Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735

Chem Catalysis

CellPress

Perspective

# Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?

Ewa Chukwu[1] and Ming Yang[1,*]

## SUMMARY

**The exploration of atomically dispersed supported metal catalysts (ADSMCs) as a class of heterogeneous catalysts featuring ~100% supported metal dispersion has greatly benefited from the intensive research on a subset of catalyst platforms named single-atom catalysts (SACs), in which isolated metal atoms are believed to be central to catalytic reactivity. Nevertheless, given the wide variety of ADSMC subfamilies, diverse metal-support synergy and interatomic interactions of the supported metal atoms should further enrich the design dome of SACs. Although most literature reports today focus on developing catalysts to host single-atom species with unique catalytic functions, there are far fewer, albeit significant, findings that clearly suggest uncertainties in the reactivities of single-atom species, where the fine-tuning of metal-support and interatomic interactions would cause reactivity shifts without altering the nominal catalyst formulation and ~100% metal dispersion. This perspective discusses these uncertainties and their implications for future work.**

## INTRODUCTION

Atomically dispersed supported metal catalysts (ADSMCs) are a class of heterogeneous catalysts featuring nearly 100% dispersion of the supported metal on the catalyst supports.[1] ADSMCs encompass any supported metal catalysts featuring multiple fully exposed supported metal centers (ensembles), e.g., dimers, trimers, and fully exposed clusters,[1] or the assembly of isolated metal centers, e.g., $M_1$-O-$M_1$, as catalytic sites.

Among the many possible variations of catalyst structures of ADSMCs, the intensively researched subfamily of single-atom catalysts (SACs) represent perhaps the cleanest platform for researchers to focus the research on those isolated supported metal atoms. This is because each supported metal atom in classic SACs represents the entire or at least the center of the actual catalytic site. Central to these research efforts is understanding and establishing structure-performance relationships to enable the rational design of high-performance SACs and promote their practical applications.[2–6] With the distinctive catalytic properties derived from the relatively well-defined geometric and electronic characteristics of each supported metal atom, the advances in SACs have benefited the development of the entire ADSMC area.

The early motivation for classic SAC research is aligned with a hypothesis of whether we can replace the catalytic functions of nanoparticles comprising tens of thousands of metal atoms with a few purposefully coordinated metal atoms.[7] This line of

## THE BIGGER PICTURE

Challenges and opportunities:

- The exploration of atomically dispersed supported metal catalysts (ADSMCs) as general heterogeneous catalysts featuring ~100% supported metal atom efficiency has benefitted substantially from one decade of intensive studies on single-atom catalysts (SACs), where each isolated supported metal atom is central to defining catalytic reactivities.
- The evolution of intrinsic reactivities for atomically dispersed supported metal atoms can be more dynamic than initially envisioned in pioneering SAC prototypes as a result of the diverse catalyst support effects and the interatomic interactions of the supported metal atoms.
- Factoring in the above research considerations is crucial for bridging fundamental studies with field applications. The consequence of these catalytic material tunings toward reactivation performances, either as compromises or as promotions, needs equal attention in future ADSMC research.

thought stems from the observations that only some of the exposed metal atoms of typical nanoparticles (e.g., the surface, edge, or corner of the nanoparticle or perimeter sites interfacing with catalyst supports)[8,9] directly catalyze the targeted reactions. To tackle this open question, early SAC studies adopted two main strategies to facilitate precise structure-function correlations.[10–14] The first common strategy was using very low metal loadings to exclusively realizesingle-atom metal species so that these isolated metal atoms could be reliably interrogated without suffering from significant interferences by co-existing nanoclusters and nanoparticles. The second strategy was to use substrates with limited direct or no catalytic roles as supports to enable unambiguous identification of the structure-reactivity relationship centering around the single-atom metal. These strategies were necessary to identify and control the explicit catalytic performance descriptors for SACs by using isolated metal atoms and their associated ligands as the exclusive catalytic centers.

Along this theme of classic SAC research, advanced catalytic materials with much higher loadings of single-atom species (e.g., 20 wt %) have been developed to enhance the accumulative reactivity per weight or volume of catalysts, where the intrinsic activity (activity per metal atom) of the supported metal atom is intact.[15–17] Conversely, recent research efforts have found dynamic and occasionally unexpected reactivity trends as a function of single-atom metal loading, either as promotions or compromises, when scaling to a per-supported-metal-atom basis (e.g., intrinsic activity) as a result of neighboring atoms and the direct catalytic role of the catalyst supports. A more stereoscopic development of atomically precise catalysts has started to form; it benefits from but is beyond the scope of classic or ideal SAC research.

In contrast to multiple excellent review articles focusing on preparation and characterization methods[1,2,18–22] and representative reactions adaptable to ADSMCs,[1,2,16,18,19,22–24] this perspective analyzes the uncertainties in the evolution of the reactivity per supported metal atom and discusses their implications for the development of next-generation ADSMCs. In the interest of space, we mainly focus on thermal catalytic reactions because their reaction systems are better understood (without layers of transport phenomena and localized field effects in photocatalysis and electrocatalysis, for example) and because there are relatively abundant and quality data on pertinent topics. Concise discussions about the uncertainties of intrinsic reactivities (e.g., reactivities per metal atom) associated with supported metal atoms will be arranged in the logic categories illustrated in Figure 1. We hope to use these analyses to highlight that fine-tuning metal-support and interatomic interactions could cause a shift of activity or selectivity even without changing the nominal catalyst formulations featuring atomically dispersed metals. These will be helpful considerations for our community to become well aware of these dynamics and leverage these extra tuning knobs for fundamental and applied studies.

## CONSTANT REACTIVITIES PER SUPPORTED METAL ATOM: SINGLE-ATOM METAL GOVERNS REACTIVITY

Let us begin with some of our authors' earlier findings: Yang et al.[13] found that isolated cationic Au species associated with nearby hydroxyl groups are the catalytic center for the low-temperature water-gas-shift reaction (Figure 2A). Intriguingly, for such a single-atom gold-centric catalytic site, the reducible supports (such as titania, ceria, and iron oxide), which were often viewed as geometric and electronic promoters to the catalytic centers, did not much influence the intrinsic catalytic

[1]Department of Chemical and Biomolecular Engineering, Clemson University, Clemson, SC 29634, USA

*Correspondence: myang3@clemson.edu

https://doi.org/10.1016/j.checat.2023.100735

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735





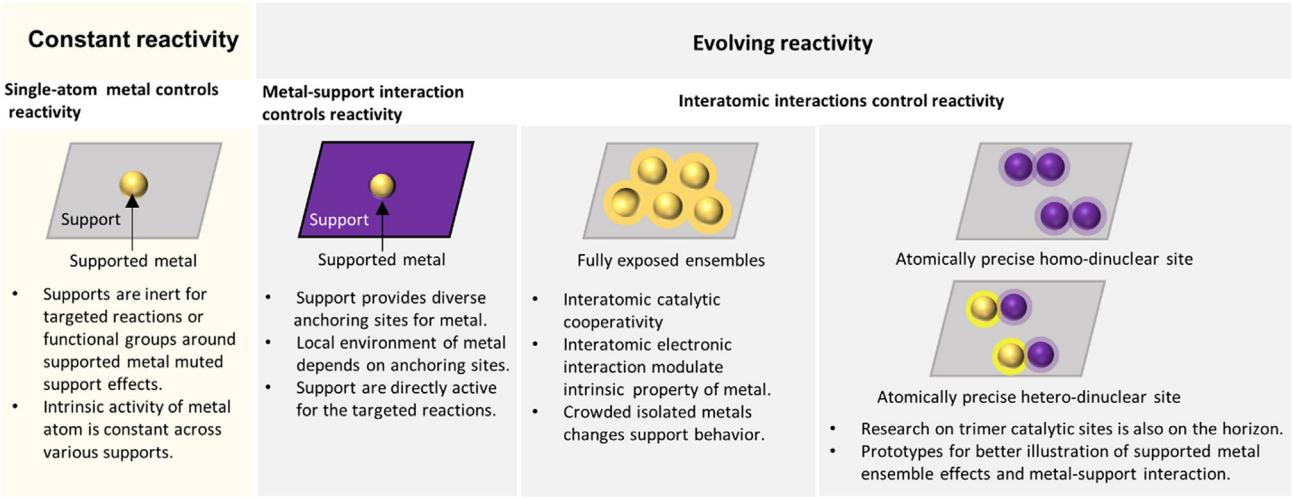



**Figure 1. Schematic overview of the content structure and layout in this perspective**

behavior of these atomically dispersed gold catalytic centers. Further, by using alkali metal-oxygen-hydroxyl as ligands to stabilize the single-atom gold[25] and platinum[14] species, the authors were able to extend the above finding to diverse types of inert supports (no reducible –O within the reaction temperature window), such as KLTL-zeolite, mesoporous MCM-41 silica, and carbon nanotubes (Figures 2A and 2B). These broad collections of single-atom Au and Pt catalysts allowed the authors to generalize that the undercoordinated $Au_1$ or $Pt_1$ species cocooned within the sheath of alkali metal-oxygen-hydroxyl linkers displayed unchanged intrinsic activity to catalyze the water-gas-shift reaction, regardless of the specific types of catalyst supports used. In these cases, the catalytic effect of catalyst supports and interatomic interactions between the neighboring supported metal atoms becomes muted because of the alkali metal-oxygen-hydroxyl linkers coordinated with the $Au_1$ or $Pt_1$ metal center. This means that one can easily scale up the accumulated activity of the given SACs by increasing the single-atom metal loading and keeping it stable, as seen for the water-gas-shift and methanol-reforming reactions.[26] In a few ideal situations, the $Au_1$– or $Pt_1$–$O_x$–$OH_y$ catalytic centers stabilized by homogeneous oxo-clusters in alkaline solutions (Figure 2C) could be readily synthesized without the involvement of catalyst supports, proving the catalyst supports as mere carriers for those valid catalytic species.[26,27]

Analogous to homogeneous molecular catalysts, the assumption of constant intrinsic activity for a stable single-atom metal site, as evidenced by some recent findings on high-loading SACs developed through novel synthesis, naturally warranted promises to promote their accumulative catalytic reactivities per weight or volume of catalysts.[15–17,28,29]

However, one should consider these findings as universal catalyst-upgrading strategies with a grain of salt. As highlighted in Figure 1, factors such as the support's heterogeneity, the support's direct catalytic contributions, and interatomic communications can profoundly alter the reactivity per supported metal atom of ADSMCs, leading to unexpected shifts of reactivity. These will be discussed in the sections "evolving reactivities by supported metal atom: metal-support interactions control supported metal reactivities" and "interatomic interactions control supported metal reactivity in ADSMCs."

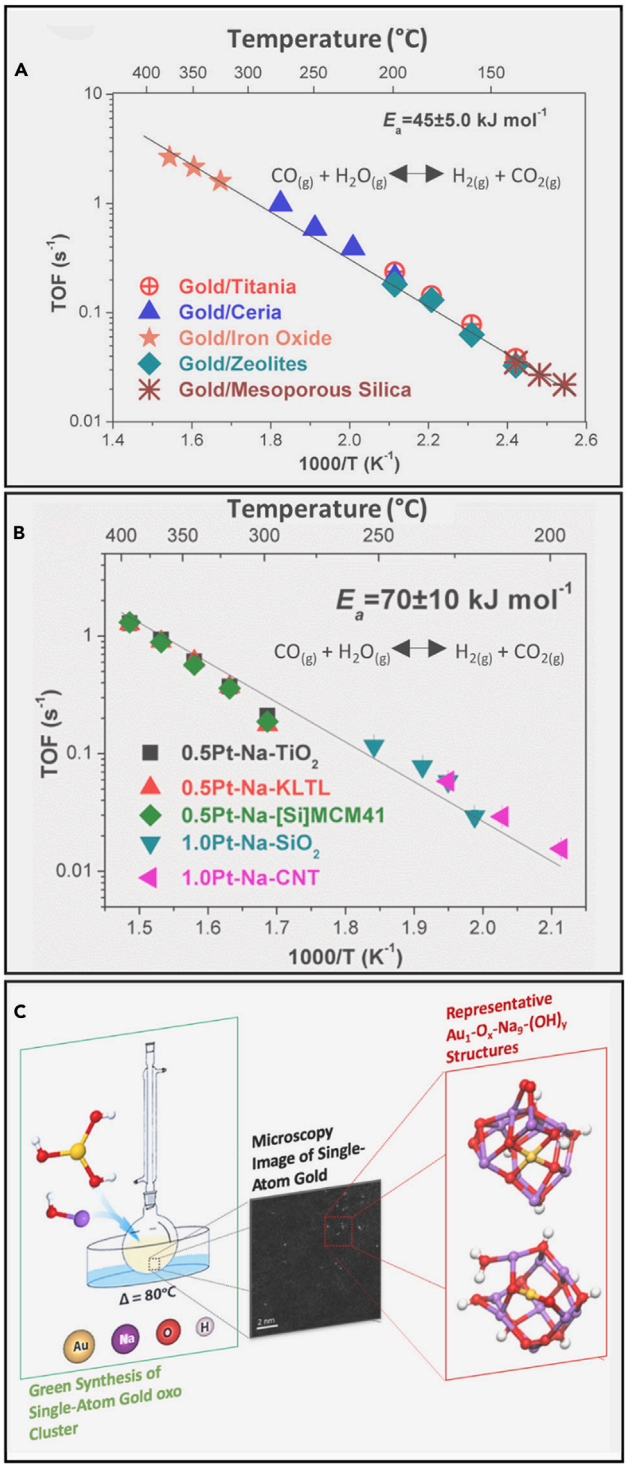



**Figure 2. Atomically dispersed supported metal controls reactivity**

(A and B) Turnover-frequency plots for the water-gas-shift reaction over SACs with either (A) $Au_1$–$O(OH)_x$ or (B) $Pt_1(II)$–$O(OH)_x$ as a common catalytic center regardless of support type. Reprinted with permission from Yang et al.[13,14] Copyright 2013 and 2015 American Chemical Society.

(C) Translational strategies for creating $Au_1$–$O(OH)_x$ species as a step of catalyst synthesis without the involvement of catalyst support materials. Reprinted with permission from Cao et al.[26] Copyright 2019 Springer Nature.

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735





## EVOLVING REACTIVITIES BY SUPPORTED METAL ATOMS: METAL-SUPPORT INTERACTIONS CONTROL SUPPORTED METAL REACTIVITIES

### Support heterogeneities influence supported metal reactivity

Support heterogeneities, unless effectively muted[14,25,26] as discussed in section "constant reactivities per supported metal atom: single-atom metal governs reactivity," can lead to diverse local environments for the supported metal. For instance, even for zeolites with relatively well-defined metal anchoring site structures, the infrared (IR) spectra of atomically dispersed iridium species within zeolite pores characterized by narrow full-width at half-maximum (FWHM) are distinct from the relatively broader FWHM IR spectra obtained when the majority of the isolated metal species are resident on other locations outside the pores (e.g., pore mouths).[30] This disparity in IR features signals that the local environment of the isolated Ir species within the zeolite pore is different from the local environment of the Ir outside the zeolite pores. These differences in local environments might translate to different catalytic behaviors for the supported metals. For example, Chen et al.[31] recently demonstrated that, for the carbon nitride scaffold supports (reputed for their relatively precise metal anchoring sites), the local electronic and coordination states of the supported isolated Pd atoms and their metal-specific reactivity in the selective hydrogenation of 2-methyl-3-butyn-2-ol to 2-methyl-3-buten-2-ol were sensitive to the structural motif arrangements and electronic properties of the carbon nitride scaffold supports, tunable by synthesis parameters.

For typical ADSMC supports, the variations in degrees of crystallinity, surface facets, and defects can all lead to heterogeneous local anchoring environments for the supported metal species. Given that these local environments determine metal-adsorbate interactions and reactivities, nominally identical catalyst formulations can exhibit distinct reactivities as a result of the varied metal-support interactions at the atomic scale. In the case of $Pt_1/TiO_2$ catalysts, different pretreatment conditions (oxidation, mild reduction, and harsh reduction) induced diverse local coordination (Figure 3A) and electronic structures for the $Pt_1$ species with no observable agglomeration. As rationalized by the authors, because the very low Pt loading (0.025 wt %) utilized in this work yielded less than one Pt atom (on average) per $TiO_2$ particle (5 nm), Pt clustering became very difficult because the Pt atoms (without vaporization) needed to transfer between $TiO_2$ particles for Pt clustering to happen. Despite the dissimilarities in local environments during CO oxidation initiation, two $Pt_1/TiO_2$ catalysts (one obtained after oxidation pretreatment at 300°C and the other after mild reduction at 250°C) with the $Pt_1$ predominantly anchored on step edges of $TiO_2$ exhibited comparable reactivities and apparent activation energies (Figure 3B). Meanwhile, $Pt_1$ stabilized on steps and terraces in defect-rich $TiO_2$ obtained after harsh reduction at 400°C possessed a different local environment and displayed significantly lower apparent activation energy with intrinsic activity two to five times better than that of the two previous catalysts (Figure 3B).[32] Tan et al.[33] observed similar surface-location-specific intrinsic activities by $Pt_1$ by tuning the preparation temperatures for identically formulated $Pt/CeO_2$ catalysts; the $Pt_1$ species mainly at the edge sites of $CeO_2$ were catalytically active for CO oxidation, and the $Pt_1$ species over-stabilized on the Ce substitution sites of $CeO_2$ terraces were far less active.

The above examples involve changing Pt-O coordination numbers on well-defined crystal surfaces to render different reactivity. It is also possible for supported metal atoms to adopt different local geometries as a result of inherent support heterogeneities, distortion of the local support structure during catalyst preparation, or

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735



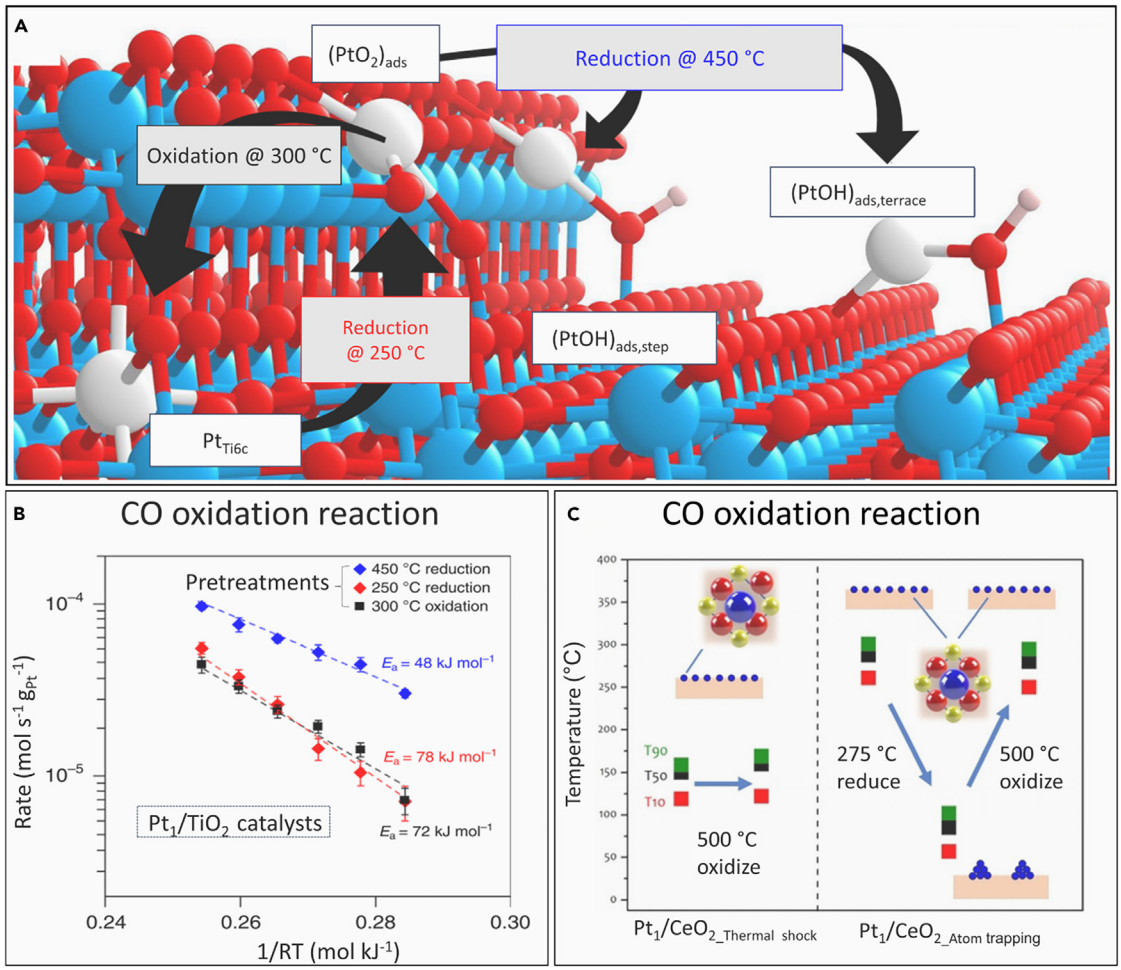



**Figure 3. Support heterogeneities control atomically dispersed supported metal's local environment and reactivity**

(A) Proposed dynamic evolution of $Pt_1/TiO_2$ catalysts after 300°C oxidation, 250°C reduction, and 450°C reduction pretreatments. Schematic structures are based on density functional theory (DFT) calculations and X-ray absorption spectroscopy (XAS) analyses. Ti, O, Pt, and H atoms are represented by blue, red, white, and light-pink spheres, respectively.

(B) Arrhenius plots for CO oxidation by the $Pt_1/TiO_2$ catalysts in (A). Black (300°C oxidation) and red (250°C reduction) data represent catalysts with $Pt_1$ predominantly anchored on step edges, whereas the blue color represents the catalyst with $Pt_1$ on anchoring sites such as steps and terraces on defect-rich $TiO_2$ obtained after 450°C reduction. Reprinted with permission from DeRita et al.[32] Copyright 2019 Springer Nature.

(C) Local $Pt_1$-$O_x$ coordination geometry of atomically dispersed metal governs CO oxidation performance (e.g., T10, temperatures required to reach 10% CO conversion) for $Pt_1/CeO_2$ catalysts and effects of pretreatment conditions on Pt structure and CO oxidation activity. The asymmetric $Pt_1$ structure in $Pt_1/CeO_2$ prepared by thermal shock (left) is thermally stable and active for low-temperature oxidation. The much less active symmetric $Pt_1$ structure in $Pt_1/CeO_2$ prepared by atom trapping (right) is thermally unstable to allow further Pt structure changes to possibly improve reactivity. Reprinted with permission from Jiang et al.[34] Copyright 2021 John Wiley & Sons.

exposure to chemical environments.[34,35] Such distorted local geometries might manifest in their intrinsic reactivities. For example,[34] a nearly perfect symmetric square-planar $Pt^{2+}$ species ($Pt_1O_4$) structure on $CeO_2$ edges for the $Pt_1/CeO_2$ catalyst prepared by the atom-trapping method involving calcination in air at 800°C was inactive for the low-temperature CO oxidation (Figure 3C). However, the $Pt^{2+}$ species (still, nominally as $Pt_1O_4$) occupying non-edge defect sites on $CeO_2$ obtained via rapid exposure (~500 ms) of $Pt/CeO_2$ to high-temperature (>1,200°C) shockwaves assumed an asymmetric geometry. Under similar reaction conditions, the asymmetric ($Pt_1O_4$) geometry readily transformed to partially reduced $Pt_1$ in $Pt_1O_{4-x}$, catalytically more active than the symmetric square-planar counterpart.

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735



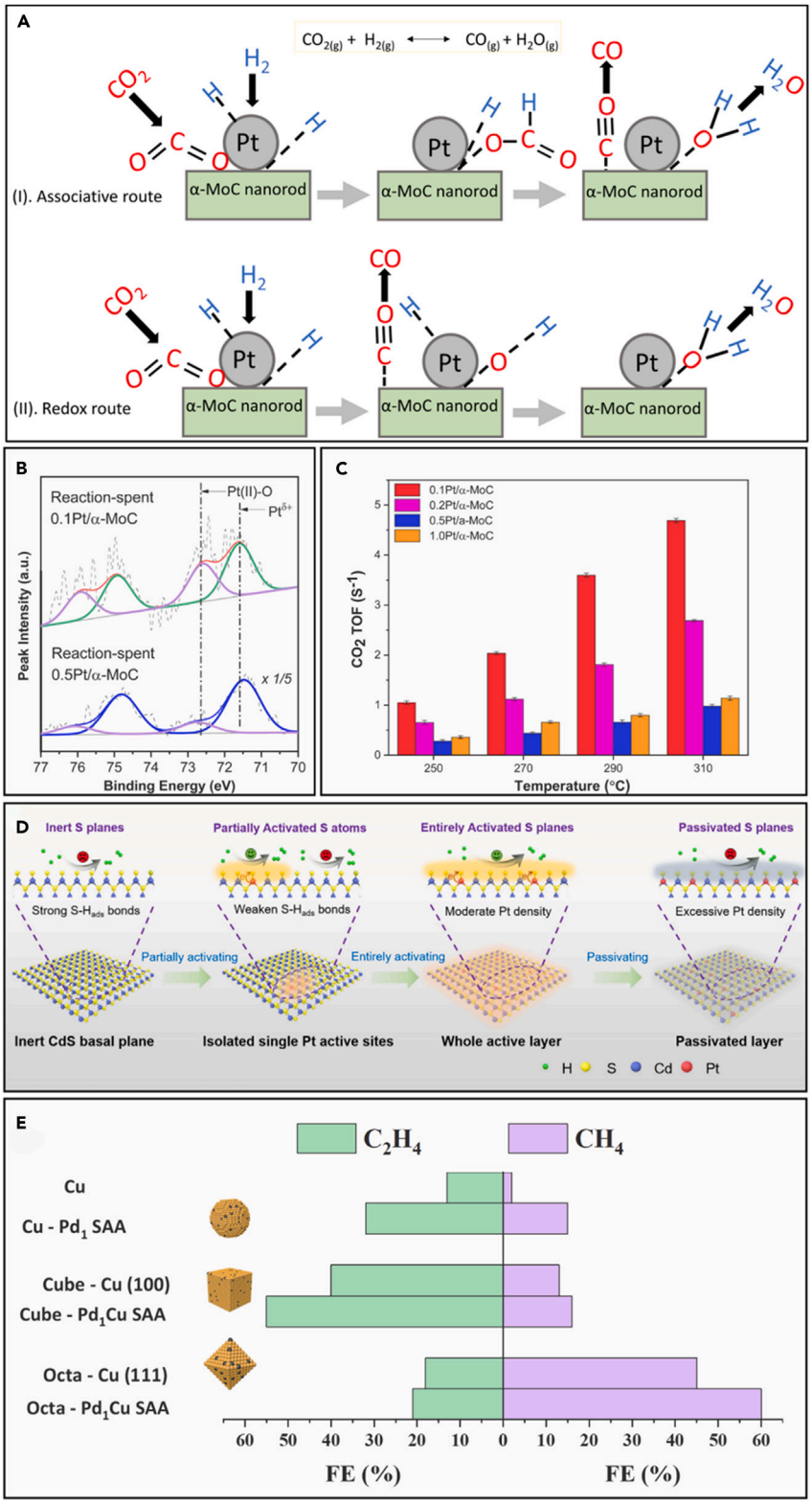


The possible impact of metal-support and metal-to-metal interactions on catalysis would seem obvious. Unfortunately, these parameters and their consequences on catalytic reactivity are often overlooked in the evaluation and definition of SACs' performance—the literature is ripe with oversimplified conclusions suggesting that the single-atom metal species in catalyst formulation XYZ is promising for a given reaction without any detailed context. As we will discuss below, these factors can dramatically shape the catalytic behaviors of the support or supported metal, resulting in an unexpected overall catalyst performance on a per-weight or -volume basis.

## Direct catalysis from supports synergize with supported metal reactivity

Performance-oriented industrial catalysts often employ catalytically active supports, an area that fundamental research will ultimately need to bridge. The direct catalytic involvement of the support, whether independently or in synergy with the supported metal, would modify the metal's intrinsic chemistry and directly affect the reaction. For example, in the case of the water-gas-shift reaction at milder temperatures, atomically dispersed metal supported on active α-MoC performs better than other catalysts reported in the literature (where supports such as $SiO_2$, $FeO_x$, $CeO_2$, and zeolite either are inert or provide limited enhancement).[36,37] In addition to the remarkable activity, the unique metal-α-MoC interface and direct activation of reactants by α-MoC induce a new reaction pathway (~35% contribution), supplementing the conventional redox/associative mechanisms in the water-gas-shift reaction. The new reaction pathway centering around the α-MoC involves direct carbon monoxide dissociation. Consequently, the new role of the catalyst support changes the anticipations for the supported metal atoms. For example, the authors found that the isolated single-atom Pt on α-MoC catalysts showed superior initial activity but compromised reaction stability. Notably, this gradual catalyst deactivation was not due to the structural instability of the single-atom Pt itself. Instead, the gradual oxidation of the carbide support surfaces during the reaction was the root cause. In such an event, the Pt clusters were necessary to protect the oxophilic α-MoC support from oxidation by oxygenate intermediates, hence retaining stable reactivity for the whole catalyst.[36]

In our recent study,[38] we leveraged the direct $CO_2$ activation and dissociation capability of pristine α-MoC to develop dual-site $Pt_1$/α-MoC catalysts for the low-temperature reverse water-gas-shift reaction. Benefitting from the synergistic interaction of Pt and α-MoC, $CO_2$ activation and CO desorption relied mainly on the electron-rich α-MoC support (Figure 4A). Unlike metal-oxide-based catalysts, where the Pt-CO* interaction is usually incrementally weakened if an electron-deficient $Pt_1$ site is in place to compromise the π-backbonding between Pt and CO, the $Pt_1$ site on α-MoC now exhibited minimal CO interaction, nearly exclusively prioritizing $H_2$ adsorption and activation. These $Pt_1$/α-MoC catalysts surpassed traditional metal-oxide-based catalysts through completely decoupled $CO_2$ and $H_2$ activation routes. With higher surface population densities for $Pt_1$, Pt species evolved predominantly as crowded yet isolated atoms covering the catalytically active α-MoC support, thereby limiting access for $CO_2$ activation at Pt-Mo interfaces. Spectator behavior of those interior Pt atoms in the crowded Pt areas during the reaction, evidenced by the reduced formation of Pt-O intermediates observed via *in situ* X-ray photoelectron spectroscopy (XPS) (Figure 4B), resulted in a sharp decline in intrinsic activity for the Pt atom (Figure 4C) without losing the nominal single-atom feature as Pt loadings increased. Although such findings have been rare, we infer their potential generality for catalysts deploying catalytically active supports as co-catalytic centers. For example, in a recent investigation of $Pt_1$/CdS catalysts for the photocatalytic


A
$CO_{2(g)} + H_{2(g)} \leftrightarrow CO_{(g)} + H_2O_{(g)}$
(I). Associative route
(II). Redox route
α-MoC nanorod
Pt
B
Reaction-spent
0.1Pt/α-MoC
Pt(II)-O
$Pt^{\delta+}$
Reaction-spent
0.5Pt/α-MoC
x 1/5
Peak Intensity (a.u.)
Binding Energy (eV)
C
0.1Pt/α-MoC
0.2Pt/α-MoC
0.5Pt/α-MoC
1.0Pt/α-MoC
$CO_2$ TOF ($S^{-1}$)
Temperature (°C)
D
Inert S planes
Partially Activated S atoms
Entirely Activated S planes
Passivated S planes
Strong S-$H_{ads}$ bonds
Weaken S-$H_{ads}$ bonds
Moderate Pt density
Excessive Pt density
Partially activating
Entirely activating
Passivating
Inert CdS basal plane
Isolated single Pt active sites
Whole active layer
Passivated layer
H S Cd Pt
E
$C_2H_4$
$CH_4$
Cu
Cu - $Pd_1$ SAA
Cube - Cu (100)
Cube - $Pd_1$Cu SAA
Octa - Cu (111)
Octa - $Pd_1$Cu SAA
FE (%)
FE (%)

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735





**Figure 4. Direct catalyst support activities influence the atomically dispersed supported metals' reactivities**

(A) Possible reverse water-gas-shift (RWGS) reaction mechanisms on dual-site $Pt_1/\alpha$-MoC nanorod catalyst. The RWGS reaction occurs through completely decoupled $CO_2$ and $H_2$ activation routes, where $CO_2$ activation relies mainly on the $\alpha$-MoC substrate and hydrogen activation on the Pt site.

(B) *In situ* XPS Pt 4*f* spectra for the representative $Pt_1/\alpha$-MoC catalysts obtained after 20 min of RWGS reaction at 250°C.

(C) Forward RWGS turnover frequency per mole of Pt as a function of temperature for different $Pt_1$ loadings. Reprinted with permission from Chukwu et al.[38] Copyright 2023 Elsevier.

(D) Influence of surface $Pt_1$ population density on photocatalytic HER over $Pt_1$/CdS. The $Pt_1$ activates the nearby "S" sites of the support substrate, the latter of which is the catalytic active site for the HER. Maximized electronic interactions among the $Pt_1$ in the CdS matrix adequately mitigate the otherwise unfavorable strong hydrogen adsorption on the neighboring "S" atoms, promoting the supported metal's reactivity for the HER. Above the optimum $Pt_1$ loading, substantially overlapping electronic footprints of the crowded $Pt_1$ metals (single-atom layer) excessively compromise the adsorption free energy for hydrogen on the neighboring "S" atoms of the support. Reprinted with permission from Xue et al.[39] Copyright 2023 Elsevier.

(E) Exposed Cu facet controls selectivity (Faradaic efficiency) in electrochemical $CO_2$ reduction reaction by $Pd_1Cu$ single-atom alloy catalysts (at −1.1 V vs. RHE). Cu(111) surfaces dominating Cu octahedra particles favored $CH_4$ formation, and Cu(100) surfaces dominating Cu cube particles favored $C_2H_4$ production. Reprinted with permission from Chhetri et al.[40] Copyright 2023 Springer Nature.

hydrogen evolution reaction (HER), Xue et al.[39] found that the single-atom Pt was necessary to activate the nearby "S" sites of the support substrate, the latter of which was the catalytic active site for the HER. As the $Pt_1$ loading was increased up to an optimal density of 0.34 Pt/nm$^2$, the maximized electronic interactions among $Pt_1$ in the CdS matrix adequately mitigated the otherwise unfavorable strong hydrogen adsorption on the neighboring "S" atoms, promoting the supported metal's reactivity for the HER (Figure 4D). However, as the $Pt_1$ loadings increased further, the substantially overlapping electronic footprints of the crowded $Pt_1$ metals (single-atom layer) excessively compromised the adsorption free energy for hydrogen on the neighboring "S" atoms of the support, inhibiting the catalytic functionality of the support substrate. This resulted in a volcano-shaped reactivity trend for the supported metal atom as a function of increasing metal loading.[39]

The profound influence of the catalytically active support's functionalities on atomically dispersed catalytic metal's reactivity could be translational to electrocatalytic reactions as well. For electrochemical $CO_2$ reduction over $Pd_1Cu$ single-atom alloy catalysts using shape-controlled Cu as hosts, our group recently demonstrated that the product selectivity is host dependent (Figure 4E).[40] In the dual-site mechanism, the single-atom Pd improved CO* coverage and energetically facilitated the rate-determining steps. Still, the SAA catalyst's reaction selectivity (Faradaic efficiency) followed the reaction pathway dictated by the copper host. Specifically, with or without the single-atom Pd, Cu(111) surfaces dominating Cu octahedra particles favored $CH_4$ formation, and Cu(100) surfaces dominating Cu cube particles favored $C_2H_4$ production.[40]

The research findings discussed in section "evolving reactivities by supported metal atom: metal-support interactions control supported metal reactivities" exemplify the evolution of intrinsic reactivities by single-atom metal sites and show that the assumption of a constant reactivity for the supported metal in ADSMCs might not hold when the support actively participates in the reaction. More so, although we can leverage active support to design good ADSMCs, the supported metal structure and density require a thoughtful assessment so that neither party's contributions are compromised.

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735



## INTERATOMIC INTERACTIONS CONTROL SUPPORTED METAL REACTIVITY IN ADSMCs

As mentioned in section "constant reactivities per supported metal atom: single-atom metal governs reactivity," developing catalysts with high population densities of supported metal atoms was considered a natural next step for linearly scaling up the overall activity for a given SAC, as long as the single-atom species is stable. However, more intriguing than pictured initially, as the surface population density of the atomically dispersed metal species increases, the increasing metal atom-to-atom proximity might physically induce intersite catalytic cooperativity or trigger substantial interatomic electronic interactions to modify the catalytic site properties intrinsically. This section will discuss these factors and their combinations in regulating catalyst reactivities.

### Interatomic catalytic cooperativity determines supported metal reactivity

An early study by Goodman and co-workers[41] demonstrates that interatomic communication between isolated supported metals can shape the intrinsic performance of single-atom metals. Their Pd/Au model catalyst investigations revealed that whereas non-contiguous Pd monomers anchored on catalytically inert Au surfaces formed the active site for ethylene acetoxylation, the intrinsic activity of the Pd monomer was influenced by the spacing between the Pd monomers, creating a volcano-type reactivity trend as a function of Pd monomer population densities. These findings hint that many ADSMCs with appreciable metal loadings might no longer be equalized as simple scaled-up classic SACs. In these ADSMCs, the specific reactivity of supported metal atoms might not stay constant as a function of the metal loading as a result of changing interatomic distances, and very different catalysis might exist for catalysts with similar formulations but very different metal loadings, even when the supported metal atoms remain fully dispersed. For example, in a recent study on the photocatalytic water-donating transfer hydrogenation reaction, the newly developed SAC clearly outperformed its Pd nanoparticle counterpart.[42] However, the authors also pointed out the intriguing observation that the reactivity per single atom was sensitive to the metal loading and that the exact mechanism would need extensive future studies.

Moving toward nanocatalysts for $C_3H_6$ and $C_3H_8$ oxidation reactions, Jeong et al.[43] found that single-atom $Rh/CeO_2$ catalysts with isolated Rh catalytic sites were inferior to the same catalyst formulation after a redox treatment, where an elusive Rh-Rh coordination started to appear (<1) in extended X-ray absorption fine structure (EXAFS) analyses without the formation of any Rh clusters or nanoparticles. Along the logic thread, our work[44] further showed that, for the CO oxidation reaction, neighboring metal sites' availability altered Pt's overall catalytic chemistry. By transforming isolated $Pt_1$ sites in the parent $Pt/CeO_2$ catalyst to a one-atom-layer, fully exposed $Pt_1$–O–$Pt_1$ ensemble (modeled as a $Pt_8O_{14}$ cluster), the intrinsic activity increased by 2–3 magnitudes (Figure 5A). Unlike the Pt–O–Ce interfacial catalysis by $Pt_1/CeO_2$, the $Pt_1$–O–$Pt_1$ site enabled facile oxygen activation, circumventing the dependence on the ceria support for low-temperature $O_2$ activation.

For ADSMCs with appreciable metal loadings, the influence of the neighboring supported metal sites on reactivity depends on the intersite distances or the number of neighboring metal atoms. According to Li et al.,[47] sparsely spaced (>3 nm apart) single-atom Pt-$S_2$ moieties on $MoS_2$ achieved with low Pt loading (<1 wt %) yielded methanol during $CO_2$ hydrogenation. But with a higher single-atom Pt loading (5.0 wt %), two adjacent closely spaced or nearly overlapping single-atom Pt-$S_2$

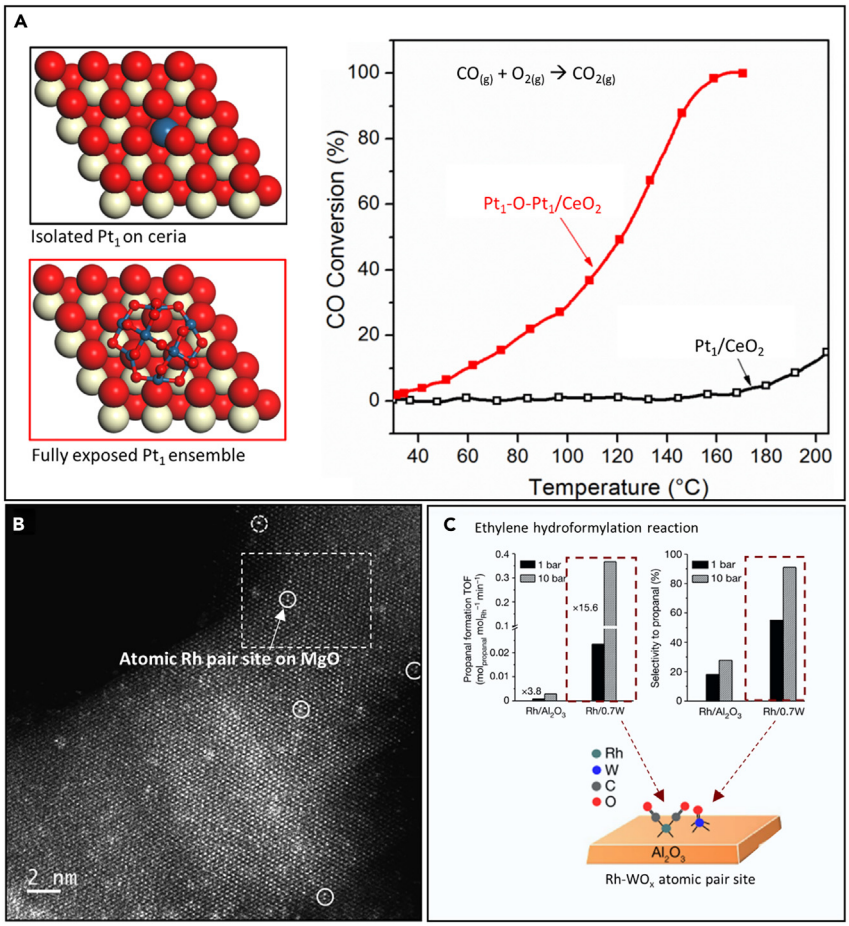



**Figure 5. Interatomic interactions control atomically dispersed supported metals' reactivities**

(A) Modeled structures of isolated single-atom $Pt_1$ (top left) and $Pt_1$-O-$Pt_1$ ensemble (bottom left) on ceria. The ensemble structure developed from the single-atom Pt promotes CO oxidation by enabling easier oxygen activation and transfer (top right).[44]

(B) High-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM) image showing a homonuclear Ir pair site anchored on MgO. The pair site is more active and stable than the single-atom analog. The hydrogen dissociation rate governing the ethylene hydrogenation reactivity is more favorable on the pair site. Reprinted with permission from Guan and Gates.[45] Copyright 2018 American Chemical Society.

(C) Comparison of the performance of the single-atom $Rh_1$ site versus the heteroatomic Rh-$WO_x$ pair site for the ethylene hydroformylation reaction, where the latter offers much improved activity and selectivity. The well-tailored proximity of the atomic pair site facilitates synergistic electronic interactions and effective intersite migration of reactive species to sustain the overall catalytic cycle. Reprinted with permission from Ro et al.[46] Copyright 2022 Springer Nature.

moeities synergistically enabled $CO_2$ hydrogenation to mainly formic acid through a pathway with a remarkably lower energy barrier. At a further increased single-atom Pt loading (7.5 wt %), single-atom ensembles consisting of three or more Pt-$S_2$ catalytic centers with suboptimal intersite distances evolved and manifested poor activity for $CO_2$ hydrogenation. Similarly, Hai et al.[29] found that as the single-atom Cu loading increased, the intrinsic activity of the Cu site for the azide-alkyne cycloaddition reaction was not constant but instead scaled positively with metal loading. The authors ascribed the enhanced intrinsic activity with the increasing population of surface metal atoms to the shortened distances between the fully dispersed Cu atoms, which promotes the cross-coupling of reactants.

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735



### Interatomic electronic communication determines supported metal reactivity

As noted at the beginning of section "interatomic interactions control supported metal reactivity in ADSMCs," interatomic electronic communication between adjacent metal atoms is another source for modulating the intrinsic chemistry of metal sites and hence altering catalytic reactivity. For example, whereas a confined single-atom Ag model wire catalyst lacking adjacent $Ag_1$ sites was inactive for low-temperature CO oxidation, an alternative model with the two opposite endings of the $Ag_1$ wire exposed to the surface exhibited remarkable activity.[48] Unlike the inactive model catalyst following the classical "inter-independent local reaction mechanism," the alternative active model counterpart catalyzes CO oxidation via an "electron-delocalized mechanism" according to the authors. In this latter mechanism, the electrons generated by the reaction on each $Ag_1$ site are transported through the interlinking conductive Ag metal wire to the neighboring site, thereby facilitating the redox half reactions on each exposed $Ag_1$ site.

For ADSMCs with appreciable metal loadings, the impact of electronic communications between metal sites depends on intersite distances, atomicity, metal type, etc. If significant, site-to-site electronic communication can alter the supported metal's local electronic structure and hence the intrinsic catalytic behavior. For single-atom Co on a 2D polymeric carbon substrate, the local coordination structure of the Co atom remained essentially unchanged regardless of its surface population density.[49] However, the strongly enhanced electronic interaction between closely spaced isolated Co sites resulted in a progressive Co 3d orbital energy downshift and a charge migration from cobalt to the support. This "charge redistribution" favoring oxygen and alkenes activation promoted the intrinsic activity of $Co_1$ during alkene epoxidation. Jin et al.[50] reported similar surface-density-dependent specific activity for cationic $Cu_1$ species supported on an inert polymer substrate for one-step selective benzene hydroxylation by hydrogen peroxide. At all $Cu_1$ loadings, phenol selectivity remained ~99%. Notably, the intrinsic activity of the Cu site increased with $Cu_1$ loadings as a result of enhanced synergistic electronic interactions between Cu atoms due to decreased intersite distances. The modulated electronic environment regulated the hydroxyl radical adsorption strength, a rate-determining descriptor in benzene hydroxylation. The translational electronic interaction effect on the intrinsic activity of a single-atom metal with increased metal population density was observed for the electrocatalytic oxygen reduction reaction on N-modified carbon-supported Fe catalysts.[51]

Nonetheless, in line with the well-established Sabatier principle in heterogeneous catalysis, we reiterate that one should not simplify the dynamic science above to mean that the more interatomic electronic interactions there are, the more beneficial it is for the reaction. This is because the essence of catalysis is that the proper catalytic sites should bind targeted reacting species neither too strongly nor too weakly. By studying the quinoline hydrogenation over Ir SACs, Jin et al. recently reported a volcano-shaped relationship between the intrinsic reactivity of the $Ir_1$ moiety and its areal density as a function of Ir metal loading.[52] The authors proposed that atomic hydrogen species' adsorption and desorption strengths on the single-atom Ir depend on the Bader charge-transfer rate, which scales up with Ir density. The maximum activity achieved coincides with the optimum Bader charge-transfer rate that is suitable for both the adsorption and desorption of H* species. Although the Sabatier principle is well known in the catalysis community, controlling its impact as a collective property of supported single-atom metals is new and deserves more attention from the community.

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735





Furthermore, considerable interatomic interactions among supported metal atoms could trigger notable structural changes (surface or bulk) in the catalyst support. These supported metal surface-density-dependent changes can modify the catalytic responses of the support substrate, ultimately shaping the overall catalytic expectations for the supported metal atom. An example is the dramatic lowering of oxygen vacancy formation energy in ceria with increasing $Pd_1$ population density caused by overlapping of Pd atoms' "electrostatic footprints."[53] Accordingly, the intrinsic activity of the $Pd_1$ on $CeO_2$ for CO oxidation increased with the surface population of $Pd_1$ as a result of the significantly enhanced $CeO_2$ reducibility for facile oxygen activation. On the other hand, as exemplified by our discussion in section "direct catalysis from supports synergize with supported metal reactivity" ($Pd_1$/CdS for photocatalytic HER) and as equally reported for the electrocatalytic HER on $MoS_2$-supported single-atom Rh[54] (where the in-plane "S" site of the support is the active site for the HER), undue overlapping of supported metal atoms' electronic interactions over the support can severely undermine the catalytic contributions of the support, inhibiting the reaction.

These uncertainties surrounding the evolution of specific activities of atomically dispersed catalytic metal centers, influenced by supported metal surface population density, warrant careful consideration in designing and evaluating high-loading ADSMCs to bridge the gap between fundamental studies and practical applications. Along this direction, to be discussed in section "prototype atomically precise supported metal catalysts," atomically precise ADSMCs featuring well-defined atomicity and interatomic distances can offer valuable insights into the nature of interatomic and metal-support interactions, thereby advancing our understanding of the matter with atomic resolution.

## Prototype atomically precise supported metal catalysts

The discussed interatomic interactions' effects on the catalytic performance of ADSMCs (oriented toward applied catalysis) can be more explicitly interrogated with atomically precise metal catalysts in the interest of deeper fundamental understandings. In investigating ethylene hydrogenation reactions, Gates and co-workers found that the catalytic reactivities of atomic pair sites, such as iridium[55] and rhodium,[45] stabilized on catalytically inert MgO are superior to their corresponding single-site analogs. The ethylene hydrogenation reactivity governed by the hydrogen dissociation rate is often known to be favored on clusters, and the paired atoms (Figure 5B) are the simplest prototypes to bridge the gap between classic single atoms and small clusters. For semi-hydrogenation of alkynes on ADSMCs, triatomic metal sites exhibit better catalytic performance (selectivity and intrinsic activity) than isolated metal sites and dimers. The triatomic ensemble site enables near barrierless $H_2$ adsorption and activation and optimal multipoint adsorption, activation, and desorption energies for the reacting species, rendering the lowest overall hydrogenation energy barrier.[56,57] These findings provided precise atomicity of the catalytic center to echo the generic consensus that heterolytic hydrogen dissociation on isolated metal sites is reportedly more thermodynamically expensive than homolytic $H_2$ dissociation on clusters.[58]

For some catalysis requiring interatomic cooperativities, i.e., ensemble effects, the number of adjacent metal atoms and the distances between these metal atoms are key catalytic performance descriptors defining the reactivity per metal atom. For example, in the selective oxidation of 2-aminobenzyl alcohol utilizing supported Ru on metal-organic frameworks (MOFs) (zeolitic imidazolate frameworks [ZIFs]), the intrinsic activity of the Ru atom for a triatomic metal site is at least ten times higher

Please cite this article in press as: Chukwu and Yang, Uncertainties in the reactivity of atomically dispersed catalytic metal: Can any single-atom catalyst work like a charm?, Chem Catalysis (2023), https://doi.org/10.1016/j.checat.2023.100735



than that of the isolated metal site analog.[59] The much less reactive stable configuration of 2-aminobenzyl alcohol adsorbing via its amino group on the single-atom Ru site blocks the Ru site, limiting its catalytic reactivity. However, the triatomic Ru metal active site induces a significantly more reactive adsorption configuration for the 2-amino benzyl alcohol such that both the amino and hydroxyl groups are adsorbed on the Ru atom. Contrastingly, Ru nanoparticles (also providing adjacent atoms such as the triatomic cluster) render the lowest reactivity as a result of overly strong adsorption of 2-amino benzyl alcohol, blocking the active site.

The above prototypical examples involve direct interatomic communication. Nevertheless, as discussed in the earlier section "interatomic interactions control supported metal reactivity in ADSMCs," interatomic communications between non-contiguous neighboring isolated metal atoms can be also established by bridging the atoms with secondary non-metallic species. For solar water oxidation, Wang and colleagues[60,61] found that a homonuclear Ir pair site linked by oxygen species ($Ir_1$–O–$Ir_1$) was catalytically superior to the isolated metal SACs because of a unique reaction pathway, faster charge-transfer kinetics, and thermodynamically efficient proton-coupled electron transfer. This Ir pair site on $\alpha$-$Fe_2O_3$ support exhibited specific activity three times more than the mononuclear Ir site homolog.

When distinct atomic metal types are in close proximity, such heterometallic structures can inherit distinct catalytic functionalities otherwise unachievable by their respective homometallic ADSMCs.[46,62–64] By employing site-specific strong electrostatic adsorption and carefully manipulating synthesis parameters, Christopher and colleagues[46,64] preferentially directed single-atom Rh species to atomic $WO_x$ (-$ReO_x$) domains rather than randomly onto an $Al_2O_3$ support. Unlike their respective monometallic single-atom analogs, these heterodimeric structures could selectively catalyze the $C_2H_4$ hydroformylation reaction, involving the conversion of $C_2H_4$ with CO and $H_2$ to produce aldehydes. The well-tailored proximity of the atomic pair site facilitated synergistic electronic interactions and effective intersite migration of reactive species to sustain the overall catalytic cycle. For instance, strong CO adsorption on the $Rh_1/Al_2O_3$ catalyst poisoned the Rh and forbid $C_2H_4$ adsorption, whereas $C_2H_4$ activation on $WO_x/Al_2O_3$ was energetically unfavorable.[46] However, with the Rh-$WO_x$ atomic active pair-site structure (Figure 5C), the $WO_x$ species weakened CO adsorption on $Rh_1$, effectively withdrawing CO from the Rh site. Concurrently, the atomic $WO_x$ site acted as a stop gap to adsorb and transfer $C_2H_4$ to the electron-deficient $Rh_1$. Plus, the Rh-$WO_x$ interface facilitated $H_2$ dissociation. These distinct cooperativities yielded significant activity and ca. 100% propanol formation selectivity (Figure 5C). Fu et al.[63] adopted a similar heterometallic pair-site strategy in designing $Ir_1Mo_1/TiO_2$ to selectively catalyze the hydrogenation of 4-nitrostyrene to 4-vinyl aniline with $Ir_1$ sites responsible for $H_2$ activation and $Mo_1$ sites dedicated to 4-nitrostyrene adsorption and activation. These examples of this relatively young field highlight the potential for rational exploitation of the distinct catalytic properties of different metals to overcome the limitations of homometallic ADSMCs to control catalytic synergies for complex multisite reactions.

## CONCLUSION AND OUTLOOK

The exploration of ADSMCs as general heterogeneous catalysts has benefited substantially from over one decade of intensive studies on SACs. The explosive growth of reports on the topical area of classic SACs could easily leave researchers with an overly simplified impression that the success of creating some sort of single-atom

supported metal species for any given catalyst formulation will be the one-step approach to encounter specific new and universal catalytic chemistry. We present a non-exhaustive overview and discussion on the general topic of ADSMCs to highlight that the intrinsic reactivities of the atomically dispersed metal species can be more dynamic than the ideal SACs would project. Even within the same catalyst formulation, the intrinsic activity and selectivity of the supported metal atoms can be heavily altered by metal-support interactions and interatomic interactions between supported metal atoms. From a practical point of view, one should be very careful with oversimplified research conclusions indicating that SACs inheriting formulation XYZ will be guaranteed to work effectively for a given reaction. Is the supported metal atom governing the reactivity? If yes, will the interatomic interactions between the supported metal atoms affect the reactivity? If the supported metal site alone is insufficient to determine reactivity, to what extent are the metal-support interactions tuned to generalize the findings?

Looking beyond classic SACs to embrace complex but robust ADSMC designs, one future research direction is scalable material engineering strategies for precisely designing and synthesizing advanced catalysts. Given the dynamic evolution of intrinsic reactivities for atomically dispersed supported metals in many catalyst systems, the common practice of reporting catalytic performance for ADSMCs on the basis of a single metal loading could hinder the community from reliably assessing and predicting their true catalytic potentials and versatility. Researchers should preliminarily probe the effects of single-atom metal loading and support heterogeneity to generalize a conclusion that single-atom XYZ catalysts will promote certain reactions.

For better-nuanced knowledge, decoupling and elucidating the specific role of intersite distances and atomicity (number of neighboring atoms) and their combined impacts in shaping catalytic performances is a valuable research direction. It is also essential to note that the location and environments of active sites might not remain static, especially under reaction conditions.[65,66] More so, the somewhat underappreciated kinetic studies these days can often offer a deeper understanding of the structure-performance relationship of ADSMCs, and they are excellent tools to complement materials-science-oriented research prevalent in the catalysis community. Combined with microkinetic computational studies, these can provide a thorough mechanistic understanding of catalytic reactions, echoing various characterization implications.

## ACKNOWLEDGMENTS

M.Y. appreciates the support provided by the start-up fund of Clemson University, National Science Foundation award 2146591, and American Chemical Society PRF Doctoral New Investigator Award 65606-DNI5. This perspective is dedicated to M.Y. and Lingxi's newborn daughter, Caroline, and to the loving memory of E.C.'s father, who passed away on August 2, 2023.

## AUTHOR CONTRIBUTIONS

Writing – original draft, E.C.; writing – review & editing, E.C. and M.Y.

## DECLARATION OF INTERESTS

The authors declare no competing interests.

## REFERENCES


1. Liu, J. (2017). Catalysis by supported single metal atoms. ACS Catal. *7*, 34–59.
2. Yang, X.F., Wang, A., Qiao, B., Li, J.U.N., Liu, J., and Zhang, T. (2013). Single-atom catalysts: a new frontier in heterogeneous catalysis. Acc. Chem. Res. *46*, 1740–1748. https://doi.org/10.1021/ar300361m.
3. Flytzani-Stephanopoulos, M., and Gates, B.C. (2012). Atomically dispersed supported metal catalysts. Annu. Rev. Chem. Biomol. Eng. *3*, 545–574.
4. Liu, L., and Corma, A. (2018). Metal catalysts for heterogeneous catalysis: from single atoms to nanoclusters and nanoparticles. Chem. Rev. *118*, 4981–5079.
5. Datye, A.K., and Guo, H. (2021). Single atom catalysis poised to transition from an academic curiosity to an industrially relevant technology. Nat. Commun. *12*, 895.
6. Mitchell, S., and Pérez-Ramírez, J. (2021). Atomically precise control in the design of low-nuclearity supported metal catalysts. Nat. Rev. Mater. *6*, 969–985.
7. Thomas, J.M. (2015). Tens of thousands of atoms replaced by one. Nature *525*, 325–326.
8. Shekhar, M., Wang, J., Lee, W.S., Williams, W.D., Kim, S.M., Stach, E.A., Miller, J.,T., Delgass, W.N., and Ribeiro, F.H. (2012). Size and support effects for the water-gas shift catalysis over gold nanoparticles supported on model $Al_2O_3$ and $TiO_2$. J. Am. Chem. Soc. *134*, 4700–4708.
9. Cargnello, M., Doan-Nguyen, V.V.T., Gordon, T.R., Diaz, R.E., Stach, E.A., Gorte, R.J., Fornasiero, P., and Murray, C.B. (2013). Control of metal nanocrystal size reveals metal-support interface role for ceria catalysts. Science *341*, 771–773.
10. Qiao, B., Wang, A., Yang, X., Allard, L.F., Jiang, Z., Cui, Y., Liu, J., Li, J., and Zhang, T. (2011). Single-atom catalysis of CO oxidation using $Pt_1/FeO_x$. Nat. Chem. *3*, 634–641.
11. DeRita, L., Dai, S., Lopez-Zepeda, K., Pham, N., Graham, G.W., Pan, X., and Christopher, P. (2017). Catalyst architecture for stable single atom dispersion enables site-specific spectroscopic and reactivity measurements of CO adsorbed to Pt atoms, oxidized Pt clusters, and metallic Pt clusters on $TiO_2$. J. Am. Chem. Soc. *139*, 14150–14165.
12. Resasco, J., DeRita, L., Dai, S., Chada, J.P., Xu, M., Yan, X., Finzel, J., Hanukovich, S., Hoffman, A.S., Graham, G.W., et al. (2020). Uniformity is key in defining structure-function relationships for atomically dispersed metal catalysts: the case of $Pt/CeO_2$. J. Am. Chem. Soc. *142*, 169–184.
13. Yang, M., Allard, L.F., and Flytzani-stephanopoulos, M. (2013). Atomically dispersed $Au-(OH)_x$ species bound on titania catalyze the low-temperature water-gas shift reaction. J. Am. Chem. Soc. *135*, 3768–3771.
14. Yang, M., Liu, J., Lee, S., Zugic, B., Huang, J., Allard, L.F., and Flytzani-stephanopoulos, M. (2015). A common single-site $Pt(II)–O(OH)_x$ species stabilized by sodium on "active" and "inert" supports catalyzes the water-gas shift reaction. J. Am. Chem. Soc. *137*, 3470–3473.
15. Zheng, J., Lebedev, K., Wu, S., Huang, C., Ayvalı, T., Wu, T.S., Li, Y., Ho, P.L., Soo, Y.L., Kirkland, A., and Tsang, S.C.E. (2021). High loading of transition metal single atoms on chalcogenide catalysts. J. Am. Chem. Soc. *143*, 7979–7990.
16. Xia, C., Qiu, Y., Xia, Y., Zhu, P., King, G., Zhang, X., Wu, Z., Kim, J.Y.T., Cullen, D.A., Zheng, D., et al. (2021). General synthesis of single-atom catalysts with high metal loading using graphene quantum dots. Nat. Chem. *13*, 887–894.
17. Mehmood, A., Gong, M., Jaouen, F., Roy, A., Zitolo, A., Khan, A., Sougrati, M.T., Primbs, M., Bonastre, A.M., Fongalland, D., et al. (2022). High loading of single atomic iron sites in Fe–NC oxygen reduction catalysts for proton exchange membrane fuel cells. Nat. Catal. *5*, 311–323.
18. Samantaray, M.K., D'Elia, V., Pump, E., Falivene, L., Harb, M., Ould Chikh, S., Cavallo, L., and Basset, J.M. (2020). The comparison between single atom catalysis and surface organometallic catalysis. Chem. Rev. *120*, 734–813.
19. Dhiman, M., and Polshettiwar, V. (2018). Supported single atom and pseudo-single atom of metals as sustainable heterogeneous nanocatalysts. ChemCatChem *10*, 881–906.
20. Ji, S., Chen, Y., Wang, X., Zhang, Z., Wang, D., and Li, Y. (2020). Chemical synthesis of single atomic site catalysts. Chem. Rev. *120*, 11900–11955.
21. Xia, Y., Sayed, M., Zhang, L., Cheng, B., and Yu, J. (2021). Single-atom heterogeneous photocatalysts. Chem Catal. *1*, 1173–1214.
22. Lang, R., Du, X., Huang, Y., Jiang, X., Zhang, Q., Guo, Y., Liu, K., Qiao, B., Wang, A., and Zhang, T. (2020). Single-atom catalysts based on the metal-oxide interaction. Chem. Rev. *120*, 11986–12043.
23. Doherty, F., Wang, H., Yang, M., and Goldsmith, B.R. (2020). Nanocluster and single-atom catalysts for thermocatalytic conversion of CO and $CO_2$. Catal. Sci. Technol. *10*, 5772–5791.
24. Shan, J., Ye, C., Jiang, Y., Jaroniec, M., Zheng, Y., and Qiao, S.Z. (2022). Metal-metal interactions in correlated single-atom catalysts. Sci. Adv. *8*, eabo0762.
25. Yang, M., Li, S., Wang, Y., Herron, J.A., Xu, Y., Allard, L.F., Lee, S., Huang, J., Mavrikakis, M., and Flytzani- Stephanopoulos, M. (2014). Catalytically active $Au-O(OH)_x$- species stabilized by alkali ions on zeolites and mesoporous oxides. Science *346*, 1498–1501.
26. Cao, S., Yang, M., Elnabawy, A.O., Trimpalis, A., Li, S., Wang, C., Göltl, F., Chen, Z., Liu, J., Shan, J., et al. (2019). Single-atom gold oxo-clusters prepared in alkaline solutions catalyse the heterogeneous methanol self- coupling reactions. Nat. Chem. *11*, 1098–1105.
27. Cao, S., Wang, Y., Wang, H., Chen, H., Zhang, G., Kritikos, A., Li, M., Ouyang, M., Wang, D., Sykes, C.H., et al. (2020). High-loading single Pt atom sites $[Pt–O(OH)_x]$ catalyze the CO $PRO_X$ reaction with high activity and selectivity at mild conditions. Sci. Adv. *16*, 1–12.
28. Beniya, A., and Higashi, S. (2019). Towards dense single-atom catalysts for future automotive applications. Nat. Catal. *2*, 590–602.
29. Hai, X., Xi, S., Mitchell, S., Harrath, K., Xu, H., Akl, D.F., Kong, D., Li, J., Li, Z., Sun, T., et al. (2022). Scalable two step annealing method for preparing ultra-high-density single-atom catalyst libraries. Nat. Nanotechnol. *17*, 174–181.
30. Hoffman, A.S., Fang, C.Y., and Gates, B.C. (2016). Homogeneity of surface sites in supported single-site metal spectra. J. Phys. Chem. Lett. *7*, 3854–3860. https://doi.org/10.1021/acs.jpclett.6b01825.
31. Chen, Z., Vorobyeva, E., Mitchell, S., Fako, E., López, N., Collins, S.M., Leary, R.K., Midgley, P.A., Hauert, R., and Pérez-Ramírez, J. (2018). Single-atom heterogeneous catalysts based on distinct carbon nitride scaffolds. Natl. Sci. Rev. *5*, 642–652.
32. DeRita, L., Resasco, J., Dai, S., Boubnov, A., Thang, H.V., Hoffman, A.s., Ro, I., Graham, G.W., Bare, S.R., Pacchioni, G., et al. (2019). Structural evolution of atomically dispersed Pt catalysts dictates reactivity. Nat. Mater. *18*, 746–751.
33. Tan, W., Xie, S., Le, D., Diao, W., Wang, M., Low, K.B., Austin, D., hong, S., Gao, F., Dong, L., et al. (2022). Fine-tuned local coordination environment of Pt single atoms on ceria controls catalytic reactivity. Nat. Commun. *13*, 7070.
34. Jiang, D., Yao, Y., Li, T., Wan, G., Pereira-Hernández, X.I., Lu, Y., Tian, J., Khivantsev, K., Engelhard, M.H., Sun, C., et al. (2021). Tailoring the local environment of platinum in single-atom $Pt_1/CeO_2$ catalysts for robust low-temperature CO oxidation. Angew. Chem. Int. Ed. *60*, 26054–26062.
35. Resasco, J., and Christopher, P. (2020). Atomically dispersed pt-group catalysts: reactivity, uniformity, structural evolution, and paths to increased functionality. J. Phys. Chem. Lett. *11*, 10114–10123. https://doi.org/10.1021/acs.jpclett.0c02904.
36. Zhang, X., Zhang, M., Deng, Y., Xu, M., Artiglia, L., Wen, W., Gao, R., Chen, B., Yao, S., Zhang, X., et al. (2021). A stable low-temperature $H_2$-production catalyst by crowding Pt on α-MoC. Nature *589*, 396–401.
37. Yao, S., Zhang, X., Zhou, W., Gao, R., Xu, W., Ye, Y., Lin, L., Wen, X., Liu, P., Chen, B., et al. (2017). Atomic-layered Au clusters on α-MoC as catalysts for the low-temperature water-gas shift reaction. Science *387*, 389–393.
38. Chukwu, E., Molina, L., Rapp, C., Morales, L., Jin, Z., Karakalos, S., Wang, H., Lee, S., Zachman, M.J., and Yang, M. (2023). Crowded supported metal atoms on catalytically active supports may compromise intrinsic activity: a case study of dual-site Pt/α-MoC catalysts. Appl. Catal. B Environ. *329*, 122532.

39. Xue, Z., Gao, X., Zhang, Y., Yan, M., Xu, J., and Wu, Y. (2023). Site-coverage dependent single-atom-layer catalysts toward hydrogen production. Chem Catal. *3*, 100538. https://doi.org/10.1016/j.checat.2023.100538.

40. Chhetri, M., Wan, M., Jin, Z., Yeager, J., Sandor, C., Rapp, C., Wang, H., Lee, S., Bodenschatz, C.J., Zachman, M.J., et al. (2023). Dual-site catalysts featuring platinum-group- metal atoms on copper shapes boost hydrocarbon formations in electrocatalytic $CO_2$ reduction. Nat. Commun. *14*, 3075. https://doi.org/10.1038/s41467-023-38777-y.

41. Chen, M., Kumar, D., Yi, C.W., and Goodman, D.W. (2005). Chemistry: the promotional effect of gold in catalysis by palladium-gold. Science *310*, 291–293.

42. Zhao, E., Li, M., Xu, B., Wang, X.L., Jing, Y., Ma, D., Mitchell, S., Pérez-Ramírez, J., and Chen, Z. (2022). Transfer hydrogenation with a carbon-nitride-supported palladium single-atom photocatalyst and water as a proton source. Angew. Chem. Int. Ed. *61*, e202207410. https://doi.org/10.1002/anie.202207410.

43. Jeong, H., Lee, G., Kim, B.S., Bae, J., Han, J.W., and Lee, H. (2018). Fully dispersed Rh ensemble catalyst to enhance low-temperature activity. J. Am. Chem. Soc. *140*, 9558–9565.

44. Wang, H., Liu, J.X., Allard, L.F., Lee, S., Liu, J., Li, H., Wang, J., Wang, J., Oh, S.H., Li, W., et al. (2019). Surpassing the single-atom catalytic activity limit through paired Pt-O-Pt ensemble built from isolated $Pt_1$ atoms. Nat. Commun. *10*, 3808. https://doi.org/10.1038/s41467-019-11856-9.

45. Guan, E., and Gates, B.C. (2018). Stable rhodium pair sites on MgO: influence of ligands and rhodium nuclearity on catalysis of ethylene hydrogenation and H–D exchange in the reaction of $H_2$ with $D_2$. ACS Catal. *8*, 482–487.

46. Ro, I., Qi, J., Lee, S., Xu, M., Yan, X., Xie, Z., Zakem, G., Morales, A., Chen, J.G., Pan, X., et al. (2022). Bifunctional hydroformylation on heterogeneous Rh-$WO_x$ pair site catalysts. Nature *609*, 287–292. https://doi.org/10.1038/s41586-022-05075-4.

47. Li, H., Wang, L., Dai, Y., Pu, Z., Lao, Z., Chen, Y., Wang, M., Zheng, X., Zhu, J., Zhang, W., et al. (2018). Synergetic interaction between neighbouring platinum monomers in $CO_2$ hydrogenation. Nat. Nanotechnol. *13*, 411–417.

48. Huang, Z., Liang, J.X., Tang, D., Chen, Y., Qu, W., Hu, X., Chen, J., Dong, Y., Xu, D., Golberg, D., et al. (2022). Interplay between remote single-atom active sites triggers speedy catalytic oxidation. Chem *8*, 3008–3017.

49. Jin, H., Zhou, K., Zhang, R., Cui, H., Yu, Y., Cui, P., Song, W., and Cao, C. (2023). Regulating the electronic structure through charge redistribution in dense single-atom catalysts for enhanced alkene epoxidation. Nat. Commun. *14*, 2494. https://doi.org/10.1038/s41467-023-38310-1.

50. Jin, H., Cui, P., Cao, C., Yu, X., Zhao, R., Ma, D., and Song, W. (2023). Understanding the Density-dependent activity of Cu single-atom catalyst in the benzene hydroxylation reaction. ACS Catal. *13*, 1316–1325.

51. Jin, Z., Li, P., Meng, Y., Fang, Z., Xiao, D., and Yu, G. (2021). Understanding the inter-site distance effect in single-atom catalysts for oxygen electroreduction. Nat. Catal. *4*, 615–622.

52. Jin, H., Zhao, R., Cui, P., Liu, X., Yan, J., Yu, X., Ma, D., Song, W., and Cao, C. (2023). Sabatier phenomenon in hydrogenation reactions induced by single-atom density. J. Am. Chem. Soc. *145*, 12023–12032. https://doi.org/10.1021/jacs.3c00786.

53. Kim, Y., Collinge, G., Lee, M.S., Khivantsev, K., Cho, S.J., Glezakou, V.A., Rousseau, R., Szanyi, J., and Kwak, J.H. (2021). Surface density dependent catalytic activity of single palladium atoms supported on ceria. Angew. Chem. Int. Ed. *60*, 22769–22775.

54. Meng, X., Ma, C., Jiang, L., Si, R., Meng, X., Tu, Y., Yu, L., Bao, X., and Deng, D. (2020). Distance synergy of $MoS_2$-confined rhodium atoms for highly efficient hydrogen evolution. Angew. Chem. Int. Ed. *59*, 10502–10507.

55. Guan, E., Debefve, L., Vasiliu, M., Zhang, S., Dixon, D.A., and Gates, B.C. (2019). MgO-supported iridium metal pair-site catalysts are more active and resistant to CO poisoning than analogous single-site catalysts for ethylene hydrogenation and hydrogen-deuterium exchange. ACS Catal. *9*, 9545–9553.

56. Vorobyeva, E., Fako, E., Chen, Z., Collins, S.M., Johnstone, D., Midgley, P.A., Hauert, R., Safonova, O.V., Vilé, G., López, N., et al. (2019). Atom-by-atom resolution of structure–function relations over low-nuclearity metal catalysts. Angew. Chem. Int. Ed. *58*, 8724–8729.

57. Ji, S., Chen, Y., Zhao, S., Chen, W., Shi, L., Wang, Y., Dong, J., Li, Z., Li, F., Chen, C., et al. (2019). Atomically dispersed ruthenium species inside metal–organic frameworks: combining the high activity of atomic sites and the molecular sieving effect of MOFs. Angew. Chem. Int. Ed. *58*, 4271–4275.

58. Aireddy, D.R., and Ding, K. (2022). Heterolytic dissociation of $H_2$ in heterogeneous catalysis. ACS Catal. *12*, 4707–4723.

59. Ji, S., Chen, Y., Fu, Q., Chen, Y., Dong, J., Chen, W., Li, Z., Wang, Y., Gu, L., He, W., et al. (2017). Confined pyrolysis within metal-organic frameworks to form uniform $Ru_3$ clusters for efficient oxidation of alcohols. J. Am. Chem. Soc. *139*, 9795–9798.

60. Zhao, Y., Yang, K.R., Wang, Z., Yan, X., Cao, S., Ye, Y., Dong, Q., Zhang, X., Thorne, J.E., Jin, L., et al. (2018). Stable iridium dinuclear heterogeneous catalysts supported on metal-oxide substrate for solar water oxidation. Proc. Natl. Acad. Sci. USA *115*, 2902–2907.

61. Zhao, Y., Yan, X., Yang, K.R., Cao, S., Dong, Q., Thorne, J.E., Materna, K.L., Zhu, S., Pan, X., Flytzani- Stephanopoulos, M., et al. (2018). End-on bound iridium dinuclear heterogeneous catalysts on $WO_3$ for solar water oxidation. ACS Cent. Sci. *4*, 1166–1172.

62. Huang, F., Peng, M., Chen, Y., Cai, X., Qin, X., Wang, N., Xiao, D., Jin, L., Wang, G., Wen, X.D., et al. (2022). Low-temperature acetylene semi-hydrogenation over the $Pd_1$−$Cu_1$ dual-atom catalyst. J. Am. Chem. Soc. *144*, 18485–18493. https://doi.org/10.1021/jacs.2c07208.

63. Fu, J., Dong, J., Si, R., Sun, K., Zhang, J., Li, M., Yu, N., Zhang, B., Humphrey, M.G., Fu, Q., and Huang, J. (2021). Synergistic effects for enhanced catalysis in a dual single-atom catalyst. ACS Catal. *11*, 1952–1961. https://doi.org/10.1021/acscatal.0c05599.

64. Ro, I., Xu, M., Graham, G.W., Pan, X., and Christopher, P. (2019). Synthesis of heteroatom Rh−$ReO_x$ atomically dispersed species on $Al_2O_3$ and their tunable catalytic reactivity in ethylene hydroformylation. ACS Catal. *9*, 10899–10912. https://doi.org/10.1021/acscatal.9b02111.

65. Xu, L., Papanikolaou, K.G., Lechner, B.A.J., Je, L., Somorjai, G.A., Salmeron, M., and Mavrikakis, M. (2023). Formation of active sites on transition metals through reaction-driven migration of surface atoms. Science *380*, 70–76. https://doi.org/10.1126/science.add0089.

66. Tang, Y., Asokan, C., Xu, M., Graham, G.W., Pan, X., Christopher, P., Li, J., and Sautet, P. (2019). Rh single atoms on $TiO_2$ dynamically respond to reaction conditions by adapting their site. Nat. Commun. *10*, 4488.