$$T_s(x) = T_{s,in} - \frac{T_{s,out} - T_{s,in}}{\ell} x. \tag{5.41}$$

For a given inlet temperature of cooling water and total length of tubing, the lengths of tubing in each heat exchanger can be chosen to minimize the supersaturation over the total length of tube while also maximizing the total yield. In an analogous example to the design of the multi-bath system above (Eq. (5.36)), design of a slug-flow system with four double pipe heat exchangers in series would use the optimization:

$$\begin{aligned} &\min_{\substack{\ell_1,\ell_2,\ell_3 \\ \dot{m}_{c,1},\dot{m}_{c,2},\dot{m}_{c,3},\dot{m}_{c,4}}} \left[S_{max} + \varepsilon_1 \max\left\{ C_f - C_{sat}(T_{c,in}), 0 \right\} \right] \\ &0 < \ell_i \le \ell_{total},\ i = 1,\ldots,n \\ &\ell_n = \ell_{total} - \sum_{i}^{n-1} \ell_i \\ &0 < \dot{m}_{c,i} \le \dot{m}_{c,max},\ i = 1,\ldots,n. \end{aligned} \tag{5.42}$$

where the value of ε_1 specifies the tradeoff between maximum supersaturation and yield in a system with fixed tube length.

5.5 Controlled Nucleation before Slug Formation

Two of the most effective methods are discussed for continuous nucleation of uniform non-aggregating seeds, with detailed design criteria and operational suggestions (Figure 5.15).

5.5.1 Micromixers

Micromixers were well studied and commonly used to generate uniform particles/crystals from combining solution streams for antisolvent or reaction crystallizations.[39,40] In continuous crystallization, these slurry-borne crystals will then go through further growth towards target size and shape.

Recently, laminar-regime micromixers were also developed for cooling crystallization, which combines two solutions of hot and cold temperature for generating crystals.[41–43] High local supersaturation (much higher than the average supersaturation) can be obtained near the interface between hot and cold solutions when the thermal diffusivity is much larger than the molecular diffusivity, as experimentally demonstrated and theoretically explained.[41,42] Cooling micromixers of various configurations (*e.g.*, Figure 5.2a) were tested, resulting in crystals of improved size uniformity and reduced aggregation, compared to direct cooling of hot solution in tubing (poor mixing in laminar flow).[2]