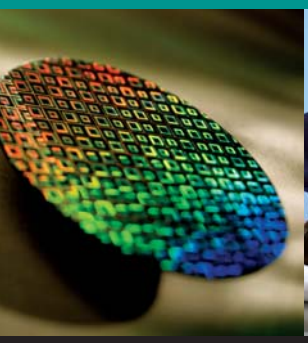
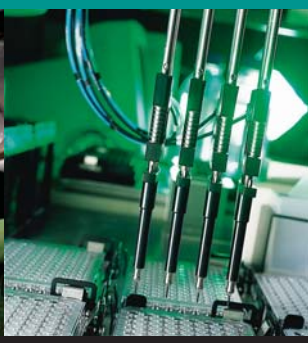
NMS Innovation News

Incorporating the former MET Newsletter

2008 | issue 02







ADVANCED MATERIALS | MEDICAL | COMMUNICATIONS | ENERGY | MANUFACTURING

Depth Profiling of Organic Materials: An Aid to the Design of Functional Coatings

Virtually every object in the world is coated with organic material. Usually this is a result of the adventitious accumulation of environmental molecules and serves no useful purpose. In a wide variety of products, however, the coating is deliberately applied to enhance performance or enable the product to function. In everyday life organic and polymeric thin films have become ubiquitous as a glance around any home or workplace will reveal. Examples include lubricants, paints, inks, adhesives, laminations for paper, coatings for glass and the many functional layers in a common crisp packet. A number of emerging technologies rely upon controlling the thickness and composition of organic layers and ensuring that the distribution of organic components is fully understood when used or exposed to different environments. Significant examples of emerging technologies include plastic electronics and the controlled release of drugs. In plastic electronics, individual devices comprise of a minimum of two organic layers: control of the absolute and relative thickness of these layers as well as homogeneity across the device are critical for reliable operation. Controlled release systems commonly comprise of a therapeutic agent (a drug) dispersed in a biodegradable polymer: the distribution of the drug determines the release rate, and this must be above a minimal therapeutic level but below toxic levels throughout the lifetime of the system. The advantage of controlled release is that it avoids the fluctuating levels of drug associated with repeat injections and removes the risk of patients or carers forgetting to administer the drug, or administering the incorrect dose.

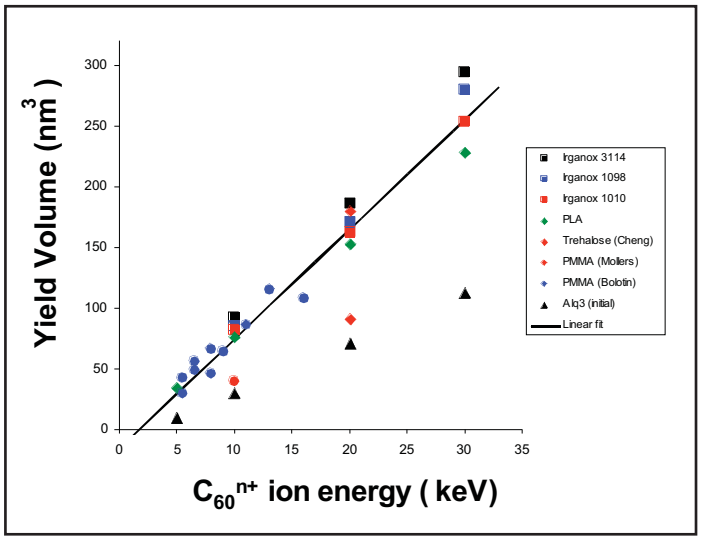


Figure 1: The volume of material sputtered per incident C_{60} ion (Yield Volume) as a function of C_{60} kinetic energy from a variety of materials. The initial Yield Volume is shown to be very similar for most organic materials and appears to increase linearly with energy. It should be appreciated that the volume of a C_{60} molecule is less than 1 nm^3.

Having a means to measure the distribution of organic components in thin films will enable designers to confirm that the predicted distributions have been achieved and to determine the cause of poor function or failure. Appropriate methods must be able to deliver the necessary depth resolution of a few tens of nanometres and have the ability to uniquely identify delicate organic species. Until recently, this was thought to be impossible and indirect methods were employed which either did not have the chemical

nel technology for life

LGC Setting standards in analytical science

NPL National Physical Laboratory

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specificity required to uniquely identify organic components or did not have the requisite depth resolution. However, in the last ten years it has been recognised that organic material may be sputtered with cluster ions without causing significant damage to the underlying material. By using a surface sensitive and chemically specific spectroscopy, such as secondary ion mass spectrometry (SIMS) it is possible to record signals from individual organic components as a function of depth by repetitively 'shaving' a thin layer of material with a cluster ion beam and analysing the remaining surface. In this way a depth profile of organic components can be achieved.

One of the most promising set of cluster ions for organic depth profiling are fullerene ions, particularly C_{60}^{n+}. Seminal work using C_{60}^{n+} ion sources has been carried out at Pennsylvania State University, USA and the University of Manchester. The research has demonstrated that organic depth profiling is possible, but has not demonstrated the general utility of the technique. As part of MET2.2, 'Nanostructured Organic Multilayer Characterisation' NPL (in partnership with the University of Nottingham, Cambridge Display Technologies, Novalia, Kodak, ICI and NTERA) has been developing C_{60} depth profiling to determine important metrological parameters, explore the limitations of the technique and to demonstrate its utility on real devices.

By accurately measuring the sputtering rate of a variety of organic materials (Figure 1), we have shown that most organic materials *initially* sputter at the same rate. This observation is very encouraging, as it suggests that the application of a depth scale to data from mixed organic materials should be straightforward. The volume of material liberated by each ion impact is very large and is the key to the success of the technique. The sputtered volume is large enough to remove most of the damage created by previous impacts. However, for some materials the remaining damage acts to decrease the sputtering rate and the yield rapidly declines until sputtering rates are a hundred times lower, more typical of inorganic materials such as silicon. Our investigations indicate that there are two limiting factors that undermine the success of organic depth profiling. Some materials cross-link under ion bombardment and this leads to a rapid decline in sputtering yield. Others develop a high degree of roughness and this leads to a slow decline in sputtering yield. We are currently exploring experimental methods to reduce these effects, yet a wide range of materials do not display these limiting behaviours and profiles of up to a micrometer in depth with a depth resolution of 50 nm at the end of the profile have be achieved.

To obtain a deep understanding of organic depth profiling, we have constructed novel layered organic films. By making some of the layers very thin, the resolution of the technique can be directly visualised (Figure 2). Such films are called 'delta-layers' and have been used to understand the depth profiling process within inorganic materials, particularly by the semiconductor industry. Experiments on the NPL organic delta layers have provided a wealth

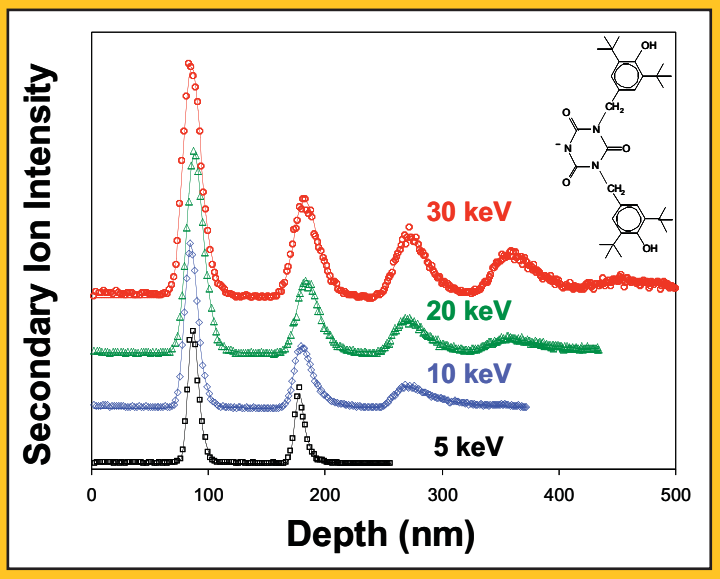


Figure 2: C_{60} sputter depth profile of an NPL organic delta layer, the ion detected is shown in the inset. The signal from a delicate organic compound deposited in 2.5 nm thick layers within another organic material reveals the sputter rate, depth resolution and sensitivity during a profile. Higher energies have poorer depth resolution, but a greater useful depth of sputtering. Analysis shows that the relative concentration of the compound in each layer can be determined to within 10%.

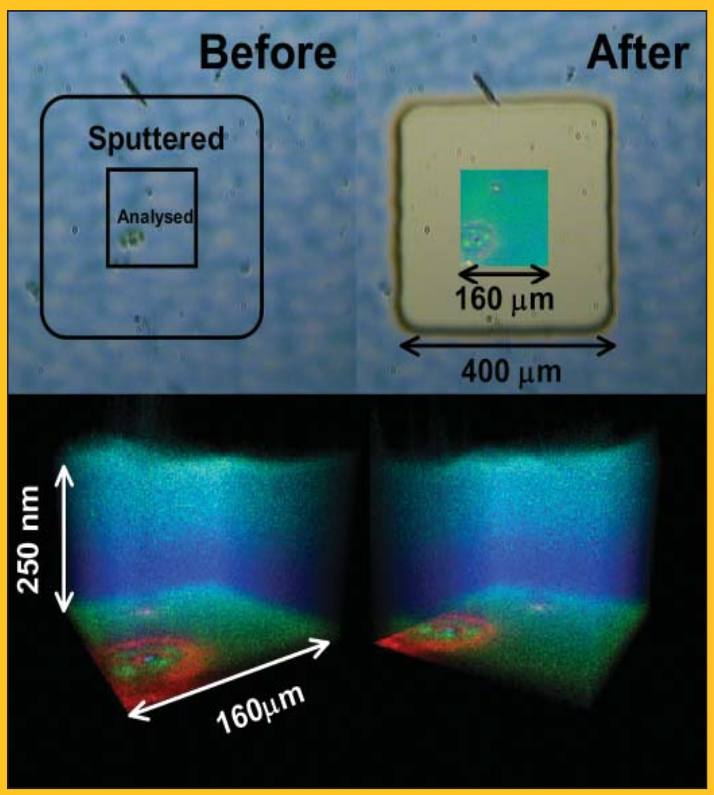


Figure 3: Upper images show optical micrographs of a defective drug-loaded polymer film before and after analysis. The 'after' image is overlaid with a composite image to show that the optical features correlate with components in the film. The lower images show two views of a 3 dimensional reconstruction of the film components, sodium contamination is red, intact drug molecules are green and polymer is blue. Defects are associated with sodium contamination on the underlying substrate and the drug has segregated to the top and bottom of the film.

of understanding of the depth profiling process. For example, by comparison with atomic force measurements we have proven that the resolution is determined solely by the roughness of the sputtered surface and not by any mixing processes. NPL organic delta layers will be used to find ways to limit the development of surface roughness and to compare different cluster ion sources.

Having obtained a thorough and detailed understanding of the organic depth profiling process, the interpretation of results from samples of technological importance becomes possible. In Figure 3 we show example results from a drug delivery material. Because SIMS can be used as an imaging spectroscopy with good spatial resolution, three-dimensional reconstructions are possible. The dataset from any experiment is actually four dimensional, since any point in space has a full mass spectrum associated with it. Processing, visualising and understanding the results of such an experiment are all extremely challenging. The surface and nanoanalysis team at NPL is world-leading in providing analysts with the necessary tools for this task.

For further information please contact alex.shard@npl.co.uk or visit http://www.metprog.org.uk

Advances in Cell Based Technologies

With the increasing average age of the UK population, industry is turning more and more to cell based technologies in the drive to develop more effective therapies. This is fuelling the strong UK position in the development and exploitation of stem cell based therapies for the cessation of organ degeneration and in bioprocessing for the development of pharmaceuticals. To help enhance this position, LGC has led three projects under the current programme aimed at answering several of the measurement challenges that currently hinder technology development.

In recent years, the media spotlight has centred on the emergent potential of stem cells. These cells are purported to be able to divide indefinitely offering a limitless supply of cells which can be transformed into any cell type in the human body. Predictably, this has put them at the forefront of one of the most rapidly developing and heavily invested areas of science "regenerative medicine". To realise the potential of this new technology and aid its commercialisation, intelligent and controllable culture systems need to be in place to ensure that cell manufacture can be scaled beyond the logistical capabilities of standard culture technology. In addition, robust methods also need to be in place to measure cell status as they differentiate into the organ specific cell type of choice.

LGC has developed a bioreactor system which allows cells to be grown on microcarrier support structures in a controlled environment. The system allows the cells to be maintained for long culture periods (50 days) and has an inferential measurement capability which monitors cell growth using the biochemical profile of the growth medium. Cells have not only been grown but also induced to differentiate along a neuronal lineage. These key findings validate the concept of the bioreactor setup and its potential to aid regenerative medicine commercialisation.

LGC has also examined a range of platform technologies to measure the signatory biomarker profiles of the differentiating cells in a multiplexed manner. These include mass spectroscopy, protein micro-arrays and flow cytometry. Cross platform comparisons have shown that in isolation each technology can detect biomarker profiles but have different limitations in terms of sensitivity, sample preparation or ability to multiplex. These limitations could be overcome, however, using a multiplatform approach to ensure measurement robustness, which in turn can have a huge impact for product quality control in the regenerative medicine marketplace.

Technological development in the bioprocessing sector is also essential to the continued success of modern medicine.

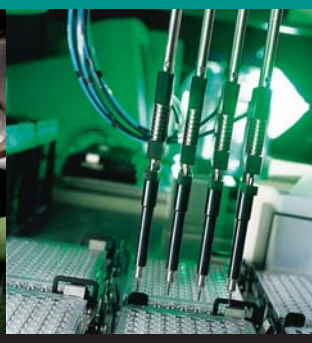
The use of modified cell lines for the production of biopharmaceuticals is well established, but these frequently fail to make the desired product as a result of adjustment to any modification in their environment. LGC has focussed efforts on improvements in the monitoring of metabolic engineering to ensure effective control of the bioprocess. Establishment of a dedicated, small-scale bioproduction facility has led to the development of methods for the monitoring of carbon and nitrogen flux coupled to novel data analysis techniques. This provides a novel, instrument-independent, data analysis 'pipeline' for identifying metabolite variations in direct response to pathophysiological stimuli of the biological system. The software is also easily extensible to on-line monitoring.

Taken together, these cell based measurement projects for emerging technologies have demonstrated how the provision of intelligent, robust and integrated technologies can drive innovation, cost optimisation and competitiveness for new medicinal products aimed at the future provision of healthcare in the UK.

For further information on these projects please contact neil.harris@lgc.co.uk or visit http://www.metprog.org.uk







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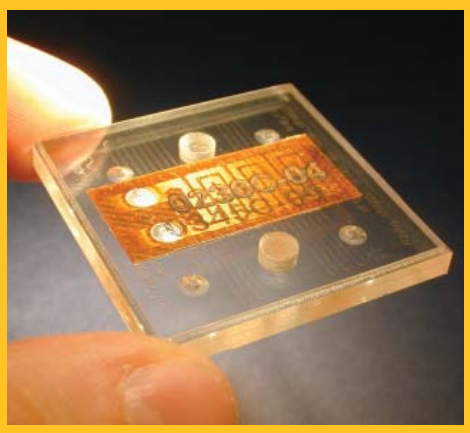
If you would like further information on any aspect of NMS Innovation R&D Programme, see www.metprog.org.uk
National Physical Laboratory | Teddington | Middlesex | United Kingdom | TW11 0LW
Helpline: 020 8943 6880 | Fax: 020 8614 0446 | E-mail: enquiry@npl.co.uk

Micro Flow Challenges



Polymeric microfluidic chip with heating element (courtesy of Epigem)

Microfluidic technologies have seen a huge surge in their utilisation and development in recent years by both industrial and academic communities. This growth has been paralleled by the accelerated progression to ever smaller dimensions and into the nanofluidic domain. The rapid uptake and commercialisation of microfluidic technology has been observed globally across a huge range of sectors. These include medical diagnostics, life science, chemical production and analysis, and fuel cells, with new applications constantly emerging. Many developing applications are critically dependant on the accurate and precise determination of flow rates, an area that is actively being investigated by NEL.

Indeed there has been a noticeable increase in the number of new commercial flow rate sensors specifically aimed at microfluidic applications to quantify ultra-low flow rates. However, users of these sensors have reported numerous complications with their calibration and have questioned their accuracy. Traceable flow measurements to ensure consistent and repeatable results could improve confidence in microfluidic technologies, devices and flow sensors. However, to date no fiscal or regulatory drivers for traceability in ultra-low flow applications have been identified, and the majority of UK companies using these technologies are still at an early development stage. Hence most companies consider that it is too early for them to consider traceable flow measurements. Besides certifying accuracy and repeatability for commercially available devices, traceability in flow measurements should lead to greater consistency of results between research organisations at different locations.

Other issues that have surfaced following NEL's extensive review of UK industries using microfluidic technologies include the often erroneous assumption of Newtonian properties for fluids and the continuing low confidence in microfluidic flow modelling. The latter is primarily due to the lack of accurate experimental data to validate flow modelling results and the expense of acquiring such data. This highlights the need for further research in this area.

For further information please contact egraham@tuvnel.com or visit http://www.flowprogramme.co.uk

Forthcoming Events

Overview of Ultrasound Research at NPL
21 February 2008 (11:00)
Bajram Zequiri – NPL (Interwise Event Number 123139)
Join this online meeting via mset.org.uk

A Node Discovery Service for Partially Mobile Sensor Networks
22 February 2008 (15:00)
Vladimir Dyo - University College London (Interwise Event Number 348235)
Join this online meeting via mset.org.uk

Measurement and Modelling Tools being developed by NPL for the Fuel Cell Industry
27 February 2008 (11:00)
Gareth Hinds – NPL (Interwise Event Number 450389)
Join this online meeting via mset.org.uk

Surgery by Soundbeam - the use of High Intensity Focussed Ultrasound to Treat Cancer
5 March 2008 (11:00)
Adam Shaw – NPL (Interwise Event Number 756380)
Join this online meeting via mset.org.uk

Anamet Meeting
RF and Microwave Metrology Club
6 March 2008
Rohde & Schwarz UK, Fleet, Hampshire
Contact: chris.eio@npl.co.uk

Nanoscale Surface Analysis for the Characterisation of Fibres
19 March 2008 (11:00)
Joanna Lee – NPL (Interwise Event Number 308065
Join this online meeting via mset.org.uk

Power Harvesting for MEMS
26 March 2008 (11:00)
Markys Cain – NPL (Interwise Event Number 361045)
Join this online meeting via mset.org.uk

CEM 2008 – Seventh International Conference on Computation in Electromagnetics
7 – 10 April 2008
Quality Hotel, Brighton
http://conferences.theiet.org/cem

7370/K0108