

also reconfigurable and 25% smaller [0.5 m (width)  $\times$  1.0 m (length)  $\times$  1.3 m (height)],<sup>14</sup> which was achieved among other things by applying PI principles for continuous crystallization (e.g., a compact two-stage MSMR cascade with pressure-driven slurry transfer).<sup>26</sup>

Ultimately, the increasing trend towards continuous manufacturing in the pharmaceutical industry and the accompanying academic research for compact manufacturing platforms<sup>12,14</sup> requires the attention of the vendors of process analytical technology (PAT) to provide solutions for the customers' needs.<sup>304,305</sup> For instance, Mettler Toledo has developed their in-line ATR FT-IR system, known as FlowIR, to meet the demands of flow chemistry.<sup>306</sup> Similar necessary innovative solutions will be needed to support the PI efforts in small-scale continuous crystallization integrated in compact platforms to monitor and maintain the process within its design space (see Chapter 4 for further details on control strategies). For instance, key challenge often overlooked is the physical size of probes in combination with control boxes. Thus, PATs suitable in size (miniaturization) but with the same accuracy as laboratory bench devices are needed.<sup>305</sup> In this context, handheld PATs, already implemented in the pharmaceutical industry for raw material validation and cleanliness checking,<sup>307</sup> could be a potential solution besides innovative compact sensor arrays. However, commercially available handheld devices are currently lacking in adaptors to allow them to be used as plug-and-play PAT in everyday crystallizer setups and thus require further development efforts in the future.

## References

1. ACS, Sustainable US Manufacturing: Chemical and Allied Industries Technology, Technology Area 4: Next Generation Chemical Manufacturing, <https://www.acs.org/content/dam/acsorg/sustainability/acsandsustainability/sustainablemanufacturing/roadmaps/smrt-technology-area-4-next-generation-chemical-manufacturing-pdf.pdf>, accessed September 28, 2017.
2. K. Knoerzer, P. Juliano and G. W. Smithers, *Woodhead Publishing Series in Food Science, Technology and Nutrition*, Woodhead Publishing, 2016.
3. C. Jiménez-González, P. Poehlauer, Q. B. Broxterman, B.-S. Yang, D. am Ende, J. Baird, C. Bertsch, R. E. Hannah, P. Dell'Orco, H. Noorman, S. Yee, R. Reintjens, A. Wells, V. Massonneau and J. Manley, *Org. Process Res. Dev.*, 2011, **15**(4), 900–911.
4. A. Stankiewicz, *Chem. Eng. Prog.*, 2000, **96**(January), 22–34.
5. J.-C. Charpentier, *Chem. Eng. J.*, 2007, **134**(1–3), 84–92.
6. S. Becht, R. Franke, A. Geißelmann and H. Hahn, *Chem. Eng. Process.*, 2009, **48**(1), 329–332.
7. T. van Gerven and A. Stankiewicz, *Ind. Eng. Chem. Res.*, 2009, **48**(5), 2465–2474.