probes have become popular for *in situ* measurement of the CSD and crystal morphology with ample examples presented in literature.[19,53,54] The obvious advantage of PVM probes is that full information of the crystal shape distribution can be obtained. However, dense crystal suspensions pose challenges for effective use of PVM probes, especially when automated software is used to extract size and shape information, due to overlapping crystals. Furthermore, the method is based on optical measurements with visible light and limited magnification, which reduces the ability to identify fines.

Raman spectroscopy is comparable to FTIR but uses different (and complementary) vibrational and rotational modes to generate scattering of electromagnetic radiation. Therefore, probes for Raman spectroscopy and ATR-FTIR can be combined to obtain complementary data from a crystallization process.[41,55] In particular, in addition to the measurement of solute concentration, Raman is capable of measuring *in situ* the polymorphic form of crystals in suspension.[56–59] Févotte[60] provided a review on the use of *in situ* Raman spectroscopy with a focus on pharmaceutical crystallization and industrial applications. The purity of crystals is difficult to measure in an on-line fashion as spectroscopic methods usually do not have sufficient resolution to measure small quantities of impurities. However, for purity, some form of inferential control can be used by limiting the crystal growth rate *via* supersaturation control.

A more comprehensive and multi-disciplinary review with current trends in PAT, including imaging, spectroscopy, acoustic and electronic sensors has recently been provided by Simon *et al.* (see also Chapter 9).[8] Finally, generally within the pharmaceutical industry, it has been observed that the role of PAT is different during development compared to commercial manufacturing.[34] In particular, during development the use of PAT is widespread and focuses on understanding by using multi-variate measurements from different types of instruments, whereas the use of PAT during commercial manufacturing is more limited and has a more targeted and simplified role with a focus on robustness and reliability. Reasons for the observed limited role during commercial manufacturing include more stringent quality requirements during manufacturing (*e.g.*, GMP compliance, data storage requirements, maintenance, *etc.*), lack of human resources, and the fact that the use of PAT during development may have led to an understanding of how simpler process variables that are critical for quality control can be used as controlled variables during commercial manufacturing.[34]

4.4 Model-free Control Strategies

All model-free strategies are in essence feedback control methods commonly based on real-time measurements of the concentration (ATR-FTIR, ATR-UV/Vis), temperature, or particle counts (FBRM) or their combination. The overall performance of these methods depends significantly on the accuracy and reliability of the PAT. The aim is to either control some property of the