growth is commensurate with achieving almost complete desupersaturation within the target residence time whilst also producing crystals with the required size distribution. Typical strategies for commodity materials manufacture revolve around making large particles which are easy to isolate by filtration and washing. This is usually achieved by actively suppressing nucleation and operating at modest supersaturations with extended residence times.

1.2.1.3.1 Ultrasound-induced Nucleation. Sonocrystallization is the application of ultrasound to influence crystallization processes. The most common approach may be more accurately termed "sononucleation" where ultrasound is used to trigger controlled primary nucleation. Insonation can also make a distinctive contribution by generating new particles through breakage of existing crystals (see next section on secondary nucleation) allowing operation at low supersaturation levels whilst maintaining a large population of crystals which are appropriately small for direct formulation. This can allow breaking of the constraints of conventional continuous crystallization process design.

The mechanism by which ultrasound triggers nucleation is not fully understood, however, it is widely accepted that cavitation plays a central role. A sound wave propagates through a solution as alternating periods of compression and rarefaction. Acoustic intensity, the amplitude of the wave, can be expressed in microns of displacement of the source of the sound. When the amplitude of the sound wave is sufficiently large cavitation occurs and bubbles form from the release of dissolved gas and evaporated solvent vapor. These bubbles shrink during the compression phase and then they expand again during the subsequent rarefaction phase as the sound wave propagates (this repeating oscillation is known as stable cavitation). If the amplitude of the sound wave is large enough bubbles of solvent vapor form during the rarefaction. These bubbles can coalesce and transient cavitation may occur. Under appropriate conditions bubbles increase in size cycle by cycle until they reach a critical size, perhaps 100–200 μm, when they collapse catastrophically. This transient cavitation phenomenon is linked with triggering nucleation.

Much of the literature relates to aqueous solutions where the range over which transient cavitation is possible is limited to about 15–20 cm from the acoustic source, due to the shielding effect of cavitation bubbles reducing the intensity of insonation further from the acoustic source. This results in a design constraint for large scale operation. Tubular geometries with multiple acoustic sources are required to insonate large volumes with a maximum duct diameter of around 40 cm.

There are a number of reported applications with APIs in organic solvents for example, however the essential physical data required for modelling *i.e.*, velocity of sound and solution density as a function of temperature and concentration and the cavitation threshold, are rarely available. A consequence