

The Process Spectroscopy Column

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What is process spectroscopy? Should my organisation be considering it, and if so, how should we approach it? These are the questions this column will try to address over the forthcoming editions of *Spectroscopy Europe*. We will look at the spectroscopic techniques that can be used, emerging and new technologies and stories where spectroscopy has been successfully applied to industrial processes. Maybe we can even prompt some discussion of the topic in these pages.

To start at the beginning, what is it and why should we be doing it? We can define process spectroscopy as the application of a spectroscopic technique to perform an analytical measurement on a manufactured product in a more timely and cost effective way than traditional laboratory analysis. This can range from a simple at-line or near-line analysis performed on a spectrometer located nearby the process to a full blown in-process measurement providing a signal which is used not only to monitor but

also to control the process. A good example of the at-line approach is the acceptance of NIR spectroscopy to measure Iodine Value in place in the traditional wet chemistry method,^{1,2} where a two minute spectrum accumulation and partial least squares (PLS) calculation replaces a titration method taking some twenty minutes. An example of full control is the use of Raman spectroscopy to control the manufacture of titanium dioxide and ensure the correct ratio of the two crystal forms in the finished product,³ with substantial cost savings to the company concerned.

The first reason for doing process spectroscopy is already becoming obvious: cost savings; the second and equally important driver is measurement, control and improvement of product quality. Finally, safety can also be a key factor in adopting on-line spectroscopic measurements. Cost reduction can be achieved through increased plant utilisation, for example monitoring of reac-

tion end-points can enable more production batches to be run on existing plant. Getting it right first time through monitoring and control reduces scrap and re-work. Faster analysis at the point of manufacture or use reduces inventory and speeds up time to market. Most spectroscopic techniques will produce results every few minutes compared with the traditional single sample measured in the lab at the end of the batch. So, spectroscopy often gives a better measure of quality than other methods and the ability to run multiple spectra quickly throughout the manufacturing cycle provides more data to work with. In-process data can flag problems early allowing corrective action to be taken before costly re-work becomes necessary. Many spectroscopic techniques are non-invasive and provide the opportunity to measure hazardous chemicals without exposing operators and analysts to the risks involved with taking samples for off-line analysis.

The US Food and Drug Administration, in partnership with the pharmaceutical industry has recently set up an initiative to promote the use of process analysis, mainly, but not exclusively, using spectroscopic techniques. Readers interested in more detail on cost and quality drivers for process analysis are referred to www.fda.gov/cder/OPS/PAT.htm.

If you are still with us, and as a reader of *Spectroscopy Europe*, you will probably agree that process spectroscopy is a good thing. So why isn't everybody doing it already, what are the barriers that hold us back? There are probably three: **Cost**, **Culture** and **Calibration**. First, spectrometers can be expensive (at least when compared with the thermocouples and pH probes that have traditionally been used) and designing them for reliable on-line operation doesn't make them any cheaper! So it's important to quantify the benefits early in any project, because eventually the men with the money will want a cost-benefit analysis and it's sensible to address this during the project selection phase. While instrumentation can be expensive, it is a drop in the ocean when compared with the cost of new plant and increasing the throughput of existing plant using spectroscopy rather than building new capacity makes financial sense. There are savings to be made in time, inventory, materials for the existing analytical methods and labour, which can readily justify the capital cost of spectrometers. This means that process spectroscopy is often applied to

either high volume or high value products.

Culture can be another major hurdle. Asking plant operators to make spectroscopic measurements (albeit with automated analytical methods) isn't always received with boundless enthusiasm, although the more enlightened will see the improvements gained by changes in working practice as being to their long term benefit. Lab analysts may feel threatened by "their" measurement being taken out of the lab, but the analyst then becomes the guru who can implement and support multiple process spectroscopy projects. Maybe the biggest cultural barrier is the "them and us" attitude between manufacturing and the laboratory. Manufacturing rightly see their job as making as much material as possible as rapidly as possible and the analytical department are perceived as the "police" who suddenly pounce and declare a batch of newly-manufactured material to be out of spec. Changing the culture to one where manufacturing and analytical work together to produce product "right first time" is not always a trivial task and requires commitment from both sides, together with support from management.

Calibration is always seen as an issue for process spectroscopy, but needn't be. The perception that all spectroscopic techniques absolutely require lengthy and costly calibration with hundreds of calibration and validation samples may have been true of some spectroscopic techniques and some instrumentation in the past, but is rapidly becoming a modern myth. It is true that, NIR, for

example, requires calibration and validation, but some types of instrumentation require far fewer samples than others. Calibration-free methods for NIR are being researched and even simpler algorithms such as rolling standard deviation can detect reaction end points without any requirement for calibration. Many other spectroscopic techniques also have only a small calibration burden: mid-infrared and Raman spectroscopy often require only a simple univariate model (peak height/area), as does mass spectrometry. UV/vis spectroscopy is ideal where a colour change is involved and again simple univariate models often suffice.

In conclusion, process spectroscopy is an exciting and growing field, poised to become far more important to all of us. Next time we will look at the relative merits of the plethora of spectroscopic techniques available for on-line use.

References

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