

Mid-Infrared Spectro-Microscopy of Living Cells: Quantitative Studies of Reactions and Metabolic Networks

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Over the last two decades mid-infrared spectromicroscopy has seen increasing application into the study of cells and tissue due to its sensitivity to the molecular properties of the sample. Recently, developments have focused on the possibility to use of the technique to characterize biochemical reactions in living cells. [1]

The main challenge in vibrational spectroscopy studies of living cells is the complexity of the spectra, which involve hundreds of overlapping absorption bands from all the cellular components present at detectable concentrations. Our current work is focused on the analysis of the relative contribution of small-molecule metabolites to the spectra of cells and tissue. We address specifically the glycolytic metabolism of cancer cells. Several metabolites involved in glycolysis are identified by using an approach that we call Correlated Cellular Spectro-Microscopy (CSM). [2] The results show the limitations of current interpretative schemes that rely on a small number of macromolecules for band assignment.

We now extend this analysis to the two-dimensional case by performing IR imaging on single cells and cell clusters. The result is the variation of metabolite concentration in time and space across the sample. The molecular detail obtained from this analysis allows its use in evaluating the pharmacological effect of inhibitors of glycolytic enzymes with potential consequences for *in vitro* drug testing. Finally, we highlight the consequences of a spectroscopic analysis of cellular metabolites on the spectral histopathological applications of infrared microscopy.

References

- [1] *Analyst* 136(16), 3219-32 (2011).
- [2] *Anal Chem.* 86(14), 6887-95 (2014).