SIGNIFICANCE: Crystals are found all over the world in a myriad of shapes, and aesthetic forms. In particular, humans have been fascinated by the morphological diversity of biologically created minerals for centuries. Mineral morphology is determined in a process called crystallization, probably on the very first step, that is, nucleation. In a classical picture, crystals are born in an ordered fashion by successive addition of the building blocks to the incipient crystallization grain.

However, the recent advances in high-resolution transmission electron microscopy have revealed that nucleation is a much more complex phenomenon than previously thought. It turns out that there is a large diversity of the non-classical nucleation pathways that are exploited by nature. These pathways typically involve the self-assembly or self-organization of the stable (pre)nucleation precursors – phenomena being in a striking contraction with the classical picture.

Despite the numerous observations of this non-classical nucleation, the major knowledge gaps remain. For instance, the interplay between kinetically and thermodynamically controlled steps, role of molecular interactions, reactivity, solution structure and dynamics or the nature of the driving forces are still poorly understood.

Among many fundamental aspects lacking our understanding, the earliest nucleation stages are the most challenging ones. Probably due to their transient and metastable character that makes experimental detection very problematic.

OBJECTIVE: The focus of this project is to develop molecular level understanding of the earliest stages of crystallization, in particular, minerals and proteins prenucleation. The occurrence of prenucleation precursors is a manifestation of the non-classical crystallization pathway, which seems to prevail in all naturally formed (bio)minerals and bimolecular crystals.

PROPOSED RESEARCH: To address the knowledge gaps in minerals and proteins prenuclation, the synergistic combination of molecular modeling with the time-resolved liquid transition electron microscope monitoring will be critical. In this project, we ask the fundamental questions about the physicochemical processes behind the formation of nucleation precursors, in particular the prenucleation clusters and dense, solute-rich liquid droplets. We seek an understanding of the acid-base and additives control over the chosen nucleation pathway, stability and structure of the transient intermediate phases, and finally the kinetics of the self-assembly.

IMPLICATIONS: The predictive understanding of the earliest stages on nucleation in both minerals and biologically relevant systems hold a promise to affect many areas of research: from protein crystallization – a limiting step in the protein structure determination, to more comprehensive understanding of the environmental elements cycling and the biogeochemical past and present of our planet. The ultimate goal is to control the crystallization routes to produce the property- size- and shape-targeted monocrystals.