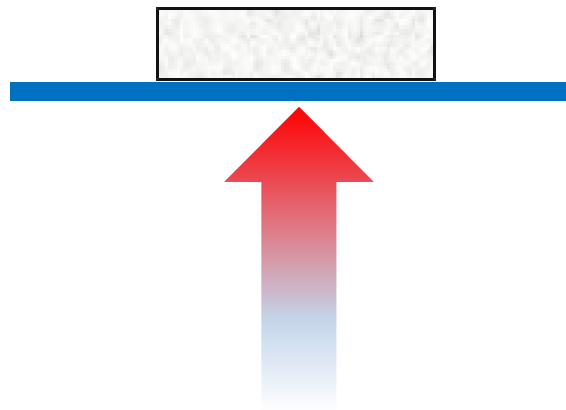


Enhancement of Transmission Raman Signal Using a 'Photon Diode'



Transmission Raman is a powerful technique for analysis of chemical and pharmaceutical mixtures. Where signal intensity or sensitivity is low a technique developed by Cobalt that uses a unidirectional mirror, or photon diode, can boost signals from powders and tablets by up to 10x.

Transmission Raman spectroscopy (TRS) can be used for rapid and accurate compositional analysis of pharmaceutical tablets and powders. TRS is well suited to this as it provides information on sample composition for the entire volume, thus avoiding subsampling issues.^{i,ii} The sensitivity of the Raman method in general is typically limited by the signal-to-noise ratio (S/N) of spectra collected from the sample. Improving collectable Raman signal is highly desirable and results directly in improved S/N ratios.

Here we describe a proprietary method developed specifically for boosting detected signals in powders or tablets by TRS. This is accomplished without changing laser power or acquisition time. The

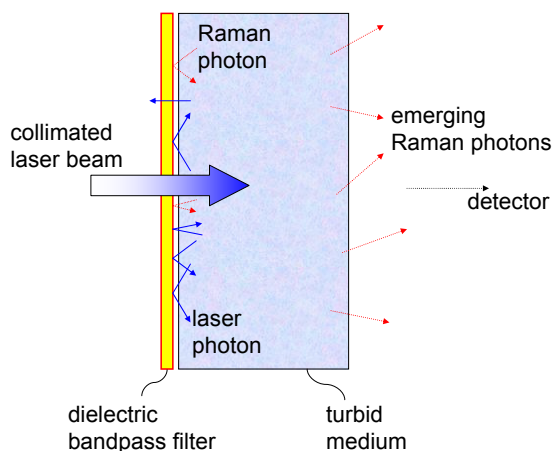


Figure 1: 'Photon Diode' principle.

enhancement is achieved using a multilayer dielectric element placed in the proximity of the sample, which is typically a highly scattering formulation. This can yield an increase in the TRS signal of 5-10x. The benefits are an enhanced signal-to-noise ratio and therefore higher sensitivity or increased penetration depth. Comprehensive details have been published elsewhere.ⁱⁱⁱ

Photon Diode

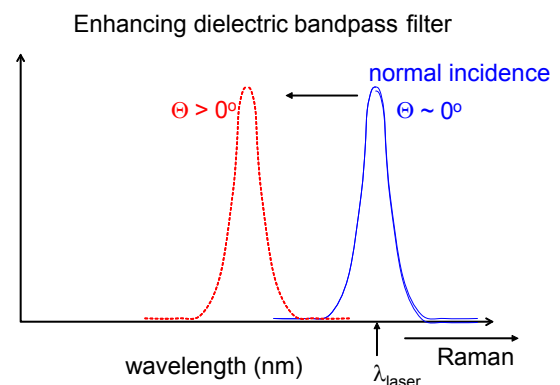
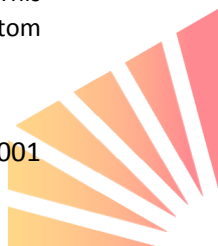


Fig 2: Reflectivity changes with angle of incidence.

Typically, most photons do not penetrate much past the sample-to-air interface on the laser illumination side of the sample. This loss is caused by the turbidity (scattering nature) of the sample allowing the light to re-emerge and escape from the sample – often more than 90% of the laser light is 'lost' in this way. This loss can be greatly reduced by placing a custom



‘unidirectional’ mirror in near contact with the sample. The properties of the mirror are such that the incident semi-collimated laser radiation is allowed to transfer into the sample through the mirror, but the escaping photons, re-emerging from the sample at random directions, are reflected from the mirror back into the sample (see Fig. 1).

Spectral transmission and reflection of dielectric elements are strongly dependent on the angle of photon incidence, with the profile shifting to shorter wavelengths as angles increase from normal incidence (see fig. 2). A narrow bandpass filter designed to transmit the laser beam at normal incidence acts as a mirror for randomly scattered photons as they re-emerge from the sample at non-normal angles and reflects them back into the sample. This increases the photon density in the sample and consequently the signal collected by TRS.

Results

A demonstration of the enhancement was carried out in a TRS experiment on a 6-7mm thick acetaminophen (Paracetamol) powder sample. The measurement was performed with the enhancing element first inserted and then removed (see Figs. 3 and 4). A substantial enhancement of $\approx 8x$ was achieved with the enhancing element.

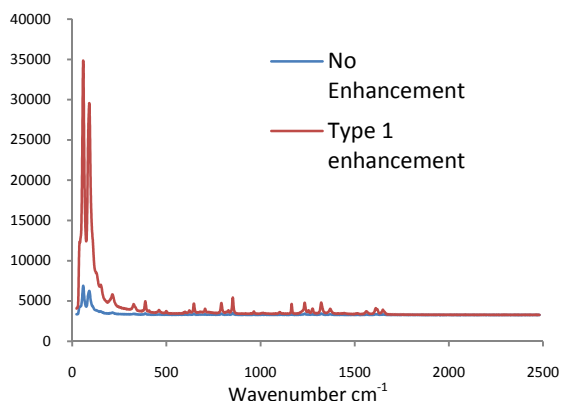


Figure 3: Demonstration of the enhancement of a 6-7mm thick acetaminophen powder sample.

The observed enhancement exhibits good reproducibility and no undue signal fluctuation was observed when the filter was in place. In addition,

the signal was enhanced uniformly across the entire spectrum comprising also the low wavenumber phonon mode region (the more intense components, which are directly due to crystal/polymorph vibrations) as would be expected for a linear enhancement process. This is important in analytical applications involving complex analytes where the spectral pattern serves as means of identifying and quantifying the relative concentrations of individual components.

The spectra were obtained in transmission Raman geometryⁱⁱⁱ on a Cobalt TRS100 platform. The probe beam power was 2W and laser wavelength 830nm. The laser illumination and Raman collection areas were $\approx 4\text{mm}$ in diameter. The acquisition time was 1s.

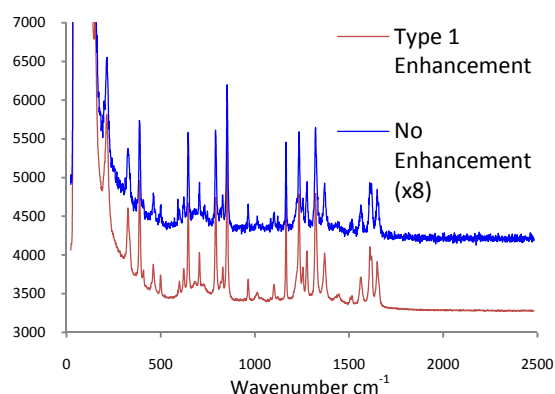


Fig. 4: The acetaminophen spectra scaled to the same height to illustrate the benefits to signal-to-noise.

The photon diode is most easily applied to flat or near-flat samples and is most useful for tablets or powders.

Conclusions

It is shown that a substantial signal enhancement can be achieved using a ‘photon diode’ inserted in the proximity of a scattering sample such as a tablet or powder. This results in greatly reduced acquisition times or in improving S/N ratio for an increase in analysis sensitivity.

i P. Matousek, A.W. Parker, *Appl. Spectrosc.* **60**, 1353 (2006).

ii C. Eliasson, N.A. Macleod, L. Jayes, F.C. Clarke, S. Hammond, M.R. Smith, P. Matousek, *J. Pharm. Biomed. Anal.* **47**, 221 (2008).

iii P. Matousek, *Applied Spectroscopy*, **61**, 845 (2007).