Design criteria based on physicochemical properties for cooling micromixers suitable for slug-flow crystallization are summarized below, with suggestions included for controlled nucleation:[42]

- The Lewis number $\alpha/D \gg 1$, so that the heat transfer is much faster than mass transfer, resulting in a supersaturation sufficiently high to nucleate crystals even at low spatially averaged supersaturation;
- The solute concentration on the hot side of the interface should be as high as allowed for chemical stability of the solute molecule, in order to increase the probability of nucleation;
- The residence time of solution can be increased by decreasing the inlet jet velocity, and/or increasing the distance between the two jets.

5.5.2 Sonication

Ultrasonication has been widely used to facilitate crystallization processes, including continuous crystallization. The sonication intensity is intrinsically non-uniform in spatial distribution (*e.g.*, with exponential decay along distance[44]), making it very difficult to narrow product crystal size distribution while avoiding contact contamination. A recent sonication-aided nucleation design[1,44] narrowed the sonication time and intensity distribution, and was used in a continuous slug flow crystallization process. In the design, the nucleation zone is localized to only a small portion of the tubing ("sonication zone", right under the probe tip, Figures 5.2a and b) which receives the highest sonication intensity.[44] Additional control can be achieved by increasing the degree of freedom such as the sonication amplitude.[1]

Below are main justifications and operational considerations for the focused indirect sonication design for the slug-flow crystallization process:[1,44]

- The inlet air and liquid flow rates are selected so that stable slugs form spontaneously and there is enough time for the liquid solution to experience cavitation (this time is the *ultrasonication residence time*).[1] For example, the mass flow rate of the inlet liquid solution in a designed experiment was 4.03 g min^{-1} with a linear velocity of 0.89 cm s^{-1}, and ultrasonication residence time of 3 seconds.[1] A reasonable sonication amplitude was chosen, so that the energy was enough for nucleation induction, but not so high that the system temperature would increase and dissolve some nuclei.[1]
- The probe tip was pressed tightly against the tubing wall to minimize the distance between the fluid in the tubing and the probe tip to maximize acoustic energy intensity. A tube outer diameter (~6 mm) was chosen to be smaller than the tip diameter of the sonication probe (~10 mm), to ensure that all of the fluid within the tube right under the probe is under high-intensity sonication.[44]