

1.2.2.1 Seeded Crystallization

In order to keep the crystal number constant, primary or secondary nucleation needs to be prevented, therefore a zero (or negligible) rate of secondary nucleation is required. Typically, this is difficult to achieve in suspension crystallizers because of the preponderance of secondary nucleation. In continuous stirred tank (CST) crystallization, the secondary nucleation is typically required for steady supply of new crystals, so the rate of secondary nucleation needs to be controlled. This should be the main focus of the process design such that the population density can be maintained at a modest supersaturation consistent with faceted growth, impurity rejection and delaying the onset of encrustation. The capability to manipulate CST is dominated by the ability to manipulate the secondary nucleation rate and allow the system to readjust to a new steady state through growth. Sucrose represents a special case where the seed crystals are added as very fine particles and because of the high solution viscosity, crystal collisions are relatively rare and sufficiently gentle that very few secondary nuclei form. This is why commercial granular sucrose has a tightly controlled particle size typically between 355 μm and 500 μm depending on the seed load selected.

Secondary nucleation has been defined⁵⁶ as: “nucleation which takes place only because of the prior presence of crystals of the material being crystallized”. Therefore, secondary nucleation of a solid phase of a substance occurs due to presence of particle(s) of the same substance *vs.* heterogeneous primary nucleation which occurs due to presence of other interfaces.

There are two distinct ways to form new crystals in the presence of pre-existing crystals. In the first one, small (abrasion) or large pieces (fracture) can break off from existing crystals and the resulting crystal fragments become new crystals. It can be argued that this should not be called nucleation at all, as there is no formation of a new solid phase domain, just mechanical division of an existing solid phase domain already present. This typically happens due to relatively high energy collisions of crystals with impellers, vessel walls, each other, or due to high energy turbulence eddies or cavitation caused by impellers or external fields, such as ultrasound. Mechanisms of formation of crystal fragments are related to fracture and abrasion mechanics of parent crystals.

In the second distinct way to form new crystals in the presence of pre-existing crystals, the existing crystals keep their structural integrity but induce formation of new crystals through contact with the surrounding supersaturated fluid phase, resulting in formation of new solid phase domains within the fluid phase. This typically happens under conditions of relatively low energy interactions with other solids or fluids, such as gentle tapping, sliding across surfaces or sedimenting. Such mechanisms of secondary nucleation are much less understood.

Despite decades of study and discussion on secondary nucleation, the mechanism and underlying physics are still in the center of scientists'