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Tutorial Review

Engineering Entropy in Soft Matter: The Bad, the Ugly and the Good

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The role of entropic interactions, often subtle and sometimes crucial, on the structure and properties of soft matter has a well-recognized place in the classic and modern scientific literature. However, the lessons learned from many of those studies do not always form part of the standard arsenal of strategies that are taught or used for de novo studies relevant to the engineering of new materials. Fortunately, a growing number of examples exist where entropic effects have been designed *a priori* to achieve a desired or new outcome. This tutorial review describes some recent such examples, selected to illustrate the potential benefits of a more pro-active approach to harnessing the often overlooked power of entropy.

1. Introduction

The second law of thermodynamics essentially defines entropy in a similar way as the first law defines energy. Clausius' dictum of the first and second laws of thermodynamics is most picturesque: "The energy of the universe is constant; the entropy tends to a maximum". In such a broader context, there is nothing intrinsically negative about entropy, but some negative connotations quickly arise once entropy surfaces in specific contexts. For example, for many, entropy is first taught in the historical context of processes where energy transforms among different forms, with the second law of thermodynamics asserting that the quality of energy degrades irreversibly as entropy increases; this is what limits the efficiency of heat engines and why power plants or internal-combustion engine automobiles can only make use of a small fraction of the raw fuel energy. A more general negative connotation of entropy is its association with disorder or randomness; our emotional side tells us that order is "good", disorder is "bad" (as applied to such things as the state of our desks or of our mind). Of course we are fully aware that disorder is not always bad and that entropy's association with disorder is only an oversimplification, but we can't deny the power of analogies and catch phrases in eliciting lasting human responses. Some claim that entropy is the force behind the so-called Murphy's Law that "Anything that can go wrong, must go wrong". Perhaps one aphorism that portrays entropy at its ugliest (being a consequence of its ever increasing nature) is the one brewed by the pioneers of Thermodynamics that state that the universe will end in a "heat death" (with no thermodynamic free energy) which will be the end of all physical phenomena. Yes, someone has to be blamed for the ultimate doom of the universe. Given the power of words, four semi-true aphorisms will be put forward in this review in an attempt to provide alternative perspectives on what entropy is and does.

Most scientists and engineers know of course that entropy plays some role (sometimes crucial) in explaining many complex phenomena and in determining the properties of all materials. For instance, whenever Brownian motion is alluded to as a player in colloidal behaviour, entropy has left its footprint. A number of statistical mechanical textbooks (e.g., Refs. [1-2]) and influential articles and reviews have explored the relationships between entropy and information theory, generalized variational principles that maximize some form of entropy, and the anthropomorphic nature of entropy quantification.[3-6] Excellent (and more technical) reviews on entropy-driven phase transitions (mostly related to colloidal systems) have also appeared.[7,8] However, it is fair to say that when it comes to designing new materials with target or improved properties (like super-selective drugs, super-conducting media, super-porous matrices, super-tough plastics, super-phobic surfaces, etc.), the engineering often focuses on tuning enthalpic interactions through chemistry. This focus is certainly justified, as it has been shown time and again to be a most productive way to generate new useful materials. Also importantly, tuning enthalpic interactions is appealing because they are often accessible to experimental measurement and are conceptually straightforward to understand. Rational design often boils down to tuning the strength of attractions and/or repulsions among chemical groups in a system (e.g., if it is desired to have "A" sticking to "B", one would try to make their attraction strong). This leads to the first aphorism:

Aphorism #1: Energy is intuitively easy to design. Entropy is not.

This is meant to be more provocative than true. It is very difficult to predict, e.g., how complex molecules interacting through multiple non-covalent forces of comparable strength will assemble. Predicting the folding of even a single complex molecule, like a large protein, has proven quite challenging[9] (though entropy is partially to blame). Also, it may be extremely difficult to synthesize and assemble the right pieces to realize one's energy-driven vision, and that is an area where great amounts of skills and novel tools continue to be advanced.

In engineering energetic effects, the complexity in the "how" defies the simplicity of the "why". Rational and heuristic guidelines for (mostly) energy-driven self-assembly are routinely expounded (see, e.g., Refs. [10-12]), while reviews of entropy-driven processes have been more scarce.[7,8,13] Of course, separating cleanly energy and entropy (as is presumed here) must be seen as an "artistic license": In many phenomena both are coupled in non-trivial ways (e.g., the so-called hydrophobic effect that often helps a protein fold or bind has a known entropic component resulting from the reduced mobility of water molecules forming a shell that solvates non-polar moieties[14]). In general, engineering coupled enthalpic and entropic effects can be very challenging. Nonetheless, in the design of new materials entropy often plays a minor part, as its role can be obscure, overlooked, unappreciated or even suppressed as being undesirable. One can then argue that:

Aphorism #2: Energy is designed intelligently. Entropy is designed accidently.

This is meant to emphasize the idea that, even when the role of entropy in explaining (or not) a phenomenon or material property is a highlight of a research paper (see, e.g., [15-16]), this is often the result of *a posteriori* analysis, not the result of *a priori* efforts to purposely introduce or design-in entropic effects. This is in part a reflection of the more subtle, more cooperative, and more complex ways in which entropic interactions play out or couple with energetic effects. Subtle is indeed the Lord, but especially when it comes to entropy. Several controversial aspects on its definition (and the allowance of negative temperatures[17]) and its measurability (like the Gibbs paradox in colloidal systems[18-20] and its application to non-equilibrium systems[21]) are the object of continuous interest and discussion. To be more concrete about different entropic effects in our ensuing discussions, let us first recall entropy's microscopic definition as given by Boltzmann's equation:

$$S = k \ln W \qquad (1)$$

Where k is Boltzmann's constant and W is the number of microstates (or volume in phase space) associated with the system at a prescribed energy, volume and number of particles. The more microstates accessible to a system, the larger the entropy. In counting microstates, one can group them into different flavours according to particular degrees of freedom that molecules can explore, as illustrated in Figure 1. While counting microstates or measuring phase space volumes may seem like a straightforward task, it turns out that aside from a few exceptions (with highly idealized models), it is rather complicated and simple intuition can easily miss by orders of magnitude. The subtlety of entropy is readily illustrated by packing entropy (see Figs. 1c-1d) which is responsible for the well-known isotropic-to-crystal transition in hard spheres[22] (occurring at volume fractions ~50%): The existence of such an entropy-driven ordering transition was controversial among scientists for many years in the 50's and 60's.[23]

Since some form of entropy is always present in a given system, shouldn't we try to use it to our advantage? Thankfully, Aphorism #2 is only partially true as there is a growing number of examples where entropy is designed intelligently. The following sections are devoted to highlight just a few such representative examples, mostly connected to molecular simulation studies, in order to reflect the author's experience and to leverage pictorial material from his own research. These examples are meant to illustrate the "good" that should counter "the bad and the ugly" sides of entropy described earlier, and are rooted in the third aphorism:

Aphorism #3: Energy is a selective force in Nature. Entropy is the creative force in Nature.

This is meant to (over) emphasize the idea that, while Nature is selective of states with low energy, it can only choose among those states that were made accessible by entropy to begin with. Indeed, in the process of maximizing the number of accessible configurations (subject to any prevailing constraints), entropy produces diversity in Nature and hence variety in the properties of materials.

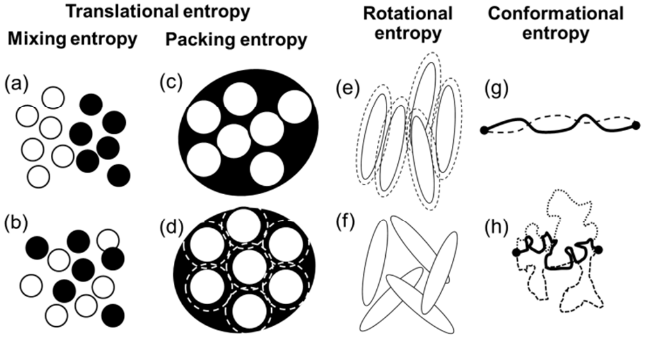

Fig. 1 Examples of different manifestations of entropy. A two-component system in states with segregated components (a) has less entropy than in states where components are spatially intermixed (b). Particles crowding in random configurations (c) could avoid jamming by arranging into orderly patterns (d), thus allowing access to more free volume around each particle (dashed circles). Rod-like particles have more rotational entropy if allowed to have uncorrelated axial orientations (f), but may align and lose orientational entropy if this is compensated by gains in packing entropy (e). Whole polymer chains typically have negligible translational or rotational entropy but have significant conformational entropy; chains lose conformational entropy when forced to have too large end-to-end distances (g) as this reduces the number of conformations accessible when less constrained (h).

2. Intelligent design of entropic interactions

2.1. Stabilizing and de-stabilizing colloidal suspensions

A well-established use of entropic interactions is the steric stabilization of colloidal suspensions via grafted oligomers or polymers.[24] Contact and aggregation of particles is precluded by the chains as they tend to extend out and avoid overlapping with chains from other particles in order to maximize their conformational entropy and reduce osmotic pressure gradients. This steric effect is less effective when polymer-grafted nanoparticles are not dispersed in a good solvent but in a polymer melt forming a nanocomposite (e.g., see [25,26]). In such cases, it has been shown that well-dispersed suspensions can be attained via chain-length polydispersity in the grafted chains to create net repulsive interparticle interactions over both short and long ranges.[27] Interestingly, for proper choices of grafting density and polymer chain length to particle size ratio, polymer-grafted nanoparticles can form well dispersed suspensions even in the absence of any solvent.[28-30]

The depletion interaction is perhaps one of the more clear examples where entropic effects have long been exploited and engineered.[31,32] A depletant is usually a non-adsorbing polymer or small particle that is added to a colloidal suspension of appreciably bigger particles to induce an effective attraction among them which can drive their aggregation and flocculation. This "attraction" is entropic in nature as it arises from the increased free volume (and translational entropy) that becomes accessible to the depletant when the larger particles come in close proximity. The range and strength of this entropic attraction can not only be tuned by the size and concentration of the depletant, but also be made selective for different surfaces of the big particles by creating therein roughness features that are either larger or smaller than the depletant size.[33] Indeed, the depletion attraction is suppressed if the depletant can fit inside the crevices of the roughness features, and roughening of selected surfaces has been exploited to microfabricate non-attractive patches on otherwise uniform (and attracting) micro-colloids to facilitate the assembly of target structures.[33-35]

2.2. Superselective nanoparticles

Many instances occur when the optimization of affinity and selectivity in the binding of ligands to substrates is not accomplished by simply creating a strong enthalpic binding but by leveraging both energetic and entropic effects. In this context multivalency has long been identified in the biology and chemistry communities as a strategy to design structure and function in living cells and soft matter.[36] As an illustration, consider the design of ligand-coated nanoparticles that can bind selectively to surfaces that display cognate receptors above a threshold surface concentration. A cartoonish setup for this system is shown in Fig. 2(a). Such superselectivity is relevant in immunology and cancer treatments where one may want to target diseased cells that overexpress a particular surface receptor, which appears at concentrations (n_R) above a certain threshold n_R*. Ideally, the binding would operate as an off-on switch so that it does not adsorb for $n_R < n_R$* (sparing normal cells) and it adsorbs strongly for n_R>n_R* only (allowing ensuing events to kill those receptor-overexpressing cells; e.g., if nanoparticles carry an active cargo). Considering first monovalent binders, i.e., a nanoparticle containing a single binding ligand (k=1), one could naively think that the binding energy could be tuned to optimize selectivity, but as Fig. 2(b) illustrates qualitatively, neither a weak nor a strong binder will approach the ideal superselective behaviour depicted by the "step function" (e.g., strong bonds will bind regardless of concentration). Using both theory, simulations, and experiments,[37,38] it has been shown that superselective behaviour can be approached by using relatively weak energetic bonds but with multiple viable ligands per nanoparticle (k>>1): For low receptor concentrations (n_R) the probability of binding is low with at most one (weak) bond, but as n_R increases, the number of simultaneous bonds (λ) increases for combinatorial (entropic) reasons making binding strong. In this case, the number of accessible bound microstates [see Eq. (1)] increases very quickly once n_R (besides k) is large enough; such a number can be estimated analytically for some limiting situations. References [37-38] show how the concentration of nanoparticles, the number of ligands, and the bonding energy can be tuned to optimize selectivity, and Ref. [39] uses similar concepts to describe superselectivity of multivalent polymers (as opposed to ligand-coated nanoparticles) to substrates. More generally, multivalency helps in these situations because it also circumvents the translational entropy loss of many monovalent ligands which opposes binding free energy; in a k-valent moiety this loss is only paid once, not k times.

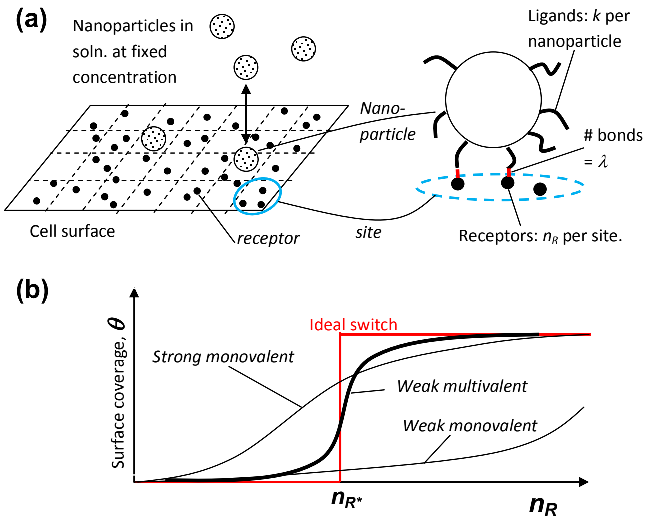

Fig. 2 Simplified model for multivalent nano-particle binding. (a) Illustration of cell surface expressing receptors (black dots) to which nanoparticles carrying a number (k) of ligands can bind; a receptor site is defined as the area covered by a bound nanoparticle. (b) Depiction of binding isotherms for different types of ligands and the ideal switch that would turn on at a receptor concentration threshold value n_R*.

2.3. Wet super-glues

One of the feats that Nature has long mastered is to create adhesives that work under water (including sea water) such as those used by tubeworms and mussels.[40] In this case, use is made of polypeptide chains with multiple charged groups (polyelectrolytes). Under some conditions, mixing oppositely charged polyelectrolytes in aqueous solution results in phase separation into two liquid phases, one aqueous polymer-dilute phase and the other a dense, polymer-rich phase called a coacervate.[41] Coacervates are ideal for dispensing adhesive proteins that allow some marine organisms to spread and adhere over selected surfaces. Surprisingly, despite the strong enthalpic interactions usually associated with charged groups, it has been found that complex coacervation (in natural and synthetic analogues) is an endothermic process (involving unfavourable enthalpic interactions); instead, it is essentially an entropy-driven process.[42,43] Indeed, coacervate formation involves the release of counter-ions (small ions that would otherwise be "bound" to the polyeletrolyte chains neutralizing oppositely charged groups) which leads to a concomitant increase of their translational entropy. Synthetic coacervates[44] have received much attention for the engineering of not only under-water and surgical adhesives and coatings but also of processed foods, cosmetics, and drug microencapsulation.[45]

2.4. Mesophase galore

Because entropy is involved with establishing structural order in materials, entropic forces are often crucial in the formation of materials whose molecular order is intermediate between crystals (having perfect order and typically reduced total entropy) and liquids (having high degree of disorder and typically high entropy). Such intermediate-order materials are called mesophases and they encompass such things as liquid crystals, plastic solids, elastomers, gels, microsegregated phases of block copolymers, glasses, and biomolecules with ordered domains like proteins (see Table 1 for a partial list). Such intermediate order is often manifested in the form of phases with novel structures and a combination of static and dynamic properties not observed in common materials. It is precisely this in-between character that has made mesophases attractive - and at times widely used - for practical applications. More recently, mesophases have been studied for such new uses as nanoporous materials for active layers in solar cells, battery electrodes, membranes for ultra-filtration, photonic devices, and high-performance plastics. Many such mesophases can occur even in the absence of enthalpic interactions and entropy can be responsible not only for the partial disorder (e.g., to optimize translational, rotational, or conformational entropy) but also for the partial order (e.g., to optimize packing or conformational entropy).

Table 1. Some mesophases and their relation to structural and dynamic behaviour. Order is understood to be long-range although in some mesophases this may not be the case.

Material	Positional order	Orientational order	Positional Immobility	Lack of flow
Typical crystal	Yes	Yes	Yes	Yes
Plastic crystal	Yes	No	Yes	Yes
Liquid crystal	Partial	Yes	No	No
Segregated	Partial	No	Partial	No
Glasses	No	No	Partial	Partial
Gels, networks	No	No	No	Yes
Typical liquid	No	No	No	No

While several mesophases from Table 1 will be featured in later sections, we here highlight simpler hard-core particle based liquid crystals (having orientational order and no positional order, like nematics and smectics) and rotator/plastic solids (having positional order but no orientational order). An early example of an entropy-driven disorder-to-mesophase phase transition is Onsager's prediction[46] for the alignment of long stiff rods above a threshold concentration to form a nematic phase (see Figs. 1e-1f). In contrast, largely because it only possesses translational degrees of freedom, no thermodynamically stable mesophase forms before the hard-sphere crystal melts as concentration decreases. These two examples suggest that particles with some anisotropy in shape such as rods[47] (or in energetic interactions like with dipolar or multipolar particles) are better suited than purely isotropic particles to form liquid crystals or rotator solids, though other mesophases may still occur due to the complex and cooperative ways entropic interactions operate. For instance, despite their isotropic interactions, hard disks in 2 dimensions exhibit a hexatic phase[48] (where particles possess short-range positional and a quasi-long-range orientational order), an elusive mesophase occurring between the isotropic phase at low concentrations and the hexagonal crystal at high concentrations. The contrasting mesophase behaviour of hard spheres in 3D and hard disks in 2D (akin to hard spheres confined to a plane) also illustrates how system dimensionality affects the types of structures that entropy can come up with.

The unpredictability of entropy can also be seen in the difficulty to predict behaviour by interpolating results from two related systems. For instance, knowing the 2D hard-disk behaviour and that hard squares in 2D form a tetratic mesophase[49] (with quasi-long range orientational order and short-range square-lattice positional order), it is hard to anticipate what kind of mesophases, e.g., hard "rounded squares" would form: a hexatic-like phase (as disks), a tetratic-like phase (as squares), or something else? It has been found that for certain degrees of roundedness, "something else" forms (see Fig. 3):[50] a dimorphic mesophase with patches having square symmetry (with high packing entropy) interspersed with patches having hexagonal symmetry (with higher orientational entropy). It is as though for such rounded squares entropy finds a hybrid solution where the two candidate symmetries are allowed to coexists (and dynamically interconvert) as "microphases", rather than as "macrophases" of either one or both.

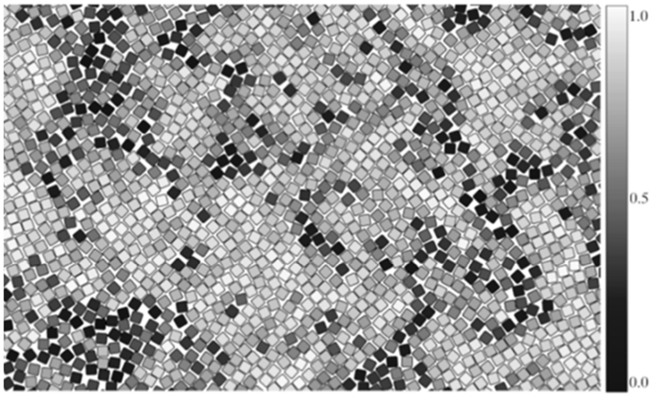

Fig. 3 Snapshot of the mesophase found for rounded squares (with round corner diameter equal to one third of the particle inradius) at an area coverage of ~78%. Particles are shaded based on the local value of the order parameter ψ_4 that captures "square-like" symmetry of neighbours around a particle (lighter/darker particles have more square/hexagonal symmetry). Reproduced from Ref. [50].

2.5. Super-tough rubbers

The effects of changes in conformational entropy of polymer chains are conveniently illustrated by the behaviour of rubbers or elastomers made up by flexible chains interacting neutrally with each other. Rubbers made of poly-dimethyl-siloxane (PDMS) chains end-linked by tetrafunctional crosslinkers provide a suitable common prototype. Elastomers are unusual in that the chains exhibit liquid-like local motions (viscous behaviour) but also have solid-like properties (elastic behaviour) arising from the crosslinks that prevent the material to flow as a liquid. As a PDMS rubber is stretched, the average end-to-end distance of the chains is increased, restricting the conformational freedom of the chains (see Figs. 1g-1h); the resulting reduction in entropy is manifested as a force that tries to restore the sample to its undeformed state.[51] If we were stretching the rubber between our two hands, we would be directly "sensing" the strength of entropy (and experiencing conformational entropy in action!). The elasticity of stretching chains has not only been extensively designed into useful man-made materials but it has been exploited for eons by Nature in such extraordinary materials as spider silk and natural adhesives and gels. In this context, a property that is often of interest is the toughness, which is the area under the force-extension curve, representing the energy that the material can absorb before it finally breaks. End-linked PDMS networks made of short chains will have high modulus (the slope of the force-extension curve) but low ultimate strain (the small extension where chain bonds start breaking) leading to limited toughness. Networks made of long chains have high ultimate strain but small modulus leading again to low toughness. See cartoons in Fig. 4a and 4b. It has been shown that networks made by crosslinking short and long chains (rather than using a single intermediate chain length) can significantly enhance toughness provided that the short chains are sufficiently abundant to percolate throughout the system and be elastically coupled to the longer chains (Fig. 4c).[52,53] In this case toughness arises from combining the strong resistance to deformation by the short chains with the facile extension of the long chain to prevent breakage (thus buffering or protecting the small chains). Note that toughness is enhanced here by purely entropic reasons: it simply combines synergistically the disparate changes of conformational entropy to deformation of two components of disparate chain length. A recent design involving a sequential crosslinking process of chains with a population of pre-stretched (low-entropy) sacrificial chains and relaxed (high-entropy) chains has been shown to provide substantial gains in toughness.[54]

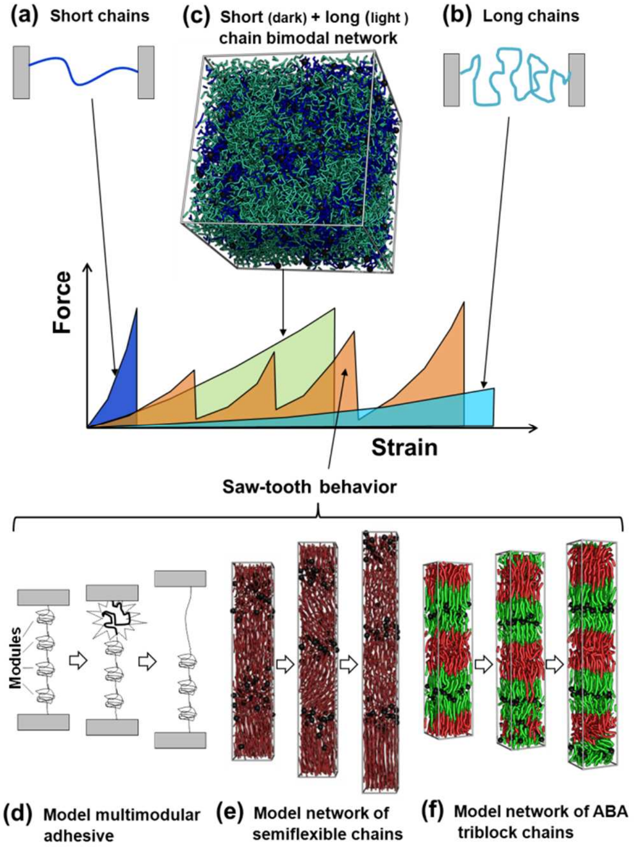

Fig. 4 Cartoon comparison of force-strain tensile responses and structural changes of various model polymer designs. The limited toughness of short (a) or long (b) chain networks can be overcome by bimodal networks[52] (c). Sawtooth response is shown for: (d) biopolymer glue in nacre,[55] (e) a model liquid-crystal elastomer, and (f) a model triblock copolymer elastomer [in (e) and (f) crosslinks are shown as dots and in (f) A/B chain blocks are green/red]. Panels (d), (e) and (f) depict how a single "tooth" arises: it is associated with the loss of a folded domain in nacre but with the creation of a new ordered domain in the elastomers.

Some natural super-tough materials such as the adhesive in abalone shells maximize toughness via a very different design principle; namely, by exhibiting a saw-tooth elastic response where the force periodically goes up but drops down each time a threshold is reached, which prevents the breakage of chemical bonds (Fig. 4d).[55] (The saw-tooth pattern cleverly increases the area under the force-strain curve). While each stress "tooth" is the free-energy barrier of an order-disorder transition associated with the loss of a folded domain in nacre, it can also be associated with the creation of a new ordered domain in nematic polydomain-forming elastomers (Fig. 4e).[56,57] In nacre, each such transition is energy-driven: the stress is absorbed by the loss of energetic contacts in the unfolding domain; in a model elastomer made up of semiflexible chains, each stress drop is entropy-driven: stretching induces the rearrangement of chains into more numerous smectic domains to better fit the space along the strain axis. Since the resistance to deformation in an elastomer composed of ordered and amorphous domains is associated with the free energy cost of rearranging those domains, the elastic properties of regular networks can be optimized by using building blocks that allow control of these free-energy barriers (their height and number). Accordingly, one could synergistically leverage the self-assembling properties of chains that are capable of forming entropy-driven liquid crystalline order (like semiflexible chains) and enthalpy-driven micro-segregated ordered phases (like block copolymers) to tune the non-linear elastic behaviour of end-chain crosslinked networks (Fig. 4f).[57]

2.6. Building new ordered phases with a little help from the polymers' entropy

Perhaps counterintuitively, increasing polymer conformational entropy may result in self-assembled structures with different or more intricate order. For instance, the trade-off gains in conformational entropy of AB diblock copolymers (DBCs) and the loss of translational entropy of nanoparticles has been shown to lead to phases where both DBCs and particles form spatially periodic structures.[58] This also happens for systems containing DBCs which can produce bicontinuous morphologies, like the gyroid (G), double-diamond (DD), and plumber's nightmare (P) phases.[59] In a bicontinuous phase, the minority-block domains (say, type A) form two interweaving networks made up by struts that merge into nodes that sit on a regular lattice. The 3D interconnectivity of these A-block networks makes them ideal candidates as precursors of porous membranes, catalytic supports, and high conductivity nanocomposites.[60,61] However, bicontinuous phases are very difficult to find in systems containing DBC melts; in fact only the G phase is stable in pure DBCs and only over a very limited region in the composition-temperature space. It has been shown that the limited stability of bicontinuous phases is due to "packing frustration"; i.e., the entropic penalty that the chains experience as they overstretch in an ineffective attempt to fill up the space inside the bulky network nodes.[62-65] Such a frustration is more severe when the nodes are bulkier (hence having a bigger "hole" to fill), explaining why the G phase is the best suited for stabilization: The G phase nodes (where 3 struts connect) are smaller than those of the DD phase (where 4 struts connect) and of the P phase (where 6 struts connect). One strategy to fight off this packing frustration is by adding to the DBC a homopolymer of type A which will preferentially "fill in" the nodal centres where the packing frustration originates.[63-65] This implies, however, a rather tricky balancing act: if the A chains are long, they may prefer to stay in the bulkier nodal regions but may also rather phase segregate to form a separate phase (of nearly pure A chains) to be more unconstrained; if they are short, they will not phase separate but could be ineffective at alleviating packing frustration as they will not tend to stay confined inside the nodal regions (potentially acting as a good solvent that also swells the interblock interfaces). The "correct" length of the A-chain additive can lead to not only an amplification of the region where the G phase is stable but also allow the DD and P phases to become stable[65,66] (see Fig. 5a). It is worth reflecting on how such a feat is attained: By maximizing the conformational entropy of both the A-chain additive (which makes it prefer the roomier nodes over the more constraining struts) and the DBC chains encasing the nodes (which would overstretch without the added A chains), highly ordered mesophases are stabilized. More entropy leads here to phases with more complex order. A similar use of selective homopolymers (that can spatially redistribute) has also been used to relieve packing frustration to allow lamellar-phase forming block copolymers deposited on a substrate to readily form defect-free non-regular patterns on chemically nanopatterned substrates (for potential use in microelectronic devices).[67]

The packing entropy of chains has also been exploited, in combination with multi-blocks having enthalpic and entropic disparities, to engineer a great variety of liquid crystals of increasing complexity. Tschierske et al., e.g., have pioneered the use of T-shaped and X-shaped molecules which are tri- or tetra-philic, having a rod-like aromatic core, polar groups at its two ends, and non-polar flexible chains at the sides.[68] These molecules often form honeycomb phases made up of columnar cells of polygonal cross sections,[68-71] with the rods (lying normal to the columns) forming the cell walls, the polar groups "gluing" the wall seams, and the lateral chains filling the interior of the cells (see Fig. 5b). Depending on the lateral chain lengths used (and temperature), the polygons may exhibit single shapes, or combinations of different polygons, including a case with 5 "colour" tiles for X-shaped polyphiles.[70] The tiling complexity arises in part to optimize the space allotted to accommodate the side-chains; e.g., single space-tiling shapes could be either too big or too small to be filled by chains of a given length. Such designers' honeycombs can not only enhance the potential technological uses of liquid crystals but also be used as mimics of some complex biological tissues.[68]

2.7. When entropy controls the assembly of patchy particles

The assembly behaviour of spherical particles with attractive patches (like Janus particles) has been extensively studied via experiments and modelling and advances in the field are periodically reviewed (see, e.g., Refs. [11-13]). Therefore, only two recent studies are highlighted here.

For a number of applications, crystal lattices with open structures (like the highly regarded diamond lattice) rather than closed packed ones are often of interest; e.g., for photonic and catalytic materials.[72] Such open structures can be accessed in a variety of ways, for example by creating binary lattices from which one of the components is etched away,[73] by creating the 'negative' of a structure formed by colloids, by inverse-designing isotropic potential interaction energies that target a desired open structure,[74-76] by soft colloids made of telechelic star polymers,[77] and even using (entropic) particle shape alone.[78]

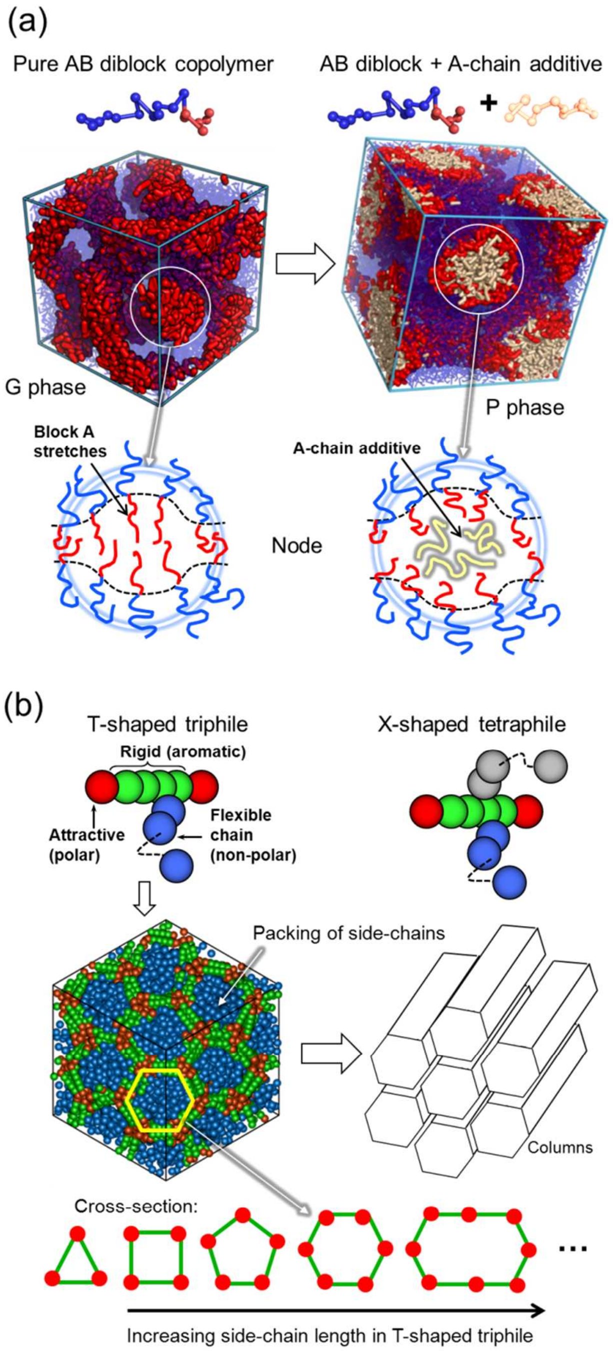

Fig. 5 Chain packing and order. (a) Left: Illustration of packing frustration inside the nodes formed by the A-block network of a gyroid (G) phase in a pure AB diblock copolymer, wherein filling the nodes forces the chains to stretch, hence reducing their conformational entropy. Right: Adding a homopolymer compatible with the A-block can alleviate packing frustration if the homopolymer length is large enough to have a marked preference to populate the nodes but short enough to avoid macrophase separation. This can allow more complex ordered phases to form, like the plumbers' nightmare (P) phase which necessitates very bulky nodes. (b) Coarse-grained architecture of T-shaped and X-shaped polyphiles and structure of some of the liquid crystalline phases formed by the former. The geometry of cross sectional tiling depends on the packing of the side-chains.

Patchy particles provide a promising avenue toward the formation of stable open crystalline structures as has been found via experiments and modeling.[12,79] For example, by using so-called triblock Janus spheres in 2D,[80] it has been found that entropy is a key player in the formation of open Kagomé lattices.[81] The explanation for this is not trivial since packing entropy typically favours lattices that pack most efficiently (and hence achieve the highest density), which for spheres in 2D would be the hexagonal lattice (see Figs. 6a-6b). But the interaction among patches (for patches of appropriately chosen size and attraction strength) constrains the problem in such a way that the "best solution" (i.e., the one with the lowest free energy) is no longer the hexagonal arrangement. For both the Kagomé and hexagonal lattices one can identify two main kinds of motions (neglecting defect dynamics): local particle rotations and cooperative vibrations. For both lattices each particle has the same number of attractive patch-patch contacts (energy) and rotations are of comparable amplitude (and associated entropy). Without this rotational entropy the open Kagomé lattice would be mechanically unstable. While at very high osmotic pressures the hexagonal lattice will necessarily be favoured, at low to intermediate osmotic pressures both lattices could form, with vibrational motions becoming determinant of thermodynamic stability. At such conditions each particle in a hexagonal lattice has additional lateral contacts (which only provide steric hindrance and no attractive energy) and hence has more constrained vibrations and less associated entropy than a particle in a Kagomé lattice.[81-83]

For patchy colloids in 3D, entropy can stabilize not only open-structure crystals over close-packed ones but also stabilize the liquid phase over any crystal even as temperature approaches the absolute zero.[84,85] This may occur, e.g., for colloidal spheres that have a small number of directional long ligands or broad patches which are monovalent, that is, satisfy the flexible-bond and the one-bond-per-patch conditions (this could be realized, e.g., via complementary DNA strands[84]). For properly chosen patch number (e.g., four in Ref. [85]), patch size, bond energy, and osmotic pressure, crystal and liquid states at low temperature are fully bonded (i.e., each particle has all its patches bonded) and hence have the same potential energy. As in the previous example, thermodynamic stability is then determined by entropy. Although the liquid's vibrational entropy will be (slightly) lower than that of the crystal due to the more efficient packing of the latter, this is more than compensated by the large configurational entropy of the liquid (associated with the large number of ways that fully-bonded disordered states can be realized). Unlike normal atomic or molecular systems for which entropy vanishes and energy rules as temperature approaches the absolute zero, in these patchy colloids entropy not only remains high but it rules! Figures 6c and 6d show a cartoonish depiction of this idea but in a 2D scenario for simplicity. Such hard-to-freeze liquids are relevant to the study of glass formers and network-forming liquids.[86]

While the examples in this Section could be seen as cases where experimentally motivated modelling efforts led to the *a posteriori* realization of the key role played by entropy, they are good candidates for future *a priori* design. For instance, the tools used in Ref. [81] for 2D models are being adopted to guide the design of open crystalline arrangements in 3D.[81-83]

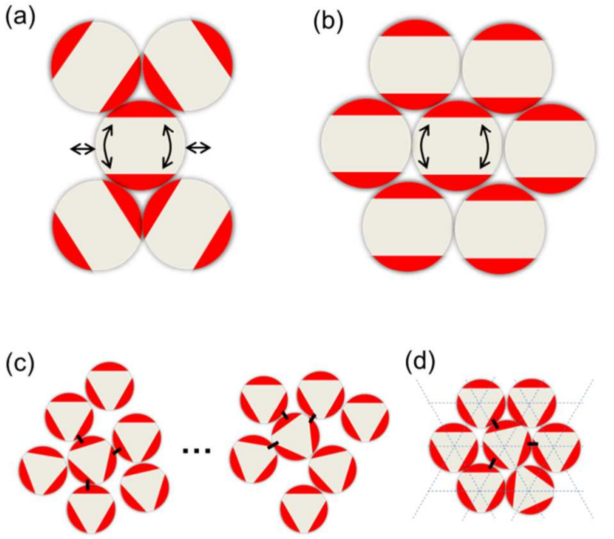

Fig. 6 Competing structures for triblock Janus particles[81] in (a) and (b), and for a 2D Smallenburg-Sciortino model[85] in (c) and (d). Attractive patches are in red. Sketch of Kagomé (a) and hexagonal (b) lattice for triblock Janus particles: The central particle in (b) experiences additional lateral constraints. In (c) and (d), each patch can only form a single bond and the bonds for the central particle only are shown in liquid configurations (c) and a solid configuration (d).

3. Polyhedral particles as potential super-assemblers

The examples in Sections 2.4 and 2.7 illustrate one of the often touted paradigm shifts in materials design that points toward a new "chemistry" of larger building-blocks, wherein rather than only relying on the usual periodic-table elements as building blocks of molecules, one can now have much more flexibility by using colloids as building blocks. Colloidal nano- (or micro-) particles would then be seen as a sort of "super-atoms" whose chemistry can be changed to suit a particular application by using any number of atomic species.[87] Crucially, such particles can be manipulated along many different axes of variability;[88] e.g., with selective patches of different size, shape, and number[12] (Janus particles being one of the most popular examples), core-shell structures, multi-axial symmetry, different levels of shape asphericity (from oblate to prolate), varying extent of faceting (as in polyhedra), etc. Polyhedral systems[74,89-102] have received significant attention in part because there currently exists many synthesis protocols that can produce large samples of highly monodisperse polyhedral shapes (e.g., those of the truncated-cube family via the modified polyol process[102]) and for different chemical compositions and surface functionalizations.[87,98]

3.1. Pure components

Among all polyhedral shapes, we focus here on studies of a subset of them, namely those that at close packing can tessellate space,[89-91,100] either completely, such as cubes, truncated octahedra, rhombic dodecahedra, hexagonal prisms, etc., or nearly, like cuboctahedra[101] (a complementary issue of interest not discussed here is finding the densest packing structure of arbitrary polyhedra[92-97]). Because such space filling polyhedra (SFPs) could be seen as encoding in their shape the instructions to assemble into perfect crystals at high concentrations, they have the potential to be the “super self-assemblers” of the polyhedral family. But not any SFP will do as good self-assemblers need to have some rotational symmetry (implying sets of repeated regular facets) so that a built-in redundancy exist - i.e., favourable combinatorial entropy - in the way local order can arise when multiple particles come together.[91] Tell-tale signs of the tendency of such particles to order can even be anticipated from the way that two such particles interact. Figure 7 illustrates the fact that the repulsive interaction between two cubes has the shortest range (or most “attractive” in relative terms) when the cubes come in contact face-to-face.[91] It is as though there is a directional entropic bond that tends to bring cubes face to face, but the strength of this “bond” is concentration dependent. It is only at high enough concentrations (when free space needed for motion is scarce) that this tendency for flat facets to align parallel to each other (and globally order) can increase packing entropy enough to compensate for any associated loss of rotational entropy in the isotropic state. This is akin to cars parking in an orderly fashion to make best use of space in a crowded unmarked parking lot or to dancers choosing to slow-dance rather than (vainly trying) to break-dance in a packed ballroom. While the basic concept is the same as Onsager’s explanation for the alignment of rigid rods,[82] the idea of entropic bonds as drivers of assembly in polyhedral particles has attracted renewed attention[91,98,99,103] and has led to theoretical efforts to generalize it in the context of other entropic interactions.[104]

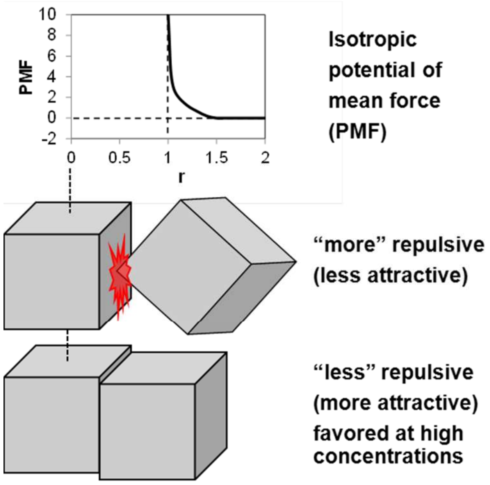

Fig. 7 Isotropic potential of mean force for hard cubes[91] (top) as a function of the distance (r) between the centres of mass of two cubes. The interaction is purely repulsive but is not isotropic; depending on the orientation of the cubes the interaction can be more repulsive (due to a longer range of the interaction) as in the middle panel or less repulsive as in the bottom panel; more or less repulsion can be re-interpreted as relatively less or more “attraction” and hence as an entropic directional bond. At high concentrations these “bonds” help particles dock into efficient-packing configurations (like cars in a crowded parking lot).

Because SFP crystals possess a structural order with multiple degrees of freedom associated with the particles’ positional and orientation order, they are good candidates to form mesophases (see Sec. 2.4). This is because while in route to the fully-disordered isotropic phase as concentration decreases, the crystal may loosen up to form structures with partial order where some of the ordering degrees of freedom are kept but others are lost. For instance, if positional (orientational) order is kept and orientational (positional) order is lost, a rotator (liquid crystalline) phase would be observed. This conjecture has been proven correct for many regular SFPs[88,100] and nearly SFPs,[99,101,105] e.g., truncated octahedra and rhombic dodecahedra form rotator plastic mesophases while prolate and oblate prisms (triangular, hexagonal, and square) form liquid crystals. Cubes exhibit a mesophase where the particle positions lie on average on a cubic lattice[100] but exhibit liquid-like fluctuations and mobility.[91] Of course, particles need not be (near) SFP to form mesophases; e.g., hard tetrahedra have been shown to form a quasi-crystal[93,94] and many low asphericity polyhedra to form rotator solid phases,[99,101,105] including truncated dodecahedra which remarkably form the structure of γ-brass that involves 52 atoms per unit cell.[99]

To be a super self-assembler, a system should have a fast disorder-to-order transition kinetics. Hard spheres, the workhorse of colloidal suspensions, can provide a suitable point of reference.[106] Truncated octahedra, rhombic dodecahedra, and cuboctahedra are all rather round-shaped SFPs that have a similar isotropic-to-solid phase transition as hard spheres, given that primarily translational order is nucleated (the rotator phase for these SFPs essentially lacks long-range orientational order).[107] Hence, one could have conjectured that the kinetics of their rotator-phase homogeneous nucleation would be comparable to that for the nucleation of translational order in hard-spheres. It has been found, however, that for comparable degrees of supersaturation these three polyhedra have significantly lower free-energy barriers and faster solid nucleation rates than hard spheres.[107] Such disparate nucleation kinetics primarily stems from the coupling of localized orientational ordering (present even in the isotropic phase) with fluctuations in local translational order. This coupling creates a positive feedback loop wherein the spontaneous local alignment of particles helps steer them toward positions with translational order; conversely, regions that have established translational order (like at the interface of the solid nucleus) in turn make fluctuations with high orientational order more common. More generally, if the goal is to form a perfect crystal by concentrating an initially isotropic colloidal suspension, then it is conjectured that (as in the previous example) the presence of a mesophase provides a “fastlane” for self-assembly by effectively chopping down the high free-energy barrier separating the fully disordered and fully ordered states into two smaller barriers: one for the isotropic-to-mesophase transition and the other for the mesophase-to-crystal transition (see Fig. 8). Hence, selecting particle shapes that form mesophases or providing conditions that induce them can be a general strategy for the entropic catalysis of ordered structures.

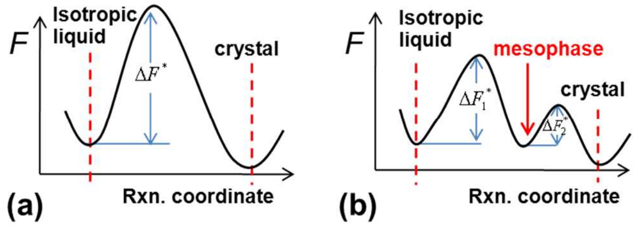

Fig. 8 Qualitative illustration of the idea that when a mesophase forms, the isotropic-to-crystal free-energy barrier (ΔF^*) as in (a) is effectively broken up into two smaller barriers (ΔF_1^* and ΔF_2^*) as in (b), hence catalysing the kinetics of the process.

3.2. Solid compounds and alloys

The potential of some SFPs and nearly SFPs as super self-assemblers can also be attested in their ability to resist the disordering effect of size polydispersity;[105] e.g., cubes have been found to be able to still form a cubic crystal for a polydispersity as high as 11.7%,[108] a value that is twice larger than that for polydisperse hard spheres.[109] This is partly due to the stabilizing effect on translational order of the orientational order correlations encoded in those SPFs.

Beyond size polydispersity, shape polydispersity can open new doors for assemblability. Colloidal nanoparticles can be used in an analogous way to atoms in traditional chemistry, where compounds can be assembled from different atoms or alloys made from different metals.[13,68] The idea of forming space-filling compounds from two types of hard polyhedra which individually do not tessellate space has already been explored and cases have been found where such compounds would be thermodynamically stable and accessible from the isotropic state (like a 1:1 mixture of octahedra and cuboctahedra of equal edge-length).[110] More generally, enhancing solid-phase miscibility between compounds is an attractive way to create new materials with properties intermediate between those of the pure constituents. Despite mixing entropy always being favourable (see, e.g., Figs. 1a-1b), it is difficult to entropically co-assemble a crystal from two components whose pure solids have different lattice motifs. Since the size of the components determines the characteristic lattice spacing of the pure solids, a key goal is to find size ratios that optimize their ordered co-assembly. Recent simulations suggest that the similarity in the order-disorder pressure (ODP) of the components is a good guide toward that goal.[108,111] This can be illustrated with a mixture of spheres and cubes. In the pressure-composition phase diagram, this mixture exhibits eutectic behaviour, with minimal inter-species mixing at high pressures where sphere-rich and cube-rich solids ensue. If one chooses, for example, the sphere diameter to be equal to the cube edge, the ODPs of the two pure components will be significantly different and minimal solubility of cubes in the sphere-rich fcc solid is achieved.[111] The ODP marks the turning point where packing entropy takes over as the dominant entropic force, hence driving the ordering of the system; i.e., it captures the readiness of a pure component to order. A loose analogy is to liken this compatibilization problem to that of trying to marry a couple A and B, and the ODP to a measure of the readiness of each partner to get married: if $\mathrm{ODP_B} << \mathrm{ODP_A}$, then for $\mathrm{ODP_B}$ < pressure < $\mathrm{ODP_A}$ individual B is ready to commit (order) while individual A is not. But if $\mathrm{ODP_A} \approx \mathrm{ODP_B}$, then above this pressure both partners are ready to commit simultaneously (having "synchronized" their tendencies to order) and stand a good chance to maximize their mixing in the ordered state. For the spheres and cubes, their ODPs match if the sphere diameter is 1.23 times the cube side edge.[108] The resulting phase diagram presented in Fig. 9 shows that at the eutectic pressure the sphere-rich fcc crystal dissolves a sizable amount of cubes (~20%), while simultaneously the cube-rich cubic solid dissolves a significant amount of spheres (~20%). It can be shown that ODP equality translates into roughly equal entropies for particles in the pure A and B ordered phases,[112] a condition that should favour their productive co-assembly. If furthermore pure A and B form the *same type* of mesophase, then their rotational entropies would be comparable and ODP equality would translate into similar *packing* entropies ("free volume" per particle), a stronger predictor of mixing compatibility. Indeed, ODP-matched polyhedra that individually form rotator mesophases lead to an even better entropic "marriage" wherein a mixed rotator phase forms for all compositions.[112]

While only entropy-driven solubility is discussed here, enthalpic interactions can readily help the co-assembly of A-B solids; e.g., by making A-B contacts more favourable than both A-A and B-B contacts.[110]

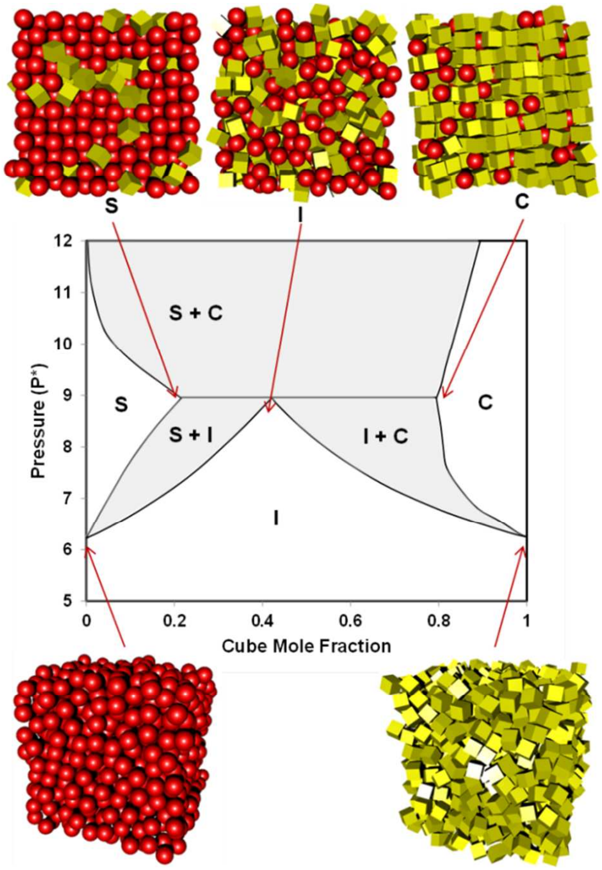

Fig. 9 Phase diagram for mixtures of hard cubes & hard spheres where the sphere diameter is 1.23 times the cube side. Two-phase regions are shaded and snapshots show coexisting phases at selected single-phase states. Phases are labelled as: I = isotropic liquid, C = cube-rich cubic solid, S = sphere-rich fcc solid. Adapted from Ref. [108].

Conclusions and Outlook

For some people still, entropy is simply an obscure player that causes disorder and chaos in a system and should hence be kept in check. Indeed, entropy is allegedly the culprit for the expected "heat death" of the universe when all order in the universe would degrade. But many scientists and engineers routinely try to understand the behaviour of systems by looking at the unique contributions and the interplay of the two fundamental driving forces: energy (or enthalpy) and entropy. The deeper understanding thus gained, however, is not always easy to translate to other systems. Indeed, while the use of models or experiments where components interact only though effectively hard-core potentials (where internal energy does not depend on density) allows the isolation of entropic effects, the addition of enthalpic interactions can sometimes bias the behaviour toward surprising solutions. Engineering entropy is highly non trivial.

The few examples provided in the previous sections illustrate that materials science is full of obvious and subtle cases where entropic forces allow a system the essential "freedom" to access different types of behaviour and even structural order (e.g., in certain crystals and mesophases) that would not occur if energetic forces were to rule unchallenged. We can let entropy create alternative viable "solutions" or ways for a structure to occur. After all, there are only two primary driving forces in Nature, energy and entropy, and there is no reason why entropy should play second fiddle. A fourth and final aphorism is hence justified:

Aphorism #4: Highly ordered and complex systems have arisen in Nature not despite of entropy but because of it.

Indeed, beyond man-made materials, even the human brain and any other marvel of high organization and order have occurred in our world, not by defeating entropy but by recruiting its help. Entropy has been at play at all length and time scales, from the tendency of mixing or stabilizing components in a solution (in cells or cell membranes) to the tendency of genome diversification via mutations in the genetic code or the "Monte Carlo-like" reshuffling of genes during various forms of reproduction. In fact, natural evolution as we know it would not have happened had entropy not played a crucial diversifying role as part of the mechanisms that gradually change a species to allow its survival.[113] In a shorter time scale, the importance of quasi random mutations to the survival of a given individual can be clearly seen in our humoral immune responses, which allow our bodies to create (via an accelerated natural mutation process) specific antibodies to neutralize antigens from invaders. The Darwinian idea of natural selection where the environment (like energy) provides a selective pressure on a purposely diverse population (as enabled by entropy) for the survival of the fittest has a loose analogy with the energy-entropy interplay as already encapsulated by Aphorism #3.

Of course, entropy can also be bad or even ugly, at least from a human perspective. Referring back to genetic mutations, their accumulation (often catalysed by external agents) in cells and tissues can lead not only to aging but also to many auto-immune diseases and cancers. But even when entropy can be perceived as the enemy, we – like any good leader - should try to "keep our friends close and our enemies even closer" as foes can be made to work toward a higher goal. In the design of therapeutics, however, enthalpic interactions as opposed to entropic ones, have often been the target. That is the basis of many drugs that seek a specific molecular target in the body; such a specificity and selectivity is encoded in the drug's chemistry and hence its energetic interactions with other molecules. In typical vaccines, of course, one can see the synergism of entropy (in allowing the immune response to sample its compositional space of antibodies) and energy (in selecting for high affinity interactions). And as the example on super-selective ligand carriers of Sec. 2.2 illustrated, the multiplicity of options provided by entropy can also play a most helpful role. Cancer and many viruses have certainly leveraged combinatorics to their advantage (they have had entropy on their side); engineering entropy could allow us to defeat cancer in its own game.[114,115]

We can all benefit from a better understanding of the bad, the ugly, and the good that entropy can do. But no matter how intimately we may get to know the non-intuitive intricacies of entropy, its mysterious veil may never be fully lifted and we may perpetually be surprised by its new, beautiful incarnations and amused by its ingenuity. After all, energy is finite, entropy is boundless.

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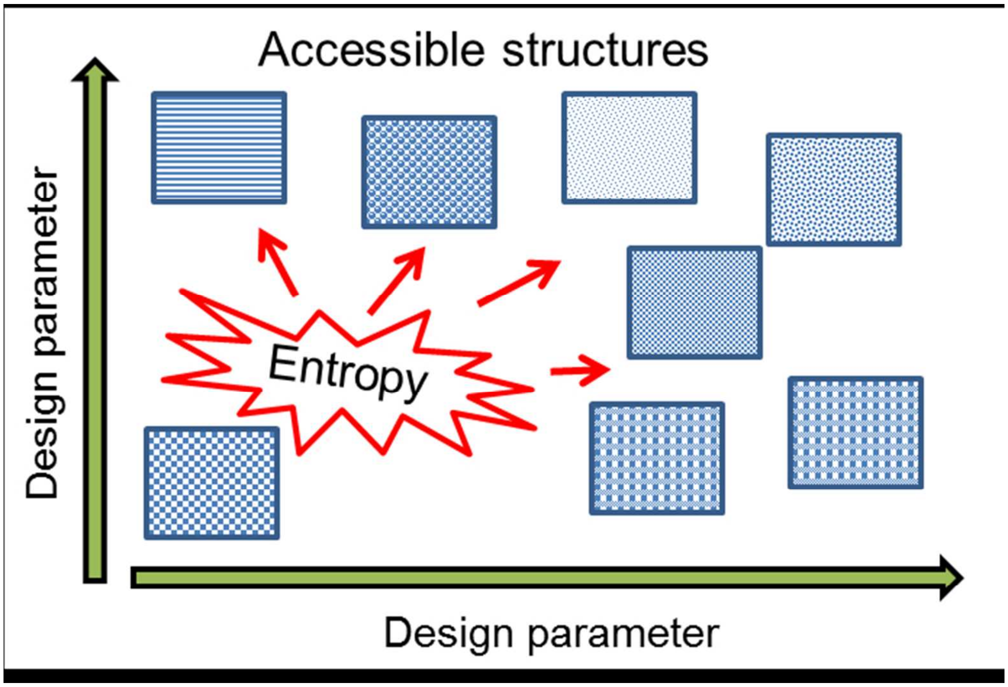

Although often fought against or designed accidentally, the intelligent design of entropy can lead to novel materials and phase behaviours