as well as the parameter estimation and validation strategies. Different parameter estimability or practical identifiability techniques were developed in many disciplines and research areas to enhance the prediction capability of the mathematical models, mitigate the effect of parameter correlation and inform the design of more optimal experiments that maximize the information content of the collected data.[109,110] A combination of a sequential orthogonalization techniques and Sobol proved particularly effective to enhance 1D and 2D population balance models and demonstrated more reliable predictions of the aspect ratio and effect of crystal shape modifiers.[111] As mentioned, the mathematical model of the crystallization process can be linearized to reduce the computational burden inherent to real time solution of the nonlinear dynamic optimization problem provided that the model remains sufficiently accurate. For instance, the Jacobian linearization can be performed over the prediction horizon at discrete operating points, in a successive linearization sequence. More recently, a more effective global state feedback linearization (SFL) technique was implemented as a multi-input multi-output MPC for batch and continuous crystallization.[112] Furthermore, the computation costs inherent to NMPC can be addressed by implementing a parallel solver based on for instance the parallel Schur complement method.[113]

4.6 Fault Detection and Isolation

Continuous crystallizers often exhibit a high level of automation, which gives a distinct advantage compared to batch crystallizers. However, automation also introduces risks due to instrumentation malfunctioning. Therefore, when defects occur in process equipment, sensors, actuators or somewhere else in the control loop, appropriate action should be taken to prevent significant loss. An effective fault control strategy should include at least reliable identification of fault occurrence (*i.e.*, detection) and some form of fault handling procedure (*i.e.*, controller reconfiguration after possibly fault isolation in case of multiple actuators), which all has to be supported by robust controllers. For example, in the case of an MSMPR crystallizer without fines dissolution and a single feed stream used as manipulated variable, a second redundant feed stream could be present as backup in case of an actuator fault in the default feed stream. Alternatively, switching between different types of control loops can be considered. For example, using either an inlet flow rate or a rate of fines dissolution as manipulated variable to control a characteristic of the CSD.

El-Farra and Giridhar proposed a systematic framework for actuator fault detection and fault-tolerant control for continuous crystallization.[99] The framework is based on a process model involving a population balance, control constraints, and a limited number of process measurements. The framework builds upon nonlinear model-based controllers and state estimation as