

This chapter aims to address each of these basic control questions. An overview of typical variables to be controlled in continuous crystallization processes is provided followed by an overview on how to measure process variables for control applications. Furthermore, a discussion on available manipulated variables will be presented, which will be structured according to the common types of crystallizers available in industry, as available manipulated variables are strongly related to the basic crystallizer design. Finally, common control strategies will be discussed that bring together controlled, measured, and manipulated variables in automated control loops. A distinction is made between three main control strategies that have been developed and implemented for crystallization processes: model-free, model-based and hybrid techniques.<sup>12</sup> The key features of model-free and model-based control strategies are presented. The focus is on solution crystallization, which is the most common and versatile type of industrial crystallization. The chapter ends with an outlook for future developments.

## 4.2 Controlled Variables

Variables that are of interest to be controlled for continuous crystallization processes include simple process variables such as temperature, pressure, volume, and liquid-phase composition and variables related to the intrinsic crystal quality attributes. With the exception of liquid-phase composition, automated control loops can be developed readily for simple process variables, as they are not unique to crystallization processes. However, crystal quality attributes are important to be controlled to improve downstream processing and product functionality, as discussed, and are much more challenging to control effectively. Common crystal quality attributes that are of interest to be selected as controlled variables include:

1. *Purity*; solvent inclusion, presence of foreign molecules
2. *Solid-state form*; various polymorphic forms, solvates, hydrates, salts, co-crystals
3. *Crystal habit*; aspect ratio, shape distribution, specific surface area, *etc.*
4. *Crystal size distribution*; various size definitions exist depending on the measurement instrument.

The purity of a crystalline product can be affected by mother liquor adhering to the crystal surface, inclusion of foreign molecules in the crystal lattice, or entrapment of mother liquor in a crystal particle. Adhesion of mother liquor is related to the crystal habit and CSD and can be mitigated *via* washing. The physical principle of crystallization does not easily allow for foreign molecules to be incorporated in a crystal lattice, but might be of significance if the foreign molecule has a similar molecular structure or when the crystal