FTIR 2D correlation analysis of prostate tumor cells exposed to anticancer agents

[1]R. Gasper, [2]T. Mijatovic, [2]R. Kiss, [1] E. Goormaghtigh

[1]Laboratory for the Structure and Function of Biological Membranes, Center for Structural Biology and Bioinformatics, CP 206/2, Université Libre de Bruxelles (ULB), Bld du triomphe, Acces 2, B-1050 Brussels, Belgium.
[2]Laboratory of Toxicology, Institute of Pharmacy, Université Libre de Bruxelles (ULB), Brussels, Belgium.

The last two decades saw the rise of IR spectroscopy as a label-free technique for the discrimination of different cell types, in particular in the field of cancer. Biochemical modifications induced by the disease lead to spectral modifications commonly evidenced with the use of chemometric tools. Our laboratory has already shown that biological modifications induced by one cardiotonic steroids on a cancer cell line can be highlighted by vibrational spectroscopy and evolves with incubation time.
Cardiotonic Steroids (CS) are well known inotropic drugs used for the treatment of congestive heart failure. Recently, several publications underlined their unique antitumoral effect. Despite similar structure, it seems CS can activate different metabolic pathways. We investigated the action of well-known molecule ouabain and new hemisynthesized CS as a function of time on PC-3 cells, a prostate cancer cell line. The metabolic modifications induced by the two drugs were monitored by recording the infrared spectra of the cells after 0, 6, 12, 24, and 36h of exposure to the drugs. Each condition was repeated 9 times. Spectra were then analysed with the use of 2D spectroscopy.
In a classical 2D experiment, a series of perturbation-induced spectra, known as dynamic spectra, are collected in a sequential order, along an induced perturbation, often as a function of time. In turn, correlation between pair of wavenumbers can be followed. Synchronous and asynchronous spectra were computed. Synchronous maps reveal spectral changes that occur at a similar pace and asynchronous ones point out spectral changes evolving at different rates.
In order to compare synchronous correlation maps for different drugs, the data were first normalized with respect to the standard deviation. The resulting correlation coefficient maps present values ranging from -1 to +1. The first advantage of the normalization is to give each wavenumber a similar weight. In turn less intense band contribution can be evidenced. The second advantage is that a map obtained for one drug can be subtracted from a map obtained for another one. We show here that map subtraction allows the identification of very specific difference in the impact of both drugs on PC-3 cells.
Analysis of both synchronous and asynchronous maps offers the possibility to define a time sequence for the spectral changes. We show here that the sequence of events occurring in prostate cancer cells can be established for both drugs along the incubation time. Yet, difference between modes of action induced by each CS can be evidenced.