Mid infra-red hyper-spectral imaging with bright super continuum source and fast acousto-optic tuneable filter for cytological applications.

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Abstract. Mid-IR imaging spectroscopy has the potential to offer an effective tool for early cancer diagnosis. Current development of bright super-continuum sources, narrow band acousto-optic tunable filters and fast cameras have made feasible a system that can be used for fast diagnosis of cancer in vivo at point of care. The performance of a proto system that has been developed under the Minerva project is described.

1. Introduction

The possibility of using mid-ir light for medical diagnostics has been recognized for some years¹. It has the potential to greatly improve the chances of early cancer diagnosis. However current systems are based on large expensive laboratory equipment that use light sources such as glow-bars, arrays of quantum cascade lasers or beams from synchrotron sources.
There is a need for a mid-ir system that can be used to measure in vivo spectra at the point of care. The light source needs to be bright, broad-band, compact and modest cost. Additionally a spectrometer is required that has a high throughput and fast scan rate so that spectra can be captured with cell level resolution on living samples. Also a sensitive infra-red camera would enable rapid capture of the spectra of many cells simultaneously.

The Minerva project was started in 2012 with the aim to develop technology solutions so that mid-ir spectroscopy can be used for medical point of care cancer diagnostics.

2. Mid-ir imaging spectrometer

The Mid-ir imaging spectrometer, which is schematically shown in fig 1, is made possible by the development of 3 key components that have been developed in the MINERVA project: a fibre laser pumped super-continuum, an acousto-optic tunable filter (AOTF) and a sensitive fast IR camera.

The super-continuum output is in a single transverse mode that has a very high brightness. As a result the beam can be collimated through the high resolution AOTF that has a narrow (0.7°) acceptance angle. An advantage of the high-resolution mid-ir AOTF is that any wavelength can be tuned to in less than 1 ms, so that a customized spectra can be sent to the sample with minimal power loss. The high brightness beam is then projected onto a high resolution IR camera. As a result a 2.5mm square sample area can be analysed with 5µm spatial resolution, which is sufficient to resolve individual cells.

Figure 1 Schematic of mid-ir cytology system
Figure 2 Bread-board mid IR hyper spectral cytology imaging system

3. System performance

The initial system performance of the breadboard system shown in Fig 2 is summarized below in table 1.

| Parameter                                | Value         |
|------------------------------------------|---------------|
| Super continuum power 2-4.5 \( \mu \)m   | 1.2 W         |
| Bandwidth                                | 2 nm          |
| Mean Power per nm                        | 2.0E-03       |
| Transmission of AOTF                     | 35%           |
| Transmission of optical elements         | 34%           |
| Power at sample                          | 0.9 mW        |
| Number of pixels                         | 300k          |
| Power per pixel                          | 4.7E-10 W     |
| Spatial resolution                       | 5 \( \mu \)m  |
| Integration time                         | 1 ms          |
| Camera Noise                             | 2000 photons  |
| Signal/noise                             | 960           |
| Minimum absorption detectable            | 0.0045dB      |

Table 1 Mid IR system performance
The performance of the short wavelength mid IR system was evaluated with a polymer film on a calcium fluoride substrate. Each image shown in Fig 3 has 300k pixels and was taken with a camera integration time of 200µseconds. The time to scan between any two wavelengths is less than 200µseconds so the limiting capture rate is governed by the frame grabber rate of 85 frames/second. Therefore a mid-IR hyper-spectral cube with 100 wavelength slices of 300k pixels each could be captured in 1.2 seconds.

Figure 3 Examples of 300 k pixel spectral images of polymer film taken at 3650 and 3970 nm and spectra of single pixel

A sample spectra of one pixel is shown in Fig 3. Spectral classification software can then be used to identify regions of the sample that match the spatial and spectral characteristics of a particular material.

One significant advantage of the mid-IR spectral imaging system is the random wavelength tuning so that 100 spectral images may be taken of a sample at specific wavelengths that correspond to fingerprint markers of cancer cells without the need to scan through wavelengths that do not give useful information hence vastly speeding up diagnosis.

4. Conclusions
We have shown the efficacy of using mid IR light from a super continuum to rapidly identify features with spectral characteristics in the 2-4.5 µm wavelength region. While this wavelength region is of interest for diagnosing cancer and other medical conditions, far greater specificity can be obtained by extending the wavelength range into the fingerprint region. Work within the Minerva project is in progress to extend the wavelength range by developing super-continuum sources, AOTF’s, IR cameras and fused fibre devices that will operate out to 12 µm.

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