

10.3 Development of Continuous Protein Crystallisation

The general strategy for developing protein crystallisation is shown in Figure 10.1. It starts with the high-throughput screening of crystallisation conditions and then proceeds to the scale-up of the crystallisation process up from the nanolitre/microlitre scale of screening experiments to a typical scale of 1 mL in batch shaking mode. Once successful, the crystallisation process can be further scaled up in batch mode in stirred tank or tubular crystallisers before converting the process into the continuous mode. The following sections will discuss these steps in depth, especially the scale-up of batch crystallisation and the conversion from batch to continuous mode.

10.3.1 Screening and Phase Diagram

Protein crystallisation starts with the screening of suitable conditions, which is often achieved with high-throughput vapour diffusion experiments in either the hanging drop or sitting drop mode.^{49–52} The results are used to construct a phase diagram (Figure 10.2), in which the solubility line indicates

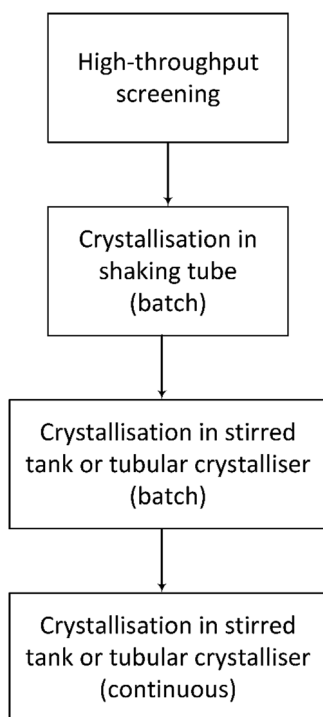


Figure 10.1 General workflow for developing continuous protein crystallisation.