REVIEW ARTICLE

Role of the Supporting Surface in the Thermodynamics and Cooperativity of Axial Ligand Binding to Metalloporphyrins at Interfaces

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Abstract: Metalloporphyrins have been shown to bind axial ligands in a variety of environments including the vacuum/solid and solution/solid interfaces. Understanding the dynamics of such interactions is a desideratum for the design and implementation of next generation molecular devices which draw inspiration from biological systems to accomplish diverse tasks such as molecular sensing, electron transport, and catalysis to name a few. In this article, we review the current literature of axial ligand coordination to surface-supported porphyrin receptors. We will focus on the coordination process as monitored by scanning tunneling microscopy (STM) that can yield qualitative and quantitative information on the dynamics and binding affinity at the single molecule level. In particular, we will address the role of the substrate and intermolecular interactions in influencing cooperative effects (positive or negative) in the binding affinity of adjacent molecules based on experimental evidence and theoretical calculations.

Keywords: Porphyrins, axial ligand binding, STM, single molecule thermodynamics, cooperative binding, Density Functional Theory calculations

1. INTRODUCTION

The properties, structures, and chemical reactivity of metal porphyrin complexes have been the subject of considerable interest recently because their relevance in diverse fields such as catalysis [1-3], chemical sensors [4-6], molecular separations [7-9], spintronics [10, 11], and medicine [12, 13]. These tetrapyrrole-based molecules are stable relative to their size and exhibit useful chemical and photoelectric properties. Considerable work has been done in the metalloporphyrin synthesis field allowing for increasingly complex molecules and unique properties. Both macrocycle substituents and metal ion transformations are used to tune the electronic, physical, and chemical properties. One significant functional chemical property of metalloporphyrins is their ability to bind axial ligands. Axial coordination of porphyrins is ubiquitous in biochemistry where porphyrins are commonly found in the active site of proteins and enzymes. Understanding the binding affinity of metalloporphyrins and the influence of surface confinement are necessary for the advancement of catalysis and sensing applications as it has been shown that the interface plays an important role in modulating axial ligand binding affinity [14, 15]. Simple metalloporphyrins have been well studied as self-assembled monolayers on conducting surfaces such as Au, Ag, Cu, and highly ordered pyrolytic graphite (HOPG) [16-18]. The self-assembled monolayers are stable and lend themselves to study at the single molecule level by techniques like scanning tunneling microscopy (STM).

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This review is concerned with the reactivity of these tetrapyrrole self-assembled surfaces with ligands. The advantage of STM over large scale, ensemble level techniques in this application is the ability to investigate reactions in real time on a per molecule basis, thus allowing for the investigation of the distribution of reacting sites, reaction

mechanisms, and binding dynamics information that may be obscured in methods that require $\gtrsim 10^8$ molecules (large scale) techniques. STM can also be used to investigate the cooperativity in surface ligation reactions in a unique way with the spatial resolution allowing for the determination of the distribution of neighboring reacted adsorbed molecules. Cooperative interactions are broadly characterized as nonadditive interactions where the behavior of a system depends on the amount of interactions present. Cooperativity is abundant in biological systems and used to alter the stability and reactivity of interaction components and is likely the source of high specificity of ligand to enzymes [19, 20].

In this review, we summarize the current state of the literature regarding axial ligand binding of various metalloporphyrins at interfaces with special focus on: (1) the role of the surface at the vacuum- and solution-solid interfaces and (2) the cooperative properties of the systems. In the final section of this review, we sum up the current progress and share our outlook for binding studies at the single molecule level. For additional readings on porphyrin chemistry and self-assembly at interfaces, the reader is directed to other recent excellent reviews [18, 21-23].

2. AXIAL LIGAND BINDING TO SURFACE SUPPORTED METALLOPORPHYRINS

2.1 General Considerations

The axial ligation of metalloporphyrin systems has been used as a functional target for a variety of applications. Axial ligands have been shown to alter the redox, photovoltaic, and magnetic properties of metal porphyrins [23-25]. Although the coordination is typically relatively weak and reversible, coordinated species tend to be thermodynamically stable. Metalloporphyrin coordination has been studied extensively in fluid solutions [26] and in various environments where the porphyrin is confined at the vacuum-solid [23] and solution-solid interfaces [22]. When confined to interfaces, porphyrins undergo surface-induced structural adaptation (ring deformation, rotation of substituents) to fit their local environments [23]. In addition to the structural changes to surface confined porphyrins, the affinity of porphyrins to axial ligands can also be modified by the surface. In some cases, the modification of porphyrin reactivity by a surface has been attributed to the surface acting as an additional coordinative bond, it has even been compared with the classical "trans-effect" in which the presence of an axial ligand can alter the bond strength of the axial ligand positioned trans to the first ligand with respect to the porphyrin macrocycle [14, 15]. Computational work has also shown that the surface can act as either a charge donor or an acceptor under differing circumstances [27]. The subsequent discussion is divided into cases of ligand binding occurring at the (1) vacuum-solid interface and (2) the solution-solid interface.

2.2 Vacuum-solid Interface

To study axial ligand coordination to surface supported porphyrins, typically the porphyrin is vapor deposited onto a solid substrate followed by exposure to the ligand. Gaseous ligands such as nitric oxide (NO), carbon monoxide (CO), dioxygen (O_2), and ammonia (NH_3) are perhaps the most well-studied types of axial ligands binding to porphyrins at the vacuum-solid interface [23]. They are of biological importance and metalloporphyrins interact with them in a range of processes from oxygen storage to muscle contraction and synaptic transmission [28, 29]. As such, there is interest in using porphyrins as sensors, single metal atom catalysis as alternative chemical storage devices, and information storage as spintronics. Many of the reactions are not observed at room temperature and require cryogenic temperatures to "freeze-out" the desired reaction product. However, nitrogen dioxide (NO_2) was shown to bind nickel tetraphenyl porphyrin (Ni-TTP) molecules at room temperature on the Cu(110) surface [30]. Bond energies of axially ligated porphyrins that are stable enough to be imaged at the vacuum-solid interface can approach the strength of covalent bonds (for reference, C-C single bond strength is ~350 kJ/mol [31]). Some examples of strong ligand-metalloporphyrin bonds are 1,3-dimethylimidazol-3-ium (IMe)-RuTTP/Ag(111), 96.5 kJ/mol from temperature programmed desorption (TPD) spectra [32], CO-RuTTP/Ag(111), 183 kJ/mol from TPD spectra [33], NO-CoP/Ag(111), 124 kJ/mol, and NO-FeP/Ag(111), 168 kJ/mol from DFT calculation [14].

The STM probe can be a powerful tool for controlling ligand-porphyrin binding chemistry at interfaces [34, 35]. One recent example is the deligation of 1,3-dimethylimidazol-3-ium (IMe) from IMe-RuTTP complex on Ag(111) [32]. When a monolayer of RuTTP deposited on Ag(111) was exposed to IMe at 300K, almost all RuTTP became coordinated, Fig. **1b**. The system was subsequently cooled to 5 K and the STM tip was positioned over an IMe-RuTTP molecule. The probe was then manipulated by turning the feedback loop off, setting the sample bias -3V, and then moving the tip 2 Å toward the surface. Scanning the same area shows the manipulated molecule returns to the unligated RuTTP state following the tip manipulation protocol.

The surface is an active participant in many coordination reactions. For example, the oxygen reduction capabilities of metal porphyrins and phthalocyanines have been of interest for a long time. Theoretical studies of homolytic oxygen cleavage by manganese porphyrins and phthalocyanines agree that the reaction pathway involving

Table 1. Comparison of ligand pKa and thermodynamic values for the formation of various 5-coordinate CoOEP-nitrogenous ligand complexes in toluene solution at 298 K.

Ligand molecule	pKa	$K_s(M^{-1})$	$-\Delta G_{(soln)}$ (kJ/mol)
Pyridine (Py)[a]	5.22	491	15.35
1-Phenyl imidazole (PhIm)[b]	5.45	1680	18.13
4-Methoxy pyridine (MeOPy)[c]	6.58	890	16.80
Imidazole (Im)[d]	6.90	7340	22.00

[a][45], [b][51], [c][49], [d][71]

the macrocycle alone has a high energy barrier and is unlikely to proceed [36-39]. The substrate must be involved in order for the cleavage of O_2 to be observed. One recent report on oxygen cleavage by iron phthalocyanine adsorbed on Ag(100) showed that Ag adatoms play an important role in the reaction mechanism and may even facilitate oxygen transfer between adjacent molecules [40]. The surface has also been known to attenuate the reactivity of certain molecules. In solution, the dioxo forms of Ru-porphyrins are known to be catalytically active for alkene/olefin epoxidations; however, when adsorbed on Ag(111) the RuTTP complex was found to be completely unreactive to molecular oxygen [41].

The presence of the surface can also significantly alter the magnetic or spin properties of an adsorbed porphyrin. Without the influence of an external magnetic field, paramagnetic metalloporphyrins have net zero magnetic moments, however, magnetic coupling between the metalloporphyrins and the surface or chemical modification of an adsorbed porphyrin have both been shown as ways to modify the spin properties of the porphyrin [42]. For example, CoTPP/Ni(001) shows ferromagnetic coupling between the porphyrin and Ni(001) surface. With NO coordination, the magnetic coupling is no longer observed leading to an *off* state of the Co spin. The *on* state of the Co spin is recovered upon thermal dissociation of the NO ligand [43]. The degree of porphyrin-surface interaction has also been shown to be tunable based on the axial ligand identity. When CoTTP/Au(111) was exposed to NH_3 and separately NO_2 gas at 80K, Scanning tunneling spectroscopy (STS) measurements, Fig. **2** showed zero bias peaks associated with net spin polarization likely originating from Kondo effect, for NO_2-CoTTP (strongest interaction) and NH_3-CoTTP (weaker interaction) and no peak for NO_2-CoTTP (no interaction) [44]. For more information on the control of magnetism of surface adsorbed molecules, see the excellent review by Kuch and Bernien [42].

2.3 Solution-solid Interface

At the solution-solid interface, it becomes possible to use STM to study reversible axial coordination. Reversibly bound ligands are especially relevant when considering biochemical system functions and applications such as catalysis or small molecule sensing. With STM, reversible binding/dissociation processes can be monitored and both qualitative and quantitative information about ligand binding affinity and the energetics that define a particular ligation reaction can be extracted. Molecular and time-dependent imaging can establish whether the process under study is at equilibrium and can also provide kinetic data and mechanisms.

Table 2. Experimental and calculated thermodynamic values for the formation of five-coordinate Im, MeOPy, and PhIm of selected metal porphyrin complexes at 298 K.

System	K_s (M^{-1})	ΔG (kJ/mol)		ΔH (kJ/mol)	
	Exp.	Exp.	Calc.	Exp.	Calc.
MeOPy-CoOEP (solution)[b]	890	-16.8±0.2	-20.7	--	-56.9
MeOPy-CoOEP/HOPG[b]	190	-13.0±0.3	-20.4	-50±5	-55.6
PhIm-CoOEP (solution)[c]	1680	-18.13	-6.6	--	-46.3
PhIm-CoOEP/HOPG[d]	--	--	-59	--	-98
Im-NiOEP (solution)[a]	--	--	--	--	-22
Im-NiOEP/HOPG[a]	590	-15.8	--	-80	-65

[a][50], [b][49], [c][71], [d]for computational details see supplementary material.

Currently, example studies that demonstrate axial ligand binding to surface supported porphyrins at the organic solution-solid interface are still rare. However, there is sufficient data reported to allow discussion of trends in ligand identity and the differences between solution phase and solution-solid interface chemistry. Examples of such ligands include nitrogenous ligands such as pyridine-based [45-49] and imidazole-based molecules [50, 51], and gases such as dioxygen [52, 53]. The surface is essential for observing binding reactions of metal porphyrins with some of these molecules. For example, Co-porphyrins do not typically bind oxygen in solution at room temperature. A notable exception here is the Co picnic basket or picket-fence porphyrins which bind molecular oxygen at 300 K [54, 55]. It is important to note that even in these special cases, oxygen binding requires the presence of an imidazole residue coordinated trans to the ligated oxygen [54, 55]. Interestingly, cobalt(II)octaethylporphyrin (CoOEP), while not reacting with O_2 in fluid solution, was shown to bind dioxygen at the phenyloctane/HOPG interface at room temperature [52]. This facile binding reaction was attributed to the presence of the HOPG surface which acts as an electron donor, thus enhancing oxygen ligation to the CoOEP supported on that substrate.

CoOEP has been studied extensively at the phenyloctane-HOPG and Au(111) interfaces and the stability and surface structure of its monolayer is well known [56, 57]. The solution phase binding chemistry of different ligands to simple porphyrins is widely known from UV-Visible spectroscopy or nuclear magnetic resonance (NMR) experiments. Many of these studies observed correlations between ligand basicity and their binding affinity (ΔG) [58-60]. In general, ligands with high pKa values tended to bind more readily to metal porphyrins than ligands with lower pKa's, although steric effects tended to modify this this trend in some instances. For example, cyclic amines have larger association constants than those of noncyclic amines because of decreased repulsion between the substituents and the porphyrin plane [59]. In solution, it has been observed that while most metalloporphyrins follow the trend of increased ligand basicity leading to higher stability constants, it has been shown that Mg(II)porphyrins and some Fe(II)porphyrins show the opposite trend [58, 61]. Ligand binding affinity to Co(II) porphyrins, on the other hand, was found to depend more on the electron donating capabilities of the porphyrin macrocycle than the nature of the ligand [62]. For reference, the binding affinity trend versus the basicity for nitrogenous ligands reacting with CoOEP in toluene solution are collected in Table **1**. Note that imidazole-based compounds show greater binding affinity than the pyridine compounds. At the phenyloctane-HOPG interface, the nitrogen bases (in Table **2**) binding affinity toward CoOEP, although not necessarily the same as in fluid solution, mainly followed the same trend as their pKa values, Table **1.**

Fig. **3** shows typical STM images obtained from ligand binding experiments with CoOEP/HOPG. In all images, the bright molecules correspond to the unligated CoOEP molecules and the dark circled molecules are coordinated with the ligand. At the extremes, the least basic ligand, pyridine (Py), Fig. **3a**, shows no surface coordinated molecules, while the most basic ligand, imidazole (Im), Fig. **3d**, causes partial dissolution of the monolayer. The dissolution may be due to the increased solubility of complexed Im-CoOEP species in solution [49]. Figures **3b** and **3c**, respectively, indicate that PhIm and MeOPy react with CoOEP [49, 50]. Furthermore, the on-surface coordination reactions of these ligands are completely reversible and can be followed in real time. Ligand concentration dependence and variation of reaction temperature studies can be carried out for quantitative evaluation of the binding affinity and thermodynamic parameters [49, 50]. At high 4-methoxypyridine concentrations, dissolution of the MeOPy-CoOEP molecules at the phenyloctane/HOPG interface was also observed [49]. One important note here is that MeOPy was found to bind to CoOEP more strongly in solution than at the HOPG/phenyloctane interface.

Another example where a surface confined porphyrin's affinity toward a ligand is different than in a solution environment is NiOEP reaction with Im. While imidazole does not react with NiOEP in organic solutions, it readily binds reversibly to the nickel ion at the NiOEP/HOPG interface in phenyloctane [50]. In a different report, zinc-5,10,15,20-*meso*-tetradodecylporphyrin adsorbed on HOPG was found to coordinate to 3-nitropyridine better than when dissolved in toluene solution [46].

Computational work has confirmed the role that the substrate plays in such reactions. DFT calculations have shown that the reactivity of imidazole toward NiOEP adsorbed on HOPG is attributable to charge donation from the graphite stabilizing the Im-Ni bond. This charge transfer pathway is supported by molecular and periodic DFT calculations which indicate that the Im ligand behaves as a π-acceptor [50]. In Table **2**, a collection of reaction enthalpies for axial ligand coordination to metalloporphyrins is presented. The reaction enthalpies for the surface adsorbed species were obtained from DFT calculations and STM experiments; the enthalpies of formation of the corresponding complexes in the gas phase were determined by DFT only. The Im-NiOEP complex is not experimentally observed in the solution phase but its computed ΔH value is approximately 3 times less favorable then the enthalpy of formation for imidazole binding NiOEP absorbed on HOPG. This result supports the experimental results of high stabilizing interaction of the substrate and the Im-NiOEP complex and absence of ligand binding in solution [50]. The calculated coordination reaction enthalpies for MeOPy-CoOEP and MeOPy-CoOEP/HOPG are approximately equal [49]. Both experimental and theoretical ΔH quantities for the MeOPy-CoOEP/HOPG system are in excellent agreement.

Examples of axial ligand binding at aqueous- and electrolyte-solid interfaces are also known. Many of these studies include analysis of the metalloporphyrins catalytic or electrocatalytic activity. For example, cobalt porphyrins adsorbed on Au(111) were found to catalyze O_2 reduction reaction (ORR) in acidic solution [63]. Imaging in aqueous and electrochemical environments utilizes electrochemical scanning tunneling microscopy (EC-STM) where the solution potential can be controlled separately from sample bias and tip-sample voltage, giving a large range of control over the adsorbed porphyrin structure and reactivity. Because of the complex chemistry that may ensue in an electrochemical environment, EC-STM studies of metalloporphyrin ligand binding are considered beyond the scope of this review. Interested readers are directed to the related review articles [18, 64].

2.4 Cooperative binding with surface supported metalloporphyrins

What is cooperativity? Cooperative interactions are broadly defined as interactions that are not additive in nature. Commonly, cooperativity is categorized as a set of multistep reactions where the free energy change for subsequent steps is different than for the initial step. Positive cooperativity refers to the decrease in free energy required per step as the number of steps increases. Negative cooperativity instead refers to the increase in free energy required for increasing number of interactions. Traditionally, cooperativity is used to describe chemical reactions, particularly the reactions between substrates and allosteric sites in enzymes, and more recently the definition has been expanded and applied to more complex instances where intermolecular interactions are highly important; such as, self-assembly, protein folding, and chelation [65]. Cooperative effects can be modulated by many complex interactions. In the case of hemoglobin, these are allosteric motions of the protein subunits in which slight changes in the histidine-Fe bond distance leading to differing amounts of charge donation from the histidine and stabilizing the oxygen adduct [54, 66]. At the solution-solid interface, it is speculated that the substrate may act as an electron source/sink which can lead to cooperative on-surface binding. It is important to understand cooperativity because it is the source of high specificity of natural systems molecular recognition.

Nearest Neighbor Analysis. The difficulty in studying many complex systems and quantifying the cooperativity is that the number of binding sites is not always known (biological systems) or might be indistinguishable. Since molecules in STM imaging are distinguishable, this methodology allows for a unique way to approach studying cooperative reactions. Metalloporphyrins are known to form stable, well-ordered monolayers on conducting surfaces. Provided that the reacted state of the porphyrin is long lived enough to observe in STM images, the state of a particular molecule can be followed as a function of time. It has been shown that when studying metalloporphyrin ligation, sometimes clusters of ligated molecules appear within the monolayer. Such clustering is indicative of positive cooperativity – a ligand binding near an existing bound system has lower energy than one binding far from another bound ligand. As a way to quantify the degree of clustering, the relative proportion of the number of porphyrin nearest neighbors that are ligated can be determined. If ligand binding was truly random, where binding to one site on the monolayer did not influence subsequent ligand binding to neighboring molecules, the proportion of ligand-bound molecules, $f_k(\theta)$ with k-ligated neighbors out of *n total* nearest neighbors would follow a binomial distribution given by:

$$f_k(\theta) = (n!/(k!(n-k)!))\theta^k(1-\theta)^{n-k} \qquad (1)$$

where θ is the fractional surface coverage of bound ligands. Cooperativity is signaled by deviations from the random distribution.

To determine the experimental distribution of k-dark nearest neighbors, a typical analysis is to collect a sufficiently large STM image such that the image captures a representative view of the surface at large while still providing molecular resolution such that the state of the molecule can be determined. Present authors recommend at least 50 x 50 nm^2 images with 100 x 100 nm^2 or larger images preferred for analysis.

The analysis described above has been used as a qualitative measure of cooperativity in some recent work with CoOEP and nitrogenous based ligands MeOPy [46] and PhIm [50]. It has also been used to describe the clustering of oxygenated manganese porphyrins; however, in this case the clustering was attributed to O atoms produced by the dissociation of O_2 binding to the nearest available Mn site [52, 67]. This was not considered cooperative in the sense that the energy of binding was not considered. Fig. **4** shows an example taken from the CoOEP and PhIm case, here you see that the fraction of clusters containing 2,3, and 4 bound (dark) nearest neighbors is greater than expected based on the binomial distribution [50]. The authors attribute the larger than expected clusters of bound molecules to cooperative binding. They confirmed computationally that the binding energy of systems with clustered PhIm-CoOEP/HOPG decreased as the number of PhIm molecules increased [50]. The nearest neighbor analysis method is useful for experiments where molecular resolution can be achieved, but it is however only a qualitative device and must be paired with computations or isothermal binding curves to comment on the energetics of cooperativity of the system.

Adsorption Isotherm Analysis. The classical way to identify cooperative binding is by constructing ligand concentration-dependent binding curves at constant temperature. This method does not require molecular resolution and can be applied to data obtained through a variety of techniques from spectroscopy such as IR and UV-Visible. Adsorption isotherms can be fit to various models. When an isotherm that does not account for cooperativity (Langmuir isotherm) fails, a new model must be selected and two of those choices are the Hill or Temkin isotherms [68, 69]. The Hill model is one that assumes that the binding of ligands is cooperative and was originally formulated to describe the oxygen binding to hemoglobin. It reflects the fraction of available binding sites that are bound by ligands. The Hill coefficient provides a way to quantify the degree of interaction between binding sites. Expressed linearly, the Hill equation is:

$$\log(\theta/(1-\theta)) = n_h \log([L]) - \log(K_a) \qquad (2)$$

where θ is the fraction of bound ligands, $[L]$ is the concentration of ligand, and K_a is the equilibrium association constant for the reaction. When a plot of $\log(\theta/(1-\theta))$ *vs* $\log[L]$ is created, the slope is equal to the Hill coefficient, n_h. A Hill coefficient of 1 means no cooperativity, <1 is anticooperative behavior, and >1 is positive cooperative behavior. The Temkin isotherm looks at the situation through a thermodynamic lens and assumes that the heat of adsorption for additional ligand binding changes linearly with coverage. The entropy change (ΔS^0) associated with ligation of surface adsorbed metalloporphyrin is taken to be coverage independent while the heat of adsorption (ΔH^0) is taken to be:

$$\Delta H^0 = \Delta H(1+\alpha_T \theta) \qquad (3)$$

where α_T is a fitting parameter and ΔH^* is the heat of adsorption when the coverage is very low (minimal influence of cooperativity). Both the Temkin and Hill equations reproduce the Langmuir equation at low coverages and/or when the systems are noncooperative. An example of the adsorption isotherm applied to a porphyrin axial ligand binding system at the solution-solid interface is NiOEP plus imidazole on HOPG. At low imidazole concentrations, the system follows a Langmuir isotherm and as the imidazole concentration increases, the behavior begins to deviate. In Fig. **5,** we see that the ratio of NiOEP/HOPG bound to imidazole is nonlinear with increasing imidazole concentration [70]. The behavior is described very well by the Temkin adsorption model and fitted $\alpha_T = -0.18$. The data is also fit to the Hill model which gives a slope of 0.49 which further supports the negative cooperativity.

2.5 Computational modeling of cooperativity in surface supported metalloporphyrins

Computational studies provide an important insight into the energetics of axial binding to surface adsorbed porphyrins, and they can also tell us about the role that the surface plays in the cooperative phenomena. PW-DFT calculations have been used to determine the binding energies and investigate the charge distributions of various surface-supported porphyrin ligation reactions. In the case of NiOEP/HOPG and Im, it was found that the binding energy of imidazole decreased by 14% between the first imidazole and a complete imidazole-NiOEP/HOPG monolayer [71]. The charge redistribution analysis showed that HOPG acts as an electronic charge acceptor from NiOEP without imidazole present but as a donor to the Im–NiOEP complex. The imidazole ligand acts as a π-acceptor when it binds to NiOEP/HOPG, contrary to the conventional understanding of imidazole as an electron donor through lone pair electrons on the nitrogen.

Another recent work [51] did a more complete set of computations using cobalt(II) porphine (CoP) as a template and was able to show that the distance between ligated CoP/HOPG molecules matters. Here, CoP neighbors directly adjacent showed positive cooperative binding affinity to PhIm ligands, but molecules further away did not exhibit the same trend [51]. Additionally, charge analysis of PhIm-CoP/HOPG models showed that HOPG acts as a donor of charge from no to low PhIm coverage, while turning out to be an acceptor at high PhIm coverage. This fluctuation in the charge distribution with high and low ligand coverage is consistent with cooperative binding.

Similar studies on the MeOPy-CoOEP/HOPG system, Fig. **5**, also show positive cooperativity using PW-DFT calculations. A comparison of binding energies of PhIm and MeOPy ligands in CoP/HOPG system showed that both ligands follow a similar trend with respect to cooperative binding, but the binding energies of MeOPy are lower than that of PhIm. Additionally, MeOPy acts as a weaker charge acceptor than PhIm on CoP/HOPG. The calculations also reproduce the experimental determination of positive cooperativity in MeOPy-CoOEP/HOPG STM results [49].

As outlined in the supplemental material, Gaussian single molecule gas and solution calculations can be paired with surface gas calculations to estimate the thermodynamics of the ligation process in fluid solution.

SUMMARY AND OUTLOOK

It is clear that understanding the interaction of the substrate with the supported complex is paramount for understanding the axial ligation of surface-confined porphyrins. To artificially reproduce the chemical specificity and catalytic capabilities observed in biology, a good understanding of porphyrin-surface interactions and the surface

influence on porphyrin axial ligation is needed. To date, experiments at the vacuum-solid interface have revealed that the surface acts as an additional coordinative bond to a metalloporphyrin and thus may influence axial ligation similarly to the classical *trans-effect*. This has been shown by measuring changes in surface-porphyrin bond lengths [14], modifications in the charge distribution between adsorbed porphyrins and the adsorbed complexes [72], and finally in changes to the molecules electronic and spin states [43]. Studies in UHV have been generally confined to systems far from equilibrium. There are currently few single molecule ligation studies at the solution-solid interface because of the dearth in the surface science techniques that may be used. However, these studies are of critical importance because they allow for the investigation of systems in dynamic equilibrium.

Theoretical studies are an important component of developing a compressive understanding of ligand binding chemistry at the solution-solid interface. To date, most calculations have not yet included solvent effects. However, plane-wave DFT calculations have indicated that the charge distribution of an absorbed porphyrin changes upon axial ligation and that the presence of a substrate stabilizes some ligation products which allow them to be observed even if they are not observed in solution [50, 53].

Axial ligation of porphyrins at interfaces is a promising system for fabricating selective chemical sensors and catalysts and has been the subject of significant research interest for the duration of the 21st century. The influence of the substrate surface means that the properties of metalloporphyrin ligated complexes may be significantly different than the properties observed in solution. It will be important for future fundamental research to learn to predict the properties of surface-confined porphyrin systems. The influence of the surface on the cooperativity of surface reactions may offer a new, unique way to control the extent and spatial orientation of reactions.

Notwithstanding the many attractive experimental features and utilities of scanning tunneling microscopy, it does have one distinct weakness, which is the fact that it is slow to collect images, typically on the order of minutes per frame. In electrochemical systems, the so called "video-rate" imaging has been employed to achieve millisecond time resolution imaging [73, 74]. Even with these advances, the data collection speeds pale in comparison with state-of-the-art spectroscopic methods which can achieve up to femtosecond time resolution. With these limitations in mind, it is necessary for the residence time of the axial ligands bound to the metalloporphyrins of interest to be greater than the time to collect one image. If the association/dissociation rates are faster than the scan rate, it is possible that instead of two distinct heights corresponding to the ligated and unligated state of the molecule, the STM image may show an approximate average height where the distinct coordination states cannot be distinguished [47]. At the vacuum-solid interface, short-lived surface species may be captured by cooling the experiment to sufficiently low temperatures, but the dynamic properties of the system will be lost. For studying ligand association/dissociation reactions at the solution-solid interface, STM measurements will need to be combined with rapidly acquired statistical data from techniques such as optical methods. Addition of advanced computations will provide a more complete picture of reversible ligand binding processes at the solution-solid interface.

CONCLUSION

This review summarizes the current literature surrounding axial ligation reactions involving surface supported metalloporphyrins. To date, many studies of porphyrin ligation have been completed at the vacuum-solid interface and a lesser number have been completed at the solution-solid interface. In general, this work has shown the surface influences the binding affinity, physical properties of the porphyrin, as well as the reaction cooperativity. The future of this field will be to continue with fundamental research on the topic in order to learn how to predict the properties of surface confined porphyrin systems. Such systems have promising applications in diverse fields such as catalysis, chemical sensors, molecular separations, and medicine.

CONFLICT OF INTEREST

The authors declare no competing financial interests.

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SUPPLEMENTARY MATERIAL

Supplementary material with details of PW-DFT calculations for PhIm-CoOEP complex formation energy is available on the publisher's website along with the published article

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