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Energy landscaping in supramolecular materials

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This review details recent developments in the design of supramolecular materials with customizable properties that can be coordinated in space and time. We highlight examples where both kinetic and thermodynamic considerations are incorporated in design, to address three challenges: control of order/disorder in supramolecular assembly; formation of structures with distinct functional domains; formation of out-of-equilibrium structures with controlled lifetimes. The examples that are discussed are based on self-assembling peptide and saccharide-based amphiphiles. These biomolecular amphiphiles are of low complexity and ideally suited to fundamental, systematic studies while they are also considered for applications in environmental remediation, food science, cosmetics and nanomedicine.

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Introduction

This review covers recent developments in the control of properties, using kinetic and thermodynamic considerations, of supramolecular materials derived from simple biomolecules [1,2]. A wide variety of synthetic and biological compounds are able to form ordered nanostructures based on reversible interactions. For applications in cosmetics, food, personal care, biomedicine and nanotechnology, simple bio-derived molecules, such as derivatives of short peptides and simple sugars, are of particular interest as they are scalable, low-cost while they are tremendously versatile. In this review we will discuss selected examples from the recent literature which demonstrate how molecular design, combined with thermodynamic and kinetic considerations can give rise to materials with uniquely addressable, customizable and tunable supramolecular properties. Examples will be discussed based on the ability to control order and disorder at the supramolecular and nanoscopic level; control separation of multiple components into separate functional domains, and to precisely regulate assembly and dis-assembly over time, by taking advantage of competing catalytic pathways. We will show that these approaches are leading to the development of systems that share similarities with biological materials but that are much simpler in composition and design, and may incorporate biological, as well as non-biological synthetic components, thus opening up new applications ranging from nanotechnology to biomedicine.

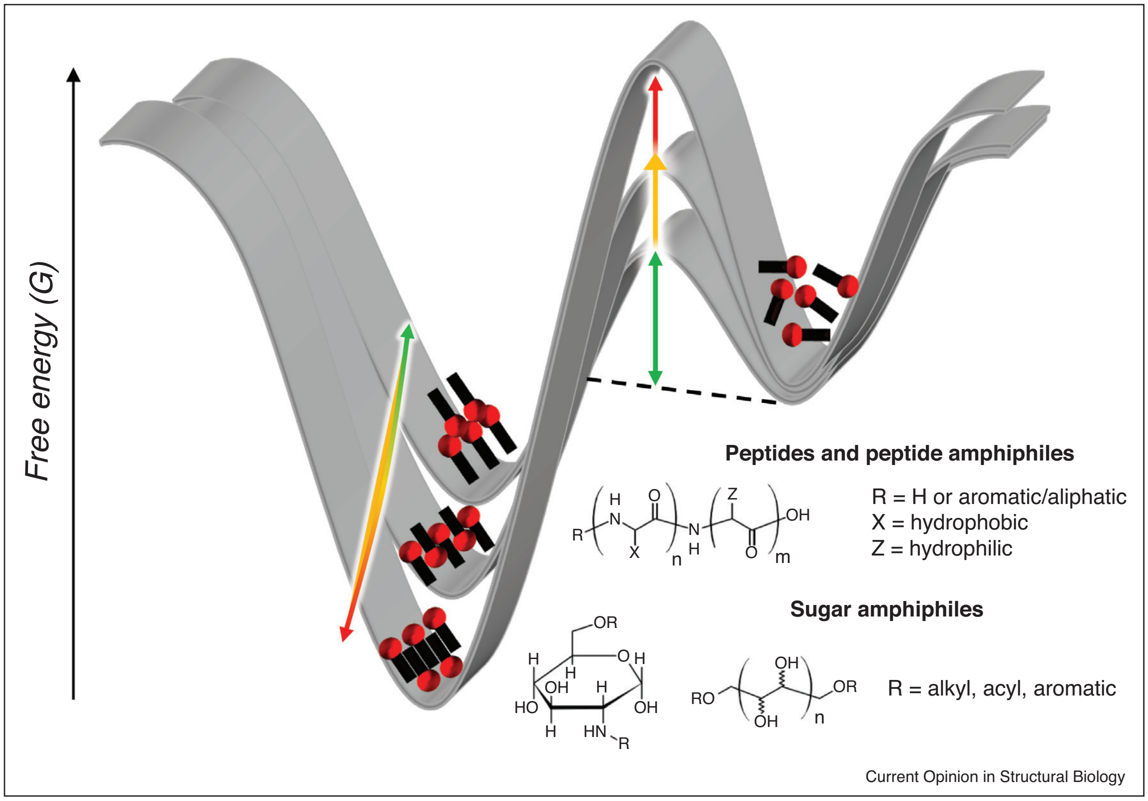
This review highlights only some of the recent developments in the extremely active field of supramolecular materials science and has the goal to inspire researchers to focus on controlling spatial and temporal aspects of supramolecular materials design, ultimately giving rise to technologies and materials with properties that start to blur the living/nonliving materials divide toward a seamless interfacing of the biological and synthetic worlds. Certainly, supramolecular biomimicry is an increasingly important strategy to devise novel materials and the focus on controlling and designing spatial and temporal variability of these materials brings us closer to the aim of achieving a more seamless interface between living and non-living matter for medicine, biotechnology, food science, and environmental science.

Supramolecular design based on simple peptides and sugars

Life's macromolecules are complex polymers whose function is dictated by the precise sequence of long chains of hundreds or thousands of monomers (saccharides, amino acids, nucleotides). It has been recognized that much simpler combinations of monomers can also give rise to structure formation, providing opportunities to design building blocks for materials with designable/customizable properties. In this review, we focus on materials based on supramolecular assembly of amphiphiles derived from simple peptides and saccharides composed of just a few amino acids or mono/di saccharides, which may be modified with aliphatic or aromatic moieties to enhance their self-assembly properties (Figure 1).

Naturally occurring amino acids constitute a formidable set of building blocks that every single living organism utilizes to construct enzymes, receptors, structural

Figure 1



Supramolecular energy landscapes dictate structure and function. Supramolecular materials derive their properties from the degree and mode of organization of their amphiphilic building blocks. The degrees of organization are, in turn, dictated by kinetic aspects, or the ease of overcoming energy barriers and accessing various assembled states. Short peptides or peptide/sugar amphiphiles are discussed in this review as building blocks with properties that can be customized for various applications by molecular design, combined with these kinetic and thermodynamic considerations.

components, etc. [3]. These provide a rich resource of inspiration for supramolecular chemists, with guidelines for their structure/function relationships resulting from systematic studies on intermolecular forces that drive their formation [4,5]. For example, collagen, the most abundant structural protein in the animal world, has fascinated scientists for its unique self-assembling, stimuli-responsive and structural properties [5,6]. Besides taking inspiration from nature's designs, there is increased interest in unbiased mapping [7] or searching [8] of short peptide sequence space to identify sequence/structure/function relationships without being guided by biology. In order to enhance the self-assembly properties of short peptides, they may be functionalized with alkyl or aryl groups, to create aliphatic [9] or aromatic peptide amphiphiles (PAs) [10]. With the virtually infinite number of combinations of the twenty natural amino acids (plus a virtually unlimited number of designed non-natural amino acids), a wide range of physicochemical and biochemical properties are accessible. Peptide synthesis, practiced mostly on a solid phase in laboratory contexts, has been developed [11] to the point that scalable processes have been established with real-world applications in food, cosmetics and pharmaceutical industries. For short peptides, biocatalytic approaches provide a cost-effective, environmentally benign and scalable alternative [12,13].

Along with amino acids, sugars represent a ubiquitous class of biomolecules, with cellulose being the most abundant biopolymer on earth. Even though in living organisms just a few saccharides dominate (glucose, lactose, galactose, etc.), they lead to an impressive variety of saccharides found in nature, arising from an extremely high level of structural and chemical variations leading to much more complex intermolecular connectivity and infinitely greater sequence diversity compared to what is achievable with oligopeptides: in mammals the number of common monosaccharides matches that of natural amino acids (20), yet, for instance, the number of obtainable *di*saccharides results to be 1600 compared to just 400 dipeptides; this gap becomes more and more marked as the chain length increases [14]. Sugars play important roles in molecular recognition and structure formation; it suffices to consider