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Theoretical Perspective on *Operando* Spectroscopy of Fluxional Nano-Catalysts

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Abstract:

Improvements in operando spectroscopy have enabled the catalysis community to investigate the dynamic nature of catalysts under operating conditions with increasing detail. Still, the highlydynamic nature of some catalysts, such as fluxional supported subnano clusters, presents a formidable challenge even for the most state-of-the-art techniques. The reason is that such fluxional catalytic interfaces contain а variety of thermally-accessible states. Operando spectroscopies used in catalysis generally fall into two categories-ensemble-based techniques, which provide spectra containing the signals of the entire ensemble of states of the catalyst and not necessarily dominated by the most active species, and localized techniques, which provide atomistic-level information about the dynamics of active sites in a very small area, which might not include the most active species. Combining many different kinds of techniques can provide detailed insight, however we propose that effective utilization of specific computational techniques and approaches within the fluxionality paradigm can fill the gap and enable atomistic characterization of the most relevant catalytic sites.

TOC Graphic:



Operando spectroscopy has become a cornerstone in catalysis research in recent years. While *ex situ* measurements, relying on surface science approaches, are increasingly recognized as inherently limited¹ for missing the dynamic changes induced in the catalyst upon exposure to reaction conditions, *operando* active site identification is valuable for probing these dynamic changes.² For example, *operando* spectroscopy can identify surface restructuring in thermal and electrocatalytic conditions, which, to a varying degree, is characteristic of bulk surfaces, amorphous interfaces, and nanoparticles.^{3–5} On the extreme end of dynamisms are supported (sub-)nano cluster catalysts, as their fluxionality under the influence of temperature, pressure, electrochemical potential and solvent, and binding reagents, causes catalysts to form a dynamic statistical ensembles of dozens if not hundreds of distinct geometric and stoichiometric states.^{6–10} A vast number of these states are typically thermodynamically and kinetically accessible, e.g. through thermal dynamics (Figure 1A),¹⁰ or collisions with incoming reagents (Figure 1B).^{16,17}



Figure 1. (A) Isomerization network connecting 30 local minima s minimum energy paths, showing that all minima are kinetically accessible within 1 From¹¹. The metastable isomer #2 is more active toward ethylene dehydrogenation t minimum, #1. (B) Cu cluster oxide on silica undergoing the attack and integration of O₂ at 400 K: (top) typical dynamic trajectory, showing atomic displacements relative to analogous thermal trajectory without the O₂ attack, (bottom) schematics of a typical minimal energy path, overlaid

with several representative dynamic trajectories, and resultant ensemble diversification. Adapted with permission from¹².

All accessible catalyst states jointly represent the chemical nature of the catalyst, and determine its properties: activity, selectivity, and *operando* spectral signatures.^{6,13,14} In fact, due to this complexity, nanocatalysts can have unique reactivity that sometimes surpasses that of the corresponding bulk catalysts, and have the ability to break past scaling relations.¹⁵ The catalysis on supported subnano clusters can be driven by higher-energy isomers rather than the most stable form of the catalyst – the global minimum (GM).^{10,16,17} Notably, this effect is characteristic also of some dynamic bulk surfaces such as WB restructuring under the hydrogen evolution reaction (HER) conditions, ³ and h-BN covered with dynamic and amorphous $B_xO_y(OH)_z$ layer catalyzes oxidative dehydrogenation (ODH) of propane.^{4,5} Hence, our general point of departure for interpreting *operando* spectra is the Boltzmann ensemble-averaged representation of the catalytic interface, proven to be reliable through numerous comparisons with experiment for, e.g., catalyst activity, and selectivity.^{5,10,16,18,19}

In this article, we aim to provide a theoretical perspective on selected popular methods of *operando* spectroscopy for active site identification, ranging from ensemble techniques, which can be X-ray (XAS: XANES/EXAFS, NAP-XPS, SAXS/XRD, often synchrotron-based) or IR-based, to more localized techniques, such as scanning probe methods, each of which has their own unique advantages and shortcomings. We capitalize on *operando* characterization of supported cluster catalysts, for their particularly dynamic nature. The reason this paper is written by theoretical chemists is because theory can aid in the process of active site identification beyond the current limits of experiment, particularly when the catalytic interface is as incredibly complex as for fluxional supported subnano clusters. Furthermore, we believe that theory gained a place more prominent than ever in this domain of catalysis research, in view of the need to describe catalysts' relentless dynamics, and tame it to extract the useful information – a road that, in our view, experiment can hardly walk alone. Thus, this is not a comprehensive review of *operando* spectroscopic methods, but rather a forward-looking account illustrating how theory can help this field, in ways previously unrecognized.

For spectroscopy, computation provides a bottom-up approach to understanding catalytic clusters atomistically, whereas the more top-down approaches are typically possible experimentally. The first responsibility of theory is to discover the maximally complete ensemble

of catalyst geometries, stoichiometries, and binding sites on the support. Fortunately, the small size, and also size-selection (if clusters are prepared in a size-selective way) make their theoretical studies feasible, with Density Functional Theory (DFT) and (grand canonical) global optimization techniques.¹³ Next, the spectral signatures of all ensemble members can be calculated, weighted by the member population in the ensemble, and an ensemble-averaged signal comparable to experiment can be predicted. Of course, experiment keeps theory accountable, and allows for method calibration. Finally, since the active site can be a minority in the ensemble, its signal can be buried by the majority species in the *operando* spectrum. In such cases in particular, it falls on theory to identify those key minority sites, through complementary reactivity studies.

Ensemble operando techniques

X-ray absorption techniques, specifically X-ray Absorption Near Edge Structure (XANES) and Extended X-ray Absorption Fine Structure (EXAFS) are considered fairly mature techniques that are highly useful for *operando* or *in situ* spectroscopy.²⁰ They have been widely used in both thermal and electrocatalysis for the identification of active sites on nanoparticles,^{2,21} in order to track changes in oxidation state and local environment of the catalytic sites throughout the reaction process (primarily XANES), as well changes in coordination number and average atom-atom distance (primarily EXAFS). This type of information is particularly useful for tracking dynamic changes in NP or cluster catalysts—XANES spectra evidence these changes in shifts in rising edge energy, white line intensity, and peak shape.²⁰ Operando XAS can additionally provide some information about morphological changes of the catalyst, which can be complemented by more detailed analysis based on X-ray scattering techniques such as SAXS.^{2,22} The combination of XAS and SAXS can inform the choice of appropriate models and approaches for computational studies, setting up a productive feedback loop with the experiment. For instance, SAXS can show if the catalyst surface restructures to become more amorphous during catalysis, informing theorists if they should account for surface restructuring via e.g. grand canonical sampling for the formation of off-stoichiometric surface layers in simulations.

XAS techniques are furthermore particularly useful because X-rays have less scatter and greater penetration in gas and liquid phases, making them ideal for probing catalysts under reaction conditions. However, the spectrum contains detail about atoms in the bulk, convoluting the signal of the active sites. This problem can be mitigated with grazing-incidence spectroscopy,² but not

totally eliminated. Furthermore, the area of incidence of the X-rays typically covers length scales much larger than that of the active species, rendering XAS inherently an ensemble technique, yielding information about all of the present sites, on all present catalyst isomers. In other words, both active sites (possibly a minority) and spectator species (possibly a majority) are represented in the data. Thus, the techniques do not directly address the question of the active site(s) for systems with sufficient surface heterogeneity. Experimentally distinguishing between active sites and spectator species is non-trivial,²³ requiring additionally measuring the rates of formation and consumption of key intermediates during the reaction process with techniques such as *operando* FTIR. This kind of analysis would determine if the bound intermediate is actually produced and consumed, or is simply so stable that it remains permanently bound to the catalyst and thus generates a strong signal under *operando* conditions.

An additional approach for distinguishing between active and spectator species involves the use of modulation excitation spectroscopy (MES).²⁴ MES involves the periodic modulation of a sample via some relevant perturbation – such as temperature, pH, or redox conditions via supplied reactant gas composition. The response to this modulation can be picked out via transformation of the resulting signal from the time domain into phase space, where the signal will only contain information about the dynamics and kinetics of the species perturbed by the modulation. Broadly we can assume that this means the signal will only contain information about active species, and with careful choice of modulation to target chemically relevant species of the catalyst. However, there are still limitations: (1) spectator species may also contribute to the signal if they experience dynamics unrelated to catalysis on the same timescales that the modulation probes, (2) the signal can be a combination of multiple signals from several co-existing active sites, (3) the timescale of the perturbation cannot be much slower than the TOF of the catalyzed reaction. There are many techniques that can be used for MES, ranging from IR-based techniques, to X-ray absorption, excitation, and diffraction-see²⁴ for review. Choice of technique must be carefully done, to match the time resolution of the technique to the periodicity of the modulation. IR-based techniques therefore have been widely used for MES, although XAS is growing in popularity. XAS does have time signal resolution issues, however this can be improved via careful eventaveraging over multiple pulses.²⁵ This can also be done for AP-XPS, which was applied to investigate the dynamics of CO oxidation on the Pd (100) surface under a variety of reactant stoichiometries, at two different pressures.²⁶ This approach not only revealed exquisite detail about

the electronic structure of the Pd surface in metallic, partially oxidized, and oxidized states, but also could track corresponding changes in the local gas composition above the surface. Similar to this, multimodal tracking via *operando* XAS and STEM-EELS of bimetallic NPs during redox cycling provided detailed insight into dynamic changes resulting from reduction and oxidation of the NPs. In both cases, the reducing conditions initially induced improved mixing of Co and Pt, ²⁷ or Ni and Cu,²⁸ but upon reoxidation, the NPs underwent increased irreversible segregation, and specific components became more oxidized than the as-prepared NPs. In the case of NiCu NPs, these changes could be tracked separately via XAS of the Ni and Cu L edges, showing that Cu underwent the significant changes, while Ni did not.²⁸ All of these cases are examples of how dynamic changes of specific active sites may be tracked via periodically perturbing the system and investigating the resulting changes in the system via combination of techniques.

The multi-stage experimental approaches can be greatly assisted and possibly simplified by use of computation. In order to computationally identify the active sites from ensemble techniques, the approach must be informed by computed ensembles, accessed through global optimization and selection of all thermally-accessible isomers. The isomers can differ in geometry, stoichiometry (changing through adsorption/desorption of reagents, and/or sintering), electronic structure, and (specifically for deposited clusters) site on the support.⁴ For accessing stoichiometric diversity of the catalyst states, the global optimization can be done in a grand canonical manner, at the relevant partial pressures and temperatures, and/or electrochemical potential. In such techniques, the number and nature of the bound adsorbates is optimized simultaneously with the system structure, with the change of chemical potential upon adsorption/desorption included in the system free energy. Once the ensemble is converged, the resulting spectral signature can be simulated as a weighted ensemble-average. We note important limitations here: (1) Sampling can be incomplete. (2) Assessing the full kinetic accessibility of all isomers in the ensemble is impracticable, and therefore, one has to make a decision to either assume a full thermodynamic equilibration described by Boltzmann statistics, or restrict the ensembles to sub-ensembles based on some knowledge about the system. One example of the latter is the energetically-prohibitive change of site on an ionic support for a cluster with a partially ionic bonding, such as PtSn on SiO₂.²⁹ Sub-ensembles can also be due to the separation of time- and energy-scales of the reorganization of the cluster core versus of the positions and numbers of adsorbates, especially at milder temperatures, e.g. in electrocatalysis. (3) Because the probability to be populated is an

exponential function of the energy difference between a given isomer and the GM, it amplifies the error in the electronic structure calculation, and therefore becomes only a qualitative metric. For example, for systems with strong static electron correlation, such as transition metal cluster alloys, DFT (and even DFT+U) cannot be trusted even to a qualitative degree, and the DFT-based probabilities will only exaggerate the problem. The quality of the agreement of the ensemble-average spectrum with the experimental *operando* spectrum can serve as a calibration for the sufficiency of sampling and/or accuracy of the computational methodology.

Next, computation can help distinguish between active sites and spectator species. As a "short-cut", the binding strength, binding mode, or degree of bond activation of the rate-limiting intermediate can be computed for every accessible catalyst isomer and every configuration of the bound adsorbate, in lieu of an activity descriptor. A more accurate and also substantially more expensive approach would involve computing the actual reaction pathway. It is clear that the approach must include numerous reaction pathways, e.g. tens or hundreds, and certainly not just one as is commonly practiced. The majority species in the ensemble will dominate the *operando* spectrum, but the activity in some cases can be dominated by a handful of metastable minority species, which would contribute "a needle into a haystack" in the measured spectrum. Unfortunately, one cannot tell *a priori* whether the active sites are the minority, and therefore studying the catalyst with one of the mentioned *operando* techniques may or may not enable active site characterization.

An example where *operando* XAS in tandem with computation was used to great effect for active site identification was by Yang at al.²² The dynamic change of a Cu atom supported on a nitrogen-carbon support, under electrocatalytic conditions of oxygen reduction reaction (ORR), was probed with *operando* XAS, EELS, and XANES simulations. After confirming that the N was anchoring the Cu to the support via EELS mapping of Cu vs N signals, *operando* XANES and EXAFS were measured at different potentials (Figure 2a), and compared to computed XANES of a model system with different N-Cu-N binding configurations (Figure 2(b)-(d)). It was determined that the Cu-N4 pre-catalyst structure underwent reduction and formed a Cu-N3 active site, with the N released from binding Cu and instead binding a proton. The calculated free energy diagram for the ORR showed that the activated Cu-N3 structure is much more active than the pre-catalyst.

Another joint *operando* experimental and computational study enabled the identification of the dynamic surface reconstruction of a Cu/Au bimetallic alloy with embedded single-atom Cu

sites (known as a single atom alloy, SAA). ³⁰ Using a combination of XAS (XANES/EXAFS) and DFT calculations, Liu et al. were able to detect the migration of the Cu atoms within the bulk Au and determine their preferential location. In this case, the authors were not attempting to identify the site completely anew, because of the relative simplicity of the SAA structure. Nonetheless, the study showcases a powerful theory-assisted approach towards active site identification.



Figure 2. (a) The *operando* XANES spectra collected on the cathode (top) and anode (bottom) at different applied potentials, showing the changes in XANES due to the applied potential. (b)-(d) The computed XANES (red) for the model active site structure shown in the inset, versus their corresponding *operando* spectra at the indicated voltages. (e) The change in Cu^{2+} : Cu^+ ratio as the potential is changed, showing total reduction of the active site during operation due to the breaking of one of the Cu-N bonds. (f) The difference in the free energy profile for the binding of relevant ORR intermediates on the pre-catalyst and active site structures, in black and red, respectively, showing that the activated structure has a much more favorable free energy profile. Figure adapted with permission from ²².

Note these examples have been focused on either single-atom catalysts (SACs), or single atom alloys (SAAs), both of which involve atomically dispersed metals acting as the active sites. Arguably, these are ideal systems for active site identification, both computationally and experimentally, since the ensemble of possible structures is limited to just a few possible configurations, at least under the assumption that SACs and SAAs do not sinter to larger clusters or domains. This is a reasonable assumption for systems where the atoms are physically anchored into a scaffold, such as zeolites or MOFs, as evidenced by the linear scaling between volume/number of sites and catalytic frameworks for zeolites.²³ However, for single metal atoms deposited on surfaces, sintering is highly likely due to their undercoordinated nature. Therefore, any analysis of single-atom active sites must ensure the stability of the system on the timescales of the *operando* measurements, and of the reaction being catalyzed. A truly thorough computational investigation of SACs would additionally investigate the activity of dimers, trimers, and/or larger-mers, and compare their spectral signatures to *operando* spectra, to either exclude them from consideration, or include in the mechanism.

The complexity of the problem grows tremendously with the cluster size, as the ensemble of metastable states accessible to the catalytic system can become significantly larger, although the ensemble size is not easily predicted without global optimization. Thus, the *operando* spectrum can contain a large number of individual signals of varying dominance. A high dispersity of NP sizes under analysis adds more complications. In our works, we typically study mass-selected surface-landed clusters, which have a fixed number of metals atoms (typically under 10). These are moderately tractable, and also fundamentally informative systems, as they report, for example, on size-dependent trends of activity.^{16,31} For such systems, the grand canonical sampling requires on the order of 10³ structures, from which the lowest free-energy minima are selected with an energy cutoff appropriate for the experimental temperature, e.g. 0.4 eV for thermal catalysis at under 700 K. The resultant ensembles can contain hundreds of structures, though occasionally contain very few or even just one structure. This ensemble is used as the starting point for computational effort towards identifying active sites, if the goal is to determine the actual species present at the catalytic interface.

In an example of this approach, we studied partially oxidized supported Cu and CuPd clusters that are active toward selective oxidative dehydrogenation of propane and cyclohexane. We used the globally optimized $Cu_4O_x^{32,33}$ and $Cu_3PdO_x^{34}$ (x=2-5) supported on amorphous alumina, for which the range of oxygen content was determined via grand canonical sampling.³³ Using FDMNES ³⁵-computed XANES of the low-energy isomers, we fit the *operando* XANES obtained during TPRx of oxidative dehydrogenation of propane on partially oxidized Cu₄ and Cu₃Pd clusters. Bulk standards are often used to estimate the composition of XANES via linear combination fitting, though this works best for systems that are much more bulk-like, which subnano clusters are not. Our fits using only computed cluster standards,³² and computed cluster

and bulk standards³⁴ are more chemically realistic, and can capture not only dynamic changes in oxygen content with temperature (reduction upon heating, oxidation upon cooling, Figure 3A, top two panels), but also irreversible sintering during heating, as evidenced by the increase in bulk fraction of the fit (Figure 3A, top). We were furthermore able to determine the degree of thermal equilibration of the system upon heating. In experiment, the clusters were landed on the support and not annealed at first, thus likely retaining some gas phase-like structures, and not equilibrating to a proper ensemble at 25°C, at which point data collection began. We drew this conclusion from the poor initial fit with thermal equilibrium-based standards, which improved rapidly upon heating (Figure 3A, bottom). This improvement of the fit was retained upon cooling. As a result, we attributed the clear hysteresis of the collected operando XANES with temperature to a combination of thermal equilibration, irreversible oxidation state change, and sintering. While in this case we used only the GM structures of each cluster composition, this was due to the dominance of the GM in the Boltzmann populations of the Cu₄O_x and Cu₃PdO_x clusters. For systems where higherenergy isomers contribute a greater fraction to the ensemble, accounting for them in the spectra is essential. We also showed that the rising-edge shift that in bulk is associated with increased oxidation is not replicated for clusters of 4 atoms,³² indicating that when interpreting the spectra for cluster catalysts, using trends that arise in bulk systems should be applied with utmost caution, if at all.



Figure 3. (A) change in composition for bulk (top) and cluster (middle) standard fractions with temperature during TPRx for $Cu_3PdO_x/alumina$ catalyzing oxidative dehydrogenation of propane. Results of the simulations producing the best fits of the *operando* XANES spectra. Note the growth

in bulk fraction during heating, after which the change in bulk/cluster fraction remains fairly stable, while the actual redox composition changes throughout- reduction upon heating, and oxidation upon cooling. The R-factor for the fit at each temperature is in the bottom panel. Adapted with permission from ³⁴. (B) (top) time-averaged image for Pt_{10}/Al_2O_3 MD trajectory at two different temperatures- brown represents oxidized Pt atoms, while blue represents the metallic atoms. (bottom) shows the experimental vs. theoretically computed XANES at two different temperatures, where the computed XANES are averaged over the MD trajectory. Note that the change in spectrum with temperature in experiment is reproduced with MD, emphasizing the importance of dynamical nature of the Pt₁₀ cluster as captured with MD. Adapted with permission from.³⁶

We note, however, that fitting operando XANES to realistic cluster standards can be regarded as mathematically ill-defined: We need to include all of the chemically meaningful cluster standards for the simulation, but many of them have significant similarities in their spectra. Thus, the fits might be not unique. However, simplification of the fits to a minimal basis, while mathematically more rigorous, limits meaningful chemical interpretation.

Other computational efforts towards interpreting operando XAS signals approach the problem differently, with more mathematical rigor but to some expense of the chemical meaning. Machine learning (ML) has been used in order to extract quantitative information, such as coordination number, nearest-neighbor distances, and oxidation states from operando XANES 37,38 and EXAFS³⁹ spectra, after training on computational spectra. The approach towards generating the computational spectra differs from our approach based on global optimization. Instead, a range of metal (e.g. Pt⁴⁰ and Cu³⁸) and stoichiometric metal oxide (e.g. Cu oxide³⁷) NPs cut from bulk are taken, and the XANES for key non-equivalent absorbing atoms of the NPs, located on edges, surfaces, or sub-surface, are simulated using both FDMNES³⁵ and FEFF⁴¹ to limit systematic errors. Some influence of different shape is included by including icosahedral NPs, as well as hcpbased structures, in addition to the classic fcc-based NPs. The effect of bond distance is also included by isotropically compressing or expanding the NPs, to generate a range of possible bond lengths. All these non-spatially averaged spectra are used to train a neural net (NN), which is then validated on particle-averaged computed XANES spectra, showing quite a good agreement for the actual and predicted coordination numbers, though for the smallest clusters- Cu₃ and Cu₄, there is more of a deviation.30 Once validated, the NNs are used to extract coordination numbers and nearest-neighbor distances of the clusters of varying size from operando XANES.

The results from the NN applied to experimental results can highlight e.g. supportdependent sintering of entirely reduced clusters, showing for instance that the XANES-extracted coordination numbers of ZnO-supported Cu nanoclusters are much higher than the ZrO₂-supported ones, indicating that sintering has taken place.³⁸ This is in contrast to the SAXS data, which indicates that all clusters agglomerate upon heating. This discrepancy is attributed to the formation of fractal-like agglomerates at the highest temperatures, where the local structure is similar to the isolated clusters, but the longer-range order indicates larger particle size. For another case of the application of the NN to experimental spectra, structural parameters of 4-, 12-, and 20-atom Cu oxide clusters on zirconia³⁷, were extracted, based on a NN trained on bulk-like oxide clusters of varying sizes, with composition Cu₂O and CuO. Different Cu₂O- and CuO-type motifs in the operando spectra were also extracted. The limitation, however, was that since the NN was trained only on stoichiometric oxides, it could not identify any off-stoichiometry of the clusters. As a result, the NN was only applied to clusters where multivariate curve resolution alternating least squares (MCR-ALS) indicated that the fraction of bulk-oxide-like nature in the spectra was the majority (70+%). While a correlation between Cu-Cu coordination number could be extracted, the error bars were significant due to the off-stoichiometric nature of subnano copper oxide clusters. Given the data on which the NN was trained, the results are impressive.

The main limitation with all of these NN studies, however, is that the training data is all based on highly symmetric structures cut from bulk. While the inclusion of non-equivalent sites and variable Cu-Cu distances likely added a certain degree of required disorder to the system, it was not enough to capture the true complexity of the system, especially at the smaller sizes of the clusters. At the smallest limits, clusters do not adhere to bulk structuring, and oxide clusters can deviate from stoichiometry and well-defined oxidation state of the metal atoms due to their small amorphous nature and interaction with support. Therefore, while NNs would likely produce quite good fits for larger NPs, the smallest clusters are unlikely to be accurately represented. This limitation could be overcome by including more realistically amorphous structures for the smallest clusters, as well as allowing for off-stoichiometry of the oxide clusters, which has been reported to occur.^{32,33}

There are various software packages that exist to simulate the XAS from structure files, ranging from the previously-mentioned FDMNES³⁵ to FEFF,⁴¹ to the newer package OCEAN.⁴² FDMNES and FEFF are widely used and often considered equivalent, both with limitations in

accurately reproducing exact relative peak intensity, or peak sharpness, leading many researchers to use a combination of software packages to cancel out any systematic errors, especially when using the theoretical spectra as a basis for ML.^{37,38,40} OCEAN, however, promises better results, thanks to the strong DFT foundation, coupled with the Bethe-Saltpeter equation approach to include exitonic effects and better capture L3/L2 ratios of light transition metals.

However, all approaches discussed up to this point miss another aspect: the intrinsic thermal dynamics of clusters at higher temperatures. Even without complete isomerization, every isomer of the supported cluster undergoes dynamic motion at catalytic temperatures, with a substantial amount of anharmonicity⁴³ (ultimately resulting in fluxionality). Adding thermal dynamics to the full ensemble picture of the catalyst would be ideal but computationally very expensive. However, it was shown that the dynamics can substantially affect the XANES signature. A Pt₁₀/Al₂O₃ cluster was simulated with *ab initio* molecular dynamic (AIMD) at two different temperatures. The trajectory-averaged XANES spectra were simulated and compared to the changes in *operando* XANES.³⁶ A clear difference in the XANES at different temperatures was observed for both experimental and theoretical spectra, showing that the dynamic changes captured by AIMD with increasing temperature were reflected in the resulting computed spectra. Further investigations into similar sized Pt_nSn_m/Al₂O₃ clusters with varying composition showed how the combination of AIMD with theoretical XAS provided key structural parameters to compare with experiment, such as fine-grained analysis of bond lengths.⁴⁴

Given that AIMD visited the states of the cluster only in the vicinity of the given starting minimum, and certainly did not sample all the structural forms accessible to the cluster through the full-extent fluxionality (i.e. barrier-crossing isomerization), the excellent fit of the experimental XANES is remarkable if not surprising. We suggest that the individual atoms in the cluster dynamically visit enough configurations to produce a representative set of atom states in AIMD, even though the chemistry of the system is not fully sampled. In other words, local environments of individual atoms visited in AIMD are likely characteristic of many different cluster isomers that the system would visit at catalytic temperatures. Thus, the chemistry of the system is not truly extractable from these XANES fits alone. However, cluster dynamics is certainly an important contributor to *operando* XANES.

(Near) ambient pressure X-ray photoelectron spectroscopy (NAP-XPS) is an ensemble operando technique, which has great surface-sensitivity due to the small inelastic mean path length

of outgoing photoelectrons. Steady improvements to the technique brought the pressures experienced by the catalyst first to near ambient (i.e. much higher that the near-vacuum conditions of typical XPS, but still orders of magnitude below industrially relevant pressures), and then up to 1 bar. In other words, the so-called "pressure gap" between surface science experiments and real catalytic conditions⁴⁵ is gradually closing through technological advances. XPS is essential for tracking changes in electronic structure of activated catalysts (e.g. oxidation state) throughout the catalytic process, and for identifying active (including transient) phases that are only present under reaction conditions, with extreme surface sensitivity. (N)AP-XPS has been widely used to investigate e.g. CO oxidation with changes in pressure,^{26,45,46} among other reactions.

In our view, it is indispensable to complement these measurements with calculations. DFT can be used to assess the shifts in the core level binding energy of electrons as a result of adsorbate binding, and/or catalyst isomerization, (shifts being most informative, since the absolute electron binding energies are subject to errors of DFT).⁴⁷ DFT XPS spectra computed on the ensembles of states can help deconvolute the experimental (N)AP-XPS, and/or follow the spectral changes with the changes of reaction conditions or with the catalyst reaching the steady state. For example, shift appearing due to adsorbate binding, and possible catalyst isomerization due to the adsorption, might report on the development of the active state of the catalyst. Should the ensemble change dramatically upon adsorbate binding or converting to a reaction intermediate, for instance, this would be reflected in the XPS. The caveat remains that the active site might provide only a minority signal. However, XPS can be an extremely valuable way to assess the majority components of different adsorbates in experiment, which can then be compared to theory for both method validation, and determination of the spectator sites, even if not always the active sites.

Combinations of first-principles and experimental XPS analyses have been used to great effect for a CuO/air interface⁴⁸ and GaN/water interface⁴⁹ in order to assign adsorbate type and configuration to specific experimental XPS peaks. In one study of a model catalyst, gas phase PdCuH₄⁻ converting CO₂ to formate and formic acid, valence photoelectron spectroscopy combined with calculations (at the CCSD(T) level) allowed us pinpointing the active isomer of the catalyst, which was not the GM (Figure 4).⁵⁰ Specifically, an intermediate forming on the reaction profile of CO₂ hydrogenation, originating from the second lowest-energy isomer (LM1), produced a photoelectron signal that was well-isolated in the spectrum, and not attributable to anything of the starting clusters, CO₂ adducts, or species originating from the GM during the reaction. Such a

clean validation of the role of metastable states in catalysis is rarely possible with current experimental methods for more complicated and realistic catalysts, and the simple model catalyst is very helpful in this regard. However, the study illustrates the power of theory in finding the active species, when combined with spectroscopy.



Figure 4. (A) CO_2 hydrogenation pathways for the two $PdCuH_4^-$ isomers, showing that the LM1 isomer is drives catalysis, while the GM isomer binds formate too strongly to complete the reaction. (B) the experimental PES of $PdCuH_4CO_2^-$ with lines indicating the computed VDEs for isomers along the GM and LM1 reaction pathways. From ⁵⁰.

Localized operando techniques

Scanning probe and transmission microscopies are a natural counterpoint to *operando* ensemble-averaged techniques. These can provide spatially resolved information about catalysts, and access ensemble information through time-averaging (as opposed to the spatial-averaging of ensemble *operando* techniques). While their access to ensemble is more limited, they can provide great insight into what conditions trigger changes in ensembles. Recent advances have been made to extend scanning probe microscopies to environmental conditions, permitting time-resolved imaging of nanoparticles and nanoclusters during catalysis. *In situ* STM in some cases can provide atomic-level detail of surfaces as well as adsorbate configuration,⁵¹ making it ideal for the imaging of small NPs. Time-resolved *in situ* STM can even image real-time growth of graphene on Ni surface, as catalyzed by adatoms.⁵² However, as the intensity of the image is proportional to the electric current between the tip of the probe and the part of the catalyst under investigation, the isomer or site that produces the most current with the tip will be the most evident, assuming that different isomers have different enough local density of states (LDOS) to impact the tunneling current. As clusters undergoes thermal dynamics, the STM signal is an average over the local

ensemble, and there is no guarantee that the dominant species seen in the STM are either the most prevalent, or the most active. Both computed LDOS and simulated STM are therefore of great utility for interpreting *operando* STM results, and attributing the information to catalytic relevant or irrelevant species at the interface.

Environmental TEM can also be used to directly image the dynamics of (sub)nano catalysts. There are many excellent recent examples of this is, such as imaging of the dynamic behavior of Pt ^{53,54} and other noble metal⁵⁵ NP catalysts under *operando* conditions, showing changes in morphology resulting from variable adsorbate binding during the catalytic process. Most notably, dynamic fluxionality of Pt catalysts as well as the in-contact oxide support layer under operating conditions for both CO oxidation⁵³ and the water gas shift reaction⁵⁴ has been shown for CeO₂-supported NPs around 1 nm (Figure 5), experimentally proving how essential it is to account for cluster (and NP) fluxionality over the course of a catalytic reaction. Dynamic restructuring of the NPs was on the same timescales as the TOF for CO oxidation, indicating that the fluxional behavior of catalysts may couple quite closely with the reaction they are catalyzing.⁵³ This suggests that computational approaches where the dynamic fluxionality of the cluster is coupled to reactant activation^{12,56} or the chemical step in catalysis⁵⁷ may be key to understanding the full scope of the catalyst behavior, despite the computational cost.





Figure 5. (a1-a6) The time evolution of a Pt NP on CeO_2 under a CO atmosphere, and (b1-b6) the time evolution the same Pt NP under WGS conditions, where the structure becomes much more rigid and faceted than in the presence of CO. The fluxionality is seen by an increased blurring of the Pt cluster, and the loss of clearly defined single atoms sites, as well as a blurring of the CeO₂ surface at the interface of the cluster. (a1/b1) A single 150 ms/frame of the NP, while d/e2-d/e5

shows the time averaged image in 1.5 second intervals, and a/b6 shows the NP structure time-averaged over 6s. From ⁵⁴.

The extent of diversity in the catalyst ensembles and factors that influence it

One may ask just how much the ensemble-based computation is really needed, for modeling catalysts in general, and for *operando* spectroscopy interpretation. Can we get away with just the GM-based view, as has been the common practice? This section is meant to illustrate the extent of the effect.

As shown above, for NPs, rapid restructuring in under 1 ns between different metastable crystalline structures on the timescale of CO oxidation reaction is seen in the TEM.⁵³ In a joint experimental and computational work, Yang et al.⁵⁸ showed how adsorbates can affect the shape of Pd/Pt NP beyond a single Wulff construct. The active sites for propene combustion in the presence of water had initially incorrectly been predicted to be terrace sites, however, the computed NP shape did not agree with post-catalysis TEM imaging. Taking adsorbates into account in the assessment of the NP shape, however, the active sites were correctly identified as undercoordinated sites stabilized by adsorbed *OH (Figure 6 a-c).

As clusters reduce in size, to just a few atoms, much more rapid and dramatic restructuring is to be expected. Reagent binding can cause cluster catalyst restructuring beyond recognition. The changes in structure as well as the number of thermally-accessible isomers depend on the intracluster bonding, and the strength of the interaction with the adsorbates, and the support, in a non-trivial and cluster size-63 and composition-dependent way. For example, CO is known to nearly disintegrate supported Au⁵⁹ and Rh⁶⁰ clusters. On the other hand, high coverage of H causes supported Pt clusters become more globular, but in a support- and coverage-dependent manner. Pt_8H_x on γ -alumina under different partial pressures of H_2 exhibit significant differences in the shape⁹ (Fig. 6 d,e). Diamond-supported partially oxidized Cu and Pd clusters under C6 molecules in conditions of oxidative dehydrogenation (ODH) of cyclohexane, show a dramatic contrast.¹⁰ Pd₄O₂ (the prevalent oxidation state present under reaction conditions) retains its tetrahedral form regardless of whether it is bare, or binds cyclohexane or cyclohexene. However, Cu₅ exhibits great fluxionality that is additionally dependent on the degree of oxidation: Cu₅O₅ is exceptionally acrobatic and populates a large number of isomers, whereas Cu₅O₃ is less so, though more than Pd_4O_2 (Figure 6f). The selectivity of cyclohexane ODH is affected: theory predicts that only Cu_5O_3 produces particularly valuable product, cyclohexene. Operando XANES in this case showed the

presence of both valences of Cu in reaction conditions, and theory was needed to decide on the more plausible active site. In electrochemical conditions, fluxionality and ensemble size are additionally affected by the electrode charging and solvation of the interface.⁶¹



Figure 6. (A-C) The change in predicted morphology of a Pd/Pt Wulff-constructed NP under conditions of vacuum vs adsorbed *OH, compared to experimental imaging,⁵⁸ (Copyright (2020) National Academy of Sciences) showing that the model requires *OH adsorption to accurately represent the experimental NP structure. (D,E) The global minima of Pt_8/γ -Al₂O₃ from grand canonical simulations under two different temperatures and partial pressures of H₂, characteristic of dehydrogenation and hydrogenation, respectively; the shape of the cluster is remarkably sensitive to the conditions.⁹ (F) Diamond-supported Pd₄O₂ and Cu₅O₃ clusters in oxidative dehydrogenation of cyclohexane exhibit element-dependent fluxionality: Cu clusters strongly changes shape and ensemble size (judged by the population of the global minima at 535K, P_{535K}), depending on the adsorbate, while Pd clusters do not.¹⁰

Larger ensembles would lead to more convoluted ensemble-averaged *operando* spectra, and likely greater dynamics observed with localized *in situ* techniques. In these cases, a

combination of ensemble and localized *operando* techniques would be valuable, as time-resolved localized techniques can provide insight into the extent of the dynamic behavior, as well as how it changes under varying conditions. Related to this, an important research direction of the future would be to find out when ensembles are large and when they are small, and how to quickly predict, and control their size, specifically with reference to what kinds of experimental conditions trigger such changes.

We believe that a more accurate computational approach towards active site identification is based on grand canonical sampling, working closely with experiment to determine which adsorbates are present and in what coverage, or at what partial pressures. It remains to be probed, but our current hypothesis is that for larger NPs, global optimization addressing NP morphology under relevant coverages of key adsorbates³⁶ should probe a few top-most layers. For sub-nano clusters and dynamic amorphous overlayers, global optimization should involve full restructuring and stoichiometric changes under the realistic reaction conditions. Cluster and NP morphology can be connected to changes in the support. For example, TiO₂-supported Pt NPs⁶² in a reducing atmosphere of H₂ get covered by a TiO_x and a Pt-Ti alloy overlayer. Under oxidizing conditions, however, the partially reduced overlayer reverts to crystalline TiO₂, and dealloys Pt and Ti. A computational approach to such a problem requires grand canonical optimization of both the cluster and the support in its vicinity, which constitutes an important advance to be made on the theory side in the near future. Hence, ensembles are not only vast, but also dramatically shifting with experimental condition. Clearly, extensive sampling is essential. Given the associated computational expense, it is also essential to find more efficient sampling strategies, and accurate simplified potentials. However, it is well-worth the time-investment, since theory, in our view, appears to be a key aid to operando spectroscopic studies in catalysis, as has been emphasized throughout this article.

While *operando* spectroscopy techniques for active site identification are powerful, and will cause a significant shift in our understanding of the dynamic behavior of active catalyst sites, alone they often lack precision for active site identification. The application of theoretical techniques is crucial in order to accelerate our understanding of active sites on an atomic level that we cannot (yet) access experimentally. However, the theoretical approaches must take into account the ensembles of accessible states of the catalyst under reaction conditions, which will contribute

to the operando spectral signatures. For instance, when working with ensemble operando techniques such as XAS, where the ensemble is accessed via both spatial and time averaging, computational approaches should account for all accessible isomers and possible surface states. Ensemble-based theoretical approaches can then allow deconvolution of the experimental signal into different chemically-informed components, the change of which throughout the reaction can be tracked to identify compositional dynamics of the system. This can also be combined with analysis of reactant binding energies and reaction pathways of the entire computed ensemble of cluster isomers or surface states in order to assess what the likely active vs. spectator species are. More localized *operando* techniques, on the other hand, such as scanning probe or transmission microscopies, can give insight into the dynamism of the ensemble. For instance, we can directly see how external factors such as presence and type of adsorbates can trigger changes in the ensemble. These factors can then be included in the computational ensemble, either via grand canonical sampling with adsorbates to account for variable coverage, or accounting for the restructuring triggered by the presence of certain adsorbates by looking at the ensemble of each intermediate separately. The accuracy of the computational approach can in turn be verified by comparison of simulated spectra to experiment. Ultimately, the combination of operando spectroscopy with ensemble-based computational results can yield a more detailed and realistic understanding of the underlying chemistry of the system, which then in turn can be used for the rational design of better future catalysts.

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