PAT tools have been seen in other types of continuous crystallisation, for example, Powell *et al.* (2016)[226] employed a combination of three components, (a) an integrated PAT array based on attenuated total reflectance ultraviolet/visible (ATR-UV/vis) spectroscopy and focused beam reflectance measurement (FBRM), (b) a crystallisation process informatics software system (CryPRINS), and (c) an ancillary PAT array based on Raman spectroscopy and particle vision microscopy (PVM) to monitor crystallisation and determine when steady state was achieved. This PAT array was also applied to a case-study for the selective crystallisation of 1 : 1 and 3 : 2 co-crystals of *p*-toluenesulfonamide/triphenylphosphine oxide.[227] *In situ* imaging and chord length distribution measurements were integrated for estimation of particle size and shape.[228] *In situ* monitoring of stirring effects on polymorphic transformations during cooling crystallisation of carbamazepine was carried out.[198] Image-based monitoring was also used for early detection of fouling in crystallisation processes.[167] Real-time image processing based online feedback control system was employed for cooling batch crystallisation[229] and for the investigation of the evolution of crystal size and shape during temperature cycling and in the presence of a polymeric additive.[230] Mathematical modelling and/or experimental validation were reported in MSMPR crystallisers for cooling crystallisation,[231] for antisolvent crystallisations,[232–234] for modelling of artefacts in estimations of particle size of needle-like particles from laser diffraction measurements,[235] for fines removal by optimizing spatial temperature profiles with controlled dissolution,[236] and for nucleation kinetics of butyl paraben.[237]

3.6 What Are the Opportunities and Challenges?

While new applications for OBC/COBC are emerging, *e.g.* sonocrystallisers,[238] microwave reactors, reactions incorporating dynamic separation, continuous hydrogenation and functional carbon nanotubes,[239] the following are some opportunities in crystallisation for COBC.

3.6.1 Reactive Crystallisation

Reactive crystallisation has been run as two separate unit operations in traditional batch operation but a tubular continuous reactor/crystalliser presents the unique opportunity of treating it as a single continuous process. One example is the reactive crystallisation of paracetamol,[240] where the solubility for crystallisation was first optimized, from which suitable reagent concentrations for the reaction part were retrospectively determined. The effects of water content and reaction temperature on reaction kinetics and mechanism as well as product purity were jointly investigated using chromatographic methods. Paracetamol form I particles were produced with the presence of water, while 4′-acetoxyacetanilide was identified in the reaction in the absence of water.[240]