Vibrational imaging of drug distributions in skin with CARS microscopy

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Coherent anti-Stokes Raman (CARS) microscopy allows label-free, non-pertubative imaging of chemical compounds based on intrinsic vibrational modes of molecules [1]. The CARS signal is due to a 3rd order nonlinear interaction of the excitation light with the sample and is resonantly enhanced in the presence of the target molecules.

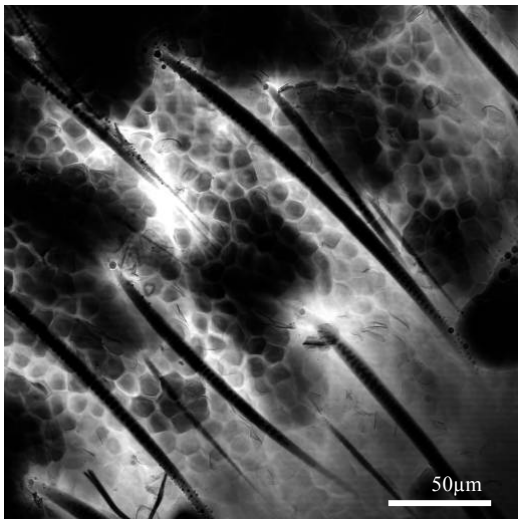

Fig.0: Transdermal delivery of the drug trans-retinol imaged with CARS microscopy in mouse skin.

Here CARS microscopy is applied to imaging of the transdermal drug delivery of the skin active trans-retinol (vitamin A) [2], illuminating the pathway of diffusion through the intercellular space of the stratum corneum. The effect of the diffusion enhancers propylene glycol (PG) and Myritol®318 are studied.

For drugs with weak Raman cross-sections or at low compound concentrations, the non-resonant background intrinsic to the CARS process limits the sensitivity of the technique. We present a new implementation of the background subtraction technique frequency-modulation CARS based on lock-in detection [3]. With a modulation frequency of 38 MHz laser noise can be suppressed successfully pushing the sensitivity limit of CARS microscopy.
Deuterium-labelling, i.e. replacing hydrogen atoms in the target molecules by the heavier isotope deuterium, shifts the Raman line of the CH-stretching vibration into the 'silent region' of the cellular spectra. The new FM-CARS setup allows to follow deuterated drugs penetrate into the skin and illuminate their biomedical functioning non-invasively and with diffraction limited resolution.

References:

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[2] Pudney, Paul D.A.; Mélot, Michaël; Caspers, Peter J.; Van der Pol, Andre; and Puppels, Gerwin J. "An In Vivo Confocal Raman Study of the Delivery of Trans-Retinol to the Skin," *Applied Spectroscopy,* **61** , 8 (2007)
[3] Ganikhanov, Feruz; Evans, Conor L.; Saar, Brian G.; Xie, X. Sunney "High-sensitivity vibrational imaging with frequency modulation coherent anti-Stokes Raman scattering (FM CARS) microscopy," *Optics Lett.*, **31**, 1872-1874 (2006).