

WHAT ROLE DOES SYNCHROTRON INFRARED MICRO-SPECTROSCOPY PLAY IN BIOMEDICAL APPLICATIONS?

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Synchrotron radiation is best known as a source of X-rays, but it is also a source for VUV to soft-X-rays photons. However, it was realised in the early 90's that this source can also be exploited in the infrared energy domain. Even if in some frequency regions (roughly 30 microns and below) the total photon flux emitted by the synchrotron source remains inferior to that of a thermal source, the brightness of a synchrotron largely exceeds that of a laboratory thermal source. Enhancement as high as three orders of magnitude has been achieved in terms of brightness (or brilliance or spectral radiance). This is essentially the feature that is most exploited in infrared spectroscopy and microscopy. Besides brightness, other characteristics like time structure (few picoseconds duration) and well-defined polarization states are being also exploited.

The main sources of infrared photons from storage rings are edge emission and bending magnet emission, and many recent infrared beamlines exploit both sources to double their experimental capacity.

Synchrotron infrared spectroscopy and micro-spectroscopy held a big promise in medical diagnosis. It is a powerful methodology to identify metabolic changes occurring at single cell level.

The brightness advantage, combined with a high beam stability (especially on recent third generation synchrotron), has resulted in fast data recording at high lateral resolution, with very good spectral quality (S/N). There exist several biological and biomedical applications which emphasize on the promising future of synchrotron infrared micro-spectroscopy in these scientific disciplines.

Among relevant examples, I will focus on the following:

- Urinary stone disease, constitutes a major health problem and is affecting an increasing number of people. Calcium oxalate, calcium phosphate, uric acid, ammonium hydrogen urate and magnesium ammonium phosphate are the main components of stones. Very

small crystals in the kidney biopsy sample, of 2.8-dihydroxyadenine (2.8-DHA) were identified, and this has direct relevant therapeutic implications. IR synchrotron microscopy is actually routinely used by doctors from Hospital for a rapid screening of kidney sections. This results in a direct implication in the patient therapy and recovery.

- The potential changes occurring in hematopoietic cells expressing BCR-ABL and BCR-ABL carrying T3151 mutation, conferring resistance to most tyrosine kinase inhibitors currently used has been evaluated using IR micro-spectroscopy. The use of the synchrotron is fully justified due to the small dimension of human leukemia cells.
- Stem cells research is a very important research topic nowadays. Several studies have shown that IR microscopy can determine the differentiation state of the stem cells. But more importantly, we have been able to show that synchrotron IR microscopy can assess unambiguously the reprogramming of stem cells, which is more difficult otherwise.
- Liver steatosis is a severe disease that can lead to hepatosteatosis, cirrhosis and cancer. The precise determination of the steatosis content during the liver transplant is crucial with recommendation to select livers exhibiting no more than 20% steatosis. This drastic recommendation contrasts with the incapacity of usual histological methods to rigorously provide an objective and non-biased assessment of steatosis. Synchrotron infrared microspectroscopy has helped determining the presence of micro vesicle with lipids content that can be directly related to the lipidomic HPLC tests. The database established with the synchrotron source is actually used to condition an IR thermal source based microscope, to be set up in hospital for direct diagnostic during liver transplant.