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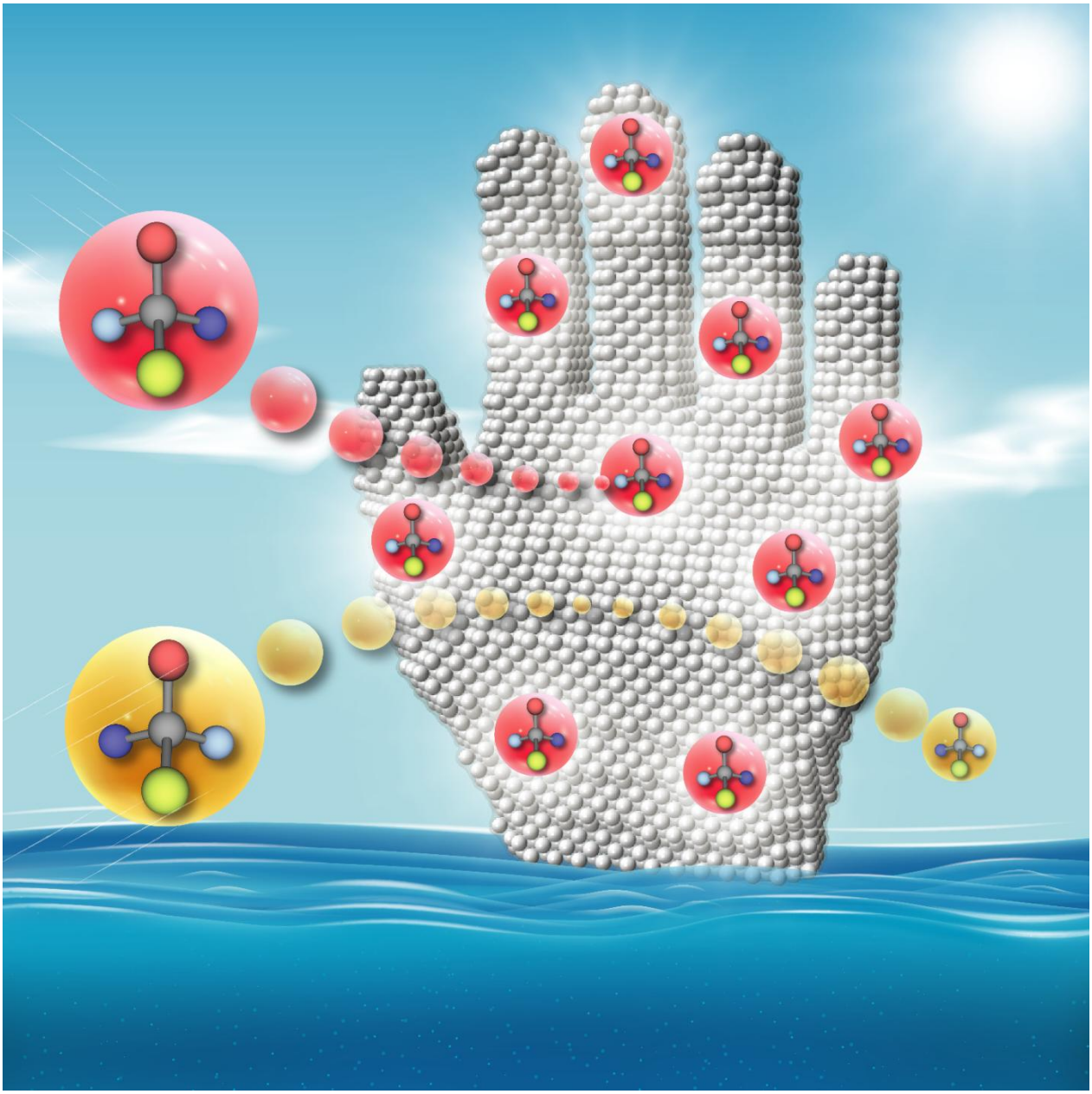
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Encoding chiral molecular information in metal structures

Chularat Wattanakit,[b] and Alexander Kuhn*[a]



The hand, made out of metal atoms symbolizes chiral features generated in or on metal structures, enabeling a differentiation between two enantiomers. The minireview illustrates some of the recent developpments in this increasingly popular field of research, including applications for enantioselective analysis, separation and synthesis.

Abstract: The concept of encoding molecular information in bulk metals has been proposed over the past decade. The structure of various types of molecules has been imprinted, including also enantiomers. Typically, to encode metals with chiral information, several approaches, based on chemical and electrochemical concepts, can be used. In this minireview we discuss recent achievements with respect to the development of such materials, including the entrapment of chiral biomolecules in metals, the chiral imprinting of metals, as well as the combination of imprinting with nanostructuring. The features and potential applications of these designer materials, such as chirooptical properties, enantioselective adsorption and separation as well as their use for asymmetric synthesis will be presented. This will illustrate that the development of molecularly encoded metal structures opens up very interesting perspectives, especially in the frame of chiral technologies.

1. Introduction

Encoding molecular information in solid matrices such as (conducting) polymers or silica has been already proposed several decades ago. Especially so-called molecular imprinted polymers (MIPs) have been studied in much detail and used for a large variety of applications from sensing to separation and catalysis[1]. However, there are some limitations of using MIPs, for example due to their flexible structure, leading to difficulties with respect to the retention of the molecular information after removal of the templates[2].

Molecular imprinted materials with chiral structures have been proposed for many potential applications, ranging from separation[3] and analysis[4], to pharmaceutical[5] and catalytic tasks[6]. Apart from the design of the above-mentioned MIPs, the encoding of molecular structures in metals has been proposed as an interesting alternative in recent years. In particular, the molecular imprinting of chiral information in metals has been studied because it can mimic biologically active sites[7]. In general the synthesis of metal structures bearing chiral features can be explored using the following five approaches: (i) adsorption of chiral molecules on metal surfaces[8]; (ii) binding or grafting of chiral ligands on a metal surface[9]; (iii) controlled breaking of the structure of a bulk metal crystal to generate chiral surfaces[10]; (iv) distortion of symmetric metal structures[11]; (v) molecular imprinting using chiral molecules as templates[7b, 12].

Generally, the introduction of chirality on metal surfaces by the adsorption approach can be achieved using either chiral/achiral molecules adsorbed on achiral surfaces[13] and chiral molecules adsorbed on achiral/chiral surfaces[8d, 14]. For example, chiral information has been generated by the adsorption of an achiral molecule on an achiral surface due to a break of symmetry in the adsorption process[13, 15]. However, this approach has limitations due to the loss of chiral information by leaching of the adsorbed molecules[16]. To improve the interaction of adsorbed species and metal surfaces, surface grafting or surface modification with chiral ligands has been proposed, for example to design chiral metal nanoparticles, namely chiral-ligand-modified metal NPs[17].

Apart from changing metal surface properties by adsorption and grafting with specific molecules, the generation of high Miller index metal surfaces by cutting along a specific crystal plane can lead to intrinsically chiral surfaces, such as Cu{531}[18] or Pt{643}[10]. In addition, the distortion of metal structures is also able to generate chirality[11]. Thiol induced passivation of gold clusters generates chiral information on gold surfaces, which is even more pronounced when using a moderate size of gold clusters[11].

To encode chiral information in metals, imprinting with chiral molecules as template is one of the most promising strategies to create and retain chiral structures or chiral imprinted cavities inside bulk metal even after removable of templates[7b, 19]. The designed materials exhibit original

properties, in particular with respect to the enantioselective recognition of chiral compounds[19]. In addition to chiral imprinting of bulk materials, in recent years the design of chiral imprinted metals in combination with mesoporous features has been proposed to generate advanced materials that combine both properties in a synergistic way.[12a-c, 20]. The obtained materials exhibit improved chiral recognition features due to the high active surface area of the mesopore walls which are imprinted with chiral information[12a].

In this minireview, several synthesis approaches will be discussed based on chemical and electrochemical concepts. In addition, the properties and applications of the designed materials such as chirooptical features, electrochemical behavior, and chemical peculiarities will be presented.



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2. Synthesis of encoded metal structures

The above-mentioned encoded metal structures can be elaborated by several synthetic pathways, including chemical and electrochemical synthesis:

2.1. Chemical Synthesis

One of the methods to design chiral metal materials is based on the modification of metal nanoparticle surfaces with molecular ligands. [21]. In brief, such materials have been obtained by the chemical reduction of precursor metal-ligand complexes such as Au2X2(BINAP), where BINAP is the

bidentate phosphine ligand 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl[21b]. Therefore, the resulting metal nanoclusters are stabilized by organic ligands. To introduce chiral information on the metal nanoparticles, three main organic ligands/macromolecules have been used including phosphine ligands, thiolate ligands, and DNA[21e].

Another possibility to introduce chiral information in metals is based on the imprinting approach. To design such materials, several metals such as Pd, Au, Pt, Ag, Cu, and Ga with the entrapped molecular structures have been reported and obtained by a chemical synthesis approach[7b, 22]. For example, imprinted metal/organics hybrid materials have been successfully prepared at room temperature using a chemical reduction in the presence of the organic molecule as a template to be entrapped within the metal matrix[22a-c]. Several chiral metal structures have been obtained in this way[18, 22g, 23], retaining the chiral information even after removal of the template[7b]. Metals such as Ag, Au, and Pd nanoparticles have been imprinted with small organic molecules, for example from the alkaloid family, using the chemical reduction of metal precursors in the presence of the chiral alkaloid molecule to generate a specific spatial configuration of the metal atoms. Interestingly, the chiral information of such materials is also retained in this case after removal of the template.

In order to integrate the benefits of mesoporous features, mesoporous bimetallic core-shell Pd@Pt nanoparticles have also been successfully synthesized by the chemical reduction route. Typically, the metal precursors were mixed with ascorbic acid (AA) together with Pluronic F127 as mesoporogen to control the mesoporous structure. Subsequently, a chiral template, 3,4-dihydroxyphenylalanine (DOPA), was added to the solution to create chiral imprinted sites in the Pt shell. Most importantly, the designed materials exhibit not only a very high surface area without the problem of aggregation, as it is often encountered for metal nanoparticles, but also have a high potential for the enantioselective recognition of the corresponding chiral compounds[24].

In addition to molecular encoded metal nanoparticles, the elaboration of thin conductive metal films such as Au and Ag by using an electroless molecular doping process, has also been demonstrated[25]. Such materials exhibit a dual functionality, combining the conductivity of metals and the functionality of the molecular templates[25].

Recently, a new concept has proposed the transfer of chirality from chiral silica to metal nanoparticles This approach comprises two main steps: (i) entrapping of metal precursors of Au and Au in chiral silica bundles containing poly(ethyleneimine); (ii) the reduction of the metal ions inside the chiral silica to metal particles. Interestingly, the resulting metal nanoparticles have a defined distortion of the atomic arrangement in their crystal lattice structures compared to the one synthesized by using achiral silica bundles[26]. This opens up interesting perspectives to design chiral metal nanoparticles using a chemical reduction process, but without adding asymmetric organic molecules, as it is often the case. Therefore, such an approach might be more versatile, as the chiral information is solely based on the local arrangement of the metal atoms and does not depend on the presence of a specific organic compound.

2.2. Electrochemical Synthesis

In order to extend the range of potential applications of chiral metals and metal oxides, such materials have been also successfully produced by using electrochemical methods[27]. Chiral encoded cavities on metals and metal oxides, have been successfully generated in CuO films deposited onto several achiral metal surfaces, for example, Au(001)[7c, 28] and Cu(111)[19, 28-29] using tartrate enantiomers as chiral templates. The stereochemical information is maintained in the CuO film even after the removable of the chiral molecules. It was found that CuO films imprinted with L-tartaric acid and D-tartaric acid show opposite configuration, having a $(1\bar{1}1)$ orientation with

an enantiomeric excess of 95% in the first case, and the latter one exhibiting a ($\bar{1}11$) orientation with an enantiomeric excess of 93%[28]. This was the first example demonstrating the possibility of creating a chiral metal oxide surface in the presence of a chiral organic molecule. In addition to the CuO film imprinted with tartaric acid, there are several other chiral templates such as malic acid that can also be used as molecules to generate chiral information in CuO films[30].

A chiral CuO film could equally be obtained by a chiral etching process[31]. In this case, the non-imprinted CuO film is electrodeposited from an aqueous solution of $CuSO_4$ in the presence of the achiral amino acid glycine. As expected, the obtained electrodeposited film does not show any evidence of enantioselectivity for the electrochemical oxidation of tartrate enantiomers. Interestingly, when the film was etched in L-(+)-tartaric acid, it showed a preferential oxidation of L-enantiomer and vice versa for the D-enantiomer when using a film etched in D-(−)-tartaric acid[31b].

Apart from this etching approach, the introduction of chiral information on metal surfaces is also possible by using other electrochemical techniques. It is well known that the surfaces of achiral materials also show chirality if they have a lack of mirror symmetry, such as the high index faces of face-centered-cubic (fcc) metals like Au. The (643) and ($\bar{6}43$) surfaces of Au are non-superimposable mirror image forms of each other and they have been successfully deposited on Si(643) wafers by electrochemically epitaxial growth of Au on the wafers. Interestingly, two enantiomeric configurations of Au(643) and Au($\bar{6}43$) are deposited on the different sides of the wafer and lead to chiral surfaces. In addition, other metal films such as Pt, Ni, Cu and Au can also be electrodeposited on the Au films and result in asymmetric surface structures. This concept is very promising for producing chiral surfaces made out of a wide range of materials on the silicon wafers[32].

In order to enhance the chiral character of metal surfaces, it has been recently demonstrated that the combination of encoding molecular structures and mesoporous features has distinct advantages, such as a significantly improved enantioselectivity due to an extremely high active surface area.[12a, 24] Chiral imprinted Pt combining chiral information and mesoporosity has been successfully obtained by electrodeposition of metals in the presence of self-assembled lyotropic liquid crystals surfactants[33] and chiral molecules as shown in Figure 1[12a]. The mesoporous structure has been induced by the surfactant's hexagonal columnar structure (H1 phase) in which the hydrophilic parts are located at the outer surface of the liquid crystal columns, resulting in the formation of a hexagonal lattice[33]. The interaction between the hydrophilic part of the surfactant and the chiral template allows orientating the chiral molecules on the surface of the columnar surfactant (a). Subsequently, the Pt structure is produced by electroreduction of a Pt salt around the chiral template and the columnar surfactant (b). Finally, the chiral imprinted cavities together with mesoporous channels are revealed after dissolution of the template molecules (c)[12a]. This new concept has been successfully applied to various types of chiral imprinted cavities using several chiral template molecules including 3,4-dihydroxyphenylalanine (DOPA)[12a], mandelic acid (MA)[12c], phenyl ethanol (PE)[20a], and tryptophan enantiomers[20b].

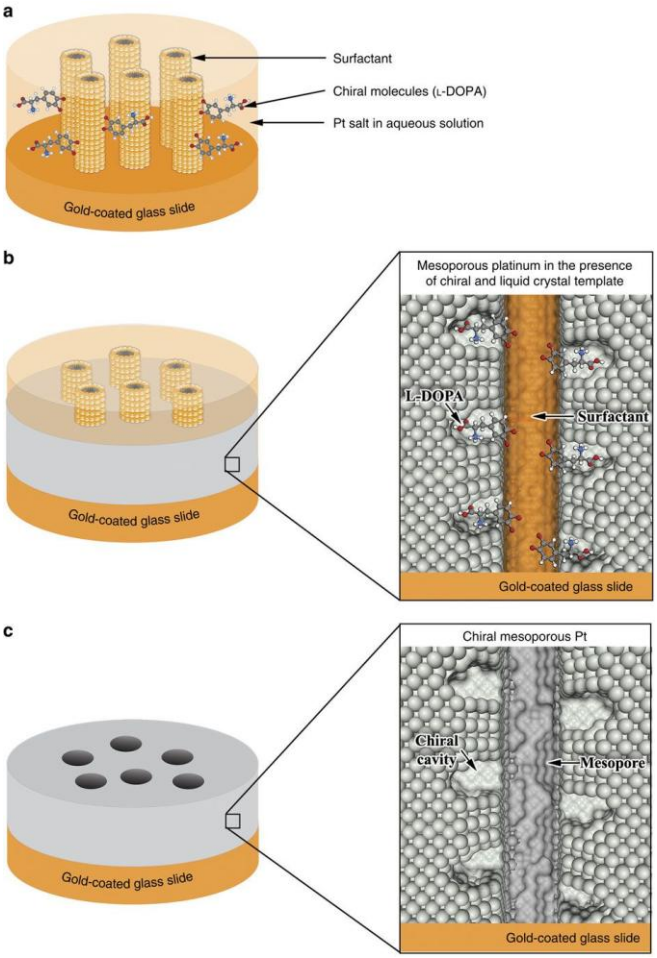


Figure 1. Schematic illustration of the preparation process of chiral imprinted mesoporous platinum in the presence of a surfactant based self-assembled lyotropic liquid crystal and chiral molecules (a) self-assembly of the lyotropic liquid crystal and the chiral template molecules; (b) electroreduction of platinum ions around the templates at a constant applied negative potential; (c) template dissolution. Reproduced with permission from Ref[12a]. Copyright (2014) Springer Nature Group.

3. Properties and Applications

As stated above, there are several types of chiral metals and metal oxides that have been successfully obtained by both chemical and electrochemical techniques. Up to date, such designer materials have been tested for various potential applications ranging from analytical chemistry and chiroptic measurements to chemical/electrochemical synthesis and separation science because they provide outstanding properties as explained in more detail below:

3.1. Optical properties

It is well-known that chiral materials are optically active because each enantiomer rotates the plane of polarized light either in a clockwise or counter-clockwise direction depending on its configuration. Several chiral metals exhibit chiroptical behaviours. There are reports describing the chiroptical behavior and circular dichroism (CD) signals generated by chiral ligand-protected metal nanoparticles. This not only reveals the existence of novel optically active materials, but also provides information of chirality effects at the nanoscale[21e].

As -mentioned above, chiral organically doped metals, such as Au, Ag, and Pd have been studied in great detail. For photoelectron emission spectroscopy, the energy distribution profiles of

the electrons, ejected by either counter-clockwise circularly polarized light (ccw-CPL) or clockwise CPL (cw-CPL) circularly polarized light, reveal a different emission yield when comparing both cases as shown in Figure 2.[7b, 18] This reflects the different diastereomeric interactions between light and the respective metal structures. Interestingly, even after the extraction of the dopant, a different photoelectron emission yield for ccw-CPL and cw-CPL can be observed. Indeed, the electron energy distribution profiles of the 'empty' metal shows the opposite trend with respect to the corresponding organically doped metals. In contrast, the non-imprinted metal exhibits insignificant variations of the photoelectron emission yield for ccw-CPL and cw-CPL[7b, 18, 22i]. This constitutes a strong evidence for an intrinsically chiral structure of the metal.

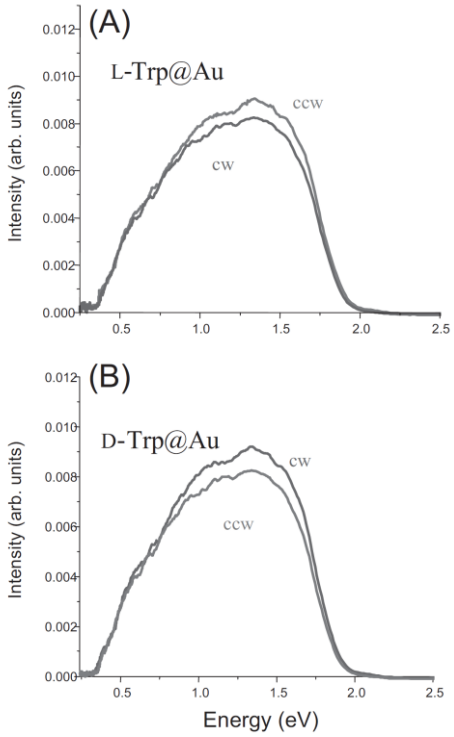


Figure 2. Illustration of the electron energy distribution profiles of photoelectrons ejected by ccw-CPL and cw-CPL on gold embedded with tryptophan enantiomers: A) L-Trp@Au and B) D-Trp@Au. Reproduced with permission from Ref[18]. Copyright (2007) WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

3.2. Electrochemical behaviour

Apart from their optical behaviour, enantiomers have identical physical and chemical properties. However, they often exhibit different features when looking at biological activity. This is due to the fact that biological receptors are mostly themselves chiral. The above discussed chiral metal structures can be considered as an artificial equivalent of a biological receptor. Their interaction with a chiral molecule should therefore allow discrimination between two enantiomers. Electrochemical techniques have been often used to study this aspect. There are several options to demonstrate enantioselective behaviour by electrochemical concepts as explained in detail below.

3.2.1. Chiral recognition at metal and metal oxides surfaces

Chiral recognition on solid surfaces is an important aspect in a pharmaceutical or biological context. Over the last decades, tremendous efforts have been made with respect to the development of chiral recognition technologies and electrochemistry offers an easy readout of such information. At the early stage of development, self-assembled monolayers (SAM) of chiral/achiral compounds on achiral/chiral electrode surfaces have been extensively studied due to the versatility of chemical functionalities which can lead to chiral surfaces[34].

Apart from molecular assemblies at electrode surfaces, intrinsically chiral metal surfaces have also played an important role in the chiral recognition [7c, 19, 28] when combined with an electrochemical readout[10a]. For example, the above-mentioned chiral surfaces produced by electrodeposition of CuO films in the presence of tartrate molecules clearly show chiral recognition in linear sweep voltammetry experiments. A CuO film encoded with (S,S)-tartrate preferentially reacts with (S,S)-tartrate compared to (R,R)-tartrate and vice versa for the (R-R)-tartrate imprinted surface[7c, 19, 28]. Cyclic voltammetry (CV) also allows investigating the chiral recognition of tartrate enantiomers at chiral CuO film obtained by etching with tartrate enantiomers as mentioned above (Figure 3)[31a].

In addition, several epitaxial metal films such as Pt, Ni, Cu and Ag that have been electrodeposited on chiral Au supported on Si wafers, as stated above, also show very promising results with respect to the enantioselective oxidation of D- and L-glucose[32]. For example, silver electrodeposited on a Au/Si(643) surface is more active for the oxidation of D-glucose compared to L-glucose and vice versa for Ag electrodeposited on Au/Si(643) as shown in Figure 4[32].

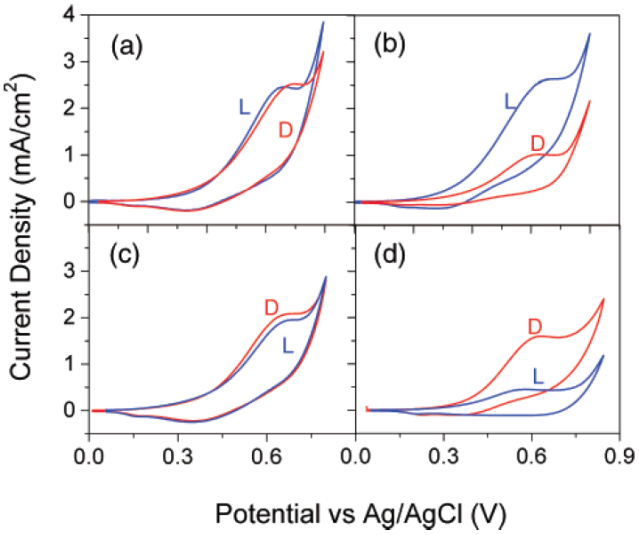


Figure 3. Illustration of the chiral recognition of tartrate ions by electrooxidation on imprinted CuO films obtained by etching with tartrate enantiomers. Cyclic voltammetry (CV) measurements in L(+)-tartrate (blue) and D(-) tartrate (red) in 1.0 M NaOH: (a) as-deposited CuO from L(+)-tartrate; (b) same film after etching in L(+)-tartaric acid; (c) as deposited CuO film from D(-)-tartrate; (d) same film after etching in D-(-)-tartaric acid. Reproduced with permission from Ref[31a]. Copyright (2007) American Chemical Society.

The beneficial effect of combining chirality with mesoporous features of the metal surfaces leads to a very significant enhancement of recognition efficiency. The enantioselectivity of molecular imprinted mesoporous platinum has been examined by using differential pulse voltammetry (DPV). A very different behaviour is observed when using mesoporous metal films imprinted with one or the other enantiomer, even after removal of the chiral templates. It was found that the chiral mesoporous platinum film imprinted with D-DOPA is much more active for the electrooxidation of D-DOPA and

vice versa for the one imprinted with the L-enantiomer. In order to confirm the presence of imprinted chiral information, the Pt electrode initially imprinted with L-DOPA was scanned in the potential range of -0.2 V to 1.25 V (vs Ag/AgCl) in 0.5 M H2SO4, resulting in the complete destruction of the chiral information due to an oxidation of the Pt surface atoms (Figure 5)[12a]. This concept can be considered as a general approach, because it can be adapted to create various chiral cavities using different templates[12b, c, 20a].

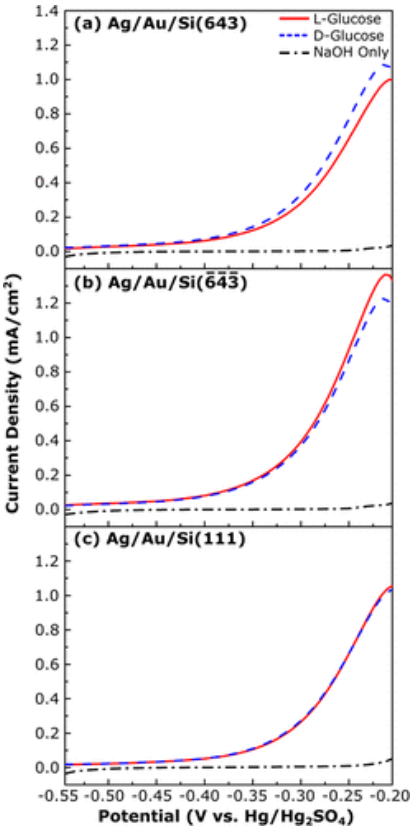


Figure 4. Illustration of chiral recognition for the electrooxidation of D- and L-glucose on (a) Ag electrodeposited on a Au/Si(643) surface (Ag/Au/Si(643)); (b) Ag electrodeposited on Au/ Si(6̄4̄3̄) (Ag/Au/Si(6̄4̄3̄)); (c) Ag electrodeposited on Si(111) (Ag/Au/Si(111)). Reproduced with permission from Ref[32]. Copyright (2018) American Chemical Society.

Apart from using molecular encoded metal structures prepared by electrodeposition, the previously discussed mesoporous bimetallic core-shell Pd@Pt nanoparticles imprinted with DOPA enantiomers allow also a differentiated electrochemical detection of the DOPA stereoisomers as shown in Figure 6[24].

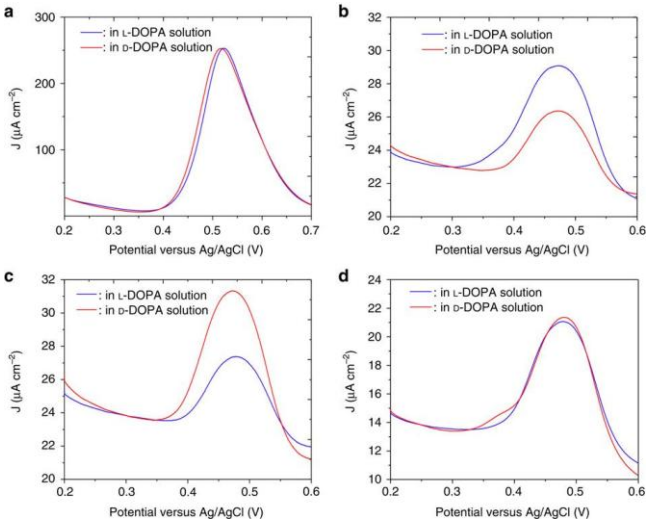


Figure 5. Chiral recognition of DOPA enantiomers revealed by differential pulse voltammetry (DPV) with molecular imprinted mesoporous platinum: (a) a flat platinum electrode; (b) a chiral mesoporous platinum electrode imprinted with L-DOPA; (c) a chiral mesoporous platinum electrode imprinted with D-DOPA; (d) chiral mesoporous platinum electrodes imprinted with L-DOPA after complete destruction of the chiral information by scanning the potential between -0.2 V to 1.25 V (vs Ag/AgCl) in 0.5 M H2SO4. Reproduced with permission from Ref[12a]. Copyright (2014) Springer Nature Group.

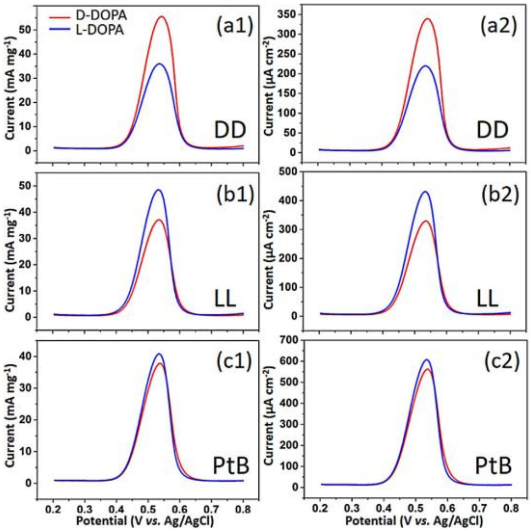


Figure 6. Chiral recognition of DOPA enantiomers recorded by differential pulse voltammetry (DPV) with (a) Pd@Pt particles that were synthesized in the presence of D-DOPA and D-AA (ascorbic acid), (b) Pd@Pt particles that were synthesized in the presence of L-DOPA and L-AA, and (c) Pt black (PtB) recorded in 4 mM DOPA in 50 mM HCl from 0.2 V to 0.8 V. Reproduced with permission from Ref[24]. Copyright (2017) Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

3.2.2. Asymmetric electrosynthesis of chiral compounds

The different chiral metal surfaces cannot only be used for analytical purposes, but also as working electrodes in electrosynthesis. Alkaloid molecules entrapped in several metals such as Ag and Cu were prepared and used as cathodes for the electrocatalytic asymmetric hydrogenation of methyl benzoylformate (MB) to methyl mandelate enantiomers and of aromatic ketones to optically

active alcohols[22g, 35]. A significant enantiomeric excess of over 70% can be obtained under mild conditions. In addition, even after the extraction of the alkaloid the metal particles retain the chiral information which is confirmed by linear sweep voltammetry[22g]. Chiral imprinted mesoporous platinum has also been used as working electrode for the asymmetric electroreduction of prochiral molecules to produce chiral compounds, like for the transformation of phenylglyoxylic acid (PGA) into mandelic acid. When using mesoporous Pt films imprinted with (R)-mandelic acid, the excess of the (R)-enantiomer is 20%. In contrast, the synthesis of (S)-mandelic acid is favored when using a Pt film imprinted with (S)-enantiomer. The observed enantiomeric excess can be attributed to the spatial orientation of the prochiral precursor in the asymmetric environment of the imprinted cavities which eventually results in the hydrogenation of the prochiral carbonyl carbon atom from one side. Interestingly, the degree of enantiomeric excess can be tuned by increasing the density of chiral cavities in the metal matrix[12c]. However, the enantiomeric excess is only moderate due to the interference with the reduction occurring on non-imprinted sites at the external surface of the Pt film.

To improve the performance of the imprinted mesoporous metal surfaces, pulsed electrosynthesis has been suggested[20a]. As mentioned above, in the case of the conventional steady-state electroreduction of a prochiral compound, the interference of the reaction at the non-imprinted external surface of metal results in a decrease in the global stereoselectivity. To circumvent this limitation, a novel concept has been proposed using pulsed electroreduction, combining a period of potential application with a relaxation time. As a model reaction, the electroreduction of a simple aromatic ketone, acetophenone, to phenylethanol (PE) has been employed as shown in Figure 7. In the first step of the reaction, the prochiral educt is adsorbed inside the chiral cavities located in the mesoporous channels. Subsequently, the adsorbed species is undergoing reduction to either (R)- or (S)-PE during a potential pulse of a certain duration. This is followed by a relaxation time without applied potential, during which the generated product is desorbed from the cavity and liberates a vacant site for the adsorption of new precursor and its transformation during the next potential pulse. Changing the relaxation time greatly influences the overall enantioselectivity and %ee values of over 90% could be obtained under optimized conditions. Very recently, similar results have also been obtained with electrodes made out of imprinted mesoporous nickel, despite the fact that it is a non-noble metal which is less stable from a chemical and mechanical point of view.[36]

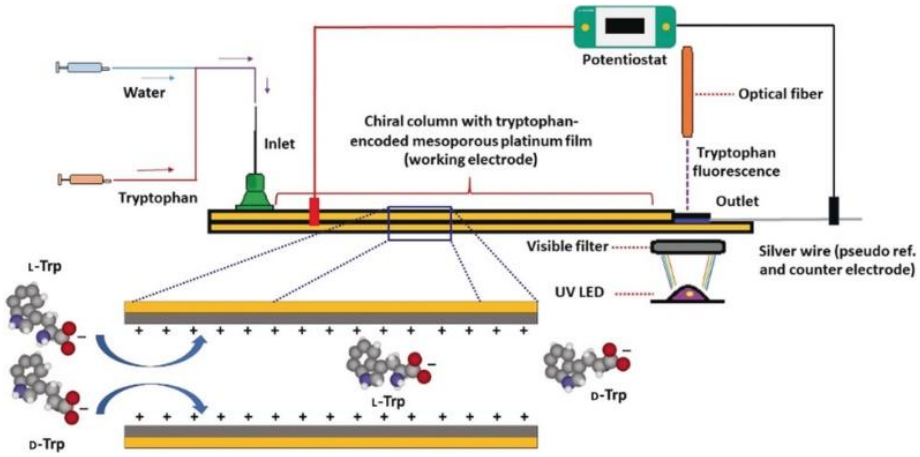


Figure 7. Schematic illustration of the pulsed electroreduction of acetophenone to phenylethanol enantiomers on molecular imprinted mesoporous platinum films including three important steps: (I) the adsorption of acetophenone in the chiral imprinted cavities of the mesoporous metal; (II) the stereoselective reduction of acetophenone to phenylethanol enantiomers; (III) the desorption of phenylethanol and the regeneration of empty chiral cavities for the next catalytic cycle. Reproduced with permission from Ref[20a]. Copyright (2017) Springer Nature Group.

3.2.3. Other electrochemical applications of chiral encoded metal surfaces

Another important aspect in the frame of chiral technologies is related to chiral separation because it can be used for many aspects such as controlling enantiopure production, checking racemization and for pharmacokinetic studies. Apart from conventional chiral separation methods

like HPLC, electroseparation techniques also have an important application potential because they allow increasing the separation efficiency of chiral molecules by an easy fine-tuning of the interaction between chiral compounds and stationary phase. Recently, molecular encoded mesoporous metals, prepared by the electrodeposition of metal salts in the simultaneous presence of a lyotropic-liquid crystalline phase and chiral templates, have been introduced as a stationary phase in a microfluidic channel for chiral separation (Figure 8)[20b]. It is possible to adjust the affinity of the imprinted metal for the chiral molecules by changing the electric potential of the stationary porous metal phase. This enhances the electrostatic interaction between the corresponding chiral molecules and the imprinted metal matrix.



Figures 8. Schematic illustration of the concept of chiral electrochromatography. A chiral mesoporous metal imprinted with L-Tryptophan is used as a stationary phase in a microfluidic electrochromatography device. The enantioaffinity can be easily tuned by applying a suitable potential to the stationary phase controlled by a potentiostat. Reproduced with permission from Ref[20b]. Copyright (2019) Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

As a proof-of principle, chiral mesporous Pt imprinted with L-tryptophan as a model template has been generated in a microfluidic channel that can be used for the separation of tryptophan enantiomers. In the case of no applied potential, an overlap of the two broad enantiomer peaks is observed at the channel outlet by fluorescence measurements. However, with a suitable potential applied to the metal walls of the channel, complete baseline separation of both enantiomers could be achieved. It therefore demonstrates that this straightforward concept can be used for the development of chiral stationary phases for electrochromatography and allows improving the separation efficiency simply by adjusting the electric potential.

In addition, another application of molecular encoded metal structures has been recently proposed via their combination with a conducting polymer in a hybrid material. A hybrid bilayer, composed of a free-standing conducting polymer film and a layer of mesoporous metal, encoded with chiral features, has been tested as enantioselective electromechanical actuator[37]. The development of efficient actuation systems is very important, for applications such as controlled robotic motion and remote sensor manipulation,[38] It opens also perspectives with respect to biomimetic actuation, reproducing for example the behaviour of muscles. Therefore, a hybrid bilayer material of chiral imprinted platinum and polypyrrole has been synthesized by electrodeposition of the metal on one side of the polymer. The synergy of both components allows the development of a wireless enantioselective electrochemical actuator[37] as illustrated in Figure 9. Preferential electrooxidation of the “good” enantiomer leads to an enhanced bending of the conducting polymer strip and therefore allows an easy optical readout of chiral information. [37].

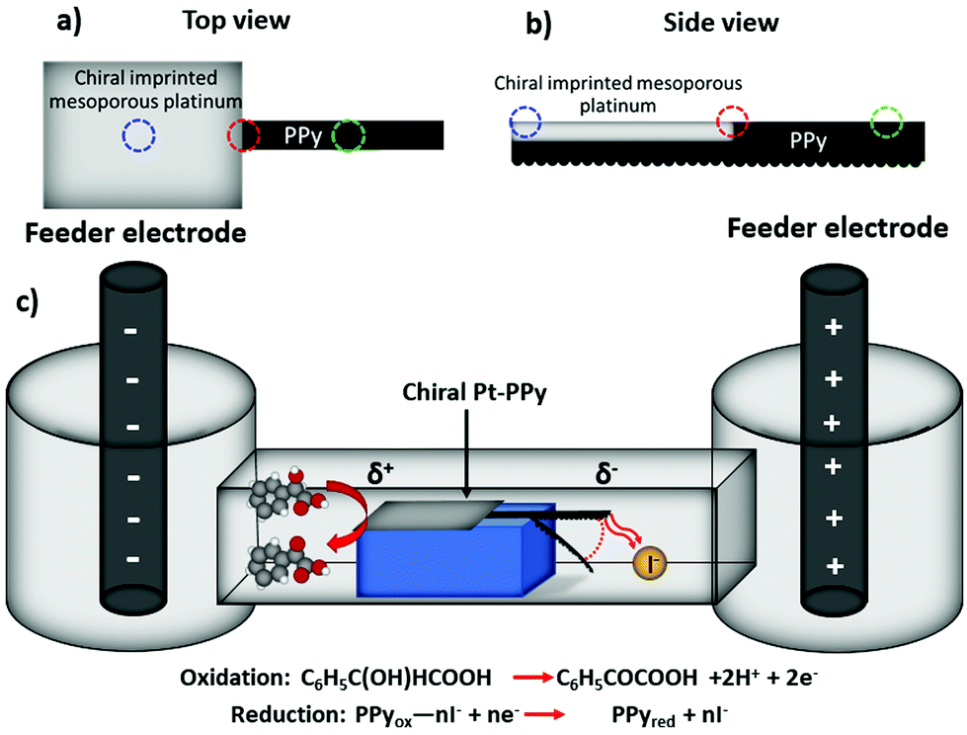


Figure 9. Schematic illustration of a hybrid bilayer composed of a free-standing conducting polymer film and a layer of mesoporous metal, encoded with chiral features (a) Top view and (b) cross section of the hybrid material (c) scheme of the bipolar electrochemical cell for the wireless optical readout of chiral information. Reproduced with permission from Ref[37]. Copyright (2019) Royal Society of Chemistry.

3. 3. Chemical features

Chiral encoded metal structures can be used for various chemical applications, like selective adsorption and separation of enantiomers. In order to illustrate this aspect, mesoporous imprinted platinum has been used for the selective adsorption of DOPA enantiomers at different temperatures. Adsorption experiments were carried out by exposing the materials to a racemic mixture of DOPA enantiomers for a given time and the remaining supernatant solution was analyzed by HPLC equipped with a chiral column. The L-enantiomer is preferentially adsorbed when using platinum imprinted with L-DOPA, whereas the one imprinted with D-DOPA shows the opposite trend. In particular, this behaviour is more pronounced when using a thicker imprinted metal film layer and carrying out the adsorption experiments at lower temperatures[12a]. The results confirm the presence of chiral information in the molecular encoded metal matrix.

Chiral imprinted alkaloid@Pd metal matrices, obtained after the extraction of cinchona alkaloids with DMSO, can selectively re-adsorb specific alkaloid molecules as has been demonstrated by carrying out time-resolved adsorption experiments followed by ultraviolet–visible spectroscopy. The ‘empty’ Pd matrix exhibits a higher adsorption capacity for the molecules with the correct configuration. Palladium imprinted with cinchonine (CN) exhibits, after removal of the dopant, a more efficient selective readsorption of cinchonine when compared with cinchonidine (CD), confirming favorable interactions between the molecule and the imprinted cavities.

In order to extend the utility of chiral metal materials for chemical applications, the sustained selective release of drugs from molecular encoded metal structures and metal oxide surfaces has been also examined as an interesting opportunity. In this context, several analgesic drugs such as

ibuprofen, naproxen, tramadol, and bupivacaine as well as antibacterial molecules have been used as dopants entrapped within metal structures (e.g., Ag and Cu). Instead of the extraction of the dopant molecules after the preparation process, their controlled release at a specific target has been studied and might become important for the development of applications in the biomedical sector[39].

One of the main challenges in modern chemistry is the development of chiral catalysts for asymmetric chemical synthesis. With this objective, chiral ligand-modified metal nanoparticles have been explored for the synthesis of enantiomers. Typically, such materials have been obtained by the following two methods: (i) using a chiral modifier as a stabilizer; (ii) ligand exchange on already stabilized metal nanoparticles[17]. The obtained materials show catalytic activity for several reactions ranging from asymmetric allylic alkylation[40] and asymmetric cross-coupling reactions[41] to hydroformylation[42], Pauson–Khand reaction[43] and 1,4-addition reactions[44].

In addition to chiral ligand-modified metal nanoparticles, several other approaches have also been proposed for employing chiral encoded metal structures as heterogeneous catalysts. The studied asymmetric synthesis schemes include the use of metal structures with entrapped organic molecules obtained by chemical reduction[22a-c]. In such cases, the organic molecules are not adsorbed on the metal surface, but are embedded in the metal crystal structure, eventually resulting in the formation of a metallo-organic hybrid structure[39f]. This constitutes an interesting complementary approach with respect to other concepts of asymmetric heterogeneous catalysis [45]. Moreover, entrapped chiral metal complexes, such as a chiral cobalt complex located in a silver matrix, can be used for the asymmetric carboxylation of benzyl bromides with CO2 under mild conditions without adding any further catalyst to the reaction medium. The composite offers a remarkable reaction yield of 73%, combined with good stability and reusability[46].

Apart from the metallo-organic hybrid materials, the doping of metal structures has been also achieved using a chemical reduction with a reducing agent.[18, 23] and the chiral information is retained even after removal of the dopant[7b]. To illustrate the catalytic activity of the metal for asymmetric synthesis, encoded palladium has been been generated by the chemical reduction of palladium salt in the presence of four pseudoenantiomers of cinchona alkaloids, cinchonine, cinchonidine, quinidine, and quinine. Such surfaces allow enantioselective catalysis of the hydrogenation of acetophenone and isophorone [7b]. For example, cinchonine@Pd exhibits an average enantiomeric excess of 16% for the hydrogenation of isophorone.

Conclusion and outlook

Encoding metals with molecular information, either in their bulk or on their surface is a very interesting challenge in the frame of the development of new materials. Due to a wide range of potential applications, a special effort is dedicated to the encoding of chiral molecular information. For the elaboration of these materials, several main synthesis approaches have been described, such as using chemical and electrochemical reduction of metal salts in the presence of molecular templates. In addition, the molecular imprinted metal structures can be also combined with mesoporous features, which leads to a very high active surface area and improved chiral recognition properties. Interestingly, such designer materials can retain the molecular information even after extraction of the molecular templates by a solvent. To confirm the intrinsically chiral structure of the imprinted cavities, several optical/spectroscopic techniques have been used. Photoelectron emission spectroscopy carried out with clockwise (cw) and anticlockwise (acw) circularly polarized light reveals that the chiral features of the metal are maintained after extraction of the chiral template. Obviously, there is still a lot of work to do with respect to an optimization of the performance of such materials.

The %ee and the yield are often not yet reaching values of practical use, but are very encouraging proof-of-concept results. Furthermore, an extremely important issue is the long-term stability of such structures. How long can the encoded information stay active in the metal matrix and what are the metals which have the highest structural stability? Can the stability of a given metal be increased by using certain alloys instead of the pure metal? Answering these and related questions will be certainly the topic of further research in this field. In conclusion, despite the fact that the utility of such materials has not yet been tested in real industrial applications, there are exciting and sometimes surprising results that hold considerable promise for the future in different fields ranging from enantioselective recognition and selective adsorption to separation and asymmetric synthesis of chiral compounds.

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