Supersaturation-independent clusters: a scaffold for nucleation and growth of crystals

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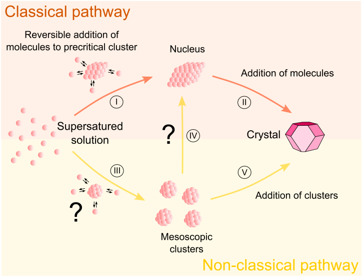
The development of multistep nucleation theory has spurred on experimentalists to find intermediate metastable states that are relevant to the solidification pathway of the molecule under interest. A great deal of studies focused on characterizing the so-called "precritical clusters" that may arise in the precipitation process. However, in macromolecular systems, the role that these clusters might play in nucleation and in the second stage of the precipitation process, i.e., growth, remains to a great extent unknown. Therefore, using biological macromolecules as a model system, we have studied the mesoscopic intermediate, the solid end state, and the relationship that exists between them. We present experimental evidence that these clusters are liquid-like and stable with respect to the parent liquid and metastable compared with the emerging crystalline phase. The presence of these clusters in the bulk liquid is associated with a nonclassical mechanism of crystal growth and can trigger a self-purifying cascade of impurity-poisoned crystal surfaces. These observations demonstrate that there exists a nontrivial connection between the growth of the macroscopic crystalline phase and the mesoscopic intermediate which should not be ignored. Our experimental data also show these clusters can significantly increase the nucleation rate and thus significantly influence the nucleation pathway.



Comparison of classical (I–II) and nonclassical (III–V, III–IV–II) pathways from the bulk liquid to the crystalline phase: contemporaneous densification and increase in crystallinity (I); temporal separation of cluster (III) and lattice (IV) formation; merging of clusters with the crystalline phase (V).