Multimodal Spectroscopic Skin Imaging

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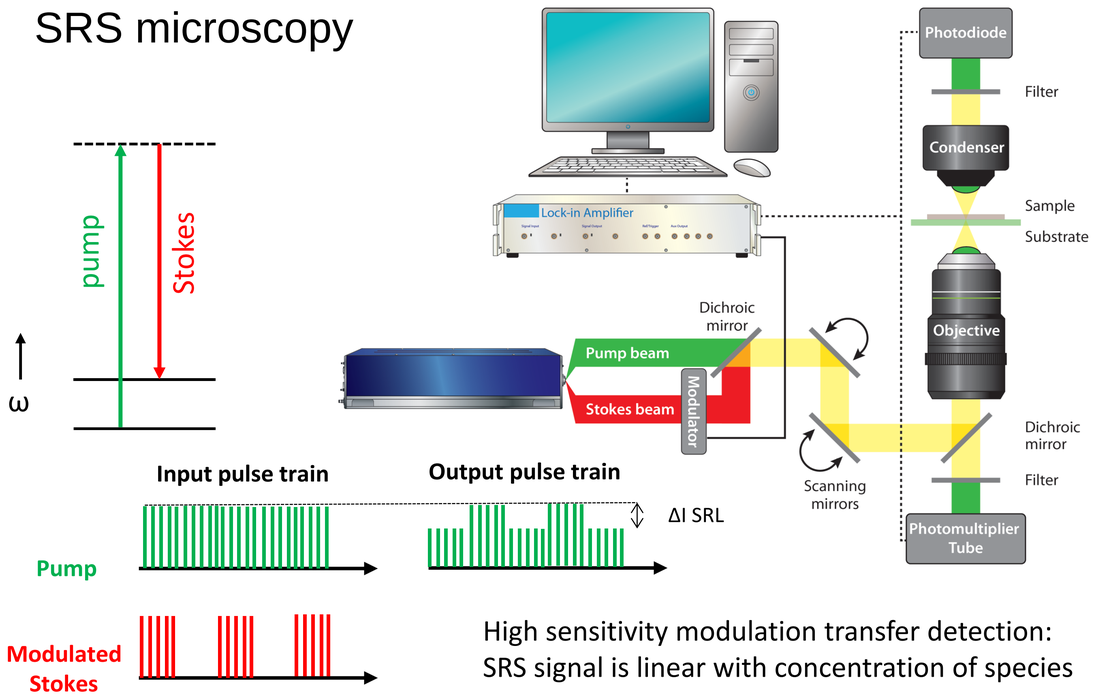
Introduction

A new generation of tools are available to asses the localisation of both endogenous compounds and xenobiotics in skin. Unlike adhesive tape stripping and other widespread bulk permeation techniques, high resolution spectroscopic imaging can reveal mechanistic insight such as penetration pathway and “metamorphosis” of active ingredients. Stimulated Raman scattering (SRS) microscopy is a non-destructive, label-free 3D imaging technique capable of video-rate examination of dermal tissue with ~500 nm spatial resolution.[1-4] Mass spectrometry imaging has also been used to study the distribution of unlabelled drugs with high chemical specificity in a diverse range of tissues and cells.[5,6] NPL is developing novel instrumentation for MSI with unique opportunities for measuring the dermal sub-cellular distribution of drugs and metabolites.

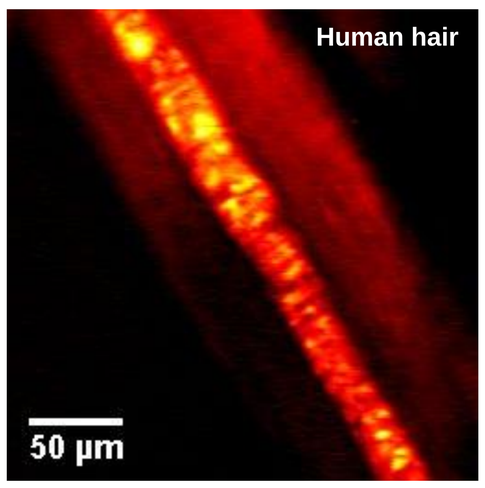
SRS microscopy

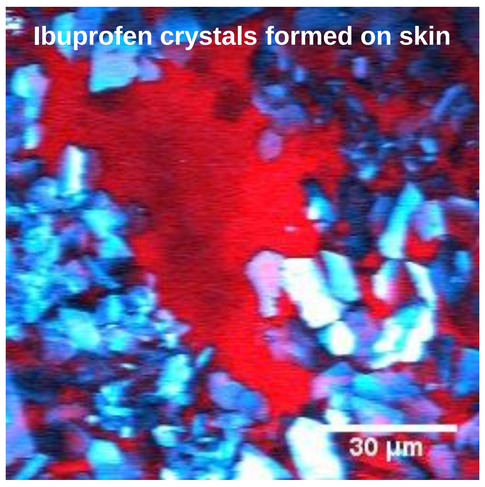


High sensitivity modulation transfer detection:
SRS signal is linear with concentration of species

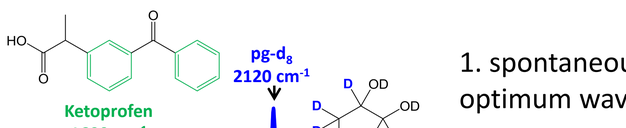
Benefits

SRS allows rapid, label-free imaging at high resolution, making it ideal for structural characterisation and drug delivery studies, including mechanistic insight, for example, penetration pathway, and crystallisation of formulation ingredients.[1,2]

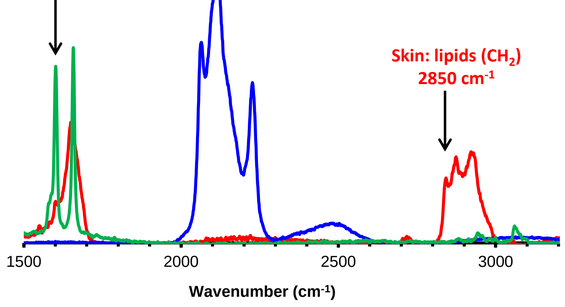


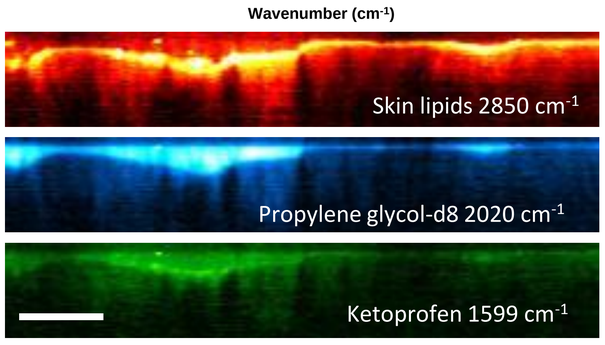


Imaging drug delivery with SRS

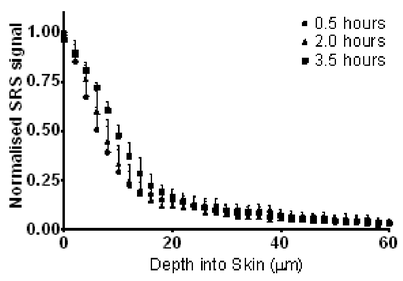


1. spontaneous Raman to determine optimum wavelength for SRS contrast

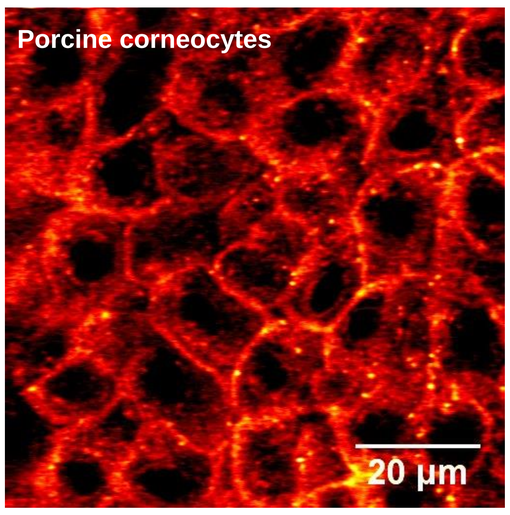


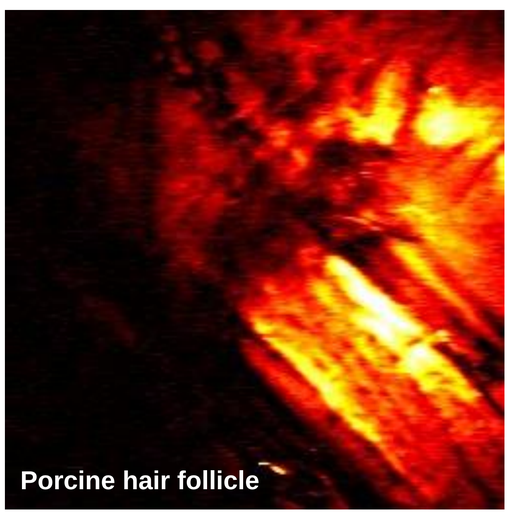


2. Rapid SRS acquisition of 3D images revealing structure, and localisation of drugs and excipients.[1]

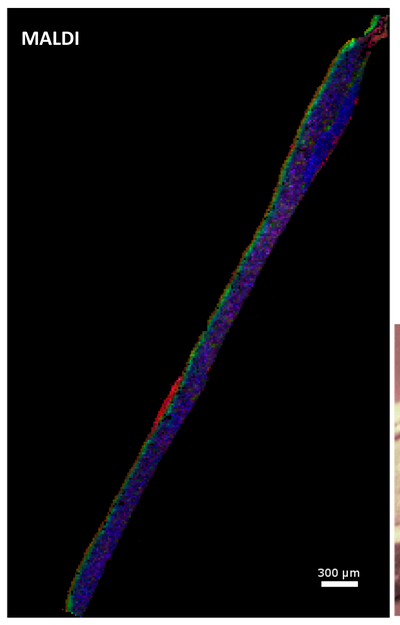


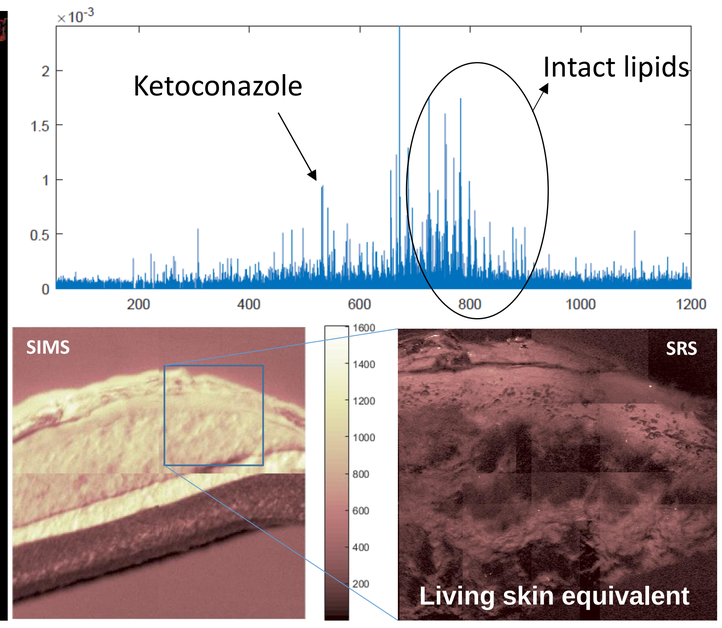
3. Extract quantitative information



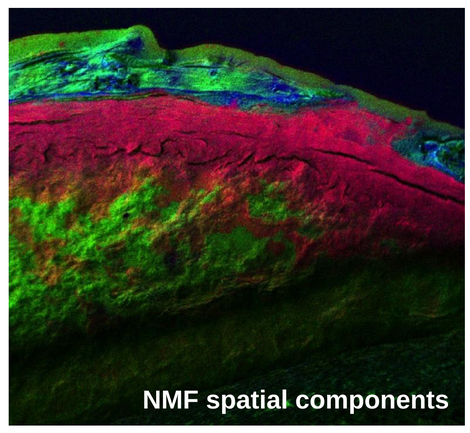


Synergistic SRS & mass spectrometry imaging (MSI)





- SRS is non-destructive, so samples can be subsequently characterised by MSI.
- SRS and MSI are highly complementary:
- Synergistic imaging: employing image fusion techniques to produce data sets with the high spatial resolution afforded by SRS with the greater chemical specificity and sensitivities attainable through MSI.
- Different techniques can be employed, depending on the sample requirements, e.g. matrix-assisted laser desorption (MALDI) or secondary ion mass spectrometry (SIMS).



Multivariate methods such as non-negative matrix factorization (NMF) are powerful approaches to identify molecular changes in tissue.

Conclusions

- SRS is a promising tool for sub-cellular mapping of drugs & nanoparticles.[1-4]
- Provides mechanistic insight to drug penetration pathways and bioavailability, not readily obtainable from tape-stripping or bulk permeation techniques.
- Ongoing efforts to improve quantitation for routines to correct for signal loss with depth due to sample scattering, and removal of parasitic signal contributions.
- Powerful multimodal imaging capability when used synergistically with MSI, which offers enhanced sensitivity and chemical specificity.

References

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