Multimodal label-free measurements for diagnostics of live cellular samples

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Label-free measurements enable the observation of live samples such as cell cultures without requiring additional processing steps as for example loading contrast agents, or cell fixation. This makes it possible to assess the sample state in different conditions, such as during drug stimulation, without influence of external protocols on cell health. However, the absence of contrast agent usually makes label-free systems less specific than measurements which can have chemical-specificity by the inserted dyes.

We present here multimodal label-free analysis of live cells based on both Raman spectroscopic measurements and quantitative phase microscopy (QPM) [1]. Raman spectroscopy enables the measurement of the vibrational spectrum under excitation from a laser source, which provides information about the intracellular molecular content based on the inelastic scattering of the excited molecules. On the other hand, QPM is an interferometric technique which provides full-field quantitative phase images, which enable the extraction of several morphological parameters in a non-invasive manner [2]. The two measurements thus provide complimentary information, respectively in the spectral/molecular domain (Raman) and dynamic/morphological one (QPM), which are also partly correlated, and can also be combined for more specific analysis [1]. Furthermore, it is possible to optimize the acquisition approach by avoiding redundancy within the multimodal measurements and forgo a full Raman imaging acquisition, hence focusing on spectral properties of the sample to reach better multimodal measurement throughput, of typically one second per sample [3].

We also present various approaches that can be employed to combine and analyze the measurements extracted from different dimensions with the multimodal system, such as temporal, spatial or spectral information, in order to extract relevant biological parameters from live cells under different stimuli.

References

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