Into the Facet-Selectivity of Sequenced Amphiphilic Peptoids at the Au-Water Interface

Xin Qi¹, Biao Jin², Bin Cai^{2,3}, Feng Yan^{2,4}, James De Yoreo^{1,2}, Chun-Long Chen^{1,2}, Jim Pfaendtner^{*1,2}

¹Department of Chemical Engineering, University of Washington, Seattle, 98195 Washington, United States

²Physical and Computational Sciences Directorate, Pacific Northwest National Laboratory, Richland, Washington 99354, United States

KEYWORDS: Adsorption free-energy, Au, peptoid, solid-liquid interface, selectivity, metadynamics

ABSTRACT: Shape-controlled colloidal nanocrystal syntheses often require aid from facet-selective solution-phase chemical additives to regulate atom addition/migration fluxes or oriented particle attachment. Because of their highly tunable chemical property and robustness to a wide range of experimental conditions, peptoids contribute to a very promising group of next-generation functional chemical additives. To generalize the design philosophy, it is critical to understand the origin of facet selectivity at the molecular level. We employ molecular dynamics simulations and biased sampling methods to investigate the origin of Au(111)-favored adsorption of a peptoid, Nce3Ncp6, that is evidenced to assist the formation of five-fold twinned nanostructures. We find

that the facet-selectivity is achieved through a synergistic effect of both molecule-surface and solvent-surface interactions. Extending beyond the single-chain scenario, the order of peptoid-peptoid and peptoid-surface energetics, i.e., $\text{peptoid-Au(100)} < \text{peptoid-peptoid} < \text{peptoid-Au(111)}$, further amplifies the distinct behavior of Nce3Ncp6 chains on different Au surfaces. Our studies set the stage for future peptoid design in shape-controlled nanocrystal syntheses by probing the facet selectivity from various perspectives.

Introduction

In the past two to three decades, the indispensability of solution-phase chemical additives in shape-controlled inorganic nanocrystal syntheses has been repeatedly addressed in experimental literature.¹⁻⁷ Regardless of the chemical composition, these solution-phase additives often, if not always, exhibit facet selectivity and consequently promote the growth of a specific facet or domain.⁸⁻¹⁴ In recent years, with the advancement in computational power and algorithm, theory and simulation works have made numerous breakthroughs in unraveling the complex role of these additives in morphological control.^{6,15-24} For example, with a very high facet selectivity (i.e., when the molecule strongly favors a specific facet over the other), the trend in facet-specific interfacial free energies can be reversed upon adsorption and thus alter the thermodynamic equilibrium shapes.²⁵ In the spectrum of weak to moderate facet selectivity, the surface-adsorbed molecules may regulate the solution-phase atom addition fluxes, which gives rise to kinetic shapes.^{16,17,21,26} In addition to the atom-by-atom growth mechanism, facet-selective binding can also guide nanocrystal formation through non-oriented⁶ or oriented attachment^{27,28} by modulating the attachment kinetic barrier, as a result of different packing densities or surface diffusivities of surface adsorbed molecules.

While these chemicals are traditionally selected from polymers, oligomers, proteins, or nucleic acids, peptoids (or N-substituted glycines) contribute to a rising group of candidates as shape-directing solution-phase chemical additives.^{6,29,30} Being a type of sequence-defined synthetic polymers, peptoids are relatively easy to synthesize and robust to a wide range of experimental conditions. Also, peptoids are chemically similar to peptides, with the side chains connected to the backbone N atom instead of the alpha C. This makes their properties highly tunable via side chain sequencing. More significantly, the side chain compositions of peptoids are much more diverse

than naturally occurring amino acids, creating a massive design space for new successful chemical additives with the desired facet-selectivity.

We herein report that a di-block amphiphilic peptoid (Figure 1(a)), Nce3Ncep6, composed of carboxyl [Nce=N-(2-carboxyethyl)glycines] side chains (hydrophilic) and aromatic [Ncp=N-[2-(4-chloro-phenyl)ethyl]glycines)] side chains (hydrophobic) has been observed to mediate the formation of five-fold twinned Au nanocrystals in a basic aqueous solution (pH=9.0). More specifically, decahedron-like five-fold twinned nanocrystals are formed with the presence of Nce3Ncep6, while branched or spherical nanocrystals are formed without the peptoid (cf. Figure 1(b) and (c)). Ideally, a single-crystalline nanocrystal of a face-centered cubic (fcc) metal is enclosed by low-index surfaces, such as {100} and {111} facets, with corners or edges smoothed with {110} or higher index facets, to minimize the total surface free energy. Any emergence of twin planes is always associated with energetic costs due to internal strain/stress.^{31–34} One way to counterbalance such energetic penalty is to lower the total surface free energy with surface-adsorbed chemical additives; otherwise, the structure would undergo reconstruction if the size is small enough (e.g., seeds) or fracture if the structure is too large.⁸ Therefore, a likely route for Nce3Ncep6 to assist the formation of structures in Figure 1(b) is to strongly adsorb to Au(111), as a decahedron is mostly {111}-faceted, such that the energy increase associated with the twin plane is sufficiently negated.

To move forward with structure-directing peptoid design for better shape homogeneity control, it is necessary to establish the linkage between the chemical composition and its influence on majorly involved crystalline facets, such as {100} and {111} facets. In this work, we use classic molecular dynamics (MD) simulations, together with biased sampling methods, to probe the affinity of Nce3Ncep6 on Au(100) and Au(111). We notice a very strong preference of Au(111)

over Au(100). We conclude that it is a synergistic effect from both the peptoid itself and the interfacial water behavior through further analysis. In the end, we move beyond the single-chain properties and shed light on how Nce3Ncp6 may collectively impose influence on the growth of the two facets.

Figure 1. (a) The atomistic structure of Nce3Ncp6 used in MD simulations. The carboxyl groups are deprotonated to reflect the basic synthetic condition. Atoms are colored as the following: C (cyan), O (red), N (blue), Cl (green), and H (white). (b) The five-fold twinned nanocrystals synthesized with the presence of Nce3Ncp6 and (c) the branched and small spherical nanocrystals synthesized without the presence of Nce3Ncp6. The twin planes are highlighted with white, dashed lines.

Materials and methods

All MD simulations are conducted using GROMACS 5.1³⁵ with PLUMED 2.4 plugin³⁶. Taking the similarity between peptoids and peptides, we describe most of the intra- and intermolecular interactions of Nce3Ncp6 using the CHARMM force field (FF),^{37,38} with few modifications on

dihedrals to account for the different backbone flexibility.³⁹ In addition, we use GoIP-CHARMM FF to describe the Au-Au and Au-solution interactions for its ability to capture the correct facet selectivity of peptides on Au surfaces in previous studies.⁴⁰ The TIP3P water model is used to be compatible with the GoIP-CHARMM parameterization. The initial configuration of each system is designed to accommodate the purpose of the study. Below, we state the configuration setup by category.

Single peptoid on Au surfaces

We choose metadynamics as the biased sampling method to obtain the adsorption free-energy profiles. To ensure sufficient sampling of the adsorbed and desorbed states of a peptoid near Au, the simulation cell should be large enough to accommodate for exploration in configurational phase space. The Au(100) system contains a $20 \times 20 \times 8$ (atoms) periodic Au(100) slab and the Au(111) system contains a $20 \times 18 \times 8$ (atoms) periodic Au(111) slab. We insert one peptoid chain near the surface and fill the rest of the simulation box with water, counter ions (Na), and extra ten pairs of NaCl. Both systems are equilibrated in the NPT ensemble using the v-rescale thermostat (300 K) and Berendsen barostat (1 bar) for 5 ns,⁴¹ with pressure coupling only applied to the z-dimension (i.e., orthogonal to the surface). Following the simulation scheme recommended by Wright and coworkers,⁴⁰ we freeze the position of Au atoms and virtual sites and only allow the dipolar rods to spin at all times. The final z-dimension is 9.98 and 9.83 nm for Au(100) and Au(111), respectively. Both systems are further equilibrated in the NVT ensemble using the v-rescale thermostat for additional 50 ns to relax the peptide structure. All production and enhanced sampling runs are carried out in the same NVT ensemble.

The adsorption free-energy of peptoids on Au surfaces are calculated using parallel-bias metadynamics (PBMetaD) with the multiple-walker scheme.⁴² In PBMetaD, numerous low

dimensional collective variables (CV) can be biased in parallel to achieve efficient exploration for high dimensional CVs. The CVs sampled in this study include the distance between the center of mass (COM) of the peptoid backbone and the Au surfaces in z-dimension, the distance between the COM of the side chain of each residue and the Au surfaces in z-dimension, and the radius of gyration (r_g) of the peptoid. The Au surface is represented by the average position of all atoms in the outmost layer. Four walkers are used for each surface, and each walker is run for 1000 ns to ensure convergence (see the Supporting Information (SI)).

Peptoid-peptoid interaction

For estimating the energetics between two peptoids, we solvate two Nce3Ncp6 chains in water, counterions, and extra NaCl ion pairs. The simulation cell dimension is adjusted to $6.04 \text{ nm} \times 6.04 \text{ nm} \times 6.04 \text{ nm}$ after a 5 ns equilibration in the NPT ensemble with isotropic pressure coupling (v-rescale thermostat and Berendsen barostat), then equilibrated in the NVT ensemble for 50 ns to relax the peptoid structures.

Again, we employ a similar scheme as described above for chain-chain interaction. Similar to single peptoid binding free-energy calculation, four walkers are used, and each walker are sampled for 1000 ns.

Monomer sidechain analogues on Au surfaces

In the effort to identify the origin of facet selectivity of Nce3Ncp6, we dissect the peptoid into residues and assess their energetic contribution by calculating the adsorption free-energy of side chain analogues. Specifically, we use 1-chloro-4-propyl benzene (Figure 4(a)) and butyrate (Figure 4(f)) for Ncp and Nce analogues, respectively.⁶ A $14 \times 14 \times 8$ (atoms) Au(100) slab and a $15 \times 16 \times 8$ (atoms) Au(111) slab are used in this study. The equilibration step is carried out in the same set of thermostat and barostat as for the Nce3Ncp6 chain, with 5 ns in the NPT ensemble

and 20 ns in the NVT ensemble. Since the side chain analogues lack structure complexity significantly as compared to Nce3Ncp6, we use well-tempered MetaD (WTMetaD) and bias only the orthogonal distance between its COM and the Au surface. The total sampling time is 200 ns for each analogue and surface combination.

Multiple peptoid chains on Au surfaces

In addition to single-chain binding on a plain surface, we look into their collective behavior by placing multiple peptoids on the surface. We use the same Au slabs for peptoid adsorption free-energy sampling here and solvate 30 Nce3Ncp6 peptoids near the surface in water. The relaxed simulation box has a z-dimension of 18.58 nm and 18.52 nm for Au(100) and Au(111), respectively. The systems are then equilibrated for 800 ns in the NVT ensemble to arrive at a steady-state structure. We repeat the same process with three more different initial configurations for each surface to ensure the reproducibility of the characteristic configuration.

Results and discussions

Peptoid-Au and peptoid-peptoid interactions

We present the free-energy profile of single Nce3Ncp6 chain adsorption on Au surfaces, as well as peptoid dimerization, in Figure 2(a). For peptoid adsorption, the x-axis indicates the distance between the COM of the Nce3Ncp6 chain orthogonal to the surface. Since the COM of the peptoid is not biased during sampling, the free-energy profiles are obtained from the bias through the standard reweighting procedure. To directly compare the preference of a Nce3Ncp6 chain to an Au surface or to another Nce3Ncp6 chain, we superimpose the peptoid dimerization free-energy profiles onto the same plot. For peptoid dimerization, the x-axis indicates the separation of the COM between two Nce3Ncp6 chains. Since the COM separation between two Nce3Ncp6 chains

is a spatial vector, we apply a volume correction following Yuan and coworkers,⁴³ comparison with and without volume correction can be found in the SI.

A clear message delivered in Figure 2(a) is that Nce3Ncp6 strongly favors Au(111) over Au(100). The adsorption free-energy ΔF_{ads} can be extracted from the free-energy difference between the adsorbed state ΔF_{surf} and the free-floating state in the solution phase ΔF_{sol} via $\Delta F_{ads} = \Delta F_{surf} - \Delta F_{sol}$.⁴⁴⁻⁴⁶ To calculate ΔF_{surf} and ΔF_{sol} from Figure 2(a), we draw boundaries (see the SI) to define the adsorbed state and the free-floating state, and obtain the Boltzmann average of free-energy in each region using

$$\Delta F = -k_b T \log \left[\frac{\int dz e^{-F_z/k_b T}}{w} \right],$$

where k_b is the Boltzmann constant, T is the temperature, z is the orthogonal distance from the surface, F_z is the instant value on the curve at each z , and w is the width of the pre-defined region for the state. This approximation yields an affinity of Nce3Ncp6 to Au(111) ($\Delta F_{ads,\{111\}} = -63.27$ kJ/mol), nearly eleven-folds higher than that to Au(100) ($\Delta F_{ads,\{100\}} = -5.44$ kJ/mol), which exhibits a facet selectivity similar to, or even greater than, other successful structure-directing agents for shape-controlled nanocrystal growth.^{10,47-49}

Figure 2. Free-energy profiles and example simulation snapshots. (a) The free-energy profiles of peptoid adsorption on Au facets and peptoid dimerization in water. For surface adsorption, the x-axis indicates the orthogonal distance of the COM of the peptoid relative to the surface, d_z . For dimerization, the x-axis indicates between the COM of two peptoid chains, d_{com} . The (b) top and (c) side views of equilibrated Nce3Ncp6 on Au(100), and the (e) top and (f) side views of equilibrated Nce3Ncp6 on Au(111). Water molecules are shown in lightened color in the side-view snapshots (oxygen atoms shown in red and hydrogen atoms shown in white) to illustrate their ordered pattern, as well as the relative position of water and peptoid, on Au surfaces. (d) A simulation snapshot of two peptoid chains in water solution. The backbone carbon (cyan) and nitrogen (blue) are shown in large spheres, and chlorobenzene rings on the hydrophobic side chains are filled in red for highlighting purposes.

In addition to the energetic preference, we note that the location of free-energy minimum is further away from Au(100) ($d_z = \sim 1.0$ nm) than from Au(111) ($d_z = \sim 0.5$ nm). Atomistic-scale visualization can be helpful to understand the location offset in this case. The side and the top views of an equilibrated Nce3Ncp6 on Au(100) and Au(111) are compared in Figure 2. Interestingly, Figure 2(e) shows that the aromatic groups on the hydrophobic side chains can lay flat and close to the Au(111) facet. In contrast, for Au(100) in Figure 2(b), a layer of water molecules persists between the peptoid and the surface, regardless of side chain hydrophilicity. We will show the later section that the offset of the free-energy minimum corresponds to the thickness of the stem water layer (i.e., the first peak in Figure 4(a)), and the water molecules in the

stem layer on Au(100) are bound tightly to the surface to prohibit general molecular adsorption. Also, in either case, the hydrophilic carboxyl side chains prefer to stay closer to the solution phase rather than the surface.

Another feature in the adsorption free-energy profiles is the relatively narrower well width for Au(111) than Au(100), implying the different conformational degrees of freedom in the adsorbed states. By comparing the top and side views in Figure 2, it is evident that, with sufficient backbone and side chain flexibility, the aromatic groups prefer to maximize their contact to Au(111) by spreading out laterally and positioning the rings parallel to the surface, whereas the peptoid appears more compact on Au(100). For a more quantitative analysis, we project the 1D free-energy profile onto an additional CV, the radius of gyration (R_g), to assess the compactness of the protein adsorbed on different facets. By reweighting with respect to both R_g and the orthogonal distance from the surface, we obtain 2D free-energy maps as shown in Figure 3.

First, the locations of energy minimum along the y-axis in Figure 3 confirm the difference in compactness as observed in simulation snapshots, that the most energetically preferred R_g is smaller on Au(100) ($R_{g,\{100\}} = 0.74$ nm) than on Au(111) ($R_{g,\{111\}} = 0.83$ nm). Moreover, by qualitatively comparing the distinct contour shapes on the two maps, we see that the peptoid acts more like compressed 2D blobs on Au(111) (i.e., more compressed along the x-axis and elongated along the y-axis in Figure 3(b) in contrast to Figure 3(a)), and such confinement stabilizes the molecule on the surface by losing conformation entropy, which lowers the free-energy of the adsorbed state.⁵⁰

Figure 3. The 2D free-energy map of R_g for (a) Au(100) and (b) Au(111), respectively. The x-axis indicates the distance between the COM of the peptoid and the surface, and the y-axis indicates the R_g of the peptoid. The values of the energy minimum are shifted to 0 for reference. Note that the color scheme corresponds to different energetics scales in (a) and (b).

Aside from the facet selectivity, a direct comparison of peptoid-peptoid interaction to peptoid-surface interaction in Figure 2(d) reveals another interesting character of this facet-selective amphiphilic peptoid, that the peptoid-peptoid affinity is in between its affinity to the two facets, which will be discussed in the last section.

The origin of facet selectivity from the peptoid perspective

The characteristically different interfacial configurations on the two facets shown in the previous section persuasively imply that the energetic preference can be attributed to the interplay among the peptoid-surface, water-surface, and peptoid-water interactions. Herein, we explore the origin of the facet selectivity from both the peptoid and water perspectives.

As pointed out in the previous section, the Ncp side chains (i.e., the hydrophobic segments) and the Nce side chains (i.e., the hydrophilic segments) exhibit significantly different binding modes on the two facets, as the aromatic groups tend to orient parallel to Ag(111) and the carboxyl groups are generally further away from both surfaces (c.f. Figure 2 (c), (e), (h), (j)). Thus, our first effort to investigate the origin of facet selectivity is to separate the energetic contribution of each residue type. Here, we assume that the influence of the side chain outweighs that of the backbone, which allows us to model the Ncp and Nce side chains using the analogues as specified in the method section. We obtain their adsorption free-energy on Au(100) and Au(111) facets and present the free-energy profiles, as well as the simulation snapshot of equilibrated configurations, in Figure 4.

A comparison of Figures 4 (a) and (f) shows that only the Ncp side chain has a strong preference to Au(111), whereas the Nce side chain exhibits weak and non-selective binding to either Au facet. It is worth noting that each Ncp analogue possesses ~ 10 kJ/mol ΔF_{ads} difference, which contributes about 1/6 of ΔF_{ads} difference for a whole chain. Our observation is consistent with the work of Dasetty,⁵¹ which also finds that the adsorption free-energy of unstructured peptides on graphene is dominated by the strong binding amino acid residues. The preference of aromatic groups to close-packed coinage metal surfaces via many-body dispersion has been documented in related *ab initio* studies^{52,53} and is well captured by the GoIP-CHARMM FF (cf. Figure 4(b) and (d)). While the location of free-energy minimum for Ncp analogue orthogonal to Au(111) in Figure 4(a) is consistent with a typical equilibrated configuration (Figure 4(e)), we observe two minima for Au(100), yet the first minimum overlapping with Au(111) is never observed in unbiased MD simulations. This is because, although the two minima on Au(100) have the comparable energy level, for a molecule that has arrived at the second minimum from the solution phase, the energy barrier to approach further to the surface is about twice the energy barrier to return to the solution

phase. Again, based on the width and location of the minima, we confirm that the barrier prohibiting direct surface contact is the stem water layer on Au(100).

On the contrary, Figure 4(f) to (j) demonstrate that, for neither surface, the interaction between the hydrophilic Nce analogue and the surface is strong enough to break the stem layer network, such that the energetically favored locations for both are above the stem water layer.

Evidence such far confirms the influence of facet selectivity from the molecular perspective of peptoid itself and is embedded with the inseparable role of surface water, which leads to our next step in investigating the facet selectivity.

Figure 4. The configurations and adsorption free-energy profiles of side chain analogues. The top and side views of Ncp analogue on Au(100) (a, b) and Au(111) (c, d), and the top and side views of Nce analogue on Au(100) (f, g) and Au(111) (h, i). The adsorption free-energy profile of Ncp and Nce analogues are shown in (e) and (j), respectively. Water molecules are shown in the side views to indicate the relative position of stem layer water and surface-adsorbed molecules.

The origin of facet selectivity from the surface water perspective

Interfacial water structures and dynamics contrast characteristically to those of the bulk-phase water, and their behavior may depend greatly on the surface chemistry. Previous DFT studies have shown that the O atoms on water molecules prefer to adopt an a-top configuration on Au. Consequently, due to different packing of Au atoms in different surface orientations, water

molecules may exhibit dissimilar orientational or network preferences, consequently affecting the adsorption of other solutes.

Similar to other reported interfaces, water molecules lose translational isotropy and layer up near Au surfaces. However, the density distribution function of O atoms in water orthogonal to the surface alone (Figure 5(a)) is too subtle to reconcile the drastic difference we see in previous discussions. On the other hand, we find that water molecules exhibit strikingly dissimilar in-plane features within the stem layer on the two facets (i.e., within the first peak from the surface in Figure 5(a)). To visualize the dissimilarity, we show an ensemble of stem layer water O atoms positions (labeled as small red dots) relative to the Au atoms underneath (labeled as large golden spheres) in Figures 5(b) and (c). It is clear that nearly all O atoms near the Au(100) surface align strictly on top of an Au atom, whereas the distribution of O atoms is less patterned on Au(111). To break such ordered water on Au(100) would require extra free-energy associated with an entropic penalty.

In addition, a patterned distribution may also result in a tighter molecular network. We present the distribution of θ , the angle between the water dipole and its projection on the Au surface, of the stem layer water molecules in Figure 5(d). An illustration of how θ is defined is given in Figure 5(e): a value of 0° indicates that the dipole is parallel to the surface, and a value of 90° indicates a dipole aligning perpendicular to the surface, regardless of whether the dipole is pointing up or down. Most noticeably, the two facets differ in the spread of the distributions, where water dipoles near Au(100) have a preferred angular orientation relative to the surface centered around 45° but do not exhibit a strongly favored orientation for Au(111). We also compute the number of hydrogen bonds per water based on the criteria stated in Qi and coworkers.⁵⁴ The number of hydrogen bonds per water molecule in the stem layer is 2.258 ± 0.006 for Au(100) and 2.222 ± 0.007 for Au(111), further evidencing for a tighter and more patterned water network on Au(100).

A more ordered molecular network inevitably makes the water molecules more “sticky” to the surface and compete with other adsorptions. To demonstrate the “stickiness,” we consider the relaxation dynamics of water in terms of the survival probability $S(t)$, which describes how likely a water molecule will reside in a given layer after a certain time, and also residence time τ within a 1 ns window (i.e., long relaxation), a characteristic time for survival probability decay.⁵⁵ More stagnant molecular dynamics is often reflected as slow decay in survival probability, i.e., a higher value in τ . The survival probability $S(t)$ is calculated from the ensemble average of N water molecules using

$$S(t) = \sum_{i=1}^N \left\langle \prod_{t_0}^{t_0+\Delta t} P_i^s(t) \right\rangle$$

where $P_i^s(t)$ is a binary value to find ($P_i^s(t) = 1$) or lose ($P_i^s(t) = 0$) the i^{th} water in the first surface layer at time t . We plot the normalized $\frac{S(t)}{S(0)}$ in Figure 5(f) for both surfaces, and note that the decay for Au(111) is much faster than Au(100), indicating that a surface water molecule on Au(111) will be more mobile than that on Au(100). To quantify the decay, we fit the curve to the following equation to find τ

$$\frac{S(t)}{S(0)} = a_f e^{-t/\tau_f} + a_s e^{-t/\tau_s} + c$$

where τ_f is for the fast component and τ_s is for the slow component in the characteristic decay, and a_f , a_s and c are coefficients. The fitted value for τ_f is 102 ps for water near Au(100), and 38 ps for water near Au(111), and the fitted values for τ_s are 384 ps and 211 ps, respectively. Therefore, as a combined result of more ordered static structure, inter-layer network, and slow dynamics, water molecules on Au(100) form a “protective” layer that effectively impedes the adsorption of any solution-phase molecules. Finally, it should also be pointed out that although the

stem layer water on Au(111) is less ordered or stagnant as compared to that on Au(100), their residency times are still admittedly higher than other surfaces documented in the literature, suggesting a moderately protective water layer. Depending on the interaction between the surface and the incoming solution-phase molecule, such a moderate protective layer may or may not be disrupted, an example of which is the different equilibrium position of Ncp and Nce analogues orthogonal to Au(111), as shown in Figure 4(d) and (i).

Figure 5. Analyses of the static and dynamic behavior of surface water on Au. (a) The vertical density of O atoms in the water near the Au surfaces. A collection of the lateral position of O atoms in the stem layer water (within the first peak in (a)) for (b) Au(100) and (c) Au(111), with surface Au atoms shown in golden spheres underneath for reference. (d) the probability distribution function of the angle between water dipole and surface, θ , for the stem layer water. The definition of θ is shown in (e). (f) The survival probability of stem layer water over a 1 ns time window.

The configurations of the amphiphilic peptoid at a collective level

Although explaining how the facet selectivity of Nce3Ncp6 is beyond the scope of this paper, we find it is necessary to briefly discuss what ties the cause (i.e., facet selectivity) and the outcome (i.e., nanostructure), that is, the configuration of multiple peptoid chains on Au surfaces. As we have pointed out in the previous section, the free-energy profiles in Figure 2(a) suggest an energetic order of: peptoid-Au(100) < peptoid-peptoid < peptoid-Au(111). An immediate inference we can draw from the trend is that peptoids prefer to maximize their contact with the surface on Au(111) but with themselves on Au(100). Together with its amphiphilic nature and that the affinity with the surface is entirely driven by the hydrophobic group, this energetic order results in multiple-chain configurations (see Figure S5) that are rarely observed in previous computational studies on other well-known structure-directing agent-mediated nanocrystal synthesis, where relatively simple polymeric or oligomer carpets are evidenced. In Figure S5, peptoids on Au(100) remain a core-shell cross-sectional structure and sit on top of the stem layer of surface water, whereas peptoids on Au(111) adopt a bell-like structure, with the aromatic segments (i.e., hydrophobic and favoring Au(111)) buried underneath a cover consisting of the carboxyl groups (i.e., hydrophilic and weakly interacting with Au(111)). These configurations may exert thermodynamics or kinetic influences, or both, on the five-fold nanocrystal formation, for example, greatly passivating Au(111) by drastically lowering the interfacial free-energy through direct contact or exposing Au(100) to solution-phase particle or atom addition because the peptoid network is free to diffuse on the surface, etc. A thorough inquiry supported by extensive examination from both the kinetic and thermodynamic aspects is needed to answer these questions.

Conclusions and future work

To this end, we have shown a very strong selectivity of Nce3Ncp6 to Au(111) over Au(100) using the adsorption free-energy profiles obtained from MD simulation and PBMetaD sampling. Through further analyses on side chain energetic contribution and interfacial water behavior, we identify that the origin of facet selectivity is twofold. From the perspective of the molecular composition of peptoids, the aromatic side chains intrinsically favor the hexagonally packed fcc(111) lattice, and both the backbone dihedrals and the ethyl group on the side chain are flexible enough to maximize the direct contact between the aromatic ring and the surface. Second, water molecules are more ordered and stagnant on Au(100), which poses a protective barrier to prevent solution-phase molecules from adsorption in general. The carboxyl side chains on Nce3Ncp6, on the other hand, bind weakly and non-selectively to either surface. Due to its hydrophilic nature, we can fairly deduce that an increase in the hydrophilic segment will weaken the peptoid-surface interaction, as the solvation effect will cause the peptoid to be more “lifted” from the surface.

Interestingly, by comparing the peptoid-peptoid and peptoid-surface interactions, we find the energetics appear in the order of peptoid-Au(100) < peptoid-peptoid < peptoid-Au(111). We shed light on how this energetic ordering, together with the amphiphilicity, affects the configuration of peptoids beyond the scope of a single chain. At a collective level, the peptoid configurations, including the fraction of direct surface contact, the molecular diffusivity, and the molecular network, are highly relevant in investigating how the peptoids assist in the nanocrystal formation mechanism and will be the major focus in future studies.

ASSOCIATED CONTENT

Additional information on simulation and analysis are stated in detail in the SI.

AUTHOR INFORMATION

Corresponding Author

*E-mail: jpfaendt@uw.edu

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was funded by the Army Research Office, the Department of Defense, grant number W911NF1920198. This work was facilitated using computational, storage, and networking infrastructure provided by the Hyak supercomputer system, supported in part by the University of Washington and National Science Foundation [CHE-1624430]. Part of this research used the National Energy Research Scientific Computing Center (NERSC) resources, a U.S. Department of Energy Office of Science User Facility located at Lawrence Berkeley National Laboratory, operated under Contract No. DE-AC02-05CH11231.

REFERENCES

- (1) Liu, S.; Guan, Y.; Sheng, Y.; Hu, Y.; Rong, Y.; Mei, A.; Han, H. A Review on Additives for Halide Perovskite Solar Cells. *Adv Energy Mater.* 2020, 10, 1902492.
- (2) Kamat, P. V.; Pradhan, N.; Schanze, K.; Weiss, P. S.; Buriak, J.; Stang, P.; Odom, T. W.; Hartland, G. Challenges and Opportunities in Designing Perovskite Nanocrystal Heterostructures. *ACS Energy Lett.* 2020, 5, 2253–2255.

- (3) Chan, C.-H.; Poignant, F.; Beuve, M.; Dumont, E.; Loffreda, D. Effect of the Ligand Binding Strength on the Morphology of Functionalized Gold Nanoparticles. *J. Phys. Chem. Lett.* 2020, *11*, 2717–2723.
- (4) Fichthorn, K. A Pathway from 3D to 2D. *Nat Mater.* 2019, *18*, 911–912.
- (5) Velázquez-Salazar, J. J.; Bazan-Diaz, L.; Zhang, Q.; Mendoza-Cruz, R.; Montaña-Priede, L.; Guisbiers, G.; Large, N.; Link, S.; Jose-Yacaman, M. Controlled Overgrowth of Five-Fold Concave Nanoparticles into Plasmonic Nanostars and Their Single-Particle Scattering Properties. *ACS Nano* 2019, *13*, 10113–10128.
- (6) Yan, F.; Liu, L.; Walsh, T. R.; Gong, Y.; El-Khoury, P. Z.; Zhang, Y.; Zhu, Z.; Yoreo, J. J. D.; Engelhard, M. H.; Zhang, X.; Chen, C.-L. Controlled Synthesis of Highly-Branched Plasmonic Gold Nanoparticles through Peptoid Engineering. *Nat. Commun.* 2018, *9*, 1–8.
- (7) Xia, Y.; Gilroy, K. D.; Peng, H.-C.; Xia, X. Seed-Mediated Growth of Colloidal Metal Nanocrystals. *Angew. Chem. Int. Ed.* 2017, *56*, 60–95.
- (8) Xia, Y.; Xiong, Y.; Lim, B.; Skrabalak, S. E. Shape-Controlled Synthesis of Metal Nanocrystals: Simple Chemistry Meets Complex Physics? *Angew. Chem. Int. Ed.* 2009, *48*, 60–103.
- (9) Xia, X.; Zeng, J.; Zhang, Q.; Moran, C. H.; Xia, Y. Recent Developments in Shape-Controlled Synthesis of Silver Nanocrystals. *J. Phys. Chem. C* 2012, *116*, 21647–21656.
- (10) Xia, X.; Zeng, J.; Oetjen, L. K.; Li, Q.; Xia, Y. Quantitative Analysis of the Role Played by Poly(Vinylpyrrolidone) in Seed-Mediated Growth of Ag Nanocrystals. *J. Mech. Phys. Solids* 2012, *134*, 1793–1801.
- (11) Silva, R. R. da; Yang, M.; Choi, S.-I.; Chi, M.; Luo, M.; Zhang, C.; Li, Z. Y.; Camargo, P. H. C.; Ribeiro, S. J. L.; Xia, Y. Facile Synthesis of Sub-20 Nm Silver Nanowires through a Bromide-Mediated Polyol Method. *ACS Nano* 2016, *10*, 7892–7900.
- (12) Shi, Y.; Lyu, Z.; Zhao, M.; Chen, R.; Nguyen, Q. N.; Xia, Y. Noble-Metal Nanocrystals with Controlled Shapes for Catalytic and Electrocatalytic Applications. *Chem. Rev.* 2020, *121*, 649–735.
- (13) Yang, T.; Shi, Y.; Janssen, A.; Xia, Y. Surface Capping Agents and Their Roles in Shape-Controlled Synthesis of Colloidal Metal Nanocrystals. *Angew. Chem. Int. Ed.* 2020, *59*, 15378–15401.
- (14) Ruan, L.; Chiu, C.-Y.; Li, Y.; Huang, Y. Synthesis of Platinum Single-Twinned Right Bipyramid and {111}-Bipyramid through Targeted Control over Both Nucleation and Growth Using Specific Peptides. *Nano Lett.* 2011, *11*, 3040–3046.

- (15) Chen, Z.; Fichthorn, K. A. Adsorption of Ethylenediamine on Cu Surfaces: Attributes of a Successful Capping Molecule Using First-Principles Calculations. *Nanoscale* 2021, *13*, 13529–13537.
- (16) Qi, X.; Balankura, T.; Zhou, Y.; Fichthorn, K. A. How Structure-Directing Agents Control Nanocrystal Shape: Polyvinylpyrrolidone-Mediated Growth of Ag Nanocubes. *Nano Lett.* 2015, *15*, 7711–7717.
- (17) Kim, M. J.; Alvarez, S.; Yan, T.; Tadepalli, V.; Fichthorn, K. A.; Wiley, B. J. Modulating the Growth Rate, Aspect Ratio, and Yield of Copper Nanowires with Alkylamines. *Chem Mater.* 2018, *30*, 2809–2818.
- (18) Hughes, Z. E.; Wright, L. B.; Walsh, T. R. Biomolecular Adsorption at Aqueous Silver Interfaces: First-Principles Calculations, Polarizable Force-Field Simulations, and Comparisons with Gold. *Langmuir* 2013, *29*, 13217–13229.
- (19) Balankura, T.; Qi, X.; Zhou, Y.; Fichthorn, K. A. Predicting Kinetic Nanocrystal Shapes through Multi-Scale Theory and Simulation: Polyvinylpyrrolidone-Mediated Growth of Ag Nanocrystals. *J. Chem. Phys.* 2016, *145*, 144106.
- (20) Heinz, H.; Pramanik, C.; Heinz, O.; Ding, Y.; Mishra, R. K.; Marchon, D.; Flatt, R. J.; Estrela-Lopis, I.; Llop, J.; Moya, S.; Ziolo, R. F. Nanoparticle Decoration with Surfactants: Molecular Interactions, Assembly, and Applications. *Surf. Sci. Rep.* 2017, *72*, 1–58.
- (21) Kim, M. J.; Alvarez, S.; Chen, Z.; Fichthorn, K. A.; Wiley, B. J. Single-Crystal Electrochemistry Reveals Why Metal Nanowires Grow. *J. Am. Chem. Soc.* 2018, *140* (44), 14740–14746.
- (22) Fichthorn, K. A.; Chen, Z. Surface Science of Shape-Selective Metal Nanocrystal Synthesis from First-Principles: Growth of Cu Nanowires and Nanocubes. *J Vac. Sci. Technol. A* 2020, *38*, 023210.
- (23) Tang, Z.; Zhang, Q.; Yin, Y.; Chang, C. A. Facet Selectivity of Ligands on Silver Nanoplates: Molecular Mechanics Study. *J. Phys. Chem. C* 2014, *118*, 21589–21598.
- (24) Murshid, N.; Kitaev, V. Role of Poly(Vinylpyrrolidone) (PVP) and Other Sterically Protecting Polymers in Selective Stabilization of {111} and {100} Facets in Pentagonally Twinned Silver Nanoparticles. *Chem. Commun.* 2014, *50*, 1247–1249.
- (25) Qi, X.; Fichthorn, K. A. Theory of the Thermodynamic Influence of Solution-Phase Additives in Shape-Controlled Nanocrystal Synthesis. *Nanoscale* 2017, *9*, 15635–15642.
- (26) Salvalaglio, M.; Vetter, T.; Mazzotti, M.; Parrinello, M. Controlling and Predicting Crystal Shapes: The Case of Urea. *Angew. Chem. Int. Ed.* 2013, *52*, 13369–13372.

- (27) Balankura, T.; Yan, T.; Jahanmahin, O.; Narukatpichai, J.; Ng, A.; Fichthorn, K. A. Oriented Attachment Mechanism of Triangular Ag Nanoplates: A Molecular Dynamics Study. *Nanoscale Adv* 2020, 2, 2265–2270.
- (28) Liu, C.; Chen, Q. Interfacial Crystallization under DNA Control. *Nat Mater.* 2020, 19, 704–705.
- (29) Yang, W.; Yin, Q.; Chen, C.-L. Designing Sequence-Defined Peptoids for Biomimetic Control over Inorganic Crystallization. *Chem. Mater.* 2021, 33, 3047–3065.
- (30) Li, R.; Smolyakova, A.; Maayan, G.; Rimer, J. D. Designed Peptoids as Tunable Modifiers of Zeolite Crystallization. *Chem. Mater.* 2017, 29, 9536–9546.
- (31) Cleveland, C. L.; Landman, U. The Energetics and Structure of Nickel Clusters: Size Dependence. *J. Chem. Phys.* 1991, 94, 7376–7396.
- (32) Casillas, G.; Velázquez-Salazar, J. J.; Jose-Yacaman, M. A New Mechanism of Stabilization of Large Decahedral Nanoparticles. *J. Phys. Chem. C* 2012, 116, 8844–8848.
- (33) Patala, S.; Marks, L. D.; Cruz, M. O. de la. Elastic Strain Energy Effects in Faceted Decahedral Nanoparticles. *J. Phys. Chem. C* 2013, 117, 1485–1494.
- (34) Patala, S.; Marks, L. D.; Cruz, M. O. de la. Thermodynamic Analysis of Multiply Twinned Particles: Surface Stress Effects. *J. Phys. Chem. Lett.* 2013, 4, 3089–3094.
- (35) Abraham, M. J.; Murtola, T.; Schulz, R.; Páll, S.; Smith, J. C.; Hess, B.; Lindahl, E. GROMACS: High Performance Molecular Simulations through Multi-Level Parallelism from Laptops to Supercomputers. *Softwarex* 2015, 1, 19–25.
- (36) Tribello, G. A.; Bonomi, M.; Branduardi, D.; Camilloni, C.; Bussi, G. PLUMED 2: New Feathers for an Old Bird. *Comput. Phys. Commun.* 2014, 185, 604–613.
- (37) Vanommeslaeghe, K.; Hatcher, E.; Acharya, C.; Kundu, S.; Zhong, S.; Shim, J.; Darian, E.; Guvench, O.; Lopes, P.; Vorobyov, I.; MacKerell, A. D. J. CHARMM General Force Field: A Force Field for Drug-Like Molecules Compatible with the CHARMM All-Atom Additive Biological Force Fields. *J. Comput. Chem.* 2010, 31, 671–690.
- (38) Huang, J.; MacKerell, A. D. CHARMM36 All-atom Additive Protein Force Field: Validation Based on Comparison to NMR Data. *J Comput. Chem.* 2013, 34, 2135–2145.
- (39) Mirijanian, D. T.; Mannige, R. V.; Zuckermann, R. N.; Whitlam, S. Development and Use of an Atomistic CHARMM-based Forcefield for Peptoid Simulation. *J Comput. Chem* 2014, 35 (5), 360–370.

- (40) Wright, L. B.; Rodger, P. M.; Corni, S.; Walsh, T. R. GoIP-CHARMM: First-Principles Based Force Fields for the Interaction of Proteins with Au(111) and Au(100). *J. Chem. Theory Comput.* 2013, 9, 1616–1630.
- (41) Berendsen, H. J. C.; Postma, J. P. M.; Gunsteren, W. F. V.; DiNola, A.; Haak, J. R. Molecular Dynamics with Coupling to an External Bath. *J. Chem. Phys.* 1984, 81, 3684–3690.
- (42) Pfaendtner, J.; Bonomi, M. Efficient Sampling of High-Dimensional Free-Energy Landscapes with Parallel Bias Metadynamics. *J. Chem. Theory Comput.* 2015, 11, 5062–5067.
- (43) Yuan, F.; Wang, S.; Larson, R. G. Potentials of Mean Force and Escape Times of Surfactants from Micelles and Hydrophobic Surfaces Using Molecular Dynamics Simulations. *Langmuir* 2015, 31, 1336–1343.
- (44) Mao, C. M.; Sampath, J.; Sprenger, K. G.; Drobny, G.; Pfaendtner, J. Molecular Driving Forces in Peptide Adsorption to Metal Oxide Surfaces. *Langmuir* 2019, 35, 5911–5920.
- (45) Sampath, J.; Pfaendtner, J. Amphiphilic Peptide Binding on Crystalline vs. Amorphous Silica from Molecular Dynamics Simulations. *Mol. Phys.* 2019, 1, 1–9.
- (46) Sultan, A. M.; Westcott, Z. C.; Hughes, Z. E.; Palafox-Hernandez, J. P.; Giesa, T.; Puddu, V.; Buehler, M. J.; Perry, C. C.; Walsh, T. R. Aqueous Peptide–TiO₂ Interfaces: Isoenergetic Binding via Either Entropically or Enthalpically Driven Mechanisms. *ACS Appl. Mater. Interfaces* 2016, 8, 18620–18630.
- (47) Balankura, T.; Qi, X.; Fichthorn, K. A. Solvent Effects on Molecular Adsorption on Ag Surfaces: Polyvinylpyrrolidone Oligomers. *J. Phys. Chem. C* 2018, 122, 14566–14573.
- (48) Liu, S.-H.; Fichthorn, K. A. Interaction of Alkylamines with Cu Surfaces: A Metal–Organic Many-Body Force Field. *J. Phys. Chem. C* 2017, 121, 22531–22541.
- (49) Ruan, L.; Ramezani-Dakhel, H.; Chiu, C.-Y.; Zhu, E.; Li, Y.; Heinz, H.; Huang, Y. Tailoring Molecular Specificity Toward a Crystal Facet: A Lesson From Biorecognition Toward Pt{111}. *Nano Lett.* 2013, 13, 840–846.
- (50) Rubinstein, M. and Colby, R. *Polymer Physics*, 1st ed.; Oxford University Press, 003.
- (51) Dasetty, S.; Sarupria, S. Advancing Rational Control of Peptide–Surface Complexes. *J. Phys. Chem. B* 2021, 125, 2644–2657.
- (52) Jiang, Y.; Yang, S.; Li, S.; Liu, W. Aromatic Molecules on Low-Index Coinage Metal Surfaces: Many-Body Dispersion Effects. *Sci. Rep.* 2016, 6, 1–8.
- (53) Liu, W.; Carrasco, J.; Santra, B.; Michaelides, A.; Scheffler, M.; Tkatchenko, A. Benzene Adsorbed on Metals: Concerted Effect of Covalency and van Der Waals Bonding. *Phys. Rev. B* 2012, 86, 245405.

- (54) Qi, X.; Zhou, Y.; Fichthorn, K. A. Obtaining the Solid-Liquid Interfacial Free Energy via Multi-Scheme Thermodynamic Integration: Ag-Ethylene Glycol Interfaces. *J. Chem. Phys.* 2016, *145*, 194108.
- (55) Debnath, A.; Mukherjee, B.; Ayappa, K. G.; Maiti, P. K.; Lin, S.-T. Entropy and Dynamics of Water in Hydration Layers of a Bilayer. *J. Chem. Phys.* 2010, *133*, 174704.