Potential applications of non-linear optical spectroscopy in medicine

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In recent years the surface specific non-linear optical technique of sum-frequency generation spectroscopy (SFG) has emerged as a complementary experimental technique to characterize biological molecules at interfaces. SFG relies on the generation of signals through a second order non-linear optical process which can only occur when inversion symmetry is broken. This suppresses spectral contribution from bulk phases making SFG spectroscopy inherently surface specific. We already introduced SFG as a useful complementary technique to current linear spectroscopy methods for studying films of single stranded DNA[1] or the extracellular matrix of adhered cells[2]. Here we intend to introduce SFG for characterizing membrane bound ion channels.

Membrane bound ion channel proteins perform a multitude of biological functions including neuronal signaling and regulation of cardiac rhythm. Drug-induced blockade of cardiac hERG potassium channels, one prominent member of this family, causes ventricular arrhythmias and sudden cardiac death. The hERG ion channel interacts with a wide range of pharmaceuticals and is used as a mandatory industry-standard for early detection of potential side effects of new drugs. We will use linear and especially non-linear spectroscopic methods in combination with in-silico modelling to investigate and characterize hERG binding mechanisms of active compounds. We will develop a hERG-specific interaction model (in-silico and experimental) to predict side effects of potential drug candidates early in the development cycle. These data will be functionally validated using electrophysiological recordings of hERG potassium currents in *Xenopus laevis* oocytes and native cardiac myocytes. Since side-effects are often noticed only late in the billion-dollar development-cycle of a new drug, such a model will reduce the risk of patients exposed to these drug candidates and drastically lower development costs of generic new drugs in the pharmaceutical industry.

References:

[1] C. Howell, R. Schmidt, V. Kurz, P. Koelsch, *Biointerphases* 3, FC47 (2008).
[2] C. L. Howell, M. Diesner, M. Grunze, P. Koelsch, *Langmuir* 24, 13819 (2008).