Experimental Investigation of Nucleation Phenomena on the Nanoscale: Classical or Nonclassical?

Kevin Gorman Literature Seminar November 7th, 2019

Nucleation is a rare event process by which new phases of materials are formed; as such it is fundamental and crucial in such areas as cloud formation and climate science, condensed protein phases found in pathology such as Alzheimer's, and crystallization methods central in pharmaceutical applications.[1] Experimental observation of nucleation on the nanoscale was not possible for many years due to the limitations of techniques; recent developments have led to new data providing points for comparison to established knowledge from theory and simulation. Such studies have been performed with a variety of different microscopies including optical, x-ray, atomic force (AFM), scanning electron (SEM), and cryogenic transmission electron (cryo-TEM) in addition to static and dynamic light scattering experiments.[2-10]

The prevailing theory and models in this field were developed in the mid-twentieth century for the most part. Classical nucleation theory (CNT) has its basis in the works of Gibbs in the late nineteenth and early twentieth centuries in thermodynamics,[11] while the first literature on nucleation-specific kinetics came later in 1926 from Volmer and Weber.[12] Subsequently, the full formulations were developed by Becker and Döring in the 1930s,[13] along with many others providing key descriptions of different aspects of the problem at hand. The central tenants of CNT are the existence of a critical nucleus size where nuclei larger will persist and those smaller will dissolve, that all clusters involved are of the same phase as the final bulk phase, and that the process is described by a single-step barrier caused by the thermodynamic arguments. This has been challenged by numerical investigations and simulations arguing for a nonclassical multi-step nucleation (MSN) process in which clusters of higher density nucleants form before then coming together to form a larger, ordered nucleus. In addition, current research indicates that there are system that exhibit complex behavior bridging the two schools of thought with more elaborate mechanisms. Each thermodynamic representation can be seen in Figure 1 with the free energy for formation of the nucleus given along a reaction coordinate.[7]

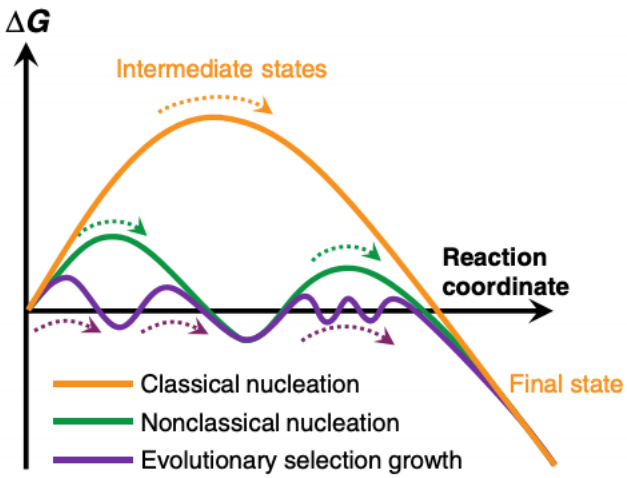

Figure 1. Thermodynamic representation of different nucleation theories.

Glucose isomerase (GI) is a macromolecule of particular interest due to its exhibition of classical nucleation and multi-step nucleation mechanisms when at different conditions. Sleutel and Alexander Van Driessche found that certain biological macromolecules, including GI, form mesoscopic clusters that are liquid-like in nature which is directly associated with a nonclassical pathway and an increase in rates of nucleation.[14] The surface structures are tracked using noninvasive laser confocal differential interference contrast microscopy (LCM-DIM) and

demonstrate clusters of GI performing 3D nucleation on surface sites. The (011) sites on orthorhombic GI experience looped macrostep formation when exposed to the solution containing clusters (Figure 2A), yet when solutes with a much lower concentration are used there is no such crystal growth (Figure 2B). As a follow up, Sleutel et al. performed a study putting GI and divalent cations into solution where heterogeneous nucleation on a mica surface was observed (Figure 2C).[8] Through the use of tapping mode AFM, the local structure of small clusters of macromolecules is probed. This reveals a classical procedure where even clusters as small as 4 molecules exhibit the same ordering as the lattice seen at much larger sizes (Figure 2D). The AFM experiments were also able to capture subcritical clusters which then redissolved before reaching the requisite critical size. The classical nucleation observed was also confirmed to not be an artifact of the substrate surface as nucleation also took place on a different, albeit similar, substrate as well as the adsorbing of the molecules onto the mica surface at random orientations.

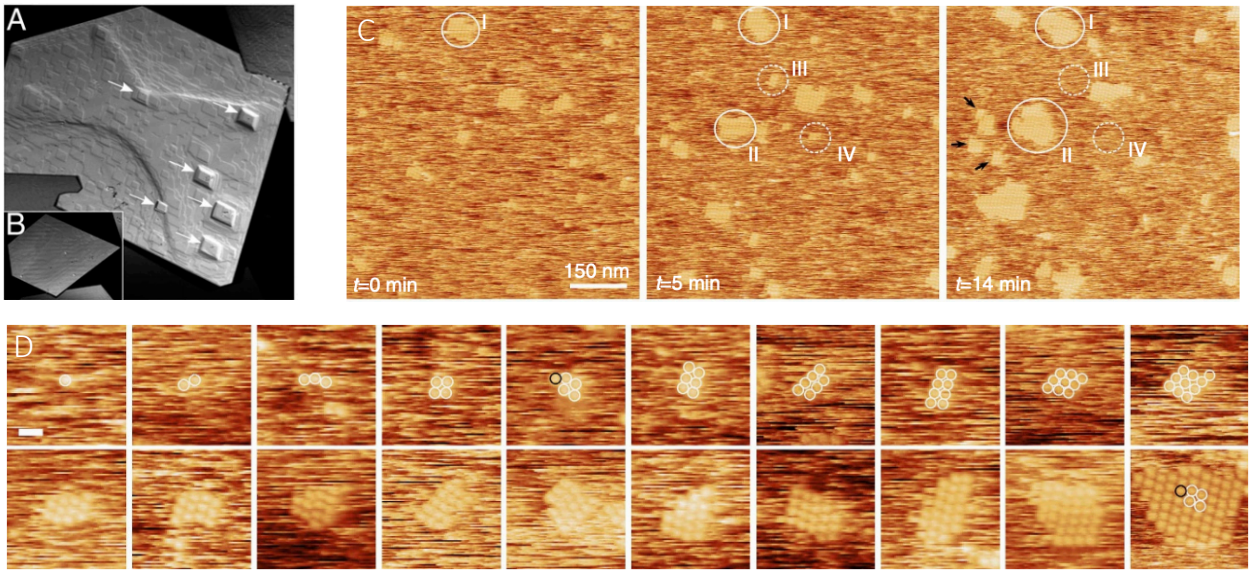

Figure 2. Nucleation of glucose isomerase: 3D nucleation on orthorhombic GI (A), filtration of solution to remove GI clusters before experiment (B), GI nucleation over time in dication solution on mica (C), nucleus size distribution on mica (D).

Organic molecules have also been studied within a similar context. It was found that amphiphilic organic semiconductors demonstrate what the authors term "crystallization-driven self-assembly".[7] Using thin film x-ray diffraction and AFM methods entire self-assembly trajectories were imaged and kinetic information was extracted. This set of data supports a sophisticated nucleation process involving nonclassical aspects as well as what is known as Ostwald ripening, where nuclei consume one another. Researchers observed five distinct steps of a complex nucleation process. The techniques utilized are able to capture nanometer resolutions and perform complicated analysis in situ, showing the continued development of experimental work.

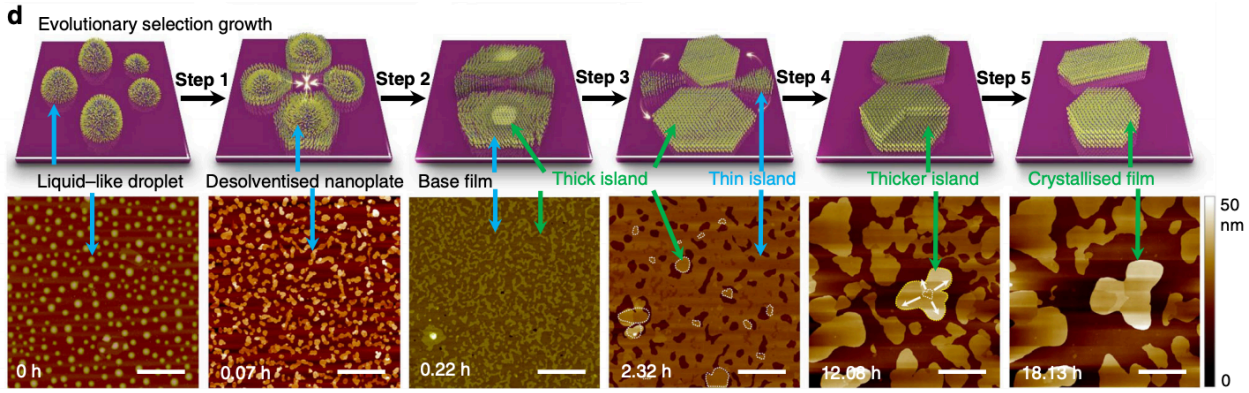

Figure 3. Nucleation of amphiphilic organic semiconductor molecules on an SiO_2 surface captured over time.

The field of nucleation attempts to study rare events, often taking place on the nanoscale, which are intrinsically difficult to observe experimentally and have proved challenging to quantitatively model through theory and simulation. Recent advances in methods used to probe such processes have led to different mechanistic insights depending on the specific system being examined. Inorganic nanoparticles, biological macromolecules, and organic molecules are among systems recently studied using various AFM and TEM techniques; different experiments have represented classical nucleation pathways, others have demonstrated MSN, and others contain aspects of both. What remains clear is that describing the mechanism of any particular nucleation process remains a formidable task. The future of the field will rely on a combination of more numerous, high resolution experiments along with advances in theoretical frameworks building off of CNT and MSN and continued simulation work.

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