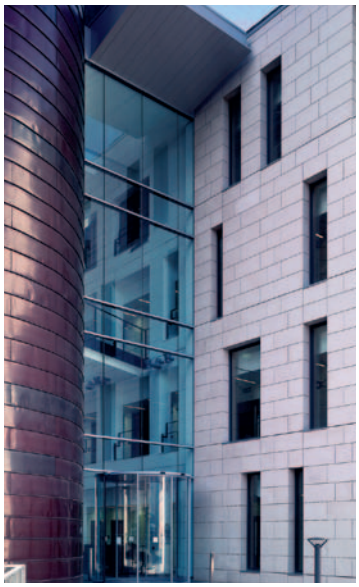
Spectroscopy
in biomedical research



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Introduction

The field of spectroscopy is vast and it would be difficult to cover in an article such as this. As ever, however, certain areas of the discipline under go periods of rapid growth, driven by developments in instrumentation, computational capabilities or by trends in research funding. One such area, is the use of infrared and Raman spectroscopy in biomedical research.

Infrared and Raman spectroscopies are analytical techniques that have been used for many years in chemical R&D mainly for the analysis and identification of molecules. Traditionally the spectra are analysed by a trained spectroscopist who can interpret each peak in the spectrum and thus identify the molecule present in the sample. The interest in large biological molecules, particularly analysis of proteins initiated a change in the way spectra could be analysed. The use of more statistical analysis and pattern recognition methods opened up the field to the study of complex biological systems including cells and tissue where interpretation at the molecular level is not necessarily the objective.

Cancer diagnosis

The diagnosis of many forms of cancer is often made primarily from the analysis of a biopsy, where a small sample of the lesion is examined under an optical microscope by a highly trained pathologist. This tissue is analysed for the presence of cancerous cells and often the cancer is graded. This process, however, is slow, expensive and subjective. In the case of prostate cancer, for example, studies have shown that pathologist agree on a grade in only about one third of cases. This can have important implications on clinical decision making and highlights the need for more objective methods of analysis. Several groups including my own have shown that Infrared spectroscopy can be used as a very rapid, reliable, and cost effective method of analysing prostate biopsies. The analysis is completely objective, based on the chemical content of the tissue rather than the observable tissue architecture. Furthermore, in principle the system can be automated so that a large number of biopsies can be analysed. This is important since prostate cancer is an age related disease and with an ageing population the number of biopsies to be analysed is increasing rapidly. The development of infrared spectroscopic imaging has revolutionised this field and now similar studies of other cancers e.g. colorectal, breast, and lung are also showing that disease detection is relatively straight forward.

Raman spectroscopy offers other advantages. Infrared spectroscopy is not practical for in vivo analysis since water is a very strong absorber. Raman spectroscopy, however, is relatively unaffected by water and so in vivo Raman probes have been developed that are suitable for in vivo tissue analysis.

Spectroscopic cytology

The coupling of both infrared and Raman spectrometers to microscopes led to a surge of interest in spectroscopic cytology. Cervical and oral cancers are often detected by looking at single cells collected from a Pap smear or an oral swab. Developments in infrared imaging technology means that it is now possible to collect spectra from hundreds of cells on an infrared compatible microscope slide in a few minutes and with newly developed scatter correction routines such as RMieS-EMSC spectral distortion can be removed. Thus with reference to in-house databases it is possible to identify the type of cells present in a sample and their disease state. Several groups are also developing Raman optical tweezer systems in which cells in an aqueous environment are held in an optical trap and identified by their Raman spectrum. It is envisaged that these analysis systems can be coupled to microfluidic systems for high throughput analysis.

Drug screening.

An ability to obtain a spectral signature of cells on a cell-by-cell basis means that variation in cell populations can easily be studied. This is being exploited in the field of drug discovery where new drugs can be compared with existing drugs of known mode of action. Infrared spectroscopy does not detect the cytotoxic agent directly, since these are usually at very low concentrations, but the presence of the cytotoxin initiates a cellular response that involves significant changes in the biochemistry of the cell. The cellular response is different depending on how the drug works so the spectral signature observed can be related to the mode of action. Since the cells are measured individually, the influence of the cell cycle and the development of drug resistance can be identified.

The future

The future for both infrared and Raman spectroscopy for biomedical research is looking healthy. Part of the key to success is the creation of institutes like the Manchester Interdisciplinary Biocentre that house researchers from disciplines as diverse as chemical engineering, computer science, life science and medicine and creates an environment that encourages real and effective collaboration.

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