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Foundations and strategies of the construction of hybrid catalysts for optimized performances

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Catalysts are generally classified into three categories: homogeneous, heterogeneous and enzyme, each evolved as an independent field. Efforts to bridge these fields are scarce but desirable. In this Perspective, we first describe how numerous classes of reactions can be achieved by all three categories of catalysts. Examples are given based on a selective survey of the literature. Next, a selection of important approaches, the benefits and challenges of constructing heterogeneous–homogeneous, heterogeneous–enzyme and homogeneous–enzyme hybrid catalysts are discussed based on published researches. Hybrid catalysts not only increase the performance, including activity, selectivity, lifetime and recyclability compared to one of the components, but also offer extra functions such as a microenvironment for different reaction pathways, and cascade catalysis for products that are challenging to produce. We expect future tailor-made hybrid catalysts will combine the advantages of the components and be optimized for industrial applications.

Life would have been very different, if not impossible, without catalysts, as catalysts play vital roles in life-maintaining processes including photosynthesis and metabolism. In the human realm, catalysts have also been utilized for centuries; for example, in production of cheese, bread and wine. Yet, the quest for better catalysts has never ended due to ever-increasing societal demands.

Catalysts are conventionally divided into three categories: homogeneous, heterogeneous and enzyme. Homogeneous catalysts, as the name suggests, operate in the same phase of matter (generally liquid or gas phase) as the reactant(s). Organometallic compounds and metal complexes represent important homogeneous catalysts, along with protons, ions, radicals and other small molecules. Enzyme catalysts refer to proteins: amino-acid-derived biomacromolecules with three-dimensional structures. Enzymes are typically most active in the aqueous phase, and are sometimes considered special versions of homogeneous catalysts. However, the unique chemical complexity and the unparalleled turnover rates distinguish enzymes from homogeneous catalysts. Heterogeneous catalysts reside in a different phase from the reactant(s). They can be outer (or inner) surfaces of dense (or porous) solids, or species attached to these surfaces or other insoluble materials, for example, polymers. Metal crystals, porous materials such as zeolites and metal-organic frameworks (MOFs), supported nanoparticles, and an organometallic compound or an enzyme attached to a surface via covalent bonds all fall into the category of heterogeneous catalysts.

Over time, each category of catalysts developed as independent fields often considered to have little overlap. Differences in reaction conditions, methodologies (synthetic and characterization techniques) and perhaps research focuses, led to the separation of the three fields. Special expressions and jargons served to intensify these differences. For example, the word substrate can have different meanings depending on the field. In homogeneous and enzyme catalysis, a substrate generally refers to the reactant consumed during a catalytic reaction. By contrast, to researchers of heterogeneous catalysis, especially those with a materials science background, the first impression of a substrate is to the material on which the catalyst is supported (for example, a silicon wafer).

Despite their differences, the three categories of catalysts actually share many of the same principles. They all consist of inorganic and/or organic components, and their active components are typically nanometre-sized. Charge, coordination, interatomic distance, bonding and orientation of catalytically active atoms are molecular factors that impact the three fields of catalysis[1]. Even for enzyme catalysts with the highest chemical complexity, their structures show a myriad of functional groups assembled near the substrate(s) binding site(s), with a capacity to participate in acid/base, hydrogen bonding, dipolar, electrostatic and hydrophobic interactions. These types of interactions are also commonly important features of homogeneous or heterogeneous catalysts.

Due to these intrinsic similarities, unsurprisingly, many reactions are accelerated by all three categories of catalysts, which lays the foundations of bridging the gaps of the three fields by examining hybrid catalysts. We will survey the strategies of accomplishing heterogeneous–homogeneous, heterogeneous–enzyme and homogeneous–enzyme hybrid catalysts, and comment on the benefits and challenges of each strategy. Overall, hybrid catalysts can be greater than the sum of their parts in terms of the performances, and may provide a promising method to synthesize elusive end products.

Reactions catalysed by all three categories of catalysts

There are many cases where the three categories of catalysts accelerate the same transformation (Table 1). We will analyse the pros and cons of each category of catalysts on alcohol oxidation and ammonia synthesis. Due to the scope of this perspective, only selective examples in each case are chosen as illustrative.

Alcohol oxidation. Primary alcohols can be oxidized into aldehydes, which can also be easily oxidized further to produce carboxylic acids. Selective formation of aldehydes is a fundamentally important laboratory and commercial procedure. However, when it

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Table 1 | A list of reactions that can be accelerated by three categories of catalysts.

Reaction type	Homogeneous	Heterogeneous	Enzyme
Alcohol dehydration	Concentrated H_2SO_4	Various zeolites[38]	Dehydratase[39]
Aldol reaction	Proline[40]	Chitosan aerogel[41]	Aldolase[42]
Alkene epoxidation	Fe complex[43]	A family of isoreticular chiral MOFs[44]	P450 BM-3 139-3[45]
Alkene hydration	H^+	Acidic zeolite[46]	Phenolic acid decarboxylases[47]
Alkene hydrogenation	Fe complexes[48]	Supported metal clusters[49]	Old Yellow Enzymes[50]
Benzoin condensation	*N*-heterocyclic carbene[51]	Polymer-supported imidazolium salts[52]	Benzaldehyde lyase[53]
Epoxide ring opening	(salen)Co[54]	Chromium complexes bound to silicates[55]	Halohydrin dehalogenase[56]
Esterification	NaOH	Silicates MCM-41[57]	Coenzyme A[58]
Glucose isomerization	Organic Brønsted base[59]	Tin-containing zeolites[60]	Glucopyranose mutarotation[61]
Halogenation	Pd complexes[62]	Pd@MOF nanocomposites[63]	Halogenases[64]
Hydrolysis of esters	Cyclodextrin dimer[65]	MOF UiO-66-NH_2[66]	Candida lipase[67]
Hydrolysis of nitrile to amide	Arene-Ru(II) complexes[68]	Manganese dioxide[69]	Nitrile hydratase[70]
Ketone hydrogenation	Frustrated Lewis pairs[71]	Porous Hybrid Solids[72]	Carbonyl reductases[73]
Methane activation	Ir, Rh and Ru complexes[74]	Silica supported Mn_xO_y-Na_2WO_4 catalysts[75]	Methane monooxygenase[76]
Olefin isomerization	High-spin cobalt(II) complexes[77]	SiO_2-Al_2O_3[78]	Old Yellow Enzyme[79]
Polymerization	Group VIII carbene complex[80]	Immobilized Grubbs' catalyst[13]	Oxidoreductases[81]
Sulfides Oxidation	(salen)Mn(III) complexes[82]	Silica-based tungstate[83]	Peroxidases[84]

An example catalyst is given in each category.

comes to the metabolism of ethanol in human bodies, oxidation of acetaldehyde is desired, as it is a highly toxic substance.

Traditionally, oxidations of alcohols are performed with relatively expensive stoichiometric amounts of toxic heavy-metal inorganic oxidants, notably chromium(VI) reagents. An emerging alternative process is the implementation of a catalyst in combination with molecular oxygen as the oxidant, which is inexpensive, readily available and produces benign by-products (water). A recent review by Parmeggiani and Cardona[2] provides an overview of aerobic oxidations of alcohols by homogeneous and heterogeneous catalysts. Notably, Sheldon and colleagues[3] first reported a water-soluble palladium(II) bathophenanthroline complex, which is a stable catalyst for the selective aerobic oxidation of a wide range of alcohols in water. The reactions were performed at a substrate/catalyst ratio of ~200, pH 11.5, 100 °C, 30-bar air pressure, and the typical initial turnover frequency (TOF) is 10^2 h^{-1}. This system is a breakthrough in homogeneous catalysis, but water solubility of the alcohol is required and the selectivity is not guaranteed in certain cases.

As for heterogeneous alcohol oxidation, Hutchings and coworkers[4] developed Au–Pd/TiO_2 catalysts for solvent-free oxidation of primary alcohols to aldehydes. Typical reaction conditions in this study involved 1 bar pO_2 at 100 °C, with a TOF of alcohols on the order of 10^5 h^{-1}. These catalysts offered high activity and selectivity in general, but could be further optimized for aromatic unsaturated alcohols (for example, vanillyl alcohol and cinnamyl alcohol).

In the case of enzyme-catalysed alcohol oxidation, an alcohol dehydrogenase (ADH), such as horse liver ADH, offers a catalytic efficiency k_{cat} K_M^{-1} of over 10^5 min^{-1} M^{-1} at 25 °C, 1.5 mM NAD^+ and 35 mM ethanol[5]. The enzyme catalyst seems the most active at the mildest condition among the three examples; but stoichiometric amounts of the co-factor NAD^+ are required to carry out the reaction, which presents a challenge for industrial applications. In addition, ADH is highly selective and it does not catalyse the further transformation of acetaldehyde; a second enzyme called aldehyde dehydrogenase (ALDH2) is required for the synthesis of acetic acid. Thus, people having ALDH2 Deficiency (common in Asia) suffer from acetaldehyde accumulation after consuming alcoholic beverages, with facial flushing known as alcohol flush.

Ammonia synthesis. Plants use nitrogen to generate biologically essential compounds, such as amino acids and nucleic acids. Even though N_2 accounts for 78% of the volume of air, the nitrogen triple bond (having a bond strength of 226 kcal mol^{-1}) makes it too inert for most organisms to handle. Most living things can only use 'fixed' nitrogen, for example, chemical compounds such as NO_3^- or NH_4^+. Animals and humans benefit from nitrogen fixation, as they absorb essential amino acids from food. In nature, 90% of the biologically available nitrogen is produced by the enzyme nitrogenase, which is found in some prokaryotic organisms. These plants produce ammonia themselves and provide ammonia to the soil.

The active site of nitrogenase is a metal–sulfur cluster with the stoichiometry [Mo–7Fe–9S–N]. Nitrogenase catalyses the biological ammonia synthesis according to the following reaction scheme: $N_2 + 8H^+ + 8e^- + 16ATP \rightarrow 2NH_3 + H_2 + 16ADP + 16P_i$. This scheme reveals interesting features of the biological ammonia synthesis: (1) protons and electrons are used instead of molecular hydrogen; (2) the activation barrier is overcome by the hydrolysis of adenosine triphosphate (ATP) to adenosine diphosphate (ADP) and inorganic phosphate (P_i), a common means of energy transfer in biology; (3) there is at least one H_2 produced per N_2 consumed[6]. Even though nitrogenase works efficiently under ambient conditions, the growing human population calls for ammonia as an industrial fertilizer.

Haber and Bosch developed an industrial process that produces ammonia from N_2 and H_2 with an alkali-promoted iron catalyst[7]. The Haber–Bosch process has been thoroughly studied and optimized industrially[8]. Considering both thermodynamics and kinetics, high temperatures and pressures are used to ensure high rates and conversion. However, a less energy-intensive process, like one that mimics nitrogenase, is highly desired.

Coordination of N_2 to a homogeneous transition metal complex is sought to achieve nitrogen fixation under mild conditions, but reports of the catalytic reduction of N_2 to NH_3 are limited[9]. Chirik and colleagues[10] reported zirconium complexes that allow direct

N–H bond formation from N_2 and H_2, and subsequent warming of the complex under 1 atmosphere of H_2 at 85 °C gives ammonia in 10–15% yield. Recently, the same group used the nitrogenase's strategy of proton-coupled electron transfer to yield free ammonia electrochemically[11]. However, the turnover number of the system requires further developments for practical applications.

Other examples. A selective list of important reactions catalysed by different catalysts is displayed in Table 1. Acid/base catalysed reactions — for example, the esterification and hydration of alkenes — can be accelerated by homogeneous acids/bases, their heterogeneous counterparts, or the enzymes. Similarly, Pd catalysts in a homogeneous metal complex form or in a heterogeneous nanocomposite form, as well as enzymes, can carry out the halogenation catalysis. All of these examples demonstrate the feasibility of capitalizing hybrid catalysts for these reactions.

Methods and the pros and cons of constructing hybrids

Many reactions can be achieved by all three categories of catalysts, although each catalyst has its own advantages within a limited scope. As most catalysts are nanometre-sized (Fig. 1) and share the same principles, hybrid catalysts that combine the advantages, or compliment the effective scopes of the components are highly desirable. Thanks to the rapid development in nanocatalyst synthesis, as well as advancements in characterization techniques, the field has matured enough for the study of hybrid catalysts. The essential components of hybrid catalysts can be controlled synthetically, investigated in various reaction conditions, and optimized to obtain the maximum catalytic performance, especially turnover rate and product selectivity. The versatile characterization techniques reveal the chemical reasons for unusual catalytic activity and/or selectivity, which in return guide the fabrication of next-generation catalysts focusing on these key chemical features with the aid of nanotechnology. General approaches of hybrid catalysts are discussed below with selective references. All these approaches are illustrated in Fig. 2.

Heterogeneous–homogeneous hybrids. Heterogeneous–homogeneous hybrid catalysts are also known as heterogenized homogeneous catalysts or immobilized molecular catalysts[12]. The goals, and ultimately the advantages of such catalysts are environmentally friendly chemical production due to long-term stability of the catalysts in storage and operation conditions; possible use in continuous, fixed-bed operations; facile product separation; reduced waste and contamination; and the reuse of the catalysts. However, a key challenge is the preservation of the intrinsic high activity and selectivity of the homogeneous components during the immobilization processes, which may change the chemical and electronic structure of the catalytic centres. In addition to the molecular composition, properties originated from the heterogeneity including the particle size, morphology, surface area, hydrophobicity/ hydrophilicity, density of active sites and mass transfer limitations require judicious optimization. Another challenge is the development of robust immobilization methods that prevents the leaching of active components, for example, metals, in harsh reaction conditions.

Covalently tethering homogeneous catalysts to insoluble supports with a linker (Fig. 2ai) has been the most widely investigated method of constructing heterogeneous–homogeneous hybrids so far. Surface functional groups (for example, silanol groups of silica or phosphino groups of polymer resins) are bonded to one end of a linker (tether), whose other end is bonded to the metal centre[13]. The research focus has been shifted away from maintaining the reactivity of the metal complexes to the synergistic effects, including the nanoconfinement (that is, confinement within the nanostructure) effects and multifunctional surfaces[14]. A second approach is the grafting or chemisorption, also known as surface organometallic chemistry (Fig. 2aii), in which organometallic compounds are directly grafted on solid materials; for example, silica and alumina[15]. Instead of using a flexible tether, the surface serves as a conformationally rigid ligand of the metal complex[16]. Sterically unsaturated metal centres, distorted coordination geometry, and the electronic effects of the support may result in unforeseen high activity[17]. A third approach is entrapment of the metal complexes physically in a host material (Fig. 2aiii). The chemical structure of the metal complex is intact in this ship-in-a-bottle assembly[18], while the nanoconfinement effects due to intrinsic charge density, acid/base property and/or shape selectivity of the host may lead to desired activity and selectivity. Suitable host materials include zeolites[18], sol-gel[19], polymers, supramolecular complexes[20] and MOFs[21]. Another approach is metal–organic assembled homogeneous catalysts (Fig. 2aiv), where the catalytically active metal complex simultaneously constitutes the support; for example, MOFs, matrix-embedded catalysts. Reaction chambers with precise physical and chemical environment can be achieved via the extensive tunability of MOFs[22].

In addition to these approaches, we developed supported dendrimer-encapsulated metal clusters (DEMCs) using concepts similar to the grafting and entrapment methods. Forty-atom metal clusters are prepared using dendrimer as a stabilizing and capping agent, and loaded into mesoporous silica to form supported dendrimer-encapsulated metal clusters (DEMCs). The metals can be oxidized (for example, with $PhICl_2$) or reduced (for example, with H_2) in situ. These solid catalysts were employed to accomplish selective transformations that had been challenging to achieve in a heterogeneous condition (for example, π-bond activation and aldol reactions) (Fig. 1, the yellow region). Critically, the heterogeneity and stability against leaching of supported DEMCs were verified by three-phase tests, hot filtration and other indirect evidence. Moreover, we have demonstrated that supported DEMCs are also outstanding catalysts for typical heterogeneous reactions, including hydrogenation and alkane isomerization. Supported DEMCs as heterogeneous–homogeneous hybrid catalysts offer additional benefits: (1) similar or better reactivity compared to homogeneous catalysts; and (2) unique heterogeneous means of catalyst optimization for product selectivity[23].

Heterogeneous–enzyme hybrids. Heterogeneous–enzyme hybrid catalysts have been applied in the industrial production of chemicals[24,25]. They share many common approaches, benefits and challenges as the heterogeneous–homogeneous ones. An additional motivation of enzyme immobilization is for the optimum performance in non-aqueous media[26]. Traditionally, enzymes are lyophilized or freeze-dried as powders for use in organic solvents, but they often aggregate or denature during the lyophilization process. However, immobilized enzymes commonly maintain the enzyme structure for access of reactants and against deactivation. Besides, immobilization of otherwise incompatible enzymes (for example, due to mutual inhibition) allows for cascade reactions. Challenges specific to the immobilization of enzymes compared to metal complexes generally include the production of by-products during pH adjustment, and the mechanical strength and filterability for industrial scales.

General approaches of achieving heterogeneous–enzyme hybrids are support-bound enzymes[27], entrapment, and support-free cross-linking[24]. Support-bound enzymes consist of enzymes adsorped onto a support or covalently attached to a support (Fig. 2bi/ii). The adsorption of enzymes onto solid supports is spontaneous thanks to van der Waals, ionic and chelating interactions with the support. Thus, a hybrid catalyst can be obtained by simply mixing an enzyme with a proper support; for example, natural or synthetic polymers, hydrogels, minerals and ceramics. The retention of the enzyme on the support depends on the number and strength of physicochemical interactions. The major drawback of this simple adsorption approach is the detachment of the enzyme in changing working

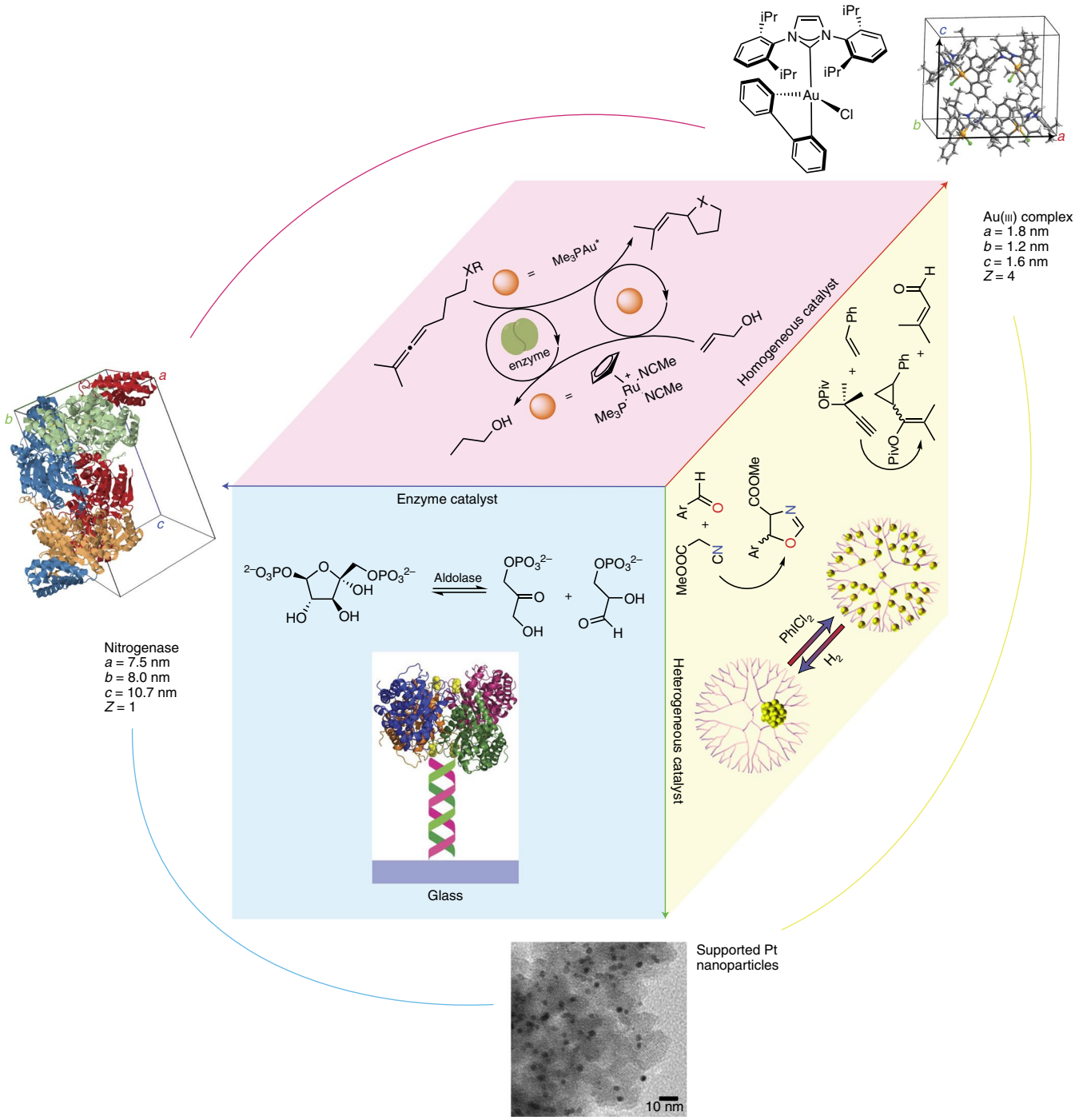

Fig. 1 | Schematic of a catalyst space with highlights on the hybrid catalysts. One example is provided at the end of the axes of homogeneous (red), heterogeneous (green) and enzyme (blue) catalysts. The unit cell dimensions (*a*, *b*, and *c*) and the scale bar show the size of the catalysts, and the value of *Z* denotes the number of chemical formula units per unit cell. The crystal structures of the Au(III) complex and the nitrogenase were from Toste et al.[85] and Sippel and Einsle[86], respectively. The three cases of hybrid catalysts along with the corresponding catalytic reactions are discussed in the text. Briefly, an example of heterogeneous–homogeneous hybrid catalyst (yellow) is supported dendrimer-encapsulated metal clusters, which can work as either traditional heterogeneous or homogeneous catalysts[23]. An aldolase enzyme immobilized on glass surfaces represent an example of heterogeneous–enzyme hybrid catalyst (cyan), and it maintains its activity toward an aldol reaction[30]. Homogeneous host–guest complexes and enzymes are compatible and are used for cascade transformations (pink)[37]. Scale bar, 10 nm. Cartoon depiction of the enzyme in the pink region is adapted from ref. [37], Macmillan publishers Ltd; cartoon depiction of the enzyme in the yellow region is adapted from ref. [23], American Chemical Society; cartoon depiction of the enzyme in the cyan region is adapted from ref. [30], American Chemical Society; the structures pointed by the red and blue arrows are adapted from refs [85,86], respectively; Macmillan Publishers Ltd.

conditions; for example, pH, reactant and product concentrations. Enzymes can be bound covalently to most supports suitable for adsorption. However, supports with proper spacing of functional groups are desired for stable links and high reactivity. The ε-amino group of lysine residues are the common target of covalent linkage, but these residues may participate in catalysis, so the downside of

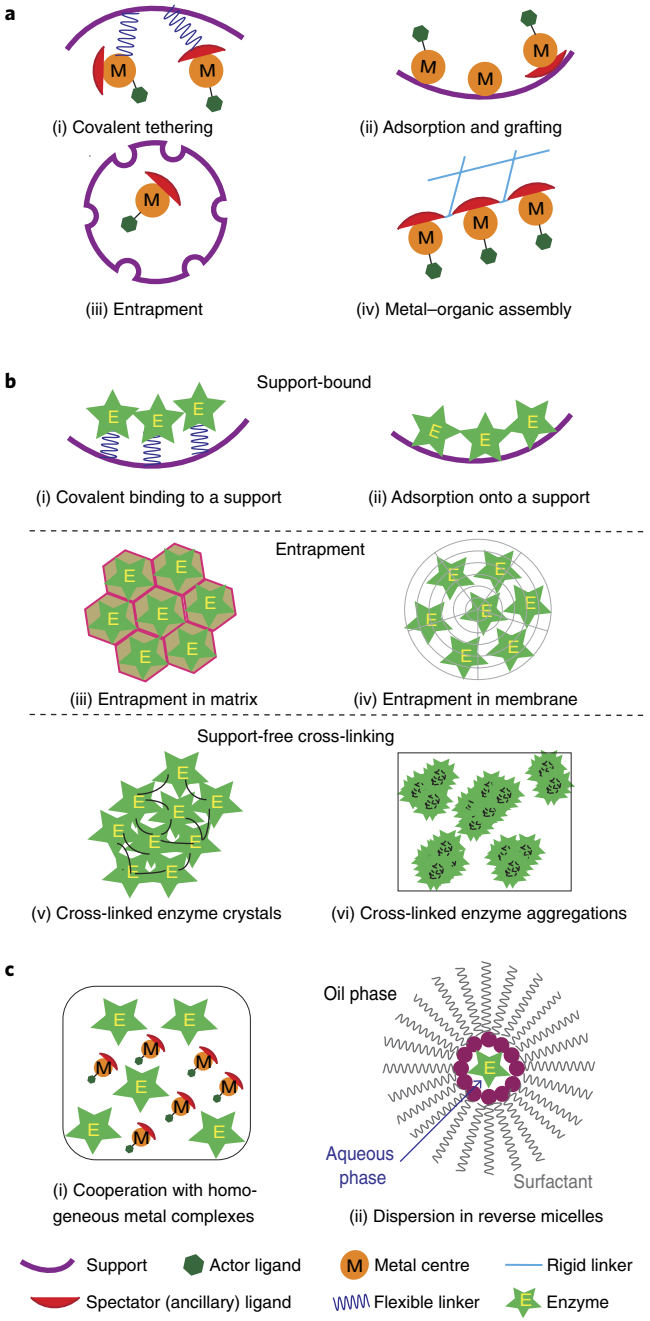

Fig. 2 | Illustrations of existing approaches to construct hybrid catalysts. **a**, Heterogeneous–homogeneous hybrids. **b**, Heterogeneous–enzyme hybrids. **c**, Homogeneous–enzyme hybrids.

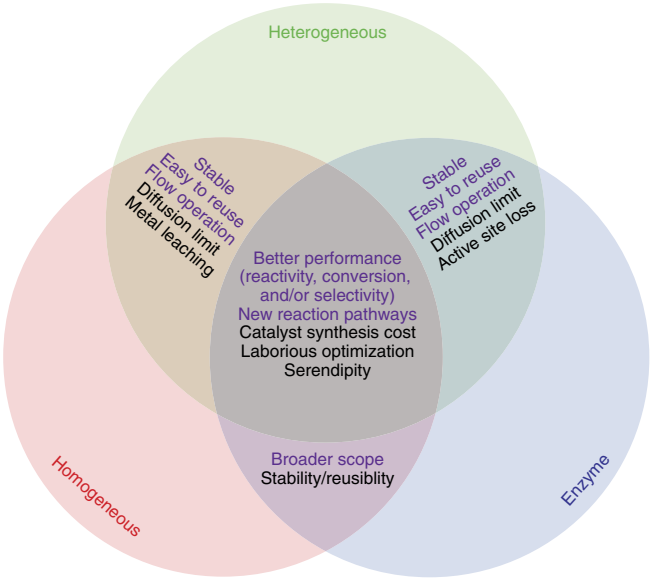

Fig. 3 | A summary of general advantages and challenges of hybrid catalysts. The information regarding specific pairs of hybrid catalysts or the general strategy is given in the corresponding overlapped region.

covalent attachment is the low residual activity after modifications of the residuals in the active sites. Similar to heterogeneous–homogeneous hybrids, enzymes can be immobilized by entrapment in a matrix or semi-permeable membranes (Fig. 2biii/iv). The structure and activity of enzymes are well maintained, but the potential leaching of enzymes requires attention. Encapsulation of enzymes in a matrix (for example, polymer network, silica or MOFs) can be accomplished by synthesizing the matrix in the presence of the enzymes. Similarly, enzymes can be embedded in semi-permeable membranes. A larger pore size of the membrane facilitates the transfer of reactants and products over the membrane but reduces the retention of the enzyme, so the choice of pore sizes is a challenge. Unique properties of enzymes allow for additional methods of enzyme immobilization, namely, support-free cross-linking (Fig. 2bv/vi), which offers highly concentrated enzyme activity, high stability and lower production costs by excluding additional supports. Covalent cross-linking of crystalline enzymes — often using bifunctional cross-linkers that react with the ε-amino group of lysine residues — generates cross-linked enzyme crystals (CLECs) 1 to 100 μm in size, which are much more stable against denaturation by heat, organic solvents and proteolysis than the original enzyme[28]. However, challenges of CLECs include costly extensive protein purification for crystallization of crystallizable enzymes and the limit of one enzyme type in the crystal. A similar but less expensive method is first precipitating the enzymes (for example, by adding salts) and subsequent crosslinking these physical aggregates[29]. The resultant materials are named cross-linked enzyme aggregates (CLEAs) of 50–100 μm in diameter. CLEAs have shown tremendous potentials as immobilized enzymes, yet it may require physical supports to increase rigidity for some applications.

As an illustrative example of the support-bound enzyme approach, we recently immobilized aldolase enzymes onto glass slides via DNA-directed immobilization to achieve heterogeneous–enzyme hybrid catalysts[30]. Briefly, a single-strand DNA is attached to a functionalized glass slide, then the complementary DNA strand is site-selectively attached to the *N*-terminus of the enzyme, resulting in the oriented arrangement of aldolase on the glass surface. Fluorescence and atomic force microscopy studies verified the validity of each step. Activity assays were conducted on the surfaces with DNA-linked aldolase to validate that the hybrid catalyst was able to retain its catalytic activity to an aldol reaction (Fig. 1, the cyan region) and the surfaces were reusable in subsequent cycles. This hybrid catalyst also allows for the modulation of surface coverage levels by varying annealing temperatures, which also affects the recyclability of the single-stranded DNA modified surfaces.

Interestingly, published works show enzyme immobilization can modify product selectivity. The enantioselectivity is shifted from >99% e.e. (*S*) when the enzyme CaL-B lipase is hydrophobically bound on one support to 95% (*R*) on another support for the hydrolysis of racemic 2-*O*-butyryl-2-phenylacetic acid[31]. Such modulation of enantioselectivity is highly desirable for the production of pharmaceutical or other fine chemicals[32].

Homogeneous–enzyme hybrids. Unlike the previous two scenarios, fewer published works specify the concept of homogeneous–enzyme hybrids[33–35]. Practical applications of dispersed enzymes usually require specific conditions compared to common homogeneous catalysts, for example, absence of noble metals and operations in an aqueous medium. Here, we define homogeneous–enzyme hybrids as systems where dispersed enzymes show acceptable activity outside these specific conditions. As such, enzymes can be used in broader reaction environments and achieve a larger synthetic scope. Two approaches are discussed in this sense. One is the compatible application of an enzyme and a noble metal complex (Fig. 2ci). Metal complexes of noble metals, for example, Au and Ru, are important homogeneous catalysts, but these metals can bind amino-acid residues of the enzymes and may undermine their activity. The collaboration of a homogeneous catalyst and an enzyme to catalyse reactions can significantly broaden the reaction scope. Supramolecular encapsulation of organometallic complexes may prevent their diffusion into the bulk solution, allowing for the simultaneous use of a complex and an enzyme in a cascade reaction. So far, this method is preliminary for general applications. Another approach is to carry out enzyme catalysis in reverse micelles (Fig. 2cii), namely, reverse water-in-oil (W/O) microemulsion[36]. This approach enables efficient enzyme catalysis in organic solvents, thus gaining access to water-insoluble but organic solvent soluble reactants. Compared to a single oil as the solvent, reverse micelles can disperse enzymes with a large interfacial area, and reduced deactivation thanks to the protection of the interfacial membrane. The challenge of this approach is the selection and costs of the surfactant for a given application.

Catalytic cascade reactions were achieved that involve esterases, lipases or alcohol dehydrogenases and Au(I) or Ru(II) complexes encapsulated in a Ga_4L_6 tetrahedral supramolecular cluster[37]. The host–guest complexes are compatible with the enzymes, and the Au(I) host–guest complex even shows enhanced reactivity compared to the free cationic guest (Fig. 1, the purple region). These observations suggest that encapsulation of reactive complexes may offer a general strategy for developing homogeneous–enzyme hybrid catalysts for carrying out organic reactions that are otherwise challenging to access.

Summary and outlook

Potential advantages of hybrid catalysts include better performance and new reaction pathways (Fig. 3). However, the goals of high reactivity, 100% product selectivity, high stability and recyclability, and low production costs remain desired. Much still has to be learned in order to obtain a good balance of these goals. Unfortunately, many of the existing successful examples of hybrid catalysts are accomplished via serendipity or laborious screening of materials and reaction conditions due to the lack of general design principles, which are urgently needed.

In our experience, collaborations between laboratories with experience in different fields of catalysis will greatly facilitate the development of hybrid catalysts. Effective discussion and facility sharing will enable researchers in one field (for example, heterogeneous catalysis) to understand and perform the synthesis and characterization that are particular to another field (for example, enzyme production), and thus lower the barrier for one another toward preparing or understanding the hybrid catalysts for a given application. We envision that with the aid of high throughput screening, machine learning and artificial intelligence, a database can be built to generalize the design principles. Then, such tailor-made hybrid catalysts can combine the advantages of their components by tuning the governing catalytic components and molecular factors, and allow for products that are unavailable to the components via new reaction channels.

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Competing interests
The authors declare no competing interests.

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