Title

Chemometric Data Evaluation

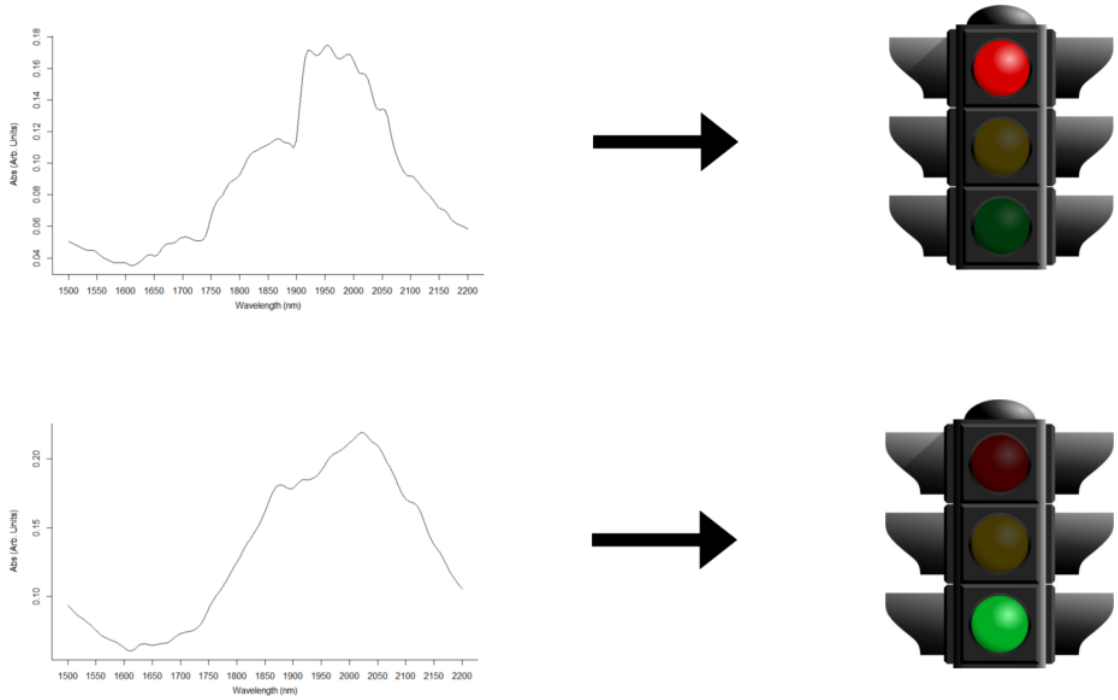
Problem Statement

There is no shortage of instrumental analysis techniques to apply to products in the pharmaceutical industry. However, ensuring that the maximum amount of actionable data is gleaned to enable better decision making is non-trivial

Approach

Application of advanced algorithms and multivariate data analysis to turn scientific data into useful information

Result



The two spectra displayed on the left are not immediately actionable, however the information required to make decisions about a process is contained within them. Using chemometric methodologies this information can be surfaced and presented in a way that makes sense – such as a “traffic light system.”

Impact

These tools enable the use of process analytical technology (PAT) to assist operators make informed, real time decisions or allow implementation advanced process control (APC) systems.

Title

Soft Sensor Modelling

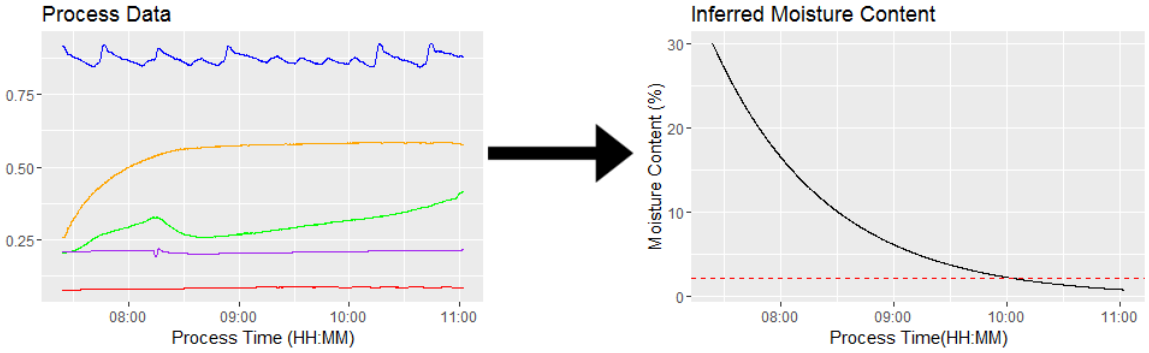
Problem Statement

The amount of data stored during manufacturing processes is increasing year on year. However, direct measurement of a key quality attribute (KQA) is sometimes not possible.

Approach

Often KQAs are intrinsically linked to other easier to measure parameters. For example, moisture content within a dynamic drying process is often not measured within the process equipment although this is a KQA. Modelling of the temperature differential between input and output air is one way to infer the moisture content without direct measurement.

Result



The image on the left is typical of what is produced during manufacturing processes, the information is hard to decipher. Analysing the signals using mathematical and statistical methodologies allows the image on the right to be produced. This shows much more relevant information from a process standpoint (*i.e.* the correct moisture content was reached at 10:00). The algorithms used are often lightweight enough to be implemented in real time.

Impact

Inferential measurements are able to estimate KQAs based on data that is routinely acquired during a manufacturing process. This enables real time tracking of desired values rather than arbitrary measurements

Title

Prediction of H_2O content of a powder using a through vial measurement

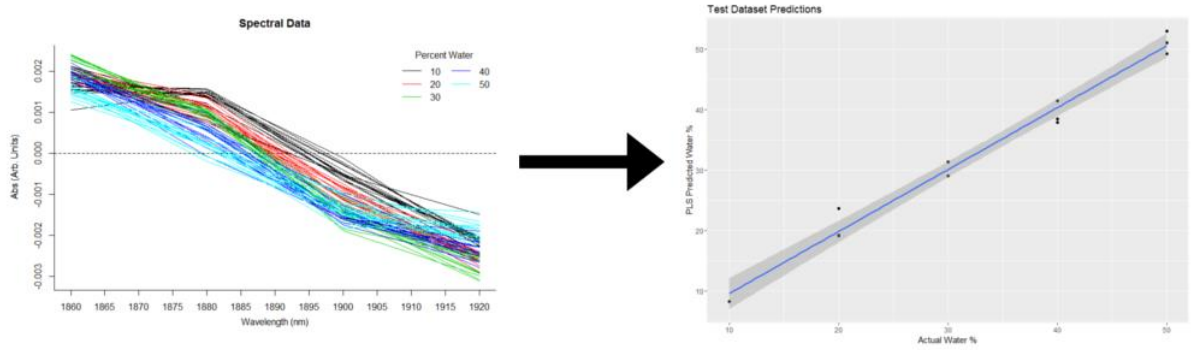
Problem Statement

Direct quantification of moisture in a powder involves a labour intensive process (LoD measurements, Karl Fischer analysis *etc.*). A faster, less invasive method would be desirable.

Approach

Near Infrared (NIR) spectroscopy is well suited to the measurement of H_2O content. A method was developed which involved a through vial measurement coupled with chemometric analysis to predict the moisture content within a powder sample.

Result



Measurement of each vial of powder takes less than one second, applying some advanced data analysis allows water content to be predicted. The graph on the right shows the predicted vs the measured (by reference method) values. The Error is within 5 %

Impact

Development of analytical methods to infer properties allow more samples to be tested in a shorter time frame and for less cost without compromising on accuracy.

Title

API Content Uniformity Across a Tablet Surface

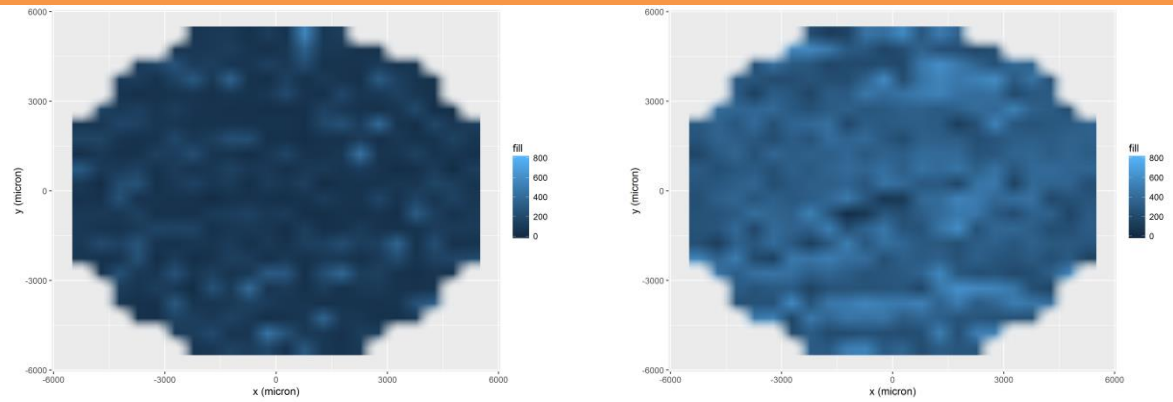
Problem Statement

When a drug formulation is tabletted it is desirable to ensure a uniform distribution of the API is each tablet. Current methods of testing this involve dissolution of the tablet and measurement of API concentration. This ensures that the API content in solution is correct but preserves no information about the solid state form of the API, or information about distribution in the tablet itself (*i.e.* if a half dose is required, can the tablet be safely split in half?).

Approach

Raman spectroscopy is tool which enables molecular specific analysis of chemical samples. For this study *ca.* 400 points were recorded across a tablet surface. From this a map was built of the distribution of the API using statistical methodology.

Result



The images show tablets with 20 (left) and 70 (right) % by weight of API, the lighter blue indicates a higher concentration of API. Domains of higher API concentration can be observed in the right hand image, suggesting that the API may stick together when flowing into the tabletting machine.

Impact

In the example above measuring content uniformity in this way allowed more information about the formulation to be gained that with traditional content uniformity methodologies. Additionally this process is highly automated and very quick. Full mapping of a single tablet takes less than one hour, with a manned time of under five minutes.

PMTC
Advanced Technology Solutions in Pharmaceutical Manufacturing

Title

Predictive Measurement of Tool Dulling

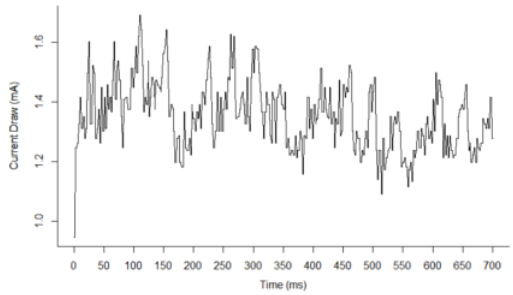
Problem Statement

During the manufacturing process for a medical device, a number of concurrent cuts are made within a work piece. Over time the blade of the cutting tool begins to dull and the process becomes less efficient causing multiple unit failures. Currently the tool is inspected at specified intervals, however by this point the problem may have already occurred causing losses in plant time; produced units and energy.

Approach

Using the current draw of the motor while a cut was taking place, some statistical data analysis was able to find patterns which gave an early indication if the tool was about to fail.

Result



Impact

Early detection of tool maintenance requirements allows for less failures during manufacturing. Additionally once a dataset of tool health versus units produced is built up the data can be further mined to create predictive algorithms to plan for tool maintenance allow better resource allocations and plant time planning.

Title

Early Deviation Detection in Batch Manufacture

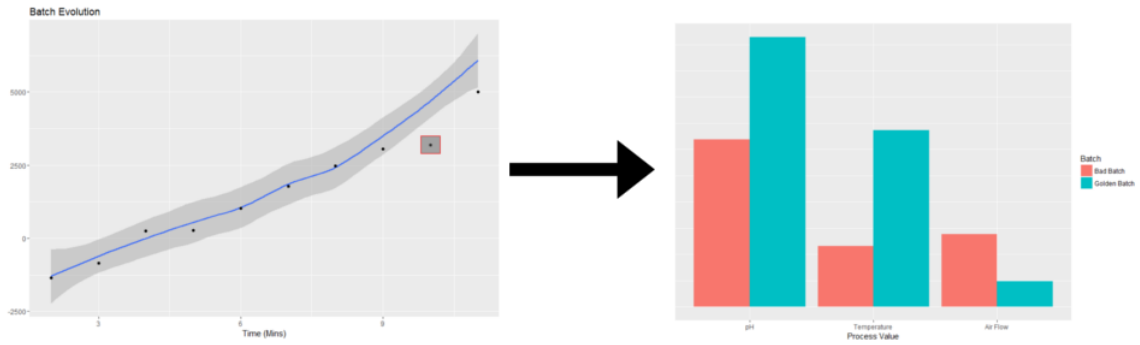
Problem Statement

During batch manufacturing it is often too late to remedy a process once it is identified as being out-of-control. This is usually because the root cause of the problem is not immediately apparent. A real-time system where misperforming batches can be identified and out-of-control parameters displayed would be advantageous.

Approach

Statistical modelling of in-control batches allow the evolution of a "golden" batch to be defined. New incoming data points can be evaluated against this evolution in real-time. Out of control points can be drilled-down into to display individual parameters (or combination of parameters) which are causing the problem.

Result



Impact

An analysis such as this allows a real-time monitoring paradigm where root causes can be displayed rapidly. This in turn will allow ill performing batches to be identified and stopped before the product is wasted.