How to include azeotropy in the design of self-assembling Patchy Particles systems

Camilla Beneduce,1 Francesco Sciortino,1 Petr Šulc,2 and John Russo1

1 Dipartimento di Fisica, Sapienza Università di Roma, P.le Aldo Moro 5, 00185 Rome, Italy
2 School of Molecular Sciences and Center for Molecular Design and Biomimetics, The Biodesign Institute, Arizona State University, 1001 South McAllister Avenue, Tempe, Arizona 85281, USA

The goal of inverse self-assembly is to design inter-particle interactions capable of assembling the units into a desired target structure. The effective assembly of complex structures often requires the use of multiple components, each new component increasing the thermodynamic degrees of freedom and hence the complexity of the self-assembly pathway. In this work we explore the possibility to use azeotropy, i.e. a special thermodynamic condition where the system behaves effectively as a one-component system, as a way to control the self-assembly of an arbitrarily high number of components. In the context of Wertheim’s perturbation theory we show how to design Patchy particle systems that exhibit azeotropic points along the desired self-assembly pathway. As an example we map the full phase diagram of a binary mixture that fully assembles into cubic (and only cubic) diamond via an azeotropic point.

INTRODUCTION

When interactions between particles in a gas phase have strength comparable or larger than the thermal energy, the system becomes unstable and the particles condense searching for a lower free energy state. The spontaneous formation of inter-particle bonds, gives rise to larger and larger particle aggregates, originating a final structure that can be either an ordered lattice, a connected percolating structure (e.g. a liquid), or a collection of finite size clusters. This spontaneous search for the lowest free energy state, when originating ordered finite size or periodic structures is called self-assembly [1, 2]. While the computation of the free energy of a structure is a laborious but solved problem in statistical mechanics, several challenges hamper our understanding of self-assembly and our ability to mimic natural systems. In the direct self-assembly problem, one starts from a set of predetermined elementary units with known inter-particle interactions and is tasked with selecting structures that correspond to free energy minima. This is done either with intuition (for simple structures), with brute force approaches (direct molecular simulations), or with specialized algorithms [3, 4]. Even more challenging is the inverse self-assembly problem, where one is tasked with designing the inter-particle interactions that will self-assemble a desired target structure [5, 6]. In this case the problems are two-fold: after designing an interaction-potential, one has the direct problem of confirming that there are no alternative routes that preempt the formation of the target structure. So far, two types of approaches have been explored: optimisation algorithms and geometrical strategies. Optimisation algorithms allow one to design a pair potential whose free-energy minima is guaranteed to be the desired structure [6, 14]. However, the inter-particle interactions that result from such procedures are often too complex and require a degree of precision that is out of reach for experimental realisation. In geometrical strategies, instead, one matches the geometric features of the target structure by tuning some interaction properties of the building units, e.g. the shape and the directionality of the bonds, in order to match the geometric features of the target structure [16–29]. Although it is an experimentally feasible route, it is system specific and it requires a high degree of geometrical intuition.

A different solution strategy to the inverse self-assembly problem is to extend the number of building blocks, going from single component systems to multi-component mixtures, shifting the problem of designing complex single particle potentials to that of optimizing simpler (and more geometrical) interactions between multiple components. Extending the alphabet of building blocks, i.e. the number of components, lowers the degree of symmetry in the final structure, allowing for a considerable reduction in competing structures, and an easier assembly pathway towards the target design. Compared to single-component mixtures, and leaving experimental challenges aside, two major problems are introduced by the increase in the number of components: a combinatorial problem and a thermodynamic problem.

The combinatorial problem arises from the fact that each new component increases exponentially the space of possible solutions, and with that the time required to find a solution. To tackle it, advanced optimization algorithms are necessary, such as genetic algorithms [24] or machine learning [15–25]. Some of us have recently introduced a novel approach called SAT-assembly [26, 27], aimed at the design of multi-component mixtures of patchy particles that spontaneously assemble into a predetermined structure. In this approach, the bond colouring is translated into a Boolean satisfiability (SAT) problem by encoding the bond topology of the target structure into a system of Boolean equations whose solution gives the interaction matrix between different patches. One
needs to fix only the desired number of species (i.e. different types of patchy particles) and the desired number of patch types (colours), and the SAT-assembly approach can efficiently search the space of all the possible patch colourings and the colour interaction matrices to find solutions that have the target structure as their energy minimum. The sophistication of modern SAT solvers [28] allows to effectively tackle the combinatorial problem for complex assemblies, including open crystalline structures, photonic crystals, and clathrate structures. Another distinct advantage of the SAT-assembly strategy is to avoid the formation of competing structures. In some cases, this can be achieved by explicitly encoding Boolean clauses that ensure that competing structures cannot be formed, or by using the SAT solvers to enumerate possible interaction matrices, which can be quickly tested for their ability to form competing structures. Iteratively, one can find the solution that is guaranteed not to have the competing structures as a minimum energy of the designed interaction potential.

The thermodynamic problem arises instead because, according to Gibbs rule of phases, each component represents an additional thermodynamic degree of freedom of the system, extending the phase behaviour phenomenology in ways that can interfere with the self-assembly pathway. Full phase diagram calculations are very time-consuming, and are often avoided in multi-component systems due to their complexity. The goal of this article is to show how to overcome the thermodynamic difficulties associated with the use of multicomponent mixtures, by explicitly encoding azeotropic points in the self-assembly designs of Patchy Particles. The azeotropic point is a point where the free-energy of the mixture can be written as that of an effective one-component system. The ability to explicitly include azeotropic points along the self-assembly pathways of these systems thus represents an attractive strategy to tame the complexity in phase behaviour usually associated with multi-component mixtures. Some of the advantages of combining azeotropic behaviour with self-assembly are listed below. 1) the ability to (considerably) increase the reaction rates of the self-assembly process by quenching the system in a region of (liquid-gas) metastability: in fact, it is well-established that nucleation rates increase in proximity of critical points [29] and spinodal locus [30]; ii) increase the kinetics of the self-assembly reaction: if the concentration of the azeotropic point is the same as the crystal composition, one can avoid slow diffusion-limited process, where the crystal nucleus has to wait for the concentration of the local environment to match the one of the target structure [31]; iii) the yield of the self-assembly process can proceed theoretically until all components are exhausted (to 100%), as the liquid phase will form at the same composition of the target crystalline structures.

In this article we will first show how to control azeotropy in mixtures of patchy particles. We will discuss the general case, but use as an example a simple binary mixture that is designed to form the cubic diamond crystal. We will show results from both Wertheim thermodynamic theory, solved with the isochoric thermodynamic’s framework, and from direct Monte Carlo simulations, employing biased moves [32] and the Gibbs ensemble [33] [34]. We will show that the simple mixture we investigate as an example presents a very interesting phase behaviour, where demixing only occurs for mixed states, and not for the pure states.

MODELS AND THEORY

Patchy particles

Our building units are patchy particles of diameter $\sigma$. They are a model of colloidal particles whose surface is decorated by attractive sites, named patches [35]. In Fig. 1 we draw schematically two particles which patches are arranged in a tetrahedral geometry. We describe the pair interaction $V_{pp}$ between two patchy particles through the Kern-Frenkel potential [36] [37]: a square well potential $V_{SW}$ of depth $\epsilon$ and range $\sigma + \delta$ modulated by a term $f$ depending on the patch particles orientation. Therefore two patchy particles cannot overlap, i.e. their distance is always larger than their diameter $\sigma$, whereas they attract in a strongly directional way if they are at distance between $\sigma$ and $\sigma + \delta$ and if a line connecting their centres intersects the volume of both patches involved in the bond. The interaction is

$$V_{pp}(\mathbf{r}_{ij}, \mathbf{r}_{\alpha,i}, \mathbf{r}_{\beta,j}) = V_{SW}(\mathbf{r}_{ij}) f(\mathbf{r}_{ij}, \mathbf{r}_{\alpha,i}, \mathbf{r}_{\beta,j}) \quad (1)$$

with

$$f(\mathbf{r}_{ij}, \mathbf{r}_{\alpha,i}, \mathbf{r}_{\beta,j}) = \begin{cases} 1 & \text{if } \mathbf{r}_{ij} \cdot \mathbf{r}_{\alpha,i} > \cos(\theta_{max}) \\ 0 & \text{otherwise} \end{cases} \quad (2)$$

For identical patches, the Kern-Frenkel potential is characterised by the two independent parameters $\delta$ and $\theta_{max}$ that specify the range and the angular width of the patches respectively (see Fig. 1) and that can be tuned giving rise to different phase diagrams [35].

As for any short-ranged patchy potential (in the single-bond per patch condition), the static properties are controlled by the bonding volume [35], i.e. the volume in which a particle can move while being bonded to another particle, which for the Kern-Frenkel potential assumes the following simple expression $V_b = \frac{4}{3}(\sigma + \delta)^3 - \sigma^3 \left[ \frac{1 - \cos(\theta_{max})}{2} \right]^2$. 

Patchy particles are an effective and easy model to tackle the inverse self-assembly task since they open up the possibility to control the valence and to encode the desired topology in the number, the placement and the type of patches. Apart from their modeling convenience, patchy particles are also experimentally viable systems: short ranged anisotropic interactions between colloidal particles have in fact been achieved via chemical patterning of their surfaces [39,42], via modelling of their shape [43] or by attaching single strands of DNA to well-defined positions on their surface [44,45] such that colloids of different types can selectively bind to each other.

In the rest of this work energy is measured in units of the square-well depth ($\epsilon$), distances in units of the patchy particle diameter ($\sigma$), and $k_B = 1$.

**SAT-assembly**

With patchy particles as elementary units, the number and the surface arrangement of the patches is chosen to reflect the geometric properties of the target structure. However, for a given number of different patches $N_p$ and species $N_s$, determining how patchy particles must interact one with the other, in such a way that the desired structure is the lowest energy fully bonded one, is a challenging combinatorial task. It can be addressed with the SAT-assembly framework first introduced in references [26, 27]. Briefly, the algorithm determines the interaction matrix, that is a square symmetric matrix of order $N_s N_p$, the same as the number of distinct patches, whose elements $a_{ij}$ are 0 if patches $i$ and $j$ do not interact or 1 if between patches $i$ and $j$ a bond can be created.

We deal with the combinatorial task of finding non-trivial interaction matrixes in which all bonds are formed in the target structure. In practice this is achieved by solving a satisfiability (SAT) problem, in which the topology of the target structure is converted in a list of Boolean clauses, and whose solution produces the interaction matrix. In the inverse design problems studied with SAT-assembly so far, the typical tasks convert into millions of Boolean equations encoding constraints that ten of thousand of Boolean variables must satisfy.

Another crucial feature of SAT-assembly is that more Boolean clauses can be inserted into the problem that select interaction matrices which do not allow the formation of competing structures (both ordered and disordered). If competing structures are known beforehand [50,51], their avoidance can be in some cases directly encoded into the satisfiability problem, or the SAT framework can be repeated iteratively excluding structures different from the target structure found in simulations at each iteration.

There are several ways to experimentally realise the obtained design. The most promising one uses DNA nanotechnologies (DNA functionalised colloids [52] or DNA origami [48,49,53–55]) to create a selective binding between particles: matchable colours [56] correspond to complementary single DNA strands.

In the results section we will present an example of a binary mixture solution obtained originally from SAT-assembly which also obeys the rules for the design of azeotropic points. Since the discussion of the azeotropic conditions represents the main focus of this work, we will not discuss the SAT-framework any further. Interested readers are referred to the original publications for all the details [26, 27].

**Wertheim perturbation theory**

We consider a multi-component mixture made by $N_s$ species of patchy particles with the same diameter $\sigma$; each species can differ from the others by the number, arrangement, and/or the type of the patches. Here we report the results of the Wertheim first order perturbation theory [57] that was originally developed to derive a mean-field theory of associating fluids and that can be easily generalised to patchy particles [58,59]. Recently [60,61,62,63], the theory has been adopted to study in detail the static (e.g. percolation) and thermodynamic (e.g. phase behaviour) properties of Patchy particle systems, both in pure components and in mixtures, showing excellent qualitative agreement with numerical simulations. The main assumptions are that each attractive site cannot be engaged in more than one bond at the same time (one-bond-per-patch condition) and that a new bond occurs only between particles belonging to different clusters (loop formations are forbidden). Wertheim developed a perturbative method that, applied to patchy particles, estimates the effect of the attractive patches on the Helmholtz free energy of the reference system of hard spheres. The power of this theory is the chance to provide a good estimate of the Helmholtz free energy of a multicomponent system of patchy particles by only knowing the structure of the reference system and the interaction potential characterising patchy particles. Here we fol-

low the conventions of Refs. \[61\] [64]. The Helmholtz free energy per particle in units of $k_B T$ can be expressed as:

$$\beta f = \beta f_{\text{reference}} + \beta f_{\text{bonding}}$$  \hspace{1cm} (3)

The reference free energy is the sum of the ideal gas contribution $\beta f_{\text{ideal}}$ and of the hard spheres excess term $\beta f_{\text{HS}}$. This hard spheres contribution takes into account the excluded volume of the patchy particles and it is given by the Carnahan-Starling formula \[66\] since the different species have all the same diameter.

$$\beta f_{\text{reference}} = \beta f_{\text{ideal}} + \beta f_{\text{HS}} \quad \text{with}$$

$$\beta f_{\text{ideal}} = \ln \rho - 1 + \sum_{i=1}^{n} x^{(i)} \ln \left(x^{(i)} V_i\right)$$  \hspace{1cm} (4)

$$\beta f_{\text{HS}} = \frac{4\phi - 3\phi^2}{(1-\phi)^2}$$

where $\rho$ is the density, $x^{(i)}$ is the molar fraction of species $i$, $V_i$ is the thermal volume and $\phi$ is the packing fraction equal to $\rho V_s$ where $V_s = \sigma^3 \pi / 6$ is the volume of a single particle.

The bonding contribution contains the sum over the species and the sum over the patches of a certain species; the number of patches of species $i$ is denoted as $n(\Gamma(i))$.

$$\beta f_{\text{bonding}} = \sum_{i=1}^{n} x^{(i)} \left[ \sum_{\alpha \in \Gamma^{(i)}} \left( \ln X^{(i)} - \frac{X^{(i)}_\alpha}{2} \right) + \frac{1}{2} n(\Gamma^{(i)}) \right]$$  \hspace{1cm} (5)

$X^{(i)}_\alpha$ is the probability that a patch $\alpha$ on a species $i$ is not bonded and it is defined by the mass balance equation:

$$X^{(i)}_\alpha = \left[ 1 + \phi \sum_{j=1,n} x^{(j)} \sum_{\gamma \in \Gamma^{(j)}} X^{(j)}_\gamma \Delta^{(ij)} \right]^{-1}$$  \hspace{1cm} (6)

where $\Delta^{(ij)}$ does not depend on the species, since the diameter is always the same, and it is given by

$$\Delta^{(ij)} = \Delta^{(i\gamma)} = \frac{1}{V_s} \int_{V_{\alpha\gamma}} g_{\text{HS}}(r)(e^{\beta \epsilon_{\alpha\gamma}} - 1) d\mathbf{r}$$  \hspace{1cm} (7)

where $g_{\text{HS}}$ is the radial distribution function of hard spheres, $V_{\alpha\gamma}$ is the bonding volume and $\epsilon_{\alpha\gamma}$ is the bonding energy both related to a bond between patches $\alpha$ and $\gamma$. $\Delta^{(i\gamma)}$ characterises the bond between the patch $\alpha$ on the patchy particle of species $i$ and the patch $\beta$ on the patchy particle of species $j$. Patches are in general different and therefore they can interact following different potentials (Kern-Frenkel in our case). In the following we consider that all bonds have the same bonding volume and we approximate the radial distribution function with an expansion around its value at contact, as detailed in Ref. \[66\]. With these approximations, affecting the results only quantitatively, but not qualitatively, equation (7) becomes:

$$\Delta^{(i\gamma)} = \frac{1}{V_s} 4\pi \lambda^2 \left\{ \left(1 + \delta\right)^3 - \frac{1}{3} A_0 \right\} +$$

$$\left[ \left(1 + \delta\right)^4 - \frac{1}{4} A_1 \right] \left( e^{\beta \epsilon_{\alpha\gamma}} - 1 \right)$$

with

$$A_0 = \frac{1 - \frac{3}{2} \chi}{\left(1 - \phi\right)^3}$$

$$A_1 = \frac{2 \chi}{\left(1 - \phi\right)^3}$$

$$\chi = \frac{1 - \cos \theta_{\text{m.m.m.}}}{2}$$

The theory allows the computation of the Helmholtz free energy for any state point. To derive phase behaviour we use isochoric thermodynamics as detailed in the following section.

**Isochoric thermodynamics**

In order to construct the binodal curve for a single component system, the Clausius-Clapeyron differential equation can be integrated. Likewise, in this section, a set of differential equations, that if integrated provides the binodal curve for multi-components mixtures, is reported. The integration of these differential equations is carried out numerically in the isochoric thermodynamics framework \[67\] \[68\]. We provide here a short summary of this framework. In the canonical ensemble, the thermodynamic state of a multi-component mixture is specified by temperature $T$, molar density $\rho$ and mole fractions $x_i$. However the mole fractions have some disadvantages: they are not independent variables and, conversely to density, they are dimensionless causing the density mole fractions space to have an ill defined metric. On the contrary, in the isochoric thermodynamics the independent variables are molar densities $\rho_i$ and the fundamental thermodynamic potential is the Helmholtz energy density $\Psi$. They are defined as:

$$\rho_i = x_i \rho$$

$$\Psi(\rho, T) = \sum_{i=1}^{n} \rho_i$$

where $A$ is the Helmholtz energy and $a$ is the molar Helmholtz energy. We must pay attention to the difference between $\rho$ and $\rho_i$: the former is the molar density of the $n$-component mixture $\rho = \sum_{i=1}^{n} \rho_i$ and the second
one is the vector of molar densities $\rho = (\rho_1, \rho_2, \ldots, \rho_n)$. The local curvature of the Helmholtz energy density is encoded in the hessian matrix:

$$H = \begin{pmatrix}
(\frac{\partial^2 \Psi}{\partial \rho_1^2})_T & (\frac{\partial^2 \Psi}{\partial \rho_1 \rho_2})_T & \cdots & (\frac{\partial^2 \Psi}{\partial \rho_1 \rho_n})_T \\
(\frac{\partial^2 \Psi}{\partial \rho_2 \rho_1})_T & (\frac{\partial^2 \Psi}{\partial \rho_2^2})_T & \cdots & (\frac{\partial^2 \Psi}{\partial \rho_2 \rho_n})_T \\
\vdots & \vdots & \ddots & \vdots \\
(\frac{\partial^2 \Psi}{\partial \rho_n \rho_1})_T & (\frac{\partial^2 \Psi}{\partial \rho_n \rho_2})_T & \cdots & (\frac{\partial^2 \Psi}{\partial \rho_n \rho_n})_T 
\end{pmatrix}_T$$  (11)

If it is positive defined, then the state is a stable state. We know that two phases ’ and ″, as the liquid phase ’ and the vapour phase ″, coexist in equilibrium at constant temperature if, along the phase boundary, the pressure and the chemical potentials of each component are equal for both phases. This means that the variation of the pressure and of the chemical potentials along the phase boundary must be the same for both phases:

$$d\mu_i = d\mu_i'' \quad \text{with } i = 1, 2, \ldots, n$$
$$dP' = dP''$$

having defined the chemical potentials and the pressure as $\mu_i = \partial \Psi / \partial \rho_i$ and $P = -\Psi + \sum_{i=1}^{n} \rho_i \mu_i$.

By exploiting these conditions, a system of first order differential equations, that integrated allows to build the coexistence region, is found. For the isothermal phase equilibrium of a binary mixture it is:

$$\begin{pmatrix}
H_{\Psi,1}' \cdot \rho'' & H_{\Psi,2}' \cdot \rho'' \\
H_{\Psi,1}'' \cdot \rho' & H_{\Psi,2}'' \cdot \rho'
\end{pmatrix}_T, \tau = \begin{pmatrix} 1 \\
1 \end{pmatrix}$$

$$H_{\Psi}''(\frac{d\rho}{dP})''_T, \tau = H_{\Psi}'(\frac{d\rho}{dP})'_T, \tau$$

where $H_{\Psi,i}$ indicates the $i$-th row of the Hessian matrix with $n = 2$ in [11] and $\tau$ stands to underline that derivatives are calculated along the phase boundary.

Finally, starting from accurate initial values, the integration of the derivatives of the molar densities in the coexisting phases over the desired range of pressure provides how molar densities of vapour and liquid change with pressure. This enables the construction of the binary mixture pressure concentration and density concentration binodal curves: by knowing only one pair of coexisting points we can determine the entire coexistence region by calculating how these points change over the binodal curve.

Monte Carlo simulations: AVB moves and Gibbs ensemble

When simulating patchy particle systems interacting via anisotropic and short-ranged interactions rototranslation moves are not always sufficient to ensure a good sampling of the phase space. Indeed patchy particles self-assembly occurs when the thermal energy is much smaller than the bonding energy $\epsilon$, which makes the Metropolis acceptance probability of a move breaking a bond extremely low. Thus almost all moves that try to break a bond are rejected not allowing the system to equilibrate. To overcome this drawback, biased moves are introduced too [32]. They are called aggregation-volume-bias-moves (AVB) and they facilitate bond breaking by enhancing the acceptance probability. In particular, there are two types of AVB moves: the AVB-B move and the AVB-U move. The AVB-B move attempts to create a bond by moving one patchy particle in the bonding volume ($V_b$) of another patchy particle, thus giving rise to a bond between two patchy particles that were not bonded to each other. Conversely, the AVB-U move tries to break a bond by taking one bonded patchy particle outside the bonding volume ($V_o = 4\pi V - V_b$) of the patchy particle to which it is bonded, thus eliminating an existing bond between a patchy particles pair. These moves are biased, and their acceptance probabilities are

$$A_{AVB-B} = \min \left\{ 1, \frac{(N-N_e-1)V_b}{(N_e+1)V_b} e^{-\beta \Delta E} \right\}$$

$$A_{AVB-U} = \min \left\{ 1, \frac{N_e V_b}{(N-N_e) V_o} e^{-\beta \Delta E} \right\}$$

where $N_e$ is the number of particles that are bonded to particle $i$. Importantly, the acceptance probability of breaking a bond is enhanced respect to the one of simple rototranslation move, as the ratio $V_o/V_b$ is much larger than one since the bonding volume $V_b$ is much smaller that its complementary volume $V_o = 4\pi V - V_b$, where $V$ is the volume of the simulation box.

In order to study the coexistence between two phases at a certain temperature, we employ Gibbs ensemble simulations [33, 34], where coexistence occurs between two simulation boxes that virtually interact among each other without an explicit interface. In addition to rototranslational moves, the Gibbs ensemble incorporates volume moves (which alter the size of the two boxes keeping the total volume fixed), and particle transfer moves (where a particle is moved from one simulation box to the other).

Azeotropy

In systems of two or more components, both the pressure-concentration and the temperature-
concentration phase diagrams exhibit a coexistence region rather than a coexistence line. The presence of a coexistence region implies that concentration of the vapor and liquid phases are not the same. From Fig. 2, showing a qualitative pressure-concentration phase diagram for a non ideal binary mixture, we notice that the coexistence pressures reduce to a single value when the first component concentration is equal to zero and to one, i.e. when the binary mixture becomes a one-component system. However, if the mixture strongly deviates from ideal behaviour, it can exist another point, named azeotropic point, at concentration different from zero and one, where the coexistence region reduces to a single point. A multi-component mixture at the azeotropic point will separate into phases at the same azeotropic concentration, therefore behaving as a pure system.

In the Results section we will show how azeotropy can be included in patchy particles design, and how to control its location.

RESULTS

How to design azeotropic mixtures

We consider a $N_s$-component mixture with all species having the same diameter $\sigma$, the same number ($N_p$) and placements of patches, and differing only in the patches type. We first notice that if the probabilities $X^{(i)}_{\alpha}$ in Eq. 4 are all equal for whatever patch $\alpha$ and species $i$, then the Helmholtz bonding free energy in Eq. 5 reduces to that of a one of a one-component system. In order to determine whether there is a thermodynamic point where all $X^{(i)}_{\alpha}$ have the same value, we turn to the mass balance condition, Eq. 6, which is a set of $N_s \times N_p$ equations in the variables $X^{(i)}_{\alpha}$. Looking for the rules under which all the mass balance equations become equivalent provides a sufficient condition for the appearance of azeotropy in a multi-component mixture.

In the following we examine three families of rules that ensure azeotropy:

- the bond exclusivity condition will generate azeotropic points at equimolar conditions;
- the bond degeneracy condition allows for azeotropic points at non-equimolar conditions;
- the fully-connected bond condition generates always-azeotropic mixtures, i.e. the coexistence line becomes a line of azeotropic points.

Bond exclusivity condition

One condition ensuring azeotropy is the bond exclusivity constraint requiring that each patch has only one bonding partner (that can be also itself in case of self-complementarity) among all patches of all species in the mixture. This means that all patches are different and that the SAT interaction matrix has a single one for each row, located at a different column for different rows. Moreover, if we consider the case where all bonds have the same bonding energy then azeotropy appears at equimolar conditions: a $N_s$-component mixture will be azeotropic if it is prepared by mixing all the $N_s$ components at the equimolar concentration $\frac{1}{N_s}$.

The bond exclusivity condition implies that the sum over the patches $(\sum_{\gamma \in \Gamma(j)})$ and the sum over the species $(\sum_{j=1}^{N_s})$ in Eq. 6 reduce to a single contribution since the patch coloured $\alpha$ belonging to species $i$ can interact only with its partner patch coloured $\gamma$ belonging to species $j$ ($j$ can be also equal to $i$ as well as $\alpha$ can be equal to $\gamma$). Therefore the $N_s \times N_p$ mass balance equations for $X^{(i)}_{\alpha}$ reduce all to equations of the form

$$X^{(i)}_{\alpha} = \left[ 1 + \phi x^{(j)} X^{(j)}_{\gamma} \Delta_{\alpha \gamma} \right]^{-1}$$

Moreover, by designing bonds with the same strength, we set $\Delta_{\alpha \gamma} \equiv \Delta$ for all patches $\alpha$ and $\gamma$. Without knowing the exact design of our patchy particles, we can assert that the $N_s \times N_p$ mass balance equations can be of two types:

$$\text{type 1} \quad X_{\alpha} + \phi x^{(i)} X^2_{\alpha} \Delta - 1 = 0 \quad \text{or}$$

$$\text{type 2} \quad X_{\alpha} + \phi x^{(i)} X^2_{\alpha} \Delta + \phi(x^{(j)} - x^{(i)}) X_{\alpha} \Delta - 1 = 0$$

FIG. 2. Pressure concentration phase diagram for a binary mixture with a negative azeotrope. The azeotropic point is located at the lowest pressure at which the liquid and the vapour phases can coexist.
depending if the two interacting patches belong to the same species or to different species, respectively. There can be \( N_s \) forms for equations of the first type and \( N_s \times (N_p - 1) \) forms for equations of the second type; the exact set of \( N_s \times N_p \) equations can be defined only if the complete design of the patchy particles is known. Nevertheless with the equimolarity condition all the \( N_s \times N_p \) equations become equal to

\[
X + \frac{\phi}{n} X^2 \Delta - 1 = 0 \tag{17}
\]

being all \( x^{(i)} = 1/N_s \) with \( i = 1, 2, \ldots, N_s \). We have thus seen that the bond exclusivity condition will generally generate an azeotrope at equimolar concentration, which is very useful in self-assembly designs where the target structure is composed of an equal number of all species.

**Bond degeneracy condition**

If the target structure has a generic concentration vector \( x \) (containing the concentration of each component), it would be advantageous if the azeotropic point appeared at that same concentration. For this purpose, in addition to the bond exclusivity constraint, we can introduce a bond degeneracy condition. A patch satisfying the bond exclusivity requirement has a unique bonding partner, whereas a patch obeying the bond degeneracy condition must be able to bind, with the same bonding energy, with two or more different patches. Considering a binary mixture where the ratio between the two species (denoted as (1) and (2)) is 1 : \( n \), in order to have an azeotrope at \( x^{(2)} = nx^{(1)} \), we must design patches interactions in such a way that:

- patches of the first species bonding with patches of the second species, as well as patches of the second species forming bonds with patches of the second species, must obey the bond exclusivity condition;

- patches of the second species bonding with patches of the first species, as well as patches of the first species forming bonds with patches of the first species, must obey the bond degeneracy condition: each patch must be able to bind with other \( n \) patches belonging to the first species.

This recipe is generalisable to multi-component mixtures with more than two species: the bond degeneracy condition will require to establish a bond with \( m \) patches belonging to certain species, where \( m \) is the least common multiple between component ratios.

For the sake of clarity we analyse the example of a binary mixture of patchy particles, with four patches tetrahedrally arranged, whose ratio is 1 : 2. An interaction matrix satisfying the previous bonding rules is:

\[
\begin{pmatrix}
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 \\
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1
\end{pmatrix}
\tag{18}
\]

It is easy to check this design by looking at the number and the placement of each 1 at each row. Patches under bond exclusivity constraint have a single one for each row, whereas patches obeying the bond degeneracy condition have two one for each row, as expected being the components ratio 1 : 2, i.e. \( n = 2 \).

In this case, in the mass balance equations for \( X^{(i)}_\alpha \) the sum over the species (\( \sum j=1,2 \)) still drops out while the sum over the patches (\( \sum \gamma \in G(j) \)) reduces to one or to two terms depending if patch \( \alpha \) satisfies the bond exclusivity condition or the bond degeneracy condition, respectively. Together with the condition \( \Delta_{\alpha\gamma} = 0 \) for all patches \( \alpha \) and \( \gamma \), this implies that the coefficient in front of \( X^{(i)}_\alpha \) is the same for all species \( i \). Patches belonging to the same species and characterised by the same row in the interaction matrix are equal and therefore they share the same probability \( X^{(i)}_\alpha \).

In our example, \( X_1^{(1)} = X_2^{(1)} \) and \( X_3^{(1)} = X_4^{(1)} \) and with simple algebraic steps we obtain the four following types of equations:

\[
\text{if } \alpha = 1, 2 \quad X_\alpha + 2\phi x^{(1)}X_\alpha^2 \Delta + \phi X_\alpha \Delta (x^{(2)} - 2x^{(1)}) - 1 = 0 \\
\text{if } \alpha = 3, 4 \quad X_\alpha + 2\phi x^{(1)}X_\alpha^2 \Delta - 1 = 0 \tag{19}
\]

\[
\text{if } \alpha = 5 \quad X_\alpha + \phi x^{(2)}X_\alpha^2 \Delta + \phi X_\alpha \Delta (2x^{(1)} - x^{(2)}) - 1 = 0 \\
\text{if } \alpha = 6, 7, 8 \quad X_\alpha + \phi x^{(2)}X_\alpha^2 \Delta - 1 = 0
\]

We notice that if \( x^{(2)} = 2x^{(1)} \) all the equations in [19] become equal to:

\[
X + \frac{2}{3} \phi X^2 \Delta - 1 = 0 \tag{20}
\]

indeed \( x^{(1)} + x^{(2)} = 1 \) and therefore \( x^{(1)} = \frac{1}{3} \) and
are two ones for each row: the first is located among the specific components ratio, and instead the entire coexistence region becomes a point not only at a specific non equimolar concentration, but whatever ratio the two species are mixed together.

In this case, in the mass balance equations for \(X^{(i)}_\alpha\) the sum over the species \(\sum_{j=1,2}\) does not drop out while the sum \(\sum_{\gamma\in\Gamma(i)} X^{(j)}_\gamma \Delta_{\alpha\gamma}\) still reduces to one term as for the case where each patch can make a bond only with another patch. Indeed now, even if each patch makes a bond with two other patches, the patches involved in the bonds are located one on the first species and the other on the second species. Hence, for each patch \(\alpha\), \(\Delta_{\alpha\gamma}\) is different from zero only for two patches, \(\gamma\) and \(\delta\), not belonging to the same patchy particle species. Therefore \(X^{(i)}_\alpha\) is recasted as

\[
X^{(i)}_\alpha = \frac{1}{1 + \phi \left[ x^{(i)} X^{(i)}_\gamma \Delta_{\alpha\gamma} + x^{(j)} X^{(j)}_\delta \Delta_{\alpha\delta} \right]} \tag{22}
\]

Now we impose the equal bonding energy condition that allows to set \(\Delta_{\alpha\gamma}\), for whatever \(\alpha\) and \(\gamma\), at the same value denoted as \(\Delta\). In this way, for each patch \(\alpha\), \(X^{(i)}_\alpha\) becomes of the form

\[
X^{(i)}_\alpha = \frac{1}{1 + \phi \left[ x^{(i)} X^{(i)}_\gamma + x^{(j)} X^{(j)}_\delta \right]} \Delta \tag{23}
\]

In particular, considering the interaction matrix \(21\) we have eight equations. For instance, the ones for the patches 1 and 2 are:

\[
X^{(1)}_1 = \frac{1}{1 + \phi \left[ x^{(1)} X^{(1)}_2 + x^{(2)} X^{(2)}_6 \right]} \Delta \tag{24}
\]

\[
X^{(1)}_2 = \frac{1}{1 + \phi \left[ x^{(1)} X^{(1)}_4 + x^{(2)} X^{(2)}_6 \right]} \Delta
\]

We notice that \(X^{(1)}_1 = X^{(2)}_6 = X\) and that \(X^{(1)}_2 = X^{(2)}_5 = X'\). This implies that

\[
X = \frac{1}{1 + \phi [x^{(1)} + x^{(2)}]} X \Delta = \frac{1}{1 + \phi} X \Delta
\]

\[
X' = \frac{1}{1 + \phi [x^{(1)} + x^{(2)}]} X \Delta = \frac{1}{1 + \phi} X \Delta
\]

By replacing the expression for \(X'\) in the equation for \(X\) and vice-versa we obtain the two equal equations:
\[X^2\phi\Delta + X - 1 = 0\]
\[X'^2\phi\Delta + X' - 1 = 0\]

Therefore, satisfying the same equations, \(X_1^{(1)} = X_6^{(2)} = X_5^{(1)} = X_5^{(2)}\). We are left to demonstrate that also \(X_3^{(1)}, X_4^{(1)}, X_7^{(2)}, X_8^{(2)}\) are defined by equations equal to the ones in Eq. 26. Firstly we notice that if \(X_7^{(2)} = X_8^{(2)}\) then \(X_3^{(1)} = X_4^{(1)}\) and this would imply that \(X_7^{(2)} = X_8^{(2)} = X_3^{(1)} = X_4^{(1)} \equiv X''\). Hence we can write

\[X'' = \frac{1}{1 + \phi(x^{(1)} + x^{(2)})} = \frac{1}{1 + \phi X'' \Delta}\]

which can be rewritten as

\[X'^2\phi\Delta + X'' - 1 = 0\]

i.e. the same equation as the ones reported in Eq. 26. Therefore if \(X_7^{(2)} = X_8^{(2)}\) then all the \(X_\alpha\), for whatever patch \(\alpha\), are equal. The equalities of all the \(X_\alpha\) are valid for whatever value \(x^{(1)}\) (and so \(x^{(2)}\) takes). This means that this binary mixture is always an azeotropic binary mixture.

Finally, the equality \(X_7^{(2)} = X_8^{(2)}\) holds because, since the physics does not change if patch 7 is replaced by patch 8 and patch 3 is replaced by patch 4, then the equations must be invariant under these exchanges satisfying equalities \(X_7^{(2)} = X_8^{(2)}\) and \(X_3^{(1)} = X_4^{(1)}\).

In conclusion the bonding Helmholtz free energy of Eq. 5 is

\[\beta f_{bonding} = x^{(1)} \left[4 \left(\ln \frac{X - \frac{X}{2}}{2}\right) + \left(\frac{M}{2}\right)\right] +
+b^{(2)} \left[4 \left(\ln \frac{X - \frac{X}{2}}{2}\right) + \left(\frac{M}{2}\right)\right] =
= \left(x^{(1)} + x^{(2)}\right) \left[4 \left(\ln \frac{X - \frac{X}{2}}{2}\right) + \left(\frac{M}{2}\right)\right] =
= 4 \left(\ln \frac{X - \frac{X}{2}}{2}\right) + \left(\frac{M}{2}\right)\]

(29)

where \(n(\Gamma(i)) = M = 4\) (with \(i = 1, 2\)) since we deal with patchy particles species having both four patches. As expected, we notice that, for whatever concentration, \(\beta f_{bonding}\) is equal to the free energy of a single component system.

FIG. 3. 3D representation of the two patchy particles species (a) and (b) of the SAT-designed N2c8 binary mixture. Equal patches colours indicate that patches can bind to each other, and the colours appearing only once are self-interacting.

**Example: self-assembly of the cubic diamond crystal**

One of the most interesting and challenging bottom-up realisation of a target structure is that of the cubic diamond. Understanding how to realise a cubic diamond on colloidal scale would open up the possibility of creating and designing a photonic crystal that allows for light manipulation in a controlled way. The self-assembly of a cubic diamond is complex since its lattice is an open structure which competes with the hexagonal diamond structure, which prevents the cubic diamond from forming without defects and stacking faults. Several studies have been performed to overcome these difficulties, including solutions obtained within the SAT-assembly framework. Because of the cubic diamond lattice topology we model patchy particles of valence four with a tetrahedral patches arrangement. The minimal SAT-designed solution (the one requiring the smallest number of distinct particles) is the so called N2c8 binary mixture that uses two species and eight patches types and it is schematised in Fig. 3.

The N2c8 interaction matrix, encoding the design, is

\[
\begin{pmatrix}
0 & 0 & 0 & 0 & 0 & 0 & 1 \\
0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 
\end{pmatrix}
\]

(30)

We notice that having a single one for each row, the bond exclusivity condition guaranteeing azeotropy is satisfied. Moreover, since the N2c8 binary mixture was discovered by SAT-assembly requiring identical bonding energies, we expect an azeotrope at concentration \(x^{(1)} = x^{(2)} = \frac{1}{2}\).
The N2c8 mixture is thus an ideal candidate to test the appearance of azeotropy, and to investigate in detail its self-assembly properties.

In order to verify the effective presence of an azeotrope when the two species are mixed at equal ratio, we first use Wertheim’s theory to determine the binodal curve in pressure concentration and density concentration phase diagrams. The thermodynamical conditions for a stable state of the mixture are found when the Helmholtz free energy per particle $f$ has a minimum. To search this minimum we work at fixed temperature and pressure and so we switch to the Gibbs free energy per particle $g$

\[ g = \frac{P}{\rho} + f \]  

where $P$ is the pressure and $\rho$ is the total density. Since the same total density can be achieved by mixing species at more than one pair of concentrations $x_1 \equiv x$ and $x_2 = 1 - x_1$, firstly we must minimise $g$ for each fixed concentration $x$ with respect to the density $\rho$. In this way the Gibbs free energy becomes only a function of concentration. Coexisting phases having the same temperature, pressure and chemical potential can be obtained by searching those points on $g(x)$ that are connected by a common tangent. Starting from a single pair of coexistence points found with the common tangent rule, we numerically integrate Eq. 13 over the desired range of pressures, obtaining the two coexisting mole fractions as a function of pressure. For all the following numerical calculations we fix the Patchy potential parameters to the values $\cos \theta_{\text{max}} = 0.98$ and $\delta = 0.2$. This choice follows from the knowledge that the nucleation is facilitated at small apertures of the angle $\theta_{\text{max}}$ [35, 38, 72]. The pressure composition phase diagrams obtained at $T = 0.07$ is shown in Fig. 4. Integration gets stiff and does not proceed further close to critical points, as the step-size of the adaptive step-size integrator [68] progressively decreases as the hessian determinant vanishes at the critical points. Hence critical points, indicated in Fig. 4 by triangles, are computed by imposing the hessian determinant to be zero and the stability conditions.

This phase diagram confirms that the N2c8 is an azeotropic mixture with the azeotropic point at concentration equal to $x = 0.5$: it is exactly at $x = 0.5$ that the bubble point curve (where the first vapour bubble appears when pressure is lowered starting from a point greater than the total vapour pressure) and the dew point curve (where the first liquid drop originates when pressure in increased starting from a point in the vapour phase) are tangent and the coexistence region reduces to a point. Moreover since the azeotrope is at the lower extremum in the pressure concentration phase diagram, the N2c8 binary mixture is a negative azeotropic binary mixture.

In Fig. 5 we plot the density-concentration phase diagram. The azeotropic point at concentration $x = 0.5$, is signalised by the tie-lines behaviour: only at $x = 0.5$ the tie-line is a vertical line indicating that if the binary mixture is prepared by mixing together half of patchy particles of both species, then the phase separation keeps this ratio in the two phases coexisting at different densities.

By constructing the binodal curve for different temperatures it is possible to analyse the phase diagram topol-
ogy. We find that the N2c8 mixture belongs to new type of binary phase diagram, in which the pure components (x = 0 and x = 1) do not have a liquid-gas transition but their mixed states does. Fig. 7 shows that decreasing temperature the coexistence region becomes larger without ever crossing the limit concentrations x = 0 and x = 1. The topology of the phase diagram is equivalent to that of an ordinary azeotropic binary mixture, but in which the binary critical point line goes to (P, T) → 0 as the concentration goes to x → 0 or x → 1.

The explanation of this characteristic behaviour is in the interaction matrix (Eq. 30) according to which patchy particles of the same species can bind to each other with no more than two bonds. Hence, in pure component conditions, they can aggregate only into chains as depicted in Fig. 7. Therefore even if particles have four patches, when x = 0 or x = 1 they behave like bi-functional particles and hence have no liquid-gas phase separation [60]. We note that the idea that systems with two-patches have a disappearing critical point at P = 0 and T = 0 was recently put forward in Ref. [76], and generalized to colored particles in Ref. [75].

Next, we study the self-assembly process through the azeotropic point. We prepare disordered configurations at equimolar composition for different state points on a regular grid, with ρ ∈ [0.1, 0.5] and Δρ = 0.05, T ∈ [0.920, 0.104] and ΔT = 0.002. For each (ρ, T) state point we run 5 independent trajectories in the NVT ensemble with AVB biased moves. The state points considered are enclosed in the green shaded area in Fig. 9, and each trajectory is run for 5 10^5 MC sweeps or until crystallization. The centers of the red circles in Fig. 9 represent the state points which crystallized within the simulation time. The diameter of each circle is proportional to the fraction of simulation runs (our of a total of 5 runs) that have crystallized at the corresponding state point. To understand why crystallization occurs only at selected state points, we superimpose (black line) the results from Gibbs Ensemble simulations that have been initialized at equimolar conditions. Error bars are computed by averaging over 5 independent simulation trajectories. Nevertheless, the trend of the numerical computed binodal curves as well as the topology of the density concentration phase diagrams are the same of the Wertheim ones as shown in the coexistence region comparison in Fig. 8. As commonly observed [35], Wertheim’s theory tends to overestimate the size of the coexistence region. Still, our Monte Carlo simulations confirm the phase diagram topology with the presence of an azeotrope at half concentration in the N2c8 binary mixture.

Equilibration of these systems at the (low) temperatures, where phase separation is located, is particularly challenging [32]: this is observed in Fig. 9, where the error bars are computed by averaging over 5 independent simulation trajectories. Nevertheless, the trend of the numerical computed binodal curves as well as the topology of the density concentration phase diagrams are the same of the Wertheim ones as shown in the coexistence region comparison in Fig. 8. As commonly observed [35], Wertheim’s theory tends to overestimate the size of the coexistence region. Still, our Monte Carlo simulations confirm the phase diagram topology with the presence of an azeotrope at half concentration in the N2c8 binary mixture.
FIG. 8. SAT-designed binary mixture density concentration phase diagrams for different temperatures. Comparison between the binodal curves obtained from Monte Carlo simulations (top) and the binodal curves computed within the Wertheim first order perturbation theory (bottom). Circles represent points belonging to the dew point curve as well as squares represent points belonging to the bubble point curve. Triangles indicate critical points.

correspondence of the phase separation boundaries. Self-assembly is aided by the formation of dense liquid regions during the phase-separation process. Interestingly some state points in Fig. 9 have nucleated outside the binodal boundaries, but close to the critical temperature. The system thus represents an interesting example of nucleation aided by critical fluctuations, as first predicted in Ref. [29] for isotropic interactions.

To summarize, the self-assembly pathway at the azeotropic point is the following: an equimolar disordered solution first demixes in an equimolar dense liquid, which then crystallizes in an equimolar crystalline structure. Self-assembly at azeotropic conditions has the advantage of bypassing the difficulties associated with concentration fluctuations, which are known to severely limit the nucleation rate.

FIG. 9. a Snapshot from a fully self-assembled solution, prepared from a random configuration at $T = 0.1$ and $\rho = 0.3$, with Patchy parameters fixed at $\theta_{\text{max}} = 0.98$ and $\delta = 0.2$. Patchy particles are colored red or white according to their species. b $T - \rho$ phase diagram obtained from Gibbs ensemble simulations (black lines). The red circles are drawn in correspondence of the state points which nucleated. The radius of the red circles is proportional to the fraction of runs that successfully assembled within the simulation time of up to $5 \times 10^8$ MC sweeps.

CONCLUSIONS

Self-assembling complex structures requires designing complex interaction potentials, that not only need to have the target structure as a free energy minimum, but that also have to avoid competing local minima that can kinetically frustrate the assembly process. In recent years it has become increasingly clear that using multi-component mixtures can shift the problem from the need to accurately design the shape of the potential (e.g. introducing torsional interactions to assemble cubic diamond and avoid hexagonal diamond) to the optimization of a generic interaction matrix between different components. We have shown that this last problem is amenable to an effective numerical solution via the so-called SAT-assembly framework, where the interactions between the different components are found by solving satisfiability
problems. But the problem remains that adding components increases the thermodynamic degrees of freedom, which considerably complicates the phase behaviour and the assembly pathway.

In this work we have shown that much of the thermodynamic difficulties can be removed by preparing the self-assembly pathway on an azeotropic point, where the system behaves effectively as a one-component mixture. Our goal was thus to show under which conditions we can include azeotropy in self-assembly designs.

As a proof of concept, we have focused on the case of Patchy particles, which represent a convenient model for systems whose interactions can be described by an isotropic repulsion and strong directional attractions. In the context of Wertheim’s thermodynamic theory, we have shown that in these systems, azeotropy can be directly included in the interaction matrix. Different cases have been considered. The simplest condition, named bond exclusivity asserts that an equimolar azeotropic point can be obtained by imposing that each patch has a unique interaction partner. The equimolar condition can be relaxed and the azeotropic point can be located at a desired concentration vector $x$, by considering the bond degeneracy condition, which requires some patches to have more than one possible interaction partner. Finally, the fully-connected bond condition, where each patch has a one interaction partner on each of the species in the system, corresponds to a always azeotropic mixture, with a line of azeotropic points extending at all concentrations.

We have then provided a fully worked example of a binary mixture designed to self-assemble colloidal diamond while avoiding the hexagonal form, and that obeys the bond exclusivity condition. We have explicitly derived its phase diagram, both within Wertheim’s perturbation theory and via Gibbs ensemble simulations, and shown that it contains the predicted negative azeotrope at equimolar conditions. The class of this phase diagram is also unique in the sense that the binary critical point line tends to $(P, T) \rightarrow 0$ for $x \rightarrow (0, 1)$, meaning that the system phase separates only upon mixing. Finally we have analyzed the self-assembly pathway for systems prepared at azeotropic conditions, and shown that the pathway is the same as in one-component systems: more precisely an equimolar mixture condenses into an equimolar liquid, which, given the coincidence in concentration between the crystal and the melt, then nucleates into a crystal that grows without defects.

We believe that the ability to explicitly include azeotropic points into artificial designs represents an exciting step towards a fully consistent framework for the self-assembly of arbitrary structures. The azeotropic conditions also serve as a criteria to select self-assembly solutions with the desired properties among the distinct solutions obtained via the SAT-assembly method. Our efforts are now geared toward experimental realization of these designs through wireframe DNA origami, that naturally encode sequence complementary.

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[1] S. Whitelam and R. L. Jack, The statistical mechanics of dynamic pathways to self-assembly, Annual review of physical chemistry 66, 143 (2015).
[2] S. K. Kumar, G. Kumaraswamy, B. L. Prasad, R. Bandypadhyaya, S. Granick, O. Gang, V. N. Manoharan, D. Frenkel, and N. A. Kotov, Nanoparticle assembly: a perspective and some unanswered questions, Current Science 1635 (2017).
[3] L. Filion, M. Marechal, B. van Oorschot, D. Pelt, F. Smallegange, and M. Dijkstra, Efficient method for predicting crystal structures at finite temperature: variable box shape simulations, Physical review letters 103, 188302 (2009).
[4] L. Filion and M. Dijkstra, Prediction of binary hard-sphere crystal structures, Physical Review E 79, 046714 (2009).
[5] A.-Y. Jee, K. Lou, H.-S. Jang, K. H. Nagamanasa, and S. Granick, Nanoparticle puzzles and research opportunities that go beyond state of the art, Faraday discussions 186, 11 (2016).
[6] M. Dijkstra and E. Luijten, From predictive modelling to machine learning and reverse engineering of colloidal self-assembly, Nature Materials 20, 762 (2021).
[7] M. C. Rechtsman, F. H. Stillinger, and S. Torquato, Optimized interactions for targeted self-assembly: application to a honeycomb lattice, Physical review letters 95, 228301 (2005).
[8] E. Marcotte, F. H. Stillinger, and S. Torquato, Optimized monotonic convex pair potentials stabilize low-coordinated crystals, Soft Matter 7, 2332 (2011).
[9] E. Marcotte, F. H. Stillinger, and S. Torquato, Communication: Designed diamond ground state via optimized isotropic monotonic pair potentials, The Journal of Chemical Physics 138, 061101 (2013).
[10] G. Zhang, F. Stillinger, and S. Torquato, Probing the limitations of isotropic pair potentials to produce ground-state structural extremes via inverse statistical mechanics, Physical Review E 88, 042309 (2013).
[11] M. Z. Miskin, G. Khaira, J. J. de Pablo, and H. M. Jaeger, Turning statistical physics models into materials design engines, Proceedings of the National Academy of Sciences 113, 34 (2016).
[12] B. A. Lindquist, R. B. Jadrich, and T. M. Truskett, Communication: Inverse design for self-assembly via on-the-fly optimization, The Journal of Chemical Physics 145, 111101 (2016).

[13] D. Chen, G. Zhang, and S. Torquato, Inverse design of colloidal crystals via optimized patchy interactions, The Journal of Physical Chemistry B 122, 8462 (2018).

[14] R. Kumar, G. M. Coli, M. Dijkstra, and S. Sastry, Inverse design of charged colloidal particle interactions for self assembly into specified crystal structures, The Journal of chemical physics 151, 084109 (2019).

[15] S. Whitelam and I. Tamblyn, Neuroevolutionary learning of particles and protocols for self-assembly, Physical review letters 127, 018003 (2021).

[16] É. Ducrot, M. He, G.-R. Yi, and D. J. Pine, Colloidal alloys with preassembled clusters and spheres, Nature materials 16, 652 (2017).

[17] D. R. Nelson, Toward a tetravalent chemistry of colloids, Nano Letters 2, 1125 (2002).

[18] V. N. Manoharan, M. T. Elsasser, and D. J. Pine, Dense packing and symmetry in small clusters of microspheres, Science 301, 483 (2003).

[19] Z. Zhang, A. S. Keys, T. Chen, and S. C. Glotzer, Self-assembly of patchy particles into diamond structures through molecular mimicry, Langmuir 21, 11547 (2005).

[20] F. Romano, J. Russo, and H. Tanaka, Influence of patch-size variability on the crystallization of tetrahedral patchy particles, Physical review letters 113, 138303 (2014).

[21] J. D. Halverson and A. V. Tkachenko, Dna-programmed mesoscopic architecture, Physical Review E 87, 062310 (2013).

[22] F. Romano and F. Sciortino, Patterning symmetry in the rational design of colloidal crystals, Nature communications 3, 975 (2012).

[23] D. F. Tracey, E. G. Noya, and J. P. K. Doye, Programming patchy particles to form complex periodic structures, The Journal of Chemical Physics 151, 224506 (2019).

[24] B. Srinivasan, T. Vo, Y. Zhang, O. Gang, S. Kumar, and V. Venkatasubramanian, Designing dna-grafted particles that self-assemble into desired crystalline structures using the genetic algorithm, Proceedings of the National Academy of Sciences 110, 18431 (2013).

[25] S. Whitelam and I. Tamblyn, Learning to grow: Control of material self-assembly using evolutionary reinforcement learning, Physical Review E 101, 052604 (2020).

[26] F. Romano, J. Russo, L. Kroc, and P. Šulc, Designing patchy interactions to self-assemble arbitrary structures, Physical Review Letters 125, 118003 (2020).

[27] J. Russo, F. Romano, L. Kroc, F. Sciortino, L. Rovigatti, and P. Šulc, Sat-assembly: A new approach for designing self-assembling systems, Journal of Physics: Condensed Matter (2022).

[28] N. Een, Minisat: A sat solver with conflict-clause minimization, in Proc. SAT-05: 8th Int. Conf. on Theory and Applications of Satisfiability Testing (2005) pp. 502–518.

[29] P. R. t. Wolde and D. Frenkel, Enhancement of protein crystal nucleation by critical density fluctuations, Science 277, 1975 (1997).

[30] L. Xu, S. V. Buldyrev, H. E. Stanley, and G. Franzese, Homogeneous crystal nucleation near a metastable fluid-fluid phase transition, Physical Review Letters 109, 095702 (2012).

[31] J. Russo, F. Romano, and H. Tanaka, Glass forming ability in systems with competing orderings, Physical Review X 8, 021040 (2018).

[32] L. Rovigatti, J. Russo, and F. Romano, How to simulate patchy particles, The European Physical Journal E 41, 59 (2018).

[33] A. Z. Panagiotopoulos, Direct determination of phase coexistence properties of fluids by monte carlo simulation in a new ensemble, Molecular Physics 61, 813 (1987).

[34] A. Z. Panagiotopoulos, N. Quirke, M. Stapleton, and D. Tildesley, Phase equilibria by simulation in the gibbs ensemble: alternative derivation, generalization and application to mixture and membrane equilibria, Molecular Physics 63, 527 (1988).

[35] J. Russo, F. Leoni, F. Martelli, and F. Sciortino, The physics of empty liquids: from patchy particles to water, Reports on Progress in Physics (2021).

[36] W. Bol, Monte carlo simulations of fluid systems of waterlike molecules, Molecular Physics 45, 605 (1982).

[37] N. Kern and D. Frenkel, Fluid-fluid coexistence in colloidal systems with short-ranged strongly directional attraction, The Journal of chemical physics 118, 9882 (2003).

[38] F. Smallenburg and S. Francesco, Liquids more stable than crystals in particles with limited valence and flexible bonds, Nature Physics 9, 554 (2013).

[39] Z. Zhang and S. C. Glotzer, Self-assembly of patchy particles, Nano Letters 4, 1407 (2004).

[40] A. B. Pawar and I. Kretzschmar, Fabrication, assembly, and application of patchy particles, Macromolecular rapid communications 31, 150 (2010).

[41] E. Bianchi, R. Blaak, and C. N. Likos, Patchy colloids: state of the art and perspectives, Physical Chemistry Chemical Physics 13, 6397 (2011).

[42] F. Romano and F. Sciortino, Colloidal self-assembly: patchy from the bottom up, Nature materials 10, 171 (2011).

[43] G. van Anders, N. K. Ahmed, R. Smith, M. Engel, and S. C. Glotzer, Entropically patchy particles: engineering valence through shape entropy, Acs Nano 8, 931 (2013).

[44] K. Suzuki, K. Hosokawa, and M. Maeda, Controlling the number and positions of oligonucleotides on gold nanoparticle surfaces, Journal of the American Chemical Society 131, 7518 (2009).

[45] J.-W. Kim, J.-H. Kim, and R. Deaton, Dna-linked nanoparticle building blocks for programmable matter, Angewandte Chemie International Edition 50, 9185 (2011).

[46] Y. Wang, Y. Wang, D. R. Breed, V. N. Manoharan, L. Feng, A. D. Hollingsworth, M. Weck, and D. J. Pine, Colloids with valence and specific directional bonding, Nature 491, 51 (2012).

[47] L. Feng, R. Dreyfus, R. Sha, N. C. Seeman, and P. M. Chaikin, Dna patchy particles, Advanced Materials 25, 2779 (2013).

[48] P. W. K. Rothemund, Folding DNA to create nanoscale shapes and patterns, Nature 440, 297 (2006).

[49] Y. Tian, J. R. Lhermitte, L. Bai, T. Vo, H. L. Xin, H. Li, R. Li, M. Fukuto, K. G. Yager, J. S. Kahn, et al., Ordered three-dimensional nanomaterials using dna-prescribed and valence-controlled material voxels, Nature materials 19, 789 (2020).
[50] N. A. Mahynski, L. Rovigatti, C. N. Likos, and A. Z. Panagiotopoulos, Bottom-up colloidal crystal assembly with a twist, ACS nano 10, 5459 (2016).
[51] F. Leoni and J. Russo, Non-classical nucleation pathways in stacking-disordered crystals, arXiv preprint arXiv:2105.05506 (2021).
[52] Y. Xiong, S. Yang, Y. Tian, A. Michelson, S. Xiang, H. Xin, and O. Gang, Three-dimensional patterning of nanoparticles by molecular stamping, ACS nano 14, 6823 (2020).
[53] W. Liu, M. Tagawa, H. L. Xin, T. Wang, H. Emamy, H. Li, K. G. Yager, F. W. Starr, A. V. Tkachenko, and O. Gang, Diamond family of nanoparticle superlattices, Science 351, 582 (2016).
[54] T. Zhang, C. Hartl, K. Frank, A. Heuer-Jungemann, S. Fischer, P. C. Nickels, B. Nickel, and T. Liedl, 3d dna origami crystals, Advanced Materials 30, 1800273 (2018).
[55] I. Chakraborty, D. J. Pearce, R. W. Verweij, S. C. Matysik, L. Giomi, and D. J. Kraft, Self-assembly dynamics of reconfigurable colloidal molecules, ACS nano 16, 2471 (2022).
[56] O. A. Vasilyev, B. A. Klumov, and A. V. Tkachenko, Chromatic patchy particles: Effects of specific interactions on liquid structure, Physical Review E 92, 012308 (2015).
[57] M. Wertheim, Fluids with highly directional attractive forces, i. statistical thermodynamics, Journal of statistical physics 35, 19 (1984).
[58] W. G. Chapman, G. Jackson, and K. E. Gubbins, Phase equilibria of associating fluids: spherical molecules with multiple bonding sites, Molecular Physics 65, 1 (1988).
[59] D. de Las Heras, J. M. Tavares, and M. M. T. da Gama, Phase diagrams of binary mixtures of patchy colloids with distinct numbers of patches: the network fluid regime, Soft Matter 7, 5615 (2011).
[60] E. Bianchi, J. Largo, P. Tartaglia, E. Zaccarelli, and S. Francesco, Phase diagram of patchy colloids: Towards empty liquids, Physical Review Letters 97, 168301 (2006).
[61] D. d. I. Heras, J. M. Tavares, and M. M. T. da Gama, Phase diagrams of binary mixtures of patchy colloids with distinct numbers and types of patches: The empty fluid regime, The Journal of chemical physics 134, 104904 (2011).
[62] L. Rovigatti, D. de las Heras, J. M. Tavares, M. M. Telo da Gama, and F. Sciortino, Computing the phase diagram of binary mixtures: A patchy particle case study, The Journal of chemical physics 138, 164904 (2013).
[63] F. Seiferling, D. de Las Heras, and M. M. Telo da Gama, Percolation in binary and ternary mixtures of patchy colloids, The Journal of Chemical Physics 145, 074903 (2016).
[64] P. Teixeira and J. Tavares, Phase behaviour of pure and mixed patchy colloids—theory and simulation, Current Opinion in Colloid & Interface Science 30, 16 (2017).
[65] R. Braz Teixeira, D. de Las Heras, J. M. Tavares, and M. M. Telo da Gama, Phase behavior of a binary mixture of patchy colloids: Effect of particle size and gravity, The Journal of Chemical Physics 155, 044903 (2021).
[66] G. Mansoori, N. F. Carnahan, K. Starling, and T. Le-land Jr, Equilibrium thermodynamic properties of the mixture of hard spheres, The Journal of Chemical Physics 54, 1523 (1971).
[67] U. K. Deiters, Differential equations for the calculation of isopleths of multicomponent fluid mixtures, Fluid Phase Equilibria 447, 72 (2017).
[68] I. H. Bell and U. K. Deiters, On the construction of binary mixture p-x and t-x diagrams from isochoric thermodynamics, AIChE Journal 64, 2745 (2018).
[69] K. Ho, C. T. Chan, and C. M. Soukoulis, Existence of a photonic gap in periodic dielectric structures, Physical Review Letters 65, 3152 (1990).
[70] C. M. Soukoulis and M. Wegener, Optical metamaterials—more bulky and less losey, Science 330, 1633 (2010).
[71] T. Ngo, C. Liddell, M. Ghebrebrhan, and J. Joannopoulos, Tetrastack: Colloidal diamond-inspired structure with omnidirectional photonic band gap for low refractive index contrast, Applied physics letters 88, 241920 (2006).
[72] F. Romano, E. Sanz, and F. Sciortino, Crystallization of tetrahedral patchy particles in silico, The Journal of chemical physics 134, 174502 (2011).
[73] A. Neophytou, D. Chakrabarti, and F. Sciortino, Facile self-assembly of colloidal diamond from tetrahedral patchy particles via ring selection, Proceedings of the National Academy of Sciences 118 (2021).
[74] L. Rovigatti, J. Russo, F. Romano, M. Matthies, L. Kroc, and P. Sulc, A simple solution to the problem of self-assembling cubic diamond crystals, arXiv preprint arXiv:2205.10680 (2022).
[75] D. Stopper, H. Hansen-Goos, R. Roth, and R. Evans, Remnants of the disappearing critical point in chain-forming patchy fluids, The Journal of Chemical Physics 152, 111101 (2020).
[76] J. Tavares and P. Teixeira, Remnants of the disappearing critical point (s) in patchy fluids with distinct interaction patches, The Journal of Chemical Physics 153, 086101 (2020).