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Front piece of article

This special issue on Fundamental Developments in Clinical Infrared (IR) and Raman Spectroscopy is focussed on the use of vibrational spectroscopy to gain biomedical insights into clinically relevant problems. It includes highlights on novel developments in methodologies and technologies as well as discussing potential ways to overcome barriers to clinical implementation of promising vibrational spectroscopic techniques.

IR and Raman spectroscopy are sensitive to biochemical markers of disease from a range of biomedical samples. The versatility of these vibrational techniques means that tailored analysis can be developed based on the clinical requirement, be it specific and highly sensitive target molecule detection or a signature based approach to try to understand the complexity of disease profiles for diagnosis. Vibrational spectroscopic techniques are generally easy to use, robust, rely upon simple sample preparation and the instrumentation can be configured to the application (e.g. probe based, hand held, imaging). These advantages combined with the fact that they are capable of highly sensitive and specific discrimination of disease from non-disease and in some cases, disease severity, means they are medically applicable and suitable for the clinical environment.

Over recent years the application of IR and Raman spectroscopy to clinical problems has progressed rapidly, not only in highlighting the potential of spectroscopy to provide objective information to aid in clinical decision making, but also in developing our fundamental understanding of how light interacts with matter. A Web of Science citation report based on a search for “FTIR” and “Clinical” publications over the period 2000 - 2015 shows an increase from 310 citations per year in 2000 to 5857 in 2015 and for “Raman” and “Clinical” from 288 citations per year to 11218 over the same period. This special issue will focus on the fundamental developments that are driving this field ever closer to the clinic.

Byrne

The analysis of vibrational data obtained from biological samples is crucial for reliable and accurate interpretation of the significance of the data. Byrne et al discusses the conditions and methods that can be used to process Infrared and Raman spectral data that take into account differing instrumental and sample preparation factors to extract accurate data from the often subtle spectral changes due to biochemical changes in the sample.

Umapathy

Umapathy *et al* then go on to discuss the quantification of vibrational data which can often be hampered by the challenging background signals often observed in biological samples as well as the sample presentation affecting the quality of the resulting data. The focus of this article is on the use of ratiometric methods to overcome these issues to allow quantitative data to be generated.

Stone

To extend the use of Raman techniques into clinical and *in vivo* will require the development of advanced instrumentation and techniques. Stone *et al* discuss the requirements for the development of fibre optic Raman probe for use *in vivo*. The focus is on the design of fibre optic probe to ensure that the materials and design is compatible with both Raman scattering and the *in vivo* environment.

Popp

Popp *et al* focus on use of Raman and stimulating Raman imaging techniques applied to biomedical samples. The article focusses on the instrumental developments in this area and the different instrumental set ups used to allow high information content imaging using spot, line and wide field imaging approaches.

Matousek

Many clinical problems require optical data to be obtained at depth whilst being as non-invasive as possible to the patient. Recent developments in Raman for biomedical application include the use of transmission and spatially offset Raman (SORS) which allows signals to be obtained from the subsurface of tissue. Matousek and Stone review the potential of these techniques for biomedical applications such as cancer diagnosis, evaluation of bone structure and glucose monitoring.

Blanch

Raman optical activity (ROA) is a technique which offers insight into the chirality of biomolecules by looking at the scattering intensity changes observed when chiral molecules are exposed to left or right-handed circularly polarised light. Blanch *et al* reviews the application of computational methods to ROA to give further insights into biomolecular structure and dynamics in increasingly complex environments.

Dluhy

Surface enhanced Raman scattering (SERS) is an advanced Raman technique which uses a roughened metal surface to enhance the intrinsically weak Raman signal. Dluhy *et al* discuss the use of SERS for the detection of the respiratory pathogen *Mycoplasma pneumoniae*. Different SERS substrates and methodologies for the detection of the pathogen are discussed as well as ways to analyse and interpret the resulting data.

Faulds

The molecular specificity and sensitivity of SERS makes it ideal for the simultaneous detection of multiple biomolecules in clinically relevant samples. Faulds *et al* review the recent literature on the use of SERS for the multiplexed detection of DNA and protein biomarkers *in vitro*.

Graham

Metal nanoparticles can be functionalised with Raman reporters and biorecognition molecules allowing them to specifically interact with and detect biomolecules using SERS. Graham et al review the use of the biofunctionalised nanoparticles for the detection of biomarkers, both *in vitro* and *in vivo*, in real clinical samples using SERS.

Porter

Porter *et al* discuss the potential for the use of SERS in a point of care (POC) environment for the detection of clinical samples with a focus on pathogen detection. This article focusses on how there is unmet need in the detection of pathogens and how SERS has the potential to meet this need as well as exploring the challenges of developing a SERS POC device in terms of limit of detection, specificity, validation and device development.

Wood

Wood discusses the contribution of Fourier Transform infrared spectroscopy has made to the understanding of DNA confirmation with a particular focus on DNA hydration / structure relationship and its role in clinical diagnostics. Highlighting advantages for biomedical spectroscopy of analysing hydrated B-DNA namely improved quantification in cells, improved discrimination and reproducibility of FTIR spectra during the cell cycle and insights into biological significance.

Sockalingum

Biofluid spectroscopy, either serum or plasma or an organ specific fluid, offer the ability for relatively non-invasive diagnostic/monitoring possibilities for the future of healthcare that are capable of rapid and reproducible diagnostics. Sockalingum *et al.* underscore recent research within the field of biofluid spectroscopy highlighting recent advances as well as issues surrounding future clinical translation.

Gardner

Histopathology is fundamental to the modern day clinical practice and disease diagnosis and is currently performed via the use of optical microscopy combined with a suite of stains depending upon the molecular epitope desired to be visualised. In this review Gardner *et al.* focus on the development and use of chemical imaging techniques, with a focus on recent advances in infrared imaging, for the development of spectral histopathology (SHP) and consider future barriers to clinical implementation.

Kazarian

FTIR spectroscopic imaging is a rapid, label-free, non-destructive and molecularly specific technique that can be applied to a wide range of biomedical applications. A promising future application is its use in live cell analysis, in this review Kazarian *et al.* focuses on the use of the attenuated total reflection (ATR) sampling mode for live cell analysis highlighting particular developments in imaging technology and particular advantages of ATR imaging.

Mahadevan-Jansen

The translation of spectroscopic equipment into the clinic or into medical use is of upmost importance for the future of biomedical vibrational spectroscopy. Mahadevan-Jansen *et al.* discuss the development of spectroscopic clinical instrumentation, focusing on Raman spectroscopy, reviewing the various considerations relevant to the implementation of Raman spectroscopy within the clinic and a focused set of applications that have successfully demonstrated the successful use of Raman in *in vivo* studies