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VIEWPOINT

Beyond Snowflakes: Heterogeneity in Nanomaterials

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> Welcome to the real world of nanomaterials; it has heterogeneity in all aspects, but you will love it.

I was reading Zihao's presentation slides for a Materials Research Society meeting. He was my first Ph.D. student and is now at Stanford studying neuroscience. To help the audience appreciate his work of pride in taking live videos of nanoscale crystallization,[1] he included an image of snowflakes, the crystalline yet chaotic forms of ice with shapes governed by crystallization pathways. Then my six-year old came to check on my progress of work, as she always did. She saw the image and giggled, "Mommy, do you know no two snowflakes are the same?" She was then interested in reading books[2] on extreme weather, such as electric skies, twisters, and icy crystals. She memorized that sentence as a fun fact.

This fact is what has fascinated me in nanomaterials. While macroscopically we seem to acquire unified measures of materials properties, such as phase, crystallinity, stoichiometric composition, and conductivity, we also start to appreciate and embrace the ubiquitous presence of heterogeneity at the nanoscale. Not perfect uniformity but variations, especially as we dive into complex, real-world materials equipped with advanced characterization tools.

Each Different in Its Own Way. The concept of "***inter-entity***" heterogeneity of snowflakes extends to nanomaterials. For example, nanoparticles colloidally synthesized even from the same reaction vessel have been increasingly shown as heterogeneous by direct high spatial-resolution imaging with electron microscopy. Three-dimensional (3D) atomic arrangements of single nanoparticles resolved by electron tomography elucidate distinctive surface structures (e.g., step, terrace, facet), which impact strain distribution, ligand adsorption energy, and consequently application in catalysis.[3] Likewise, precision synthesis of polymers with a polydispersity index of 1 remains a challenge in organic chemistry (achieved though in living systems producing biopolymers). Fundamentally, this heterogeneity can originate from the existence of multiple thermodynamically stable states or a relatively flat free energy basin, for example, the energy difference between nanoparticles of similar size and shape but different step topologies can be well below k_BT. On the other hand, local variations in material synthesis conditions such as temperature, reagent concentration, and flow field can easily occur, due to thermal fluctuation and finite rates of heat transport and/or mass transport. These variations are pronounced at the nanoscale, leading to diverse, instantaneous, and energetically favored structures at each local region. In the case of nucleation and growth, small changes of temperature, moisture, and solid surface (e.g., tree branch, glass) altogether diversify the shapes of snowflakes.

Inter-entity heterogeneity exists in the kinetic pathways along which nanomaterials interconvert among multiple thermodynamically stable states. Take proteins, Nature's nanomaterials, for an example. Cellular machineries encode identical amino acid sequence to nearly identical 3D conformation among millions of copies of the same protein, which is the basis for single particle analysis used in cryogenic electron microscopy (EM).[4] Yet it remains challenging to map the interconversion pathways of proteins associated with essentially all physiology functions ranging from enzymatic catalysis to synaptic transmission. Even the best biochemist cannot guarantee these millions of proteins are kinetically synchronized along the interconversion pathways and thus are vitrified all at once to pause at identical intermediates or metastable structures. This heterogeneity can only be more obvious in synthetic nanomaterials, where the starting and ending states of an interconversion are not necessarily identical. Future materials research to emulate the features of living organisms needs to account for and understand this heterogeneity to embed adaptive and evolving functional behaviors.

Considering kinetics furthermore, ***inter-entity*** heterogeneity can be amplified if the system is out of equilibrium, powered by various external energy inputs such as electric field, acoustic waves, chemical energy, and food. The number of available states increases. One macroscopic example is the morphogenesis of a biological organism such as embryonic development, assembly of cytoskeleton, and differential growth of leaves.[5] A common initial condition can give rise to various morphologies

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or forms through positive or negative feedback loops that augment stochastic heterogeneity. At the nanoscale, characterization of morphologies by spectroscopy mapping and EM shows that such nonequilibrium-based morphogenesis mechanisms can be applied to synthetic nanomaterials. Examples include frontal polymerization patterns induced by rapid reaction-thermal transport[6] and 3D folds and voids formed during interfacial polymerization of polyamide membranes explained qualitatively by the Turing theory.[7]

Spatial Heterogeneity Within. ***Intra-entity*** heterogeneity within a single nanomaterial entity is emergently revealed to exist in a spatial manner, accompanied by the advancements of a suite of EM characterization methods. While crystalline materials are associated with high phase purity and high structural uniformity, methods such as backscattered electron imaging and four-dimensional scanning transmission electron microscopy (4D-STEM) have been used to discover nanoscale phase orientation domains in metals,[8] oxides,[9] and conjugated polymer thin films.[10] The interfaces at the boundaries of such domains, many formed into percolated networks, can change the kinetic barriers during mass and charge transport. These findings have led to a theme of domain engineering, to utilize such heterogeneity instead of simply annealing it. For example, employing thermomechanical processing methods, such as electropulsing, Ti−Al alloy was shown to maintain a wavy dislocation morphology with enhanced twinning, which prevents early failure of the alloy under tension.[11] In some electrochemical insertion materials of ion batteries, amorphous domains or polycrystalline phases are shown to exhibit faster charge transport rates than their crystalline counterparts, likely due to enhanced ion diffusion rate along the boundaries or embedded interfaces.

Beyond crystalline materials, squishy soft materials present the other side of spatial heterogeneity at the nanoscale, structural irregularity, which calls for advances not only in characterization but also quantification. Here by "soft materials" I follow the de Gennes definition[12] to include colloidal suspensions, surfactants, polymers, and living systems at all levels, from nucleic acids to cells. By irregularity, I mean that the material's structure cannot be described by a constant value of lattice constant and symmetry or a fixed set of shape descriptors such as radius or length. This irregularity excludes the use of ensemble-averaged methods to characterize the structure. One prominent example is polymer networks, the molecular architecture underpinning tissue engineering scaffold and industrial coatings. Simplified description of their structure entails one value of mesh size defined as the distance between nodes. Recent speculations picture a much more complex structure including multiple length scales and substructures: <5 nm features of dangling ends or distances of cross-links, 5−10 nm features of cross-links and entanglements, and 10−100 nm features of collapsed multiple neighboring junctions as "frozen" blobs.[13] This multiscale structure suggests a multiscale or potentially multistep transformation and mechanical response, which EM has not yet progressed to map directly. Methods such as diffusive scattering and iterative comparison of experimental EM images with molecular dynamics simulation can potentially reveal such irregular, multiscale structures with molecular details. Structural irregularity sometimes manifests as shape irregularity. By implementing electron tomography at low doses, my group and others captured the structure of 3D crumpled polyamide membranes which are related to their separation performances.[14,15] The crumples are irregular. One had to subjectively decide a set of geometric metrics for shape quantification. Advancements can be made in using descriptor-free methods to parametrize and group the shape with the help of on machine learning (ML) to quantify "shapes" as a middle between materials synthesis/processing conditions and functions.

Film Temporal Evolution. Heraclitus said thousands of years ago "No man ever steps in the same river twice, for it's not the same river and he's not the same man." The same goes for soft materials. They are often associated with solvents during their synthesis, processing, or operation. As a result, the incessant motion of solvent molecules make these soft materials dynamic, adding yet another dimension of *time* to the heterogeneity in *space* discussed above. This aspect of heterogeneity is what my group has pursued extensively using "nanoscale cinematography"[16] coupling liquid-phase EM and ML-based data processing. Liquid-phase TEM images solution samples which are made compatible with the high vacuum of EM with "nanoaquariums"sealed by graphene or SiN_x windows. Machine learning can aid the batch processing of EM images in continuous videos, and potentially enable on-the-fly guidance of in situ experiments and detection of rare events. We studied the phase behaviors of nanoscale entities in liquids, such as nonclassical nucleation, melting, and molecular aggregation (e.g., asphaltene deposition, biofouling). These fundamental studies can be translated to practical impacts to infer design of topological mechanical metamaterials, strongly coupled magnetic/optical lattices, and nanomachines. A promising future direction in this *time* dimension is to film living systems to reveal the secrets of life and to resolve and understand the structuring, organization, and working mechanisms of nanosized biological building blocks such as proteins and lipids in various biological states. While technical hurdles are there to overcome, this direction can foster the growth of a sister to the heroic cryogenic EM method to provide a dynamic lens into the nanoscopic world of life.

■ SUMMARY

Tolstoy wrote in his famous *Anna Karenina* the ubiquity of heterogeneity at that time associated with bad fortune: "Happy families are all alike; every unhappy family is unhappy in its own way." It is somewhat consistent with the immediate prospective of heterogeneity in materials; disordered defects in a sea of highly ordered crystalline metals can serve as the heel of Achilles for the onset of mechanical failure; byproducts in a monodisperse nanoparticle synthesis are what chemists strive to remove. This Viewpoint communicates our vision on opportunities in reversing this impression, to acknowledge, to cope with, and to utilize the heterogeneity of nanomaterials.

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Notes

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