Size control in self-assembly using incommensurable subunits

(theoretical internship, possibly leading to a thesis; funding available)

The self-assembly of complex structures from engineered subunits is a major goal of nanotechnology and protein design, but controlling their size becomes increasingly difficult in larger assemblies. Existing strategies present significant challenges, among which the use of multiple subunit types or the precise control of their shape and mechanics. This project aims to **introduce an alternative, more robust approach based on a clever use of subunits with promiscuous interactions and incommensurable shapes**. It will additionally pave the way for colloidal and/or DNA origami implementations by our collaborators.

Equilibrium self-assembly is a powerful way to build nano- and microscale structures out of interacting subunits. Many biological and technological functions, however, require these structures to have a well-controlled size, requiring specific strategies for size-controlled assembly. While some such strategies have been identified *in vivo* and implemented in the laboratory, our understanding of the underlying principles is far from complete. In this project we will use statistical mechanics to analyze a new concept to this effect. In our proposed design, a small number (two or three) subunits of different sizes can bind with each other either in register or with an offset. As more and more copies of the subunits are added to the assembly, the offset between subunits increases until a specific value where binding become impossible. While the design is easy to schematize, guaranteeing its thermodynamic consistency is not trivial. How many different types of interactions are necessary to implement it? What relative strengths should they have to both provide robust on-target assembly and disfavor off-target structures? Understanding this question will require a **proper enumeration of all possible assembly structures allowed by our design**. This could be conducted by adapting existing algorithms to this problem, or by developing a suitable analytical framework.

Beyond this first thermodynamic assessment, we aim to develop a better understanding and to optimize the assembly kinetics of our design, especially with regards to the formation of **frustrated metastable intermediates**. We will also extend our concept to 2D and 3D and adapt it to the **colloidal experiments** of our collaborators Julien Heuvingh and Olivia du Roure at ESPCI and/or the **DNA origami experiments** of Friedrich Simmel's group at TU Munich. This project will be conducted in collaboration with Carl Goodrich (IST Austria, Vienna), who could co-direct a possible PhD project.
Depending on the applicant's tastes, a project on the modeling of the nonlinear mechanics and fracture of **interpenetrating double networks akin to those found in the cell's cytoskeleton** is also possible.

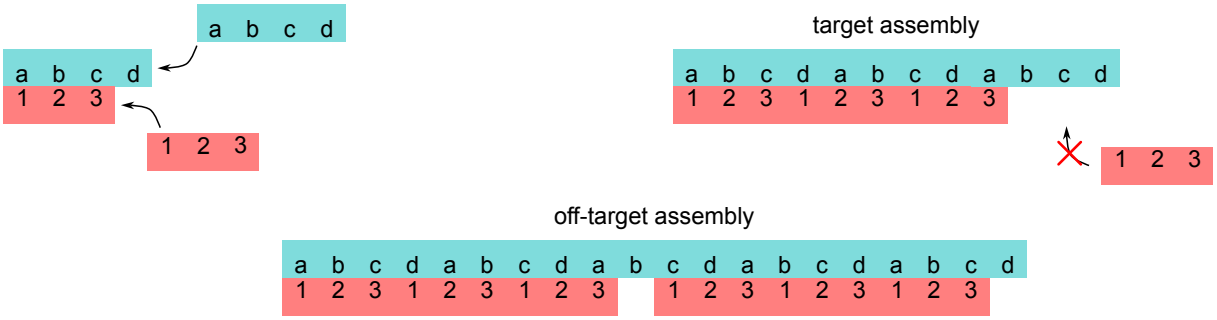

Illustration of the proposed concept with subunits of sizes 4 (blue) and 3 (red). All interactions between letters and numbers are allowed, except for b1, c2, d3. A proper choice of parameters might allow to obtain a large excess of the target assembly.

Expected skills:
A taste for statistical mechanics and numerical simulations connected to analytical aspects.
An interest in interacting with experimentalists.

Location:
PMMH at ESPCI & Sorbonne U. and/or LPTMS at U. Paris-Saclay (Orsay)

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