Ultrasound enhanced PAT: increased sensitivity of an in-line Raman spectroscopy probe

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Introduction

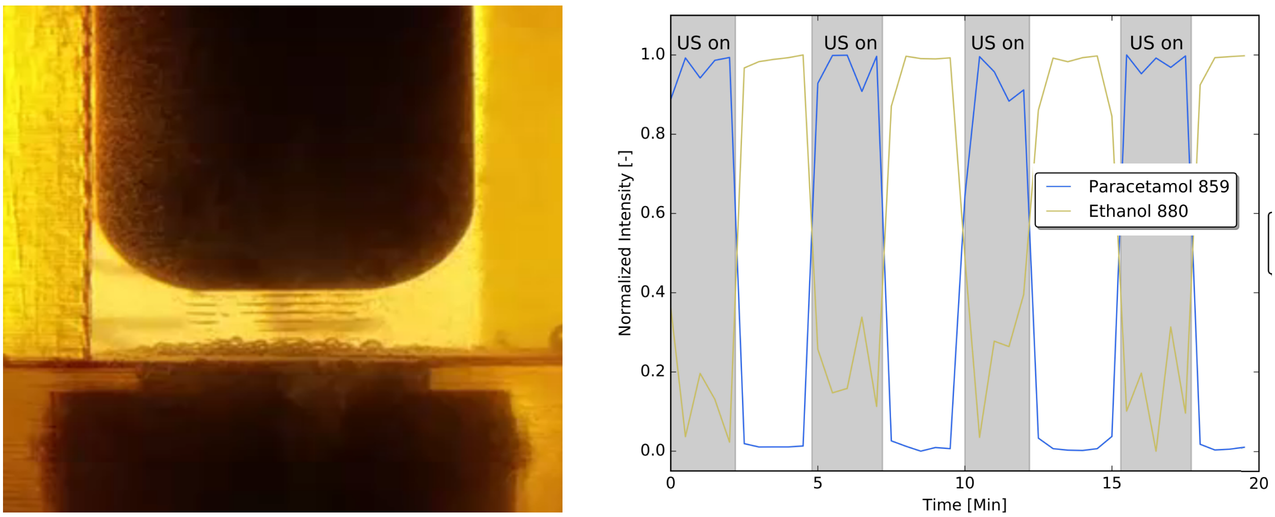
Process Analytical Technology (PAT) is a modern approach when designing and controlling manufacturing processes. One main task is the definition and assessment of Critical Control Parameters (CPP). Novel instrumentation that allow for the in-line measurement, i.e. within the process itself, of CCPs are in development these days.

Raman spectroscopy is a method holding great promise for the in-line monitoring in production processes as it delivers rich information about the analyte, among which are the chemical composition but as well for instance the type of crystal forming (polymorphism). However, due to its quantum-mechanic nature, Raman spectroscopy is inherently low in respect to sensitivity. Only one of 10^8 photons is scattered in-elastically and therefore affected by the chemical composition of the analyte and subsequently delivering the desired information. Therefore we set out to increase the sensitivity of an in-line Raman spectroscopy probe by the exploitation of the well known radiation forces exerted on particles.

These are used to increase the signal-to-noise ratio (SNR) of the measured Raman spectrum. Past work has shown, that the Raman signal of agglomerates brought about by the USW in a cuvette is comparable to the spectra of sediment [1].

Experimental and Results

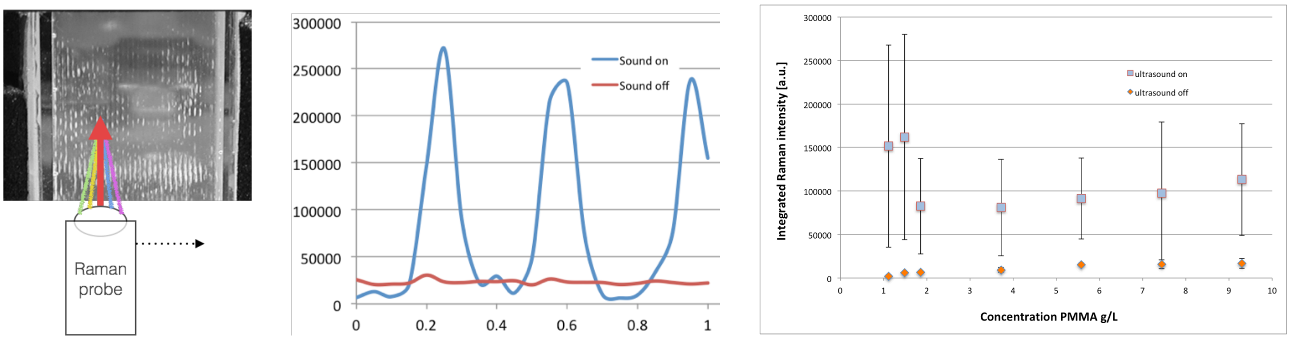
We applied an ultrasonic standing wave (USW) of approximately 2 MHz to form agglomerations of particles in the pressure nodes. This was conducted in a set-up where a Raman in-line probe was situated vis-à-vis an ultrasonic transducer like shown in Fig.1a. The agglomerations visible as thin lines in Fig.1a in the optical path of the probe led to a significant increase of the signal specific for the solid substance – in this case Paracetamol – while the suspending liquid (Ethanol) contributed less to the spectrum, when the sound was on (see Fig.1b).



(a) (b)

Figure 1: (a) Between the Raman spectroscopy probe and the Transducer the concentrated particles are visible as horizontal lines. **(b)** Raman counts for selected wavenumbers specific for the particles (Paracetamol at 859 cm^{-1}) and suspending liquid (Ethanol at 880 cm^{-1}). Clearly the influence of the agglomeration brought about by the ultrasound is detected in an increased reading for the particles and a decreased reading for the liquid when the field is applied.

It was reported before [2], that the increase of signal, when the Raman spectra were taken aiming on a agglomerate was comparable to the intensity achieved measuring a sediment. In this work the improvement was further investigated with suspensions carrying various amounts of particles. In this case a suspension of PMMA beads (ø 3µm) in water was used. The measurements were taken when the Raman probe was aiming on a cuvette equipped with ultrasonic transducers producing an agglomeration pattern like shown in Fig.2a. The relative position was changed during the measurement, resulting in a horizontal scan of the pattern of nodal planes forming when the ultrasonic field was present. Fig.2b shows the result (blue) in comparison with measurements were taken, when the sound was off. The increase, when the signals stemmed from an agglomeration was significant.



(a) (b) (c)

Figure 2: (a) The measurements were taken during a scan, i.e. when the Raman signal was collected while moving a cuvette with the pattern brought about the sound horizontally. In this case PMMA particles suspended in water were used. **(b)** The lines stemming from the nodal planes were detected as periodic increase of Raman intensity. **(c)** When comparing the Raman intensity without the ultrasonic field (red) to measurements, when the USW was present (blue), a significant increase was shown. Data shown represent the experiments repeated in triples, a rise of standard deviation was accompanying the application of the ultrasonic field.

Fig.2c shows the comparison of the averages of three respective measurements with the ultrasonic filed off (red) and on (blue), respectively. The measured spectra were reduced to a number representing specifically the used PMMA beads. Clearly an increase in "integrated Raman intensity" was found, when the ultrasonic field was applied. Although the measurements with sound showed an increased standard deviation (see Fig.2c) as well, a significant increase due the formation of lines and agglomerates brought about by the ultrasound could be detected. The high standard deviation prevents for giving precise factors for the improvement, however a rough estimation delivers at least two orders of magnitude.

Conclusion

We have shown, that applying an ultrasonic field to agglomerate particles in suspension like Paracetamol crystals in Ethanol and PMMA beads in water in the optical path of a Raman spectroscopy probe significantly increases the measured Raman intensity. This leads to an improved SNR, therefore the combination of an USW might be an interesting approach to increase the sensitivity of in-line Raman probes. That means, when taking such measurements within the production process, there is great hope, that an ultrasonic field can improve the in-line assessment of CPPs when applying Raman spectroscopy.

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References (Times New Roman 10 pt)

[1] S. Radel, J. Schnöller, A. Dominguez, B. Lendl, M. Gröschl, and E. Benes. Elektrotechnik & Informationstechnik **125**, 82–85 (2008). DOI 10.1007/s00502-008-0515-2.

[2] S. Radel. *Procs. Acoustofluidics 2017*, *p88,* San Diego, 28 - 29 August 2017.