Online Spectral Imaging in Process Analytics

Introduction to Spectral Imaging

Spectral Imaging or Chemical Imaging is the determination of the chemical identity of species and the visualization of its distribution. Optical spectroscopy is able not only to detect the chemical substrate by its wavelength specific absorption but also to detect differences in the wavelength dependent scattering behavior of particulates [1]. The laterally resolved spectroscopy produces a three-dimensional data cube with two local axes, x and y and a spectral axis λ. Figure 1 illustrates the essential differences of the different techniques used to measure spectral images. In the so-called Whiskbroom Imaging ("mapping"), defined object areas or the entire object is measured point-by-point. This type of imaging is very flexible in relation to the object and the grid size and generally requires only a single detector; such as a photomultiplier tube (PMT) or a diode array (DAD). A "staring" imager ("imaging") takes two-dimensional images in a series, one after the other, at several wavelengths. A prerequisite for this technique is that the object must remain stationary during the measurement ("Stop Motion"), thus only atline applications can be realized [2-4].

In Pushbroom imaging ("line scanning") the object is imaged along the x-axis using the line-scan method and is recorded in full through the movement of the object in the y-direction. Figure 2 illustrates this principle, which consists of a spectrograph and an appropriate camera system. Through an entrance gap in the spectrograph (x-spatial dimension), the light is routed into a prism-grating-prism optical arrangement and then spectrally resolved onto the second dimension of the camera. The second spatial dimension (y) is achieved through the movement of the object. In contrast to Whiskbroom and Staring Imaging, the Pushbroom system is fully online/inline capable, where for each line, under time-defined conditions, images can be generated and evaluated.

Example: Active Pharmaceutical Ingredient in a Tablet

Since 2002, the food and drug administration (FDA) has strongly encouraged the process analytical technique (PAT) for a better understanding of the process and to achieve a higher control of the pharmaceutical manufacturing process [1,4]. An ideal situation would be to control inline 100 % of the tablet and the particle size and the homogeneous distribution of the active ingredient. In the literature, there are numerous methods which use of NIR, IR, Tera-

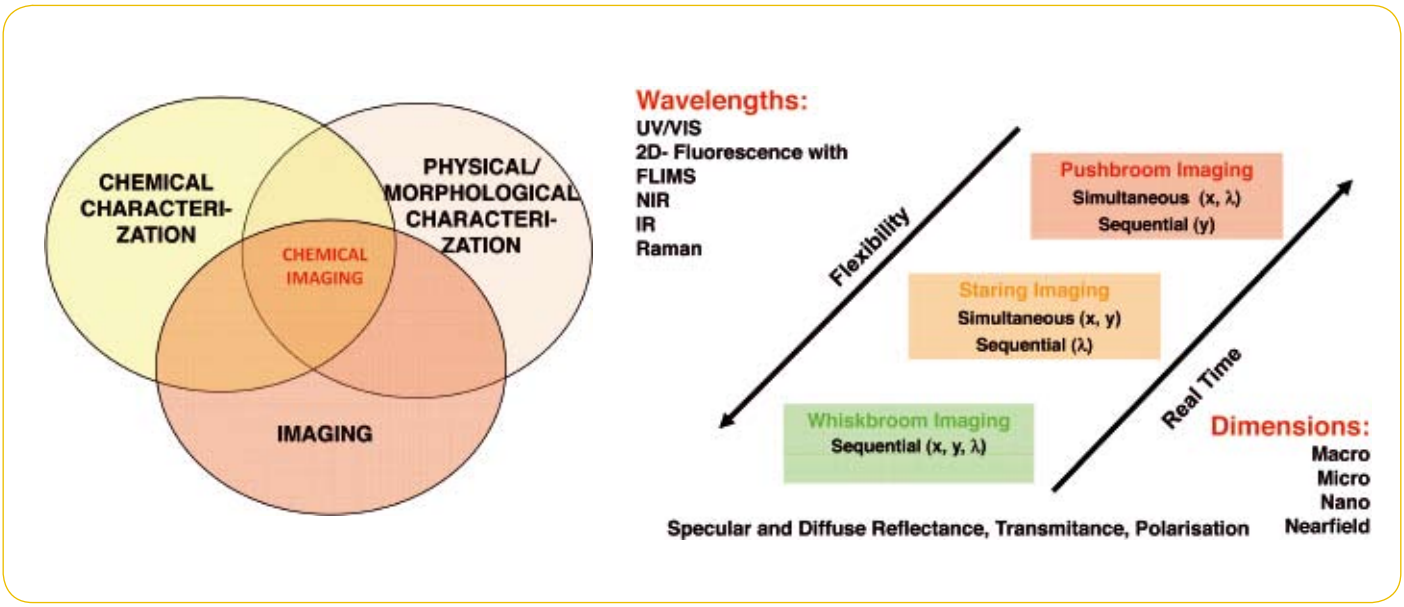

Fig. 1 left: defining Spectral (Chemical) Imaging; right: taxonomy of the imaging spectroscopy methods

hertz and Raman spectroscopic imaging[1,4,5]. Figure 2 shows as an example of an image and the spectral attributes of aspirin in cellactose. Figure 2 also shows a pushbroom imager which can be used to analyze online the spatial distribution of an API for 100 % quality control.

The problem with measurements in reflection is always the question regarding the penetration depth of the light and the scale of scrutiny, as dependent on the scattering and absorption.

Separate Absorption from Scatter: Penetration Depth

Dispersions, emulsions or solids like powders show the wavelength dependent superposition of the scatter and absorption of light. In standard multivariate data analysis in PAT, the focus of the chemometric treatment of the spectroscopic data is given on the suppression of the unwanted perturbation of multiple scatter. A better approach may be to extract not only the chemical information but also the information "morphology" from the spectra rather than to eliminate them. One of the most appropriate theories to describe multiple scattering and absorption in opaque systems is the radiative transfer equation (RTE). The approach of Kubelka and Munk (K-M) is the simplified solution of the radiative transfer theory. The diffuse reflectance and transmittance of a sample with defined thickness are described by a scattering effect S and an absorption effect K. Thus at least two independent measurements are necessary to separate S and K from the measured spectra [6,7]. Even more, specular reflected light of the surface may even produce more spectral artefacts than scatter [6,8]. However, these artifacts can easily be removed using parallel and crossed polarizers. Furthermore, if the scattered photons are locally resolved and separated from the point- illumination, the resulting spectra allow the quantification of the penetration depth of the photons through different layers. Therefore, the objective to obtain unperturbed chemical images of an API in an opaque system must include the separation of the superimposed information of the specific absorbance (labelled as "k-spectra") of the API and the excipients, the strong scattering effects (labelled as "s-spectra") induced by a diffusion of photons through the different layers of the opaque system and in addition the separate determination of the specular reflected light from the surface of the tablet. The scatter and absorption cross sections determine the penetration depth of the photons and therefore the information depth ("scale of scrutiny").

Future Trends [2]

Focus in the pharmaceutical industry is given mainly on three different uses: blend uniformity of powders and tablets, composition and morphological features of coated tablets and granules, spatial changes during hydration, degradation and active release. Counterfeit pharmaceutical

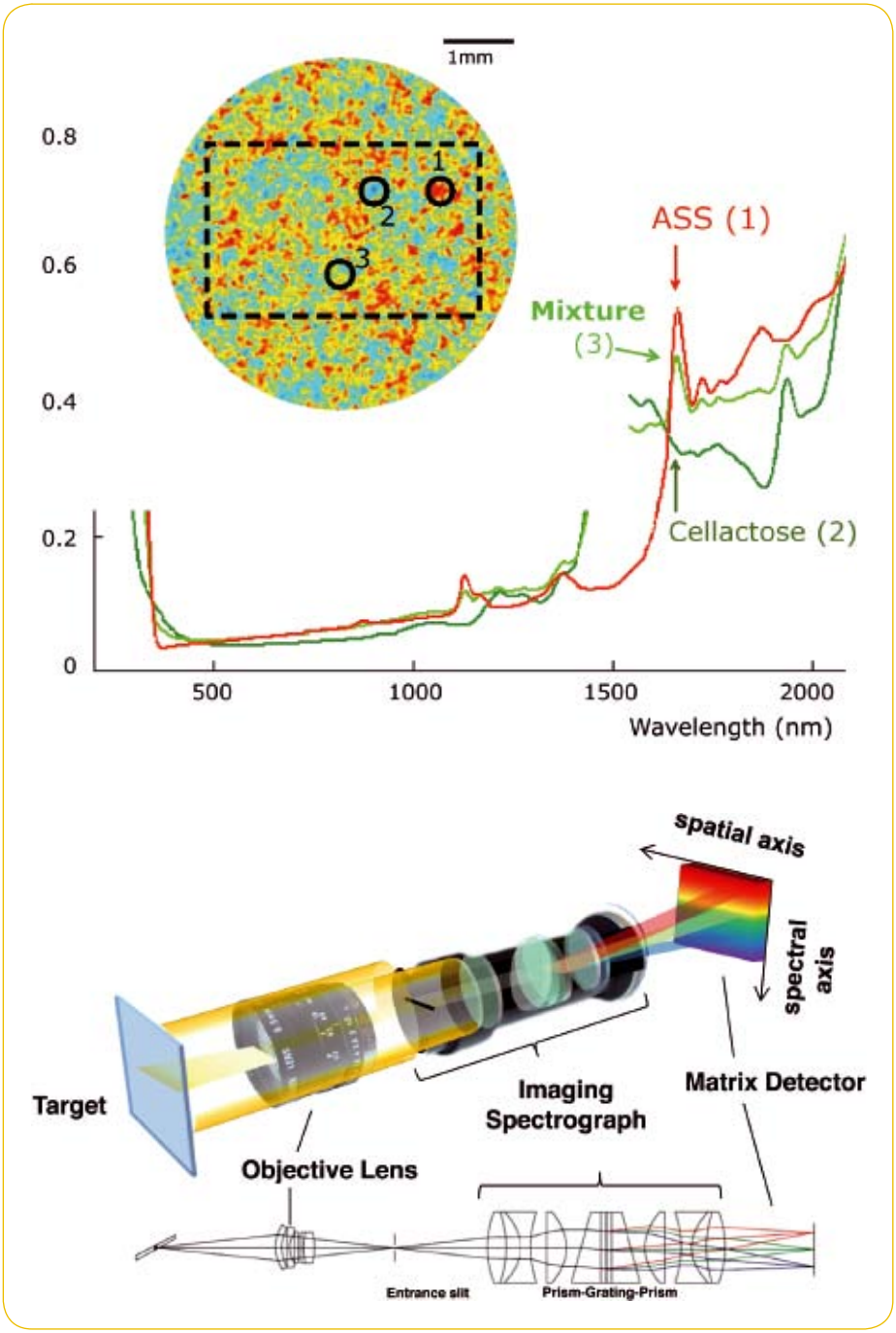

Fig. 2: VIS-NIR diffuse reflectance spectra of a 300 mg Aspirin (ASS)-tablet (insert: microscopic representation at 1660 nm); Pushbroom Imager for online control (by courtesy pf Specim Ltd.)

She highly appreciates the contributions of Yongmin Liu to the general understanding of this work and of Lukas M. Eng to the idea for this project. Moreover, she thanks Lane Martin and Pu Yu for the sample preparations, the groups of Manfred Helm and Lukas M. Eng for the NSOM measurements, and Ramamoorthy Ramesh for hosting this project. products are a real threat to the health of the patients. NIR chemical imaging provides a rapid method for detecting and comparing suspected counterfeit products without sample preparation. The advantage of imaging is that the discrimination of the tablets is not only caused by changes in the chemical composition, but also from its spatial distribution.

Online Chemical Imaging in agriculture is mainly remote sensing. Satellite or aerial remote sensing (RS) technology uses nowadays Pushbroom Imaging Technology in the Vis, s-NIR and NIR-range. Vegetation images show crop growth from planting through to harvest, changes as the season progresses and abnormalities such as weed patches, soil compaction, watering problems etc. This information can help the farmer make informed decisions about the most feasible solution. In food industry, numerous online controls are still made by human vision, especially for sorting bad looking products. Chemical Imaging in food and agriculture can also be used to identify diseases, rot and contaminations by insects e.g. larvae. Fig-

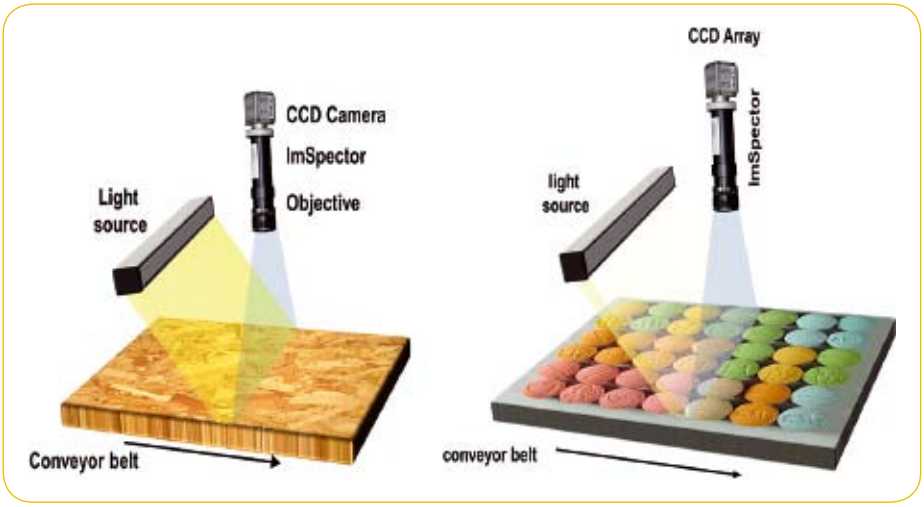

Fig. 3: left: online control of the resin distribution of a fibreboard, right: schematic of a 100 % control of tablets on a conveyor belt.

ure 3 shows the arrangement of a pushbroom imager measuring online the even distribution of the resin on a fibreboard (left) and a possible 100 % online control of tablets.

Diffuse optical imaging (DOI) is a new emerging technique for functional imaging of biological tissues. It involves generating images using measurements in the visible or s-NIR-light scattered across large and thick tissues for detecting cancer.

Instead of using at each individual production step a single spectrometer, a pushbroom imager with attached fiber bundles on its slit allows individual control of the quality at every intermediate and final step. In this case, the pushbroom imager is used as a multipoint information source and can substitute a moving multiplexer. Many fibers per spectrometer can be used for simultaneous measurements. In addition, different spectrometer technologies for UV-Vis-NIR, fluorescence or Raman can also be combined. Thereby the probe becomes a multi information system, which describes the sample in an ideal and complete way.

References are available at the author.

GDCh Kurs

Professor Dr. Rudolf W. Kessler will hold a training course on spectral imaging in September:
Spektrales Imaging (394/11)
Bildgebende Verfahren in der Prozessanalytik
27.–29. September 2011, Reutlingen, Germany, www.gdch.de/fortbildung2011

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