CONFINEMENT IN HETEROGENEOUS CATALYSIS: A CASE STUDY USING RASPBERRY-COLLOID-TEMPLATED CATALYSTS

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Confinement in catalysis: what is confined and why is confinement important?

Catalysis entails the atomic rearrangement of reactant molecules following a specific reaction pathway, facilitated by the active sites of catalysts. These catalytically active sites exist in various forms, such as a local coordination environment of metal atom(s) (typical for heterogeneous catalysis), or metal centers (typical for homogeneous catalysis). As the reactant species approaches and interacts with the active site motif, the ***reactant species becomes spatially confined,*** generally forming an adsorbate–surface atom bond (for heterogeneous catalysis), a metal-centered coordination complex (for homogeneous catalysis), or enzyme–substrate complex (for enzymatic catalysis). Since the active sites of heterogeneous catalysts are noticeably more poorly defined than their homogeneous and enzymatic catalyst counterparts (*1*), we hence focus here on highlighting the benefits, recent progress, and outlook of rational confinement in heterogeneous catalytic systems to encourage further research and discussion in this area.

In heterogeneous catalysis, confining the adsorption geometry of reactant species energetically stabilizes specific transition states to direct size-, stereo-, or regio- selective chemical transformations. Such effects were traditionally achieved using microporous materials (*e.g.,* zeolites, carbon nanotubes, and metal–organic frameworks), where the characteristic diffusion lengths of reactants are commensurate to the pore/channel dimensions, thereby enhancing the interactions between reactants and their surrounding pore walls within an internal diffusion-limited transport regime (*2*). Recently, these concepts were translated to metal oxide- or polymer-encapsulated nanoparticle (NP)-supported catalysts (*3*, *4*), ordered intermetallic NP catalysts (*5*), and bimetallic NP catalysts with somewhat defined surface domains (*6*, *7*). The overarching concept underpinning all these examples is to replicate the well-defined active site motifs of homogeneous and enzymatic catalysts to induce similar catalytic selectivity effects (*8*).

Another perspective arises when we ***spatially confine the active sites*** to a fixed position in the catalyst structure. Heterogeneous catalysts typically comprise NPs dispersed on high surface area supports, but the poor contact and adhesion between the NPs and their supports often result in NP sintering (by coalescence, Ostwald ripening, and surface diffusion/migration) (*9*), which is accelerated under harsh operating conditions of high temperature and pressure (*10*, *11*). Thus, efforts were made to entrench these NPs in the support matrix to improve their resistance against sintering. Recent efforts include overgrowing metal oxide or polymeric overlayers around NPs through solution-based chemistry (*e.g.,* sol-gel) (*4*, *12*) or physical/chemical deposition (*13*) to form inverted catalyst structures, although we remark that the overgrowth conditions should be carefully chosen to prevent complete encapsulation of the NPs, which would significantly reduce reactant accessibility to the underlying catalytically active sites on the NP surface.

Encouraged by these advantages of spatial confinement, our group has devoted research attention to gaining greater synthetic control over various confinement effects. For this purpose, we developed a modular raspberry-colloid-templated (RCT) catalyst platform, whose design, advantages, and relevant findings are summarized in the next section.

Our contribution: raspberry-colloid-templated catalysts to study confinement

To overcome the limitations of existing catalyst design—poor stability in conventional NP-supported catalysts or reduced reactant accessibility in inverted catalyst designs—we devised a RCT catalyst platform whereby NPs are partially embedded within the support to enhance resistance against sintering, while maintaining high reactant accessibility through the unembedded sections of the NP surface (*14–16*). In the RCT method (**Fig. 1a**), catalytic NPs are attached to surface-functionalized templating colloids—which can be polymeric or inorganic—to form NP-decorated raspberry colloids. These raspberry colloids are self-assembled into a 3D colloidal crystal and then infiltrated or co-assembled with support precursors (*e.g.,* metal oxides such as pre-hydrolyzed silica/alumina/titania, or pre-formed titania/alumina nanocrystals). Finally, a templating colloid removal step (calcination for polymeric templates or solution-based etching/dissolution for inorganic templates) yields the 3D macroporous RCT catalyst (**Fig. 1b**) with NPs that are, by volume, more than 50% (but not fully) embedded within the support pore walls (*17*). Hence, the RCT catalysts can serve not only as practically relevant and exceptionally stable catalysts for industrial applications, but can also serve as a model catalytic platform to elucidate clear structure–property relationships (*18–23*).

The high modularity of the RCT approach affords independent control over multiple levels of confinement as illustrated in **Fig. 1c**: (i) confinement of NP localization within and between pores, (ii) confinement of reactants within pores, (iii) confinement of NP at the pore–support interface, and (iv) confinement of reactants at the microporous voids at the embedded NP–support interface. These different levels of confinement operate at different length scales and are achieved through separate synthetic means, thus presenting their own unique confinement-related catalytic advantages, which we elaborate below.

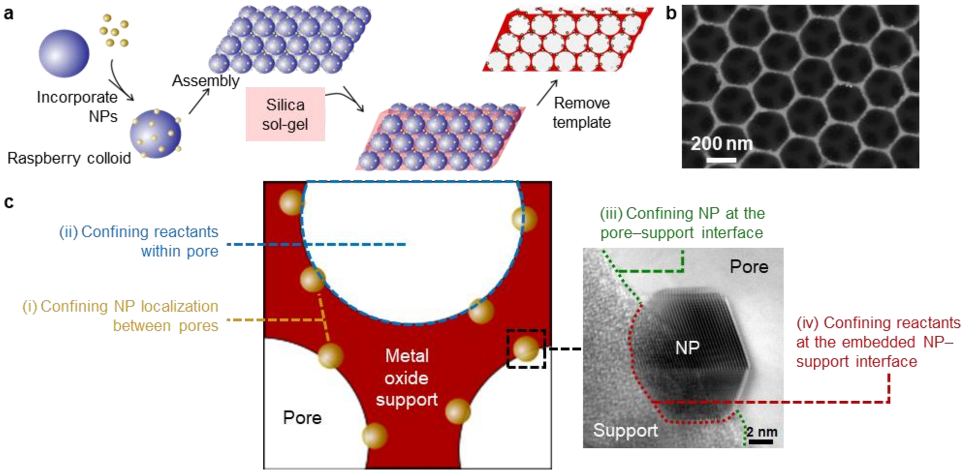

Fig. 1. RCT catalyst platform. (a) Synthetic scheme describing the preparation of RCT catalysts which comprise catalytic NPs partially embedded within a support matrix. (b) Scanning electron microscopy image of RCT catalysts depicting an ordered macroporous structure. (c) Different levels of confining reactants or catalytic NPs in RCT catalysts. (a) adapted from (*15*), (b) adapted from (*24*), (c) adapted from (*14*, *17*).

First, the placement of NPs within and between pores can be spatially confined by assembling more than one type of raspberry colloid, each bearing different catalytic NPs (**Fig. 2a**) (*14*). This design is especially useful for cascade catalytic networks where the desired product is only produced through a pre-defined sequence of active sites (*25*), or to physically separate two different sites that are chemically incompatible with each other while placing them in close proximity to facilitate the reaction cascade (*26*). One can also localize NP placement onto a pre-determined fraction of pores—by assembly with some NP-free colloids—to exploit NP proximity effects on reactant readsorption in multi-step reaction cascades (*19*), beneficially reducing the loading of (often precious) metal NPs.

Second, each individual pore acts as a discrete hollow chamber where catalytic reactions occur on the NP surfaces decorating the pore wall. By synthesizing with smaller or larger templating colloids, the macropore size can be altered to enhance or alleviate physical confinement effects from the pore walls, respectively (**Fig. 2b**) (*14*). Moreover, pore level hierarchy can be achieved by assembling templating colloids with more than one size (*27*). Separately, we note that the well-defined 3D ordered macroporous structure of RCT catalysts (**Fig. 1b**) allows one to reliably extrapolate diffusional and transport results from the single pore level to the entire catalyst structure (*28*), which highlights the unique suitability of RCT catalysts to serve as a model catalytic platform (*23*).

Third, all the NPs are partially embedded at the pore–support interface due to nanoscale wetting effects at the NP–templating colloid–support precursor interface (*17*, *24*). Our extensive tomographic analysis (*17*) reveals that, on average, 85% of the NP volume is embedded into the support (**Fig. 2c1**), which confines the NP position in place and considerably reduces surface NP migration and coalescence rates. Consequently, catalytic stability is enhanced for a variety of gas- and liquid-phase oxidation (*10*, *29–31*) and hydrogenation (*18–21*, *24*, *32*, *33*) reactions (**Fig. 2c2–2c3**). We further remark that the partial NP embedding feature creates more NP–support interfacial sites, which we exploited to increase catalytic contributions from active sites specifically confined at the interface (*21*). In summary, unlike traditional catalyst designs whereby NPs are deposited or formed onto support surfaces, the partial NP embedding feature in the RCT catalysts beneficially augments both their catalytic activity and stability.

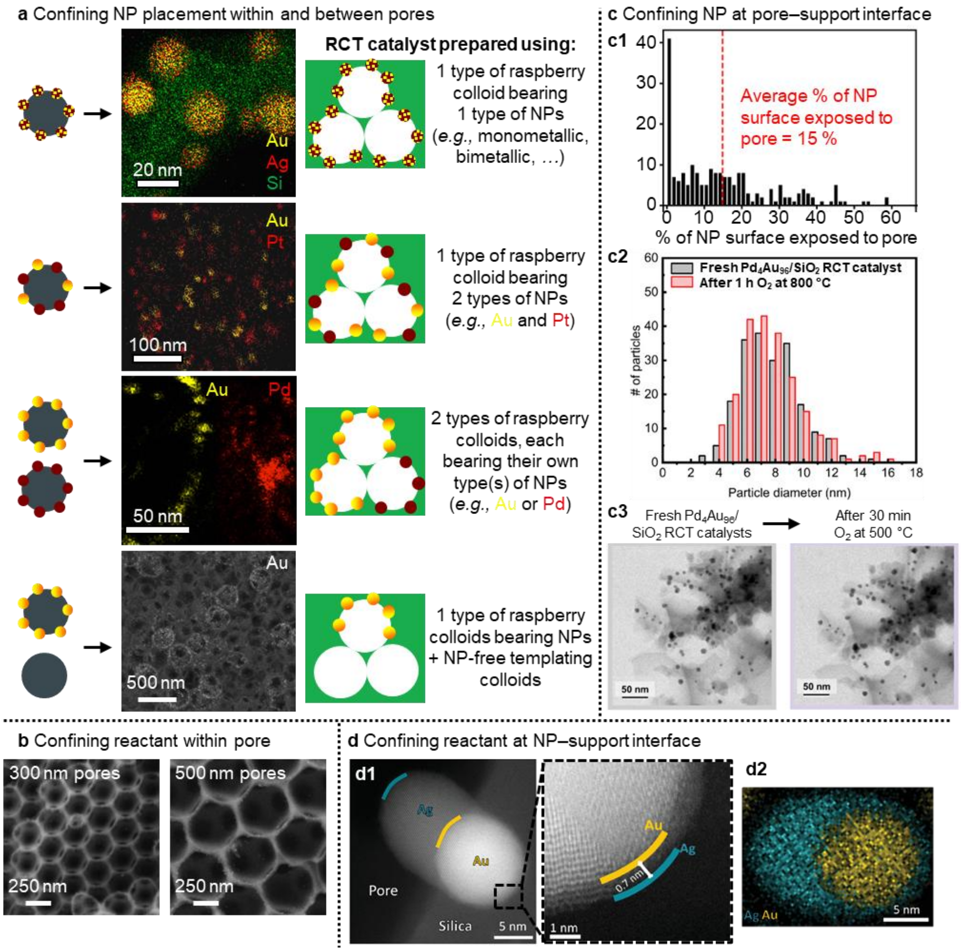

Fig. 2. Inducing confinement in RCT catalysts and their effects on catalysis. (a) NP placement within and between pores is controlled by assembling multiple types of raspberry colloids, each bearing different types of NPs. (b) Reactants are confined within macropores whose pore diameters are tuned by the size of the templating colloids used. (c) NPs are physically confined at the pore–support interface as NPs are partially, but not fully, embedded into the support, as quantified by (c1) electron tomographic analysis. As a result, (c2) NP sintering is

substantially arrested under thermocatalytic reaction conditions, as verified by (c3) *in situ* environmental transmission electron microscopy. (d) Reactants can also be confined in microporous voids at the interface between the embedded regions of the NP surface and the support. This microporosity is visualized by (d1) the successful reduction of Ag around Au NPs in Au/SiO_2 RCT catalysts, which indicate a 0.7 nm microporous pocket at the embedded NP–support interface (d1 inset). (d2) Energy-dispersive X-ray spectroscopy mapping confirms that the embedded sections of the Au NP are accessible to reactants (Ag^+ precursor in this example). (a) adapted from (*14*, *19*), (b) adapted from (*19*), (c1)–(c2), (d) adapted from (*17*), (c3) adapted from (*34*).

Finally, a microporous void exists at the interface between the embedded regions of the NP and the surrounding support (*17*), due to volume shrinkage of the support sol-gel precursor in the heat treatment step to prepare the catalysts. We visualized this microporosity by reducing Ag^+ on Au/SiO_2 RCT catalysts (**Fig. 2d**), which reveals a narrow ≈0.7 nm pocket surrounding the embedded areas of the NP surface (*17*). Hence, we posit that reactants can, in principle, access both the unembedded and embedded regions of the NP surface, with the latter potentially exerting sterically-confined catalysis effects found only in microporous materials (*2*).

Conclusions and outlook on confinement in heterogeneous catalysis

We consider confinement to be an ever-present feature in both catalyst design and in all types of catalysis, be it heterogeneous, homogeneous, or enzymatic. To gain more synthetic control over confinement effects compared to conventional catalyst design, we devised a modular RCT catalyst platform. In the RCT catalysts, a segment of the NP surface is exposed to the macropore and its open environment for reaction, while the rest of the NP is partially embedded within the support matrix to resist NP sintering. We described how NP placement can be pre-defined within and between pores to align with the diffusive pathway in which reactants flow through the catalyst structure, while affixing the NP in place by partial entrenchment into the support. For the reactants, we illustrated how controlling the pore size modulates its physical confinement effects, and how the well-ordered macroporous structure allows diffusive and transport characteristics (of reactants) in a single pore to be reliably extended to the entire structure. Finally, we provide experimental evidence for the potential of confined catalysis in the microporous pockets surrounding the embedded NP surfaces in contact with the support, which allows the RCT catalysts to uniquely function as both a macroporous and microporous catalyst.

Through the RCT platform, we demonstrate how rational colloidal design can be used to one's advantage to induce distinctly different confinement-related effects and realize newfound catalytic performance. Critically, such design principles and confinement effects are broadly applicable to a variety of reaction classes and catalyst designs for broad-based adoption. Looking forward, we anticipate future designs to incorporate multiple confinement effects into a single catalyst platform. In this regard, we postulate that tuning the spatial placement and density of different types of NPs in precise pre-defined locations will exert greater control over the reactant diffusive path across the different catalytic sites and regulate the reactant's local concentration around each catalytic NP, enabling one to steer selectivity while maintaining high catalytic activity to break archetypical activity–selectivity trade-offs. We also predict that the NP embedding levels and the size of microporous pockets around embedded NPs can be independently adjusted to tune the activity ratio from the unconfined NP surfaces to that from the confined regions at the embedded NP–support interface, forming "dual modality" macro-microporous catalysts. We close by taking the position that through confinement, we "unconfine" new catalytic possibilities to reimagine future catalyst design.

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References

1. Y. Zhang, S. Pang, Z. Wei, H. Jiao, X. Dai, H. Wang, F. Shi, Synthesis of a molecularly defined single-active site heterogeneous catalyst for selective oxidation of N-heterocycles. *Nat. Commun.* **9**, 1465 (2018).

2. J. Dai, H. Zhang, Recent Advances in Catalytic Confinement Effect within Micro/Meso-Porous Crystalline Materials. *Small* **17**, 2005334 (2021).

3. A. R. Riscoe, C. J. Wrasman, A. A. Herzing, A. S. Hoffman, A. Menon, A. Boubnov, M. Vargas, S. R. Bare, M. Cargnello, Transition state and product diffusion control by polymer–nanocrystal hybrid catalysts. *Nat. Catal.* **2**, 852–863 (2019).

4. J. Zhang, B. Wang, E. Nikolla, J. W. Medlin, Directing Reaction Pathways through Controlled Reactant Binding at Pd–TiO_2 Interfaces. *Angew. Chem. Int. Ed.* **56**, 6594–6598 (2017).

5. S. Furukawa, K. Ochi, H. Luo, M. Miyazaki, T. Komatsu, Selective Stereochemical Catalysis Controlled by Specific Atomic Arrangement of Ordered Alloys. *ChemCatChem* **7**, 3472–3479 (2015).

6. W. A. Swann, A. Yadav, N. B. Colvin, N. K. Freundl, C. W. Li, Diastereoselective Hydrogenation of Tetrasubstituted Olefins using a Heterogeneous Pt-Ni Alloy Catalyst. *Angew. Chem. Int. Ed.* **63**, e202317710 (2024).

7. W. Hong, W. A. Swann, V. Yadav, C. W. Li, Haptophilicity and Substrate-Directed Reactivity in Diastereoselective Heterogeneous Hydrogenation. *ACS Catal.* **12**, 7643–7654 (2022).

8. T. R. Ward, C. Copéret, Introduction: Bridging the Gaps: Learning from Catalysis across Boundaries. *Chem. Rev.* **123**, 5221–5224 (2023).

9. A. J. Martín, S. Mitchell, C. Mondelli, S. Jaydev, J. Pérez-Ramírez, Unifying views on catalyst deactivation. *Nat. Catal.* **5**, 854–866 (2022).

10. K. R. G. Lim, T. Shirman, T. J. Toops, J. Alvarenga, M. Aizenberg, J. Aizenberg, Active and Stable PtPd Diesel Oxidation Catalysts under Industry-Defined Test Protocols. *ChemSusChem* **18**, e202500295 (2025).

11. M. Bijl, K. R. G. Lim, S. Garg, N. J. Nicolas, N. L. Visser, M. Aizenberg, J. E. S. Van Der Hoeven, J. Aizenberg, Controlling nanoparticle placement in Au/TiO_2 inverse opal photocatalysts. *Nanoscale* **16**, 13867–13873 (2024).

12. A. Aitbekova, C. Zhou, M. L. Stone, J. S. Lezama-Pacheco, A.-C. Yang, A. S. Hoffman, E. D. Goodman, P. Huber, J. F. Stebbins, K. C. Bustillo, P. Ercius, J. Ciston, S. R. Bare, P. N. Plessow, M. Cargnello, Templated encapsulation of platinum-based catalysts promotes high-temperature stability to 1,100 °C. *Nat. Mater.* **21**, 1290–1297 (2022).

13. G. Liccardo, M. C. Cendejas, S. C. Mandal, M. L. Stone, S. Porter, B. T. Nhan, A. Kumar, J. Smith, P. N. Plessow, L. Cegelski, J. Osio-Norgaard, F. Abild-Pedersen, M. Chi, A. K. Datye, S. F. Bent, M. Cargnello, Unveiling the Stability of Encapsulated Pt Catalysts Using Nanocrystals and Atomic Layer Deposition. *J. Am. Chem. Soc.* **146**, 23909–23922 (2024).

14. E. Shirman, T. Shirman, A. V. Shneidman, A. Grinthal, K. R. Phillips, H. Whelan, E. Bulger, M. Abramovitch, J. Patil, R. Nevarez, J. Aizenberg, Modular Design of Advanced Catalytic Materials Using Hybrid Organic-Inorganic Raspberry Particles. *Adv. Funct. Mater.* **28**, 1704559 (2018).

15. K. R. G. Lim, M. Aizenberg, J. Aizenberg, Colloidal Templating in Catalyst Design for Thermocatalysis. *J. Am. Chem. Soc.* **146**, 22103–22121 (2024).

16. J. E. S. Van Der Hoeven, A. V. Shneidman, N. J. Nicolas, J. Aizenberg, Evaporation-Induced Self-Assembly of Metal Oxide Inverse Opals: From Synthesis to Applications. *Acc. Chem. Res.* **55**, 1809–1820 (2022).

17. J. E. S. van der Hoeven, S. Krämer, S. Dussi, T. Shirman, K. K. Park, C. H. Rycroft, D. C. Bell, C. M. Friend, J. Aizenberg, On the Origin of Sinter-Resistance and Catalyst Accessibility in Raspberry-Colloid-Templated Catalyst Design. *Adv. Funct. Mater.* **31**, 2106876 (2021).

18. S. K. Kaiser, J. E. S. Van Der Hoeven, G. Yan, K. R. G. Lim, H. T. Ngan, S. Garg, M. Karatok, M. Aizenberg, J. Aizenberg, P. Sautet, C. M. Friend, R. J. Madix, Identifying the Optimal Pd Ensemble Size in Dilute PdAu Alloy Nanomaterials for Benzaldehyde Hydrogenation. *ACS Catal.* **13**, 12092–12103 (2023).

19. K. R. G. Lim, S. K. Kaiser, H. Wu, S. Garg, M. Perxés Perich, J. E. S. Van Der Hoeven, M. Aizenberg, J. Aizenberg, Nanoparticle proximity controls selectivity in benzaldehyde hydrogenation. *Nat. Catal.* **7**, 172–184 (2024).

20. K. R. G. Lim, S. K. Kaiser, H. Wu, S. Garg, C. R. O'Connor, C. Reece, M. Aizenberg, J. Aizenberg, Deconvoluting the Individual Effects of Nanoparticle Proximity and Size in Thermocatalysis. *ACS Nano* **18**, 15958–15969 (2024).

21. K. R. G. Lim, S. K. Kaiser, C. J. Herring, T.-S. Kim, M. P. Perich, S. Garg, C. R. O'Connor, M. Aizenberg, J. E. S. Van Der Hoeven, C. Reece, M. M. Montemore, J. Aizenberg, Partial PdAu nanoparticle embedding into TiO_2 support accentuates catalytic contributions from the Au/TiO_2 interface. *Proc. Natl. Acad. Sci. U.S.A.* **122**, e2422628122 (2025).

22. P. K. Routh, E. Redekop, S. Prodinger, J. E. S. Van Der Hoeven, K. R. G. Lim, J. Aizenberg, M. Nachtegaal, A. H. Clark, A. I. Frenkel, Restructuring dynamics of surface species in bimetallic nanoparticles probed by modulation excitation spectroscopy. *Nat. Commun.* **15**, 6736 (2024).

23. K. R. G. Lim, M. Aizenberg, J. Aizenberg, Raspberry-colloid-templated catalysts as a versatile and stable thermocatalytic platform. *Acc. Chem. Res.*, In review (2025).

24. K. R. G. Lim, C. J. Owen, S. K. Kaiser, P. K. Routh, M. Mendoza, K.-C. K. Park, T.-S. Kim, S. Garg, J. A. Gardener, L. Russotto, C. R. O'Connor, M. Bijl, M. Aizenberg, C. Reece, J. D. Lee, A. I. Frenkel, B. Kozinsky, J. Aizenberg, Nanoscale wetting controls reactive Pd ensembles in synthesis of dilute PdAu alloy catalysts. *Nat. Commun.* **16**, 6293 (2025).

25. C. M. A. Parlett, M. A. Isaacs, S. K. Beaumont, L. M. Bingham, N. S. Hondow, K. Wilson, A. F. Lee, Spatially orthogonal chemical functionalization of a hierarchical pore network for catalytic cascade reactions. *Nat. Mater.* **15**, 178–182 (2016).

26. M. A. Isaacs, C. M. A. Parlett, N. Robinson, L. J. Durndell, J. C. Manayil, S. K. Beaumont, S. Jiang, N. S. Hondow, A. C. Lamb, D. Jampaiah, M. L. Johns, K. Wilson, A. F. Lee, A spatially orthogonal hierarchically porous acid–base catalyst for cascade and antagonistic reactions. *Nat. Catal.* **3**, 921–931 (2020).

27. M. Retsch, U. Jonas, Hierarchically Structured, Double-Periodic Inverse Composite Opals. *Adv. Funct. Mater.* **23**, 5381–5389 (2013).

28. H. Wu, D. Wang, D. K. Schwartz, Connecting Hindered Transport in Porous Media across Length Scales: From Single-Pore to Macroscopic. *J. Phys. Chem. Lett.* **11**, 8825–8831 (2020).

29. T. Shirman, J. Lattimer, M. Luneau, E. Shirman, C. Reece, M. Aizenberg, R. J. Madix, J. Aizenberg, C. M. Friend, New Architectures for Designed Catalysts: Selective Oxidation using AgAu Nanoparticles on Colloid-Templated Silica. *Chem. Eur. J.* **24**, 1833–1837 (2018).

30. A. Filie, T. Shirman, M. Aizenberg, J. Aizenberg, C. M. Friend, R. J. Madix, The dynamic behavior of dilute metallic alloy Pd_xAu_{1-x}/SiO_2 raspberry colloid templated catalysts under CO oxidation. *Catal. Sci. Technol.* **11**, 4072–4082 (2021).

31. T. Shirman, T. J. Toops, E. Shirman, A. V. Shneidman, S. Liu, K. Gurkin, J. Alvarenga, M. P. Lewandowski, M. Aizenberg, J. Aizenberg, Raspberry colloid-templated approach for the synthesis of palladium-based oxidation catalysts with enhanced hydrothermal stability and low-temperature activity. *Catal. Today* **360**, 241–251 (2021).

32. M. Luneau, T. Shirman, A. C. Foucher, K. Duanmu, D. M. A. Verbart, P. Sautet, E. A. Stach, J. Aizenberg, R. J. Madix, C. M. Friend, Achieving High Selectivity for Alkyne Hydrogenation at High Conversions with Compositionally Optimized PdAu Nanoparticle Catalysts in Raspberry Colloid-Templated SiO_2. *ACS Catal.* **10**, 441–450 (2020).

33. K. R. G. Lim, T. Azizli, S. K. Kaiser, M. Aizenberg, M. M. Montemore, J. Aizenberg, Effects of Pd ensemble size in dilute and single atom alloy PdAu catalysts for one-pot selective hydrogenation and reductive amination. *Catal. Sci. Technol.* **15**, 4179–4193 (2025).

34. M. Luneau, E. Guan, W. Chen, A. C. Foucher, N. Marcella, T. Shirman, D. M. A. Verbart, J. Aizenberg, M. Aizenberg, E. A. Stach, R. J. Madix, A. I. Frenkel, C. M. Friend, Enhancing catalytic performance of dilute metal alloy nanomaterials. *Commun. Chem.* **3**, 46 (2020).