Targeting and self-assembly using super-selective nanoparticles

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A long-standing goal of Soft Matter Physics is to understand how constructs of arbitrary complexity can be formed through self-assembly of nano-building-blocks. In principle, such constructs could act as smart and functional nanodevices with potential applications across a variety of disciplines including Biology, Medicine, Nanotechnology, and Engineering. An important step towards building complex nanodevices has been made with algorithmic [1], generation-by-generation assembly. In this scheme, the components of the target structure are made to self-assemble in an orderly fashion by carefully providing kinetically favourable pathways to the thermodynamically stable state.

In order to generalize such assembly strategies, one must first obtain excellent control over the binding events between the different docking sites on the nano-building blocks. More precisely, we need to design nanoparticles that can target a given surface or nano-object, and do so selectively in the presence of other surfaces with competing binding interactions. Besides being useful for self-assembly, such “super-selective” targeting has immediate implications for nano-medicine, as one could fabricate devices that can treat individual target cells (e.g., cancer cells) without affecting the healthy ones. Indeed, nano-targeted delivery is an active area of research [2], as it has been found that cancer cells tend to overexpress certain membrane receptors in comparison with healthy cells. [3] However, to exploit this distinctionbetween target and healthy cells, one must design nanoparticles that only bind to surfaces displaying an above-threshold coverage of a particular receptor, while leaving other surfaces intact.

Using computer simulations and a simple analytical model, we have shown that this kind of super-selectivity can be obtained with multivalent nanoparticles, which use a large number of intervening ligands that simultaneously bind to surface receptors [4]. The main idea is that in multivalent particles the number of binding arrangements rapidly increases with the number of receptors on the target surface, causing a sharp dependence of the particle’s binding free energy with receptor concentration. In effect, such particles exhibit a nearly “on-off” behaviour ideal for specific targeting. However, while this simple model accounts for the complex interplay between valence, binding strength and bulk concentration observed in systems of multivalent nanoparticles, a number of questions must still be addressed before such particles can be reliably used in real nano-technology applications. Finally, we present simulation results that shed light on the way to address some of these questions.

References

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