MID-INFRARED CHEMICAL NANO-IMAGING (MICHNI) OF ULTRASTRUCTURE AND INTRA-CELLULAR DRUG LOCALISATION.

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We describe a new way of using so-called "scattering-type" scanning near-field optical microscopy (s-SNOM) to image general biological tissue. Cell sections can now be imaged across the mid-IR spectral range at ~3nm spatial resolution, i.e. beating diffraction by ~3000x. We see the intracellular organelles (i.e. the so-called "ultrastructure") that were previously only accessible with electron microscopy (EM) at about 100x the complexity, time and cost. This is the first time these structures have been imaged optically and the images contain astonishing detail.

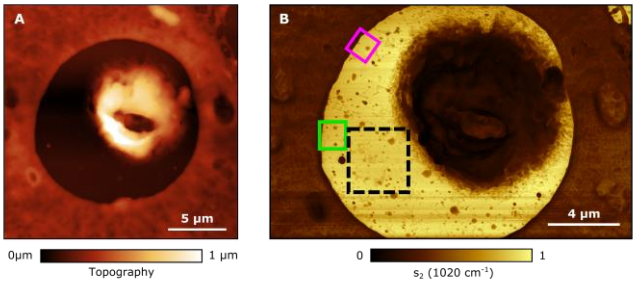

Fig. 1. Images of a human myeloma cell section. (A) AFM Topography, (B) near-field scattered amplitude, s_2, measured with an s-SNOM at λ=9.8 µm. Deep sub-cellular features, such as the cell nucleus and bilayer membrane, are clearly visible.

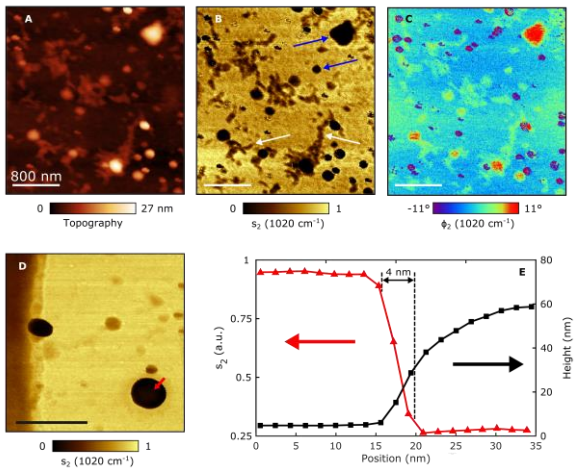

Fig. 1. Cytoplasmic ultrastructure in the 3 µm x 3 µm black dashed square in Fig. 1(B). (A) AFM topography, (B) near-field scattered signal s_2, and (C) scattered phase, φ_2. We see mitochondria (white arrows) and vesicles (blue arrows). (D) the 1.5 µm x 1.5 µm pink square in Fig. 2(B), with the red arrow designating a line-scan (E) of s_2, (red) and AFM height (black) across a vesicle boundary.

Mid-IR radiation in the so-called "chemical fingerprint" spectral region (5 µm < λ < 12µm) is absorbed in localised vibrational transitions that are characteristic of specific chemical moieties. This gives pronounced chemical contrast and allows chemical maps to be made.

As a demonstrator, we map out intracellular binding locations of the important anti-cancer drug Bortezomib (BTZ) within a single human myeloma cell.

MICHNI is label free and inherently safe, and it can be applied to any biological tissue sample. It can be used in clinical settings. In future we believe it may become an important adjunct to, or even a replacement for, EM across the whole range of the biomedical sciences.