laser used for mass spectrometry imaging (right) with less damage to surrounding tissue.

Problem addressed

Based on current methods, the generation of mid-infrared picosecond light has generally been complex as it requires the integration of two laser sources that needs to be synchronised and carefully overlapped in space. This results in unreliable and complex systems that require frequent maintenance from a trained laser technician at a high cost in time and money.

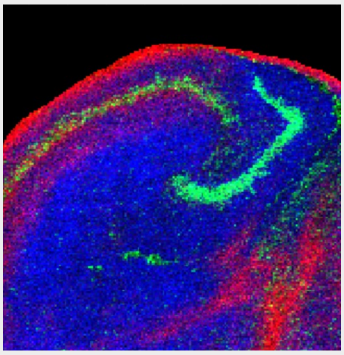
The technology developed enables the generation of light at the mid-infrared wavelength with pulse durations in the 10s-100s of picosecond range, with near diffraction limited beam quality. The high beam quality of the laser allows us to perform high resolution single cell level mass spectrometric imaging, targeting the emerging field of single-cell metabolomics. The simple architecture of the system produces reliable high-quality beams in a field-deployable footprint.

Technology overview

The architecture of the system is based on the use of more reliable, longer-lifetime diode-pumped solid-state fibre pump lasers. Through nonlinear mixing of the input light, mid-infrared pulses at 2.94µm is achieved, which have been optimised for precise ablation of tissue at the single-cell level.

Benefits

- Robust system architecture producing high quality laser beam output at 2.94 µm
- Design enables development of compact and field-deployable mid-infrared laser source
- Picosecond mid-infrared pulses for tissue ablation reduces damage to surrounding cells as compared to standard ablation methods (nanosecond or longer pulses).
- Single-cell level mass spectrometry imaging for higher resolution imaging – see single cell metabolomics, one of Nature's 2023 technologies to watch.



Example 10 um spatial resolution molecular imaging of mice brain

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Technology reference: **11333**

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Intellectual property information

PCT Application filed, September 26th, 2022.

Link to published paper(s)

1. Battle, R. A., Chandran, A. M., Runcorn, T. H., Mussot, A., Kudlinski, A., Murray, R. T., & Taylor, J. R. (2021). Mid-infrared parametric wavelength conversion seeded with fiber optical parametric sources. EPJ Web of Conferences, EOSAM 2021, 255, 11004. https://doi.org/10.1051/epjconf/202125511004
2. Battle, R. A., Chandran, A. M., Runcorn, T. H., Mussot, A., Kudlinski, A., Murray, R. T., & Taylor, J. R. (2022). Optical parametric amplification seeded by four-wave mixing in photonic crystal fibers. Proc. SPIE 11985, Nonlinear Frequency Generation and Conversion: Materials and Devices XXI, 1198502(March), 4. https://doi.org/10.1117/12.2609618
3. Battle, R. A., Chandran, A. M., Runcorn, T. H., Mussot, A., Kudlinski, A., Murray, R. T., & Roy Taylor, J. (2023). Mid-infrared difference-frequency generation directly pumped by a fiber four-wave mixing source. *Optics Letters*, *48*(2), 387. https://doi.org/10.1364/ol.476754

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