Protein aggregation: a matter of frustration?

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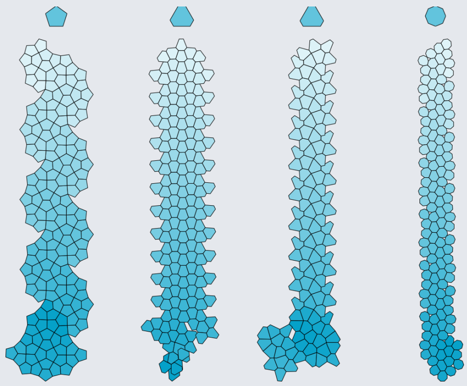
Unlike at the macroscopic scale, the interactions of objects at the micro- and nano-scales is strongly contrained by the presence of thermal agitation. As a result, structures at these scales typically form through self-assembly, be they artificial materials or supramolecular protein constructs inside the living cell. While self-assembly can be controled to some extent by tayloring the interactions between the particles involved, it is also constrained by general geometrical considerations which we are only beginning to understand.

We use theory and numerical simulations to uncover a fundamental new tenet of these generic principles of self-assembly based on the physics of geometrical frustration. Unlike many previous studies, we focus on collections of objects whose shapes do not fit together to form a straightforward supramolecular structure. Such objects cannot interlock without incurring strain, and any compact structure made out of them is thus subject to a competition between its internal geometrical frustration and the forces driving self-assembly. Using a minimal model of this competition, we demonstrate that it gives rise to a robust, distinctive morphology of nontrivial fibrous aggregates with variable widths. Due to their frustrated structures, these aggregates are systematically trapped out of equilibrium, indicating that predictable behaviors can emerge from the rich glass-like physics that underlies self- assembly.



Examples of frustrated particles and of the fibers they form when aggregated in a computer simulation

Such behaviors contain valuable lessons to understand and design structures at very small scales. Frustration indeed induces kinetic trapping in biological systems, an d is associated with fiber-like aggregation of proteins linked to several disease states. On the engineering side, this fiber-forming mechanism offers an opportunity to turn kinetic trapping from a hinderance on the path to a target structure to a fruitful design principle allowing the production of specific morphologies.

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