Molecular Mapping Beyond the Diffraction Limit
Using Tip-Enhanced Optical Spectroscopy

Non-destructive and label-free molecular mapping at the nanoscale under ambient conditions challenges the limits of most analytical techniques. Tip-Enhanced Optical Spectroscopy (TEOS) is one of the very few techniques capable of achieving this. In this article, we discuss the principles of TEOS, its application to nanoscale chemical characterisation in different areas and how it can be combined with other methods to provide multi-parameter imaging at the nanoscale.

Over the last two decades tip-enhanced optical spectroscopy (TEOS) has become a powerful nanoanalytical tool for correlative topographical and chemical mapping of a surface at the nanoscale. The most widely used method has been tip-enhanced Raman spectroscopy (TERS), which has proven useful for nanoscale chemical characterization in a wide range of research areas such as biology, catalysis, polymer-blends, semiconductors, 2D and 1D materials as well as single molecule imaging [1]. More recently, tip-enhanced photoluminescence (TEPL) spectroscopy has emerged as an effective method of probing chemical, electrical and optical properties at the nanoscale. The advantages of TEOS over other analytical techniques are the high lateral resolution (beyond the diffraction limit), the non-destructive and label-free nature of the method and the fact that it can be used under ambient conditions. TEOS works on the principle of localized surface plasmon resonance (LSPR), whereby a high intensity electric field is created at the apex of a metal-coated scanning probe microscopy (SPM) tip placed inside the focal spot of a laser beam, as schematically shown in figure 1a. The LSPR between the excitation laser and the metal nanoparticles at the tip-apex confines the electric field to a region similar to the size of the nanoparticles and enhances its intensity by several orders of magnitude thereby increasing both the spatial resolution as well as the sensitivity of optical imaging.

Visualizing Defects in Graphene and 2D Materials

Structural defects in 2D materials, such as graphene [2,3] and molybdenum disulphide [4] can significantly degrade their carrier transport properties reducing efficiency of potential 2D materials-based electronic devices such as high
performance field effect transistors, super capacitors, photonic detectors etc.

Using TERS we have shown (fig. 1b) that it is possible to map individual structural defects with radii as small as $1.9 \pm 0.1$ nm in single-layer graphene [2], under ambient conditions and even on a rough substrate such as glass.

**Mapping Catalytic Activity at the Nanoscale**

Catalysts are used in more than 90% of industrial chemical processes and contribute to almost 35% of global GDP. However, conventional spectroscopy methods of catalyst characterization typically rely upon macroscopic techniques that measure an ensemble of particles. Using TERS, we have demonstrated mapping of the catalytic activity at a heterogeneous Ag catalyst substrate employing plasmon-driven photocatalytic oxidation of $p$-mercaptoaniline ($p$MA) $\rightarrow p,p'$-dimercaptoazobenzene (DMAB) as a model reaction as shown in figure 2 [5]. In the TERS map, reaction hotspot of $p$MA $\rightarrow$ DMAB are clearly revealed with a spatial resolution of $\approx 20$ nm.

**Imaging Small Molecules in Biological Cells**

Visualizing nanoscale distribution of small molecules present inside a biological cell is crucial for understanding structure-function relationships in sub-cellular biological nanostructures. Currently, super-resolution fluorescence microscopy (SRFM) is the most popular technique for nanoscale molecular mapping in biological cells. However, SRFM suffers from the essential requirement of fluorescent labels that can sometimes change the behavior of biomolecules they are attached to. Furthermore, only the molecules tagged with fluorescent labels can be visualized using SRFM while the others remain invisible. Recently, we have demonstrated non-destructive 2D mapping of small biomolecules within a biological cell using TERS without employing any extraneous labels [6]. Figure 3 shows nanoscale chemical mapping of newly-synthesised phospholipid (NSP) molecules within a mouse pre-adipocyte cell. NSP distribution is mapped with $< 20$ nm spatial resolution using TER intensity of C-D vibration mode ($2100$ cm$^{-1}$) of the NSP molecules.

**Multi-Parameter Imaging at the Nanoscale**

The ability to directly correlate structure and function is the *holy grail* in the development of new materials and devices. This requires multi-parameter approaches (measurements of multiple properties) which becomes more challenging as higher resolution is required. Recently we demonstrated that it is possible to combine nano-optical spectroscopy (TERS, TEPL) with electrical mode scanning probe microscopy in a single, simultaneous experiment, allowing non-
destructive structure-to-function characterization with nanoscale resolution. This was achieved by developing multifunctional probes, i.e. metal-coated tips that act as both plasmonic probes and electrical contact for scanning probe measurements. Such simultaneous measurements reduce uncertainty of data analysis by facilitating registration of multiple images, diminish unwanted contamination/degradation and decrease overall measurement time. Figure 4 shows simultaneous topographical, electrical and optical microscopy (STEOM) of an organic solar cell with <20 nm spatial resolution where we used the different probe depths of each measured signal to infer the surface and subsurface molecular composition correlating it with the local photocurrent generation and used it to explain macroscopic device performance [7].

Conclusion

TEOS provides molecular information well beyond the diffraction limit and has been applied to support development of materials and devices in numerous areas, from biology to electronic devices. Recent advances in metrology [8-10] and instrumentation, such as the integration of TEOS with electrical mode SPM (STEOM) [7], are facilitating wider use of these methods, which we believe will guide the rational design of a range of nanomaterial-based optoelectronic devices.

References

topographical, electrical and optical microscopy of optoelectronic devices at the nanoscale. Nanoscale 2017, 9, 2723-2731


Authors
Naresh Kumar¹ and Fernando A. Castro¹

Affiliation
¹National Physical Laboratory, Teddington, United Kingdom

Contact
Naresh Kumar MRes MInstP MRSC
Higher Research Scientist
Chemical, Medical and Environmental Sciences
National Physical Laboratory
Teddington, United Kingdom
naresh.kumar@npl.co.uk
www.npl.co.uk

More articles on Raman Imaging

All references