boundaries and achieve enhanced performance compared to separately operating functions. A simple example in the area of crystallization is reactive crystallization, also known as precipitation, which combines reaction (liquid) and separation through the generation of a new solid phase within a crystallizer.[3,182] Combining crystallization and other separation and purification technologies (*e.g.*, chromatography, membranes, distillation) into hybrid processes is a strategy that generates synergistic effects, often attributed with cost efficiency by reducing process time, equipment size, and energy costs. Generally, hybrid processes are characterized by the combination of at least two different unit operations that contribute to the separation task by different physical separation principles and the design and optimization of these processes are highly complex due to the large number of structural and operational degrees of freedom.[183–187] While the concept of hybrid processes is generally aimed to overcome the limitations of the individual unit operations, the process integration approach within the function domain is aimed to reduce processing time, energy consumption, and equipment cost by integrating multiple unit operations (*e.g.* crystallization and agglomeration) into one.

7.4.1 Hybrid Processes

7.4.1.1 Chromatography-crystallization Process

Chromatography is a unit operation commonly used to separate mixtures of chemical substances into their individual components based on their differential partitioning, which leads to a difference in the residence time of the individual component within the chromatography column. However, due to the relatively high cost of the stationary phases (adsorbents), the capital cost of chromatography remains high compared to crystallization.[188] On the other hand, crystallization is strongly affected by the presence of impurities, especially those possessing similar/identical solid–liquid equilibria (*e.g.*, structurally similar impurities and enantiomers). Therefore, in recent years, there have been an increasing number of studies on the combination of continuous chromatography and crystallization as a hybrid separation process aimed at generating a synergistic effect, in particular for the separation of enantiomers.[188–190] The basic principle of this approach will be briefly discussed in this section. For further fundamental details on enantiomer separation by chiral crystallization in hybrid settings, the interested reader is referred to Chapter 12 and to the review by Lorenz and Seidel-Morgenstern.[190]

Generally, chiral separation can be realized by countercurrent moving bed chromatography, where the mobile phase (fluid) and stationary phase (solid) move in the opposite directions. The more retained enantiomer adsorbs to the stationary phase and the less retained enantiomer moves with the mobile phase. Consequently, collecting the concentrated enantiomers at both ends of the chromatographic column leads to the separation