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# **Achievements and expectations in the field of computational heterogeneous catalysis in an innovation context**

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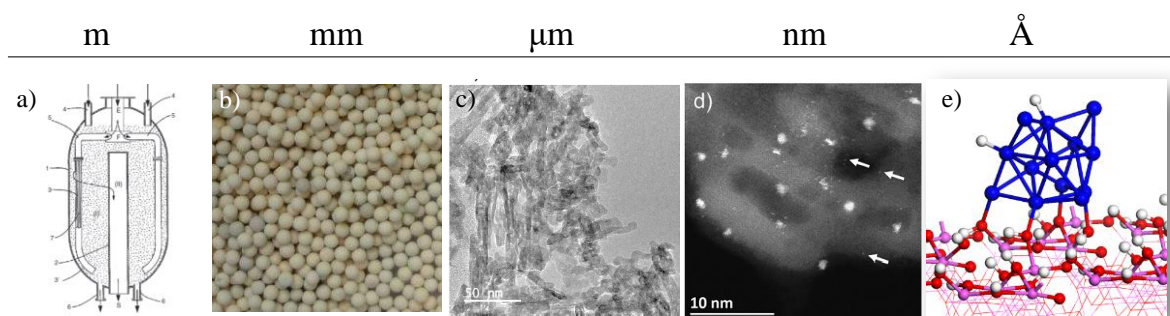
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**Abstract.** Heterogeneous catalysis is linked to industrial considerations from its origins, so is computational heterogeneous catalysis. The impact of first principles calculations on discoveries made for industrially relevant systems is growing year after year. In an innovation context, key questions are related to active site structure understanding, chemical reactivity investigations, multi-scale modeling, and prediction of new active phases with optimal catalytic performance. The present short review discusses and illustrates these various stages of the catalyst understanding and performance prediction where computational catalysis has a crucial role to play. Selected achievements in the field are reviewed, with a focus on the simulation of complex metallic and zeolite catalysts of industrial relevance. Future directions are suggested, on the basis of the need for ever more exhaustive and accurate models of catalytic sites and catalytic reactions representative of industrial systems, and for speed up in catalyst understanding and discovery.

**Keywords.** Density functional theory, multi-scale modeling, descriptors, industry.

## 1. Introduction

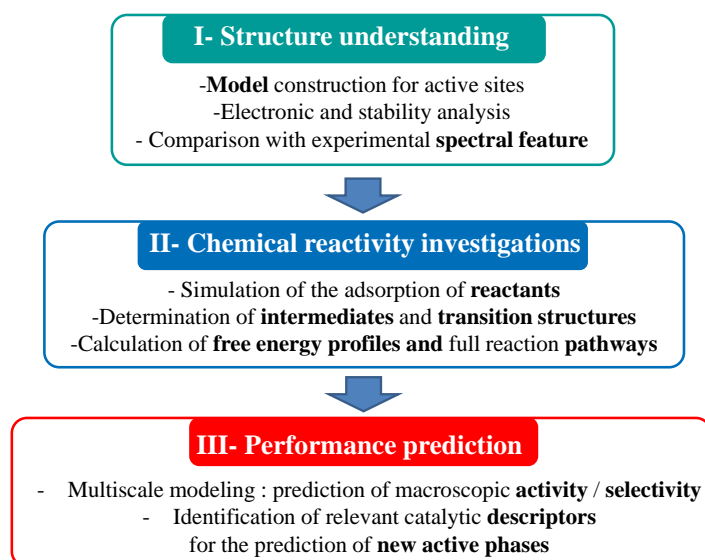
The control of the selectivity of reactions is a major issue in chemical reactivity, in particular in the transformation of multi-functional reactants undergoing several kinds of concurrent multi-step reactions. The tailoring of highly selective catalysts for each of the desired reaction pathway is key in that respect. The use of a catalyst is indeed not only a way to significantly increase the reaction rates, but also to tune the selectivity. Empirical considerations have, however, driven the choice of earlier most efficient industrial catalysts, aided by chemical intuition and serendipity. Making a breakthrough in the discovery of the most active and selective systems now requires going beyond the trial and error approach. In an industrial context, the problem needs to be addressed in a multi-scale dimension (Figure 1), keeping in mind that the catalyst is involved in a process with specific reactor geometries, flows, and pellet shape in the case of heterogeneous catalysts. An essential component of the rational design of better catalysts remains the advanced knowledge of the reaction mechanisms, of the key-elementary steps, of possible limitations by non-reactive steps (mass transfer), and of the rate constants of all of these. Atomistic simulation approaches are powerful to get a quantitative insight on some of these parameters.[1] They are more and more seriously considered by industrial actors in the field of heterogeneous catalysis,[2-7] probably more than what we can detect in the open literature. These approaches are fully connected with the fourth industrial revolution, in line with its digital transformation,[7] for the search of more sustainable processes. Significant effort was put so far on performing such investigations for catalytic reactions dealing with the transformation of hydrocarbons coming from petroleum or natural gas feedstock. Pollution abatement questions also motivated a large set of computational investigations at the atomic scale.[8, 9] Highly diverse alternative resources are now called on in the field of energy and chemistry, making the search of optimal catalysts ever more timely and challenging.[10, 11]



**Figure 1.** Various scales involved in the development of a heterogeneous catalyst: a) reactor scale (scheme of a catalytic reforming reactor, reproduced from ref.[12] with permission), b) pellet scale (catalytic reforming beads, courtesy IFPEN), c) aggregate of platelets (TEM picture of a  $\gamma$ - $\text{Al}_2\text{O}_3$  support, reproduced from ref. [13] with permission), d) single platelet scale with metallic nanoparticles (STEM picture of a Pt/  $\gamma$ - $\text{Al}_2\text{O}_3$  catalyst, reproduced from ref. [14] with permission), e) subnanometric particle scale, at the atomic scale (geometry optimized by DFT of a  $\text{Pt}_{13}$  particle on a  $\gamma$ - $\text{Al}_2\text{O}_3$  surface model, adapted from results presented in ref. [15]).

First, we aim at proposing relevant structural models of complex catalytic materials, to obtain a high level of understanding at the atomic scale (step I- in Figure 2). Thanks to quantum chemistry, electronic properties can be deduced, as well as the nature of the most stable systems as a function of the operating conditions, based on energetic data and thermodynamic considerations.[4] Then, comparison of well-chosen calculated and experimental spectroscopic features is a key step to evaluate the degree of relevance of the model, and also to assign experimental spectra, if the agreement between theory and experiments is satisfactory. On validated models, reactivity investigations can be performed (step II- in Figure 2), first by quantifying the adsorption strength between reactants and active sites, as proposed in the first step of the methodology. The determination of relevant intermediates and transition structures can then be undertaken for the reaction studied, in particular thanks to quantum chemistry calculations, often performed at the level of DFT (density functional theory[16, 17]). From the calculation of free energy profiles, some insights in the preferred reaction pathways can already be obtained. Finally, we aim at providing predictive catalytic data (step III- in Figure 2), by

integrating quantum chemistry data into higher scale models, so as to predict the activity and selectivity of a given catalyst for a given reaction, thanks to multiscale kinetic modeling.[18] If relevant descriptors of the catalyst can be found, by comparing several compositions, one may introduce them in kinetic models and even try to infer new efficient catalyst compositions for a given catalytic process.[19, 20] In the present short review, examples of results obtained at each step of the rationale are presented, for catalytic systems of industrial relevance such as metallic nanoparticles and zeolites. Some current challenges are given to make computational catalysis more deeply integrated into the innovation process. Information related to the methodologies used in the works discussed in the present article may be found in refs. [21, 22] for example.



**Figure 2.** General methodology for the simulation of heterogeneous catalytic systems of industrial relevance by atomic scale calculations.

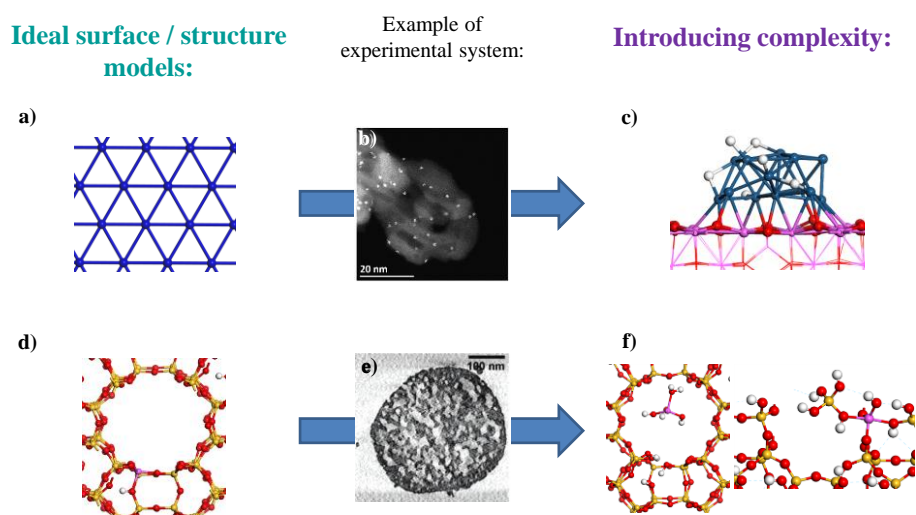
## 2. Understanding the nature of the surface active sites

Heterogeneous catalysts interact with the reactants thanks to their surface sites. Some of these sites can give birth to reaction intermediates and transition states, at the origin of the formation of products. The characterization of the structure of the surface sites is a challenge, even in the simplest case where the heterogeneous catalyst is composed of a crystalline solid.

Industrial catalysts combine several sources of complexity in that respect, due to their multi-component nature. Traditional surface models, often chosen in the literature (Figure 3-a and d), such as extended surface models of well-defined Miller indices (for metals, oxides, other crystalline materials) or perfectly crystalline structure of microporous solids (such as zeolites) bring useful general information, but are usually insufficient to account for the complexity of industrial catalysts.[4, 22]

A typical example is the case of supported metal catalysts. They play a tremendous role in the industry, for reactions involving small molecules such as  $H_2$ ,  $O_2$ ,  $CO_x$ ,  $N_2$ ,  $NO_x$ , and hydrocarbons (hydrogenation, dehydrogenation, hydrogenolysis, inter alia). Examples of industrial processes involving metallic particles are naphtha catalytic reforming,[23] propane dehydrogenation,[24] Fischer-Tropsch synthesis,[25] pollution abatement catalysts,[26] inter alia. The simulation strategy at the atomic scale depends on the size of the particles under consideration, and is limited by computational resources, in particular for the most accurate methods, using quantum chemistry approaches. Most often, when particles are larger than a few nanometers, the diversity of catalytic sites can be satisfactorily described by linear combinations of facets, edges, and corners. Whereas the two first systems are commonly investigated, much scarcer is the consideration of the latter, due to the large cells required. The simulation of the whole metallic particle by first principles may be challenging depending on its size. In this context, linear-scaling DFT options are promising.[27-29] When the support effect needs to be taken into account, in particular for small particles (Figure 3-b), an accurate model of the support needs to be developed first, accounting for the surface state in operating conditions.[30] Then, a model of the support catalyst may be elaborated by directly constructing a model containing the most relevant support model and metallic atoms or a particle on top of it.[15, 31-33] Recent findings suggest a significant ductility of the metallic particles in the presence of a support, that depends strongly on the reactive atmosphere (see for example figure

1-e and 3-c).[34-41] Elucidating these dynamic structures requires the use of advanced sampling methods, such as ab initio molecular dynamics or global optimization. This raises the question of the long-term evolution of the structure and electronic properties of the particles, knowing that at the industrial scale, catalysts stay in operation for several months. The deactivation of metallic catalysts may also be investigated by first principles approaches.[42] These questions are even more complex when dealing with metallic alloys, as the respective locations of the metals need to be addressed.[35, 43-49] The segregation of one metal with respect to the other is an important question, which is also affected by environmental parameters, such as adsorption of the reactants. This has a tremendous impact on the stability of the particles, on the electronic properties of the metals, and in the end on their reactivity.



**Figure 3.** Simple models *versus* models accounting for part of the complexity of industrial catalysts: (a) Pt(111) surface model, (b) HR-HAADF-STEM picture of a 1%Pt/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> reproduced from ref. [14] with permission, (c) Pt<sub>13</sub>/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> model adapted from results of ref. [34], (d) bulk model of zeolite mordenite, (e) TEM picture of a hierarchical ZSM-5 zeolite, reproduced from ref. [50] with permission, (f) models of extra-framework aluminum in a bulk mordenite zeolite (left, adapted from ref. [51]) and extra-framework silicon at the external surface of ZSM-5 (adapted from refs. [52]).

In the case of zeolite catalysts, extensively used industrially for the transformation of hydrocarbons[53] and pollution abatement,[54] inter alia, most computational investigations focus on the understanding of the behavior of bulk sites (Figure 3-d).[55, 56] These are located in the nanoporosity of the solid, so that the computational investigation starts from the

crystallographic structure as reported in the International Zeolite Association database.[57] In an industrial context, however, this level of description is far from being sufficient.[22] Real catalysts are scarcely purely microporous, they also exhibit mesoporosity (Figure 3-e). The latter is usually obtained by applying various post-treatments to the pristine zeolite sample, that also give birth to many defects and extra-framework species, whose structure and role is debated for a long time. As reviewed in ref. [22], many computational works have been undertaken to propose relevant models (Figure 3-f) for zeolites with defects and extra-framework species,[58-60] accounting for the mechanism of formation of extra-framework species,[51, 61-66] and for the local structure of the external surface of crystallites.[52, 67-70] Significant differences with respect to the bulk Si-(OH)-Al ideal bulk sites were revealed, in terms of structure and acidity of the defect sites. However, the way to a realistic simulation of these systems is still long, including the understanding of the structure of the surface sites at mesopores, and the interconnection of the latter with micropores. Moreover, most zeolite catalysts are used at the industrial scale as shaped pellets, in the presence of a binder (alumina, silica, clays, etc.) and many other additives.[71, 72] Notably, shaping is also often undertaken in the case of supported metal catalysts before practical use, as illustrated in figure 1-b.

The validation of the structural model proposed by a simulation approach is key before a reactivity investigation is undertaken. For atomic scale models, the confrontation of simulated structural and simulated features with experimental data coming from microscopy techniques and spectroscopies is often highly fruitful.[13, 14, 36, 43, 52, 73-75] In that respect, calculating the temperature and pressure dependent surface state of the catalysts is of utmost importance, which may be very efficiently done thanks to first principles thermodynamics.[76, 77] In an industrial context, this should motivate deeper analysis of the catalyst *operando*, meaning during the synthesis, post-treatment, catalysis, and regeneration steps.[78]



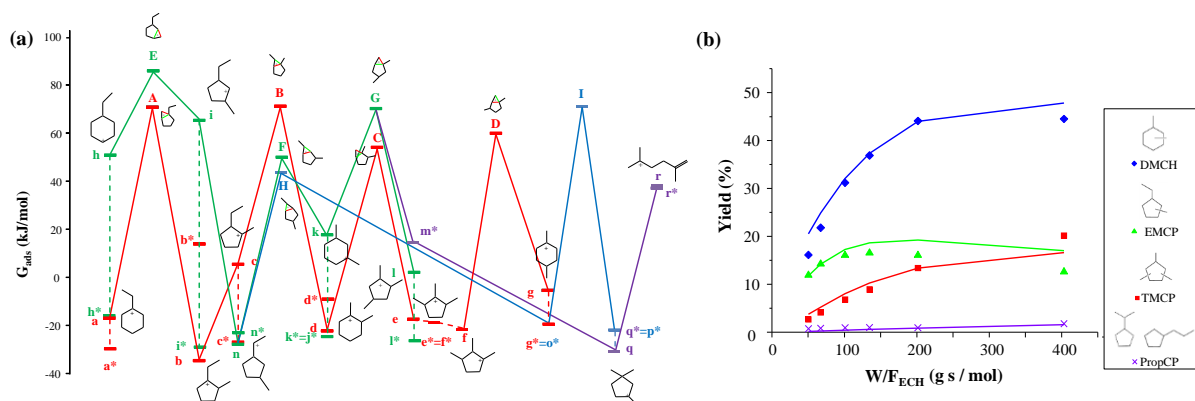
These examples illustrate the challenges that computational catalysis needs to address to reach a description of the active site of industrial catalysts. Many questions are common to the understanding of model research catalysts, but their numbers inflate with the multi-component nature of industrial catalysts, and with the multi-step nature of their life cycle. Already at the structural level, multi-scale issues are to be addressed: the accessibility of active sites is dictated by the pore system that surrounds it, which is a consequence of synthesis, post-treatment and shaping procedures. The micrometer to millimeter scale involved requires connecting the findings from quantum chemistry (atomic and molecular scales) with other simulation techniques suited for higher scales, such as dissipative particle dynamics and kinetic Monte Carlo.

### **3. Quantification of reaction profiles**

Once we have a model in which we are confident enough, thanks to the comparison of simulated and experimental spectroscopic features for example, a reactivity investigation may be undertaken at the atomic scale (step II- in Figure 2). This includes the computation of the adsorption of reactants, the identification of the reaction intermediates, and ultimately of transition states for all elementary steps for the considered reaction network. Quantum chemistry calculations, mainly at the DFT level, have proven to be powerful to elucidate the nature of active sites and mechanisms of reactions taking place at the active sites of many kinds of heterogeneous catalysts of industrial relevance. The quantification of the free energy profiles is crucial in that respect (an example is given in Figure 4-a). For metallic catalysts, usual static DFT methods appeared to be accurate, due to the highly covalent nature of the bonds between the catalytic site and the key atoms of the intermediates and transition states. For example, for alkene/alkyne hydrogenation and alkane dehydrogenation reactions (provided the chain length is short), very strong C-Metal and H-Metal bonds are involved, that make the transition state

poorly flexible close to the active center.[79-84] However, for other kinds of catalysts such as large pore proton exchanged zeolites, for reactions such as hydrocarbon isomerization and cracking, using ab initio molecular dynamics (AIMD) appeared to be crucial to correctly describe the relevant species and to properly quantify their free energy, due to their significant mobility in the large zeolite pores.[56, 85-89] This makes the static estimation poorly accurate, both from enthalpy and entropy points of view. For the latter point, the required level of theory (beyond DFT) is also currently questioned. The duality of the requirements for an accurate free energy profile quantification, in terms of quality of the sampling and of the level of theory, may be asked for any kind of catalytic system. The available computational resources often determine the choice made in practice, so that these questions may be revisited with methodological improvements.

In particular, due to limited computational resources, AIMD is limited to short time scales, basically tens or hundreds of picoseconds. Chemical reactions are very rare as such time scales, a problem that is efficiently circumvented thanks to advanced AIMD methods, to enhance the sampling of the most interesting parts of the free energy surface, for example following a given path, once a proper variable coordinate is chosen.[56] Classical forcefield molecular dynamics opens the opportunity to accelerate the calculation of the trajectories, provided accurate enough forcefields are available. This is unfortunately not the case for all systems, and generally not for the accurate description of reactions. Reactive forcefield are highly promising in that respect and have already been developed and applied to study reactions within zeolites.[90-94] However, optimizing an accurate and transferable reactive forcefield is highly challenging.



**Figure 4.** (a) Free energy profiles for the isomerization and ring opening of ethylcyclohexene in the EU-1 zeolite, calculated by periodic DFT. The structure of the intermediates and transition states is given. The species depicted by a star refer to  $\pi$ -complexes, not shown. (b) Distribution of isomerization products measured experimentally on a Pt/EU-1 bifunctional catalyst (dots) and predicted by a microkinetic model constructed from ab initio free energy profiles (lines). Adapted from ref. [95].

In an industrial context, some of the specific questions arising for this part of the work are inherited from the structural complexity (section 2). The effective catalytic behavior will not be pictured by the analysis of a single kind of active sites, but by the diversity of these, and with possible interplay between these sites. Moreover, above the complexity of the catalyst itself, the complexity (in practice, its size) of the reaction network itself is a hurdle, when considering elementary steps at the atomic step explicitly. Highly illustrative are examples such as the Methanol-to-Olefin process,[56, 96] or hydroconversion of alkanes,[97, 98] even in the case of rather small chain lengths. Some approximations can however be looked at to limit the number of transitions structure to be determined, such as unity bond index quadratic exponential potential (UBI-QEP) approaches,[99, 100] with estimation of the transition state energy from adsorption energies of fragments (for example, determined by DFT) and dissociation energy of the molecule into fragments.

The search for Brønsted–Evans–Polanyi (BEP) relationships is an interesting simplification strategy.[101, 102] This principle states that for a set of given reactions, a linear relationship between the (free) energy barrier and the corresponding (free) reaction energy may exist. Thus, once knowing the reaction (free) energy, the corresponding reaction barrier can be determined

without its explicit calculation. BEP and more generally linear scaling relations appeared to be a valuable tool for several kinds of catalyzed reactions,[103, 104] but it appears more and more often that they are not general.[105, 106]

On top of this, as mentioned in the end of section 2, the question of the accessibility of the active site within catalyst pellets, is to be asked. Non-reactive events, such as diffusion in the pore system or convection, may become limiting. The performances of industrial catalysts in large-scale reactors are indeed scarcely limited by the reaction kinetics only. This again refers to a multi-scale approach of the problem, that we address more specifically in the next section.

#### **4. Prediction of the reaction rates and of catalytic performance**

After the in-depth investigation of the structure of surface sites, and the identification of active sites in given reactions, the quantification of free energy profiles opens the door to the calculation of macroscopic catalytic data (step III- in Figure 2). The approach undertaken rather often in the literature is the integration of quantum chemistry data obtained at the atomic scale into higher scales models, so as to predict the activity and selectivity of a given catalyst for a given reaction.[107, 108] Sabbe et al. [21] proposed in 2012 an industrial perspective on first-principles kinetic modeling, that remains valid to define best practices.

Indeed, the development of predictive kinetic models is fundamentally important for any industrial process involving matter conversion reactions.[109] This makes it possible to anticipate process performance, particularly under the effect of a change in operating conditions (temperature, pressures or concentrations, etc.). It is common practice for such models to be parameterized using reaction rate constants  $k$  that are unknown in advance, the value of which is determined by adjusting rates and selectivities predicted based on reference experimental data. When several models are being considered, according to the mechanistic hypotheses advanced, the one giving the best mathematic agreement with the reference data is generally

retained. However, this approach makes developing models that are valid for ranges of conditions outside those sampled in advance an arduous task.

A recent strategy adopted to overcome this obstacle was hinged around the construction of kinetic models based on mechanisms identified by atomic scale modeling, and not only based on hypotheses.[18, 21, 107] The reaction rate constants  $k$  itself may be directly taken from the quantum chemistry approach, without the need for a parameterization step. As a result, this multi-scale approach provides a platform for moving directly to the kinetic model on the reactor scale from atomic scale calculations. Moreover, given their more robust foundations, the kinetic models thus obtained should theoretically prove better in terms of predictive capacity.

Thus, a key-ingredient of such a simulation procedure is the rate constant of each relevant elementary step, in the forward and backward directions. Microkinetics then consists in the integration of all the corresponding rate equations, in a mean-field approach of the active site. Useful information is obtained, such as the concentration of each intermediate and product, as a function of time, for a given reactor model (example in Figure 4-b). This appeared to be feasible only for reaction networks encompassing a reasonable number of elementary steps (typically, a few dozens) to allow the quantification of the free energy profile by first principles approaches. Many reports make use of the Eyring transition state theory,[110] applied to a number of elementary steps of the pathway investigated by first principles approaches, to link the free energy profile to the elementary step rate constant.[1, 95, 111-118] Notably, in some cases, the original transition state theory is known to be inaccurate.[119] Accounting for the impact of environment effects, according to the Kramers[120] or Grote-Hynes[121] theories lead to a lower rate constant than the one predicted by the transition state theory ( $k = \kappa \times k_{\text{TST}}$  with  $\kappa \leq 1$ ). This is particularly important in condensed phase. Determining  $\kappa$  requires extensive molecular dynamics simulations.[122, 123] This is frequently performed in biochemistry.[124] The lack of robust force-field for surfaces, contrary to proteins, is clearly a hurdle to the

systematic transposition of the approach to complex catalytic systems, as accumulating a large set of trajectories then exhibits a significant computational cost. Machine learning force fields[125] may be a way to circumvent this problem in the future (see section 6).

As mentioned previously, a detailed microkinetic investigation is not currently feasible for large reaction networks. Moreover, considering all elementary steps for the calculation of the reaction rates may lead to numerical difficulties, in particular when very fast events co-exist with much slower ones. In such a situation, only a few steps/intermediates/transition states actually contribute significantly to the rate of a reaction path.[126] This motivated the energetic span concept, upon identification of the rate determining intermediates and transition structures,[127] and the notion of degree of rate control.[126] Hierarchical multiscale approaches have been proposed, that consist in the determination of the most influential kinetic parameters at a semi-empirical level, considering the whole reaction network, then selecting these to be refined by first principles approaches.[107, 128, 129] With some successful case studies, these methods open the route to the construction of predictive kinetic models from first principles calculations, even for large reaction networks.

Accounting for coverage effects in the framework of meanfield microkinetic modelling is, however, not trivial. Stochastic approaches, such as on-lattice Kinetic Monte Carlo (KMC),[130-132] can bring at the same time a spatial resolution of the diversity of catalytic site and coverage effects, and introduce a stochastic treatment of chemical events. The coupling of KMC (to compute the rates) with first principles (that provide the rate constants) methods was achieved for a set of industrially important reactions, in cases where the catalyst can be described according to a (more or less simple) lattice model. In practice, ideal metallic surfaces or metal-derived compounds were mainly considered.[1, 130, 133, 134] However, the transposition of KMC to the case of more complex catalytic surfaces (non crystalline, exhibiting

ductility in the course of the reaction pathway), such as the one discussed in section 2, remains a current challenge.[1]

Moreover, the performance of heterogeneous catalysts in industrial conditions is not only determined by the kinetics of chemical reactions, but also by external and internal transport steps of reactants and products, possibly intermediates, in particular in the case of multifunctional catalysts. This is important to be considered when diffusion limitations exist. Mass transfer within the catalyst pellet, may influence the final performance. Notably, depending on the diameter of the pores, diffusion can be of several origins (molecular, Knudsen, surface diffusion) and accompanied by advection phenomena.[135] Also, experimentally measured diffusion coefficient may differ drastically from one quantification method to another, so does computational estimation of diffusion coefficients.[136] Forcefield molecular dynamics is a priori the technique of choice, that was applied often for the quantification of diffusion of molecules in the pore micropore network of zeolites.[136] However, it was recently shown that in the case of alkene diffusion in H-SAPO-34, a system that is relevant for the understanding of industrial Methanol-to-Olefin catalysts, performing ab initio molecular dynamics (instead of forcefield molecular dynamics) is required to properly describe the role of the Brønsted acid site in the diffusion process.[137, 138] Moreover, the effect of the loading of the pores with the various molecules that diffuses, was shown to have a tremendous impact on the prediction of the diffusion rates.[139] Lattice KMC models have also been built, that allow a spatial resolution of the preferred diffusion paths within the multi-dimensional porous network of zeolite catalysts, but in this case the rate of the elementary diffusion steps is an input of the model.[140-145] Such approaches are actually needed in the case of high diffusion barriers that make it become a rare event in molecular dynamics.[55] In this field, accounting for the complexity of the porous catalytic system is a real challenge that is still not overcome, although some attempts were made to simulate the effect of mesopores[146] and external surfaces of

zeolites[147-151] on the transport properties. Moreover, a full multi-scale kinetic model, that would account for reactions (from first principles calculations) and diffusion (from forcefield molecular dynamics, for example) with spatial resolution, is currently lacking, to the best of my knowledge.

At the larger industrial reactor scale (Figure 1-a), hydrodynamics is to be considered, as it directly impacts temperature and composition profiles, thus the apparent rates. For usual geometries and under ideal working conditions, chemical engineers use given reactor models (such as continuous stirred-tank, plug flow or batch reactors). This is the usual choice made in the ab initio based microkinetic models reported in the literature. However, in more specific situations, and in the case where a spatial resolution within the reactor is needed, Computational Fluid Dynamics (CFD) is a useful approach. Coupling CFD with the kinetic modeling of surface reactions is not trivial,[152] and the examples where a full multi-scale model from ab initio calculations to CFD, through kinetic modeling, are still scarce[115, 153-156] and so far restricted to ideal planar metallic catalytic systems or simple particle models. The motivation is high to go further in this direction in an industrial context, to bridge the gap between atomistic modeling and reactor scale considerations.

## **5. Prediction of new active phases**

Finally, when dealing with prediction of optimal catalysts, a very attractive computational approach is to look if the experimental rate constant is correlated to simple descriptors of the catalyst and of its interaction with the chemical environment. For several reactions, the existence of volcano plots was indeed shown (examples in Figure 5),[19, 20, 157] which can be seen as a consequence of the Sabatier principle.[158] If the existence of such simple descriptors is proven for the reaction under investigation, thanks to the combination of experiments (measurement of catalytic properties) and computations (for the estimation of the

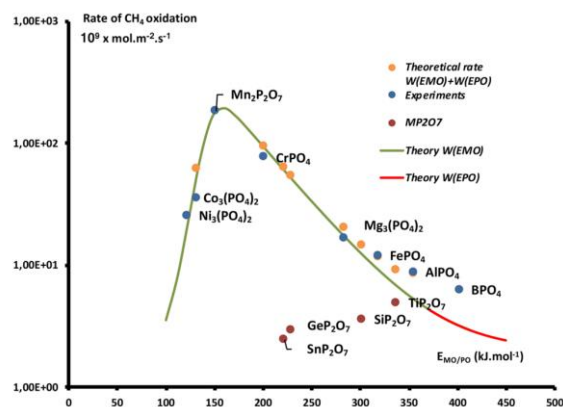


descriptor), the door is open for the fast computational prediction of new active phases, more active than the previously investigated ones, or as active but cheaper and/or more abundant. Cost of the active phase, and speed of the computational approach undertaken, are indeed high motivations in industry, that are not at the core of the approaches detailed in sections 2-4. The prediction approach by descriptors brings these parameters into the game.[159]

Notably, a very detailed knowledge of the structure of the active sites, and of the reaction profiles for specific catalytic compositions, may be helpful for the proposal of relevant descriptors. In that respect, insight brought by experimental spectroscopies are significant to propose relevant structure activity relationship. However, the current trend towards the implementation of data science in catalysis makes it possible to propose descriptors as combinations of surface features very efficiently, with improved prediction accuracy.[160-162] Whatever the strategy chosen for the identification of descriptors, a certain level of understanding remains, at least retrospectively, an asset for the clever development of new catalysts.

Descriptors can be for example the d-band level[163] or the interaction (free) energies of single atoms, simple functional groups, or reactant molecules with the surface of metals.[11, 19, 159] Similar scaling relations were explored for cation exchanged zeolites and zeotypes of various compositions (in terms of framework or exchange cations) for a given framework type.[164-169] Descriptors featuring effects linked to confinement were also found as relevant while comparing several zeolite frameworks[170, 171] or different zones of a zeolite framework,[172] for similar active sites. Even simpler properties, such as bond energies calculated on bulk structures of metal carbides, sulfides, oxides or phosphates, have been proposed, as in the Yin-Yang approach.[20, 157, 173, 174] Such descriptors appeared to be fruitful for metal, metallic sulfides, and more recently oxides catalysts, for reactions such as hydrodesulfurization, hydrogenation, and electrochemical transformation of small molecules

(N<sub>2</sub>, H<sub>2</sub>, O<sub>2</sub>, water). Recently, a method was proposed to infer the position of the maximum of volcano plots, from the thermodynamic features of the catalytic reaction,[20] making it possible to avoid the experimental screening of experimental activity patterns for a large set of catalyst compositions.



**Figure 5.** Volcano plots of methane oxidation rates versus M-O bond strength determined by the Yin-Yang approach[175]), reproduced from ref. [174] with permission.

Throughout sections 2, 3 and 4, the complexity of industrial catalysts and reactions was emphasized, that seems to be hardly conciliable with the search for simple descriptors that would hold this complexity. Indeed, looking at correlation curves linking experiments and theory, the error on the predicted trends are not negligible in many cases. One may see this as a consequence of the structure sensitivity of some catalytic reactions. Going further, one may also conclude that the reaction is not structure sensitive if the quality of the regression is excellent, whatever the structural features of the tested catalysts (surface area, proportion of sites of given coordination number, etc.). Accounting for the local structure around a considered metallic site led to the proposal of the generalized coordination number as a relevant descriptor,[176, 177] that was successfully applied to the determination of optimal environments for platinum catalysts in oxygen reduction reaction.[178] Difficulties emerge for metallic alloys, when a reconstruction of the alloy takes place upon adsorption of the reactants. [49, 179] In such cases, the reconstructions need to be taken into account separately, as the

surface structure affects the quality of the computed trends significantly. However, for very small metallic particles, it was shown that the morphology of the cluster changes as a function of the progress along the pathway,[83, 106] which breaks linear scaling rules and makes the definition of the descriptor a priori very tricky for the catalytic site. Rather than looking for a unified descriptor that would consider a huge number of sources of complexity, it is certainly more fruitful to alternate descriptor approaches to select a few promising active phases, and detailed approaches for the definition of the structure of the most active sites on a limited number of catalyst compositions.

## **6. Current challenges: towards more relevance, accuracy, efficiency**

As can be perceived through the examples selected in the previous sections, computational chemistry has gradually taken a growing importance in heterogeneous catalysis, first in an academic context, but also in strong connection with innovation up to the industrial scale. Enhancing its practical impact requires to overcome a large set of challenges. A non-exhaustive list is proposed in the next paragraphs, based on the need for ever improved exhaustivity and accuracy in the description of the active sites and of the relevant reaction pathways, but also based on efficiency requirements. Indeed, the time scale for the development of an industrial catalyst may vary strongly, but it is usually shorter than the typical time of fundamental research. Moreover, we are currently experiencing an energy transition context, that makes the target reactions change quickly. There is thus a strong motivation for speeding up discoveries, in particular those done thanks to computational chemistry.

Despite the significant efforts done so far to build realistic models of complex industrial catalysts, there is still a long way to go before reaching an accurate description of the system. For example, to obtain most relevant structural models for supported metal catalysts, instead of considering the interaction of models of clusters on models of supports, best would be to

simulate all steps of the synthesis of the catalysts. Indeed, directly simulating the catalyst without questioning its synthesis protocol requires to have a deep experimental knowledge about its structure, as computed thermodynamic features are only scarcely relevant in that respect. In the case of supported sub-nanometric metallic particles, one needs to know: i) how many atoms are present in the particles, ii) what is their arrangement (flat or 3D structures), iii) on which site of the support they are anchored, etc. High-resolution STEM provides a lot of useful information (see Figures 1-d and 3-b for examples) but cannot provide a non-ambiguous definition of all structural features. For example, in line with feature ii), STEM gives projected pictures of the 3D systems, that may be interpreted by several structural models. Tomography provides 3D insight, but not at the atomic resolution today. Point iii) is even more challenging, as atomic resolution is scarcely obtained for the supports. The synthesis usually starts from the impregnation solution (consisting in metallic salts in solution), then drying and activation atmospheres are performed (calcination, reduction, or other kinds of activation steps).[180] The latter may be composed of O<sub>2</sub>, H<sub>2</sub>, H<sub>2</sub>S, etc., depending on the target final state for the metal. After several months of operation in an industrial unit, regeneration procedures are undertaken to restore the initial performance of the catalysts. The simulation of these processes at the atomic scale are rather limited, due to the multi-step nature of the synthesis procedure and the very complex media that need to be considered.[180] For the impregnation step for example, accounting for solvent effects (often water, with proton transfers) requires its explicit simulation in the presence of the surface, which is still a challenge.[181, 182] Activation steps require high temperatures, inducing significant mobility of the metal at the support, depending on the activation atmosphere.[14, 75] The simulation of all these steps would provide kinetic information about the preferred locations of the metallic species at the support, about their nucleation state and coordination sphere. This would give insight in the possible final structures, after activation, not only from a thermodynamic but also from a kinetic point of view.

Regarding zeolite catalysts, as mentioned in section 2, works have already been devoted to the simulation of defects and external surfaces, but still, our view remains schematic in that respect.[22] Much more remains to discover about the formation mechanisms of these defects, simulating the post-treatments more realistically than currently done. This is highly challenging, in particular for treatments done in aqueous media. Moreover, much more effort must be invested in simulating the system beyond the atomic scale, as the mesopore dimensions are of the order of dozens of nanometers. The role of amorphous zones formed after post-treatments, for which only a few models are available,[183, 184] needs to be better defined, as well as the role of the binder-zeolite interaction that takes place during shaping of industrial catalysts.[185]

Regarding the quantification of the reaction profiles, the determination of the entropic terms remains most of the time the trickiest part of the problem. As shown in section 3, *ab initio* molecular dynamics is a highly relevant option, but its computational cost remains prohibitive for a systematic application.[55, 56] Moreover, the elucidation of reaction pathways and the quantification of the free energy profiles often requires the choice of appropriate reaction coordinates (collective variables CVs), which is not trivial.[186] The choice of irrelevant CVs for preliminary MD runs represents a waste of human and computational time. On top of that, the level of theory we use to propose accurate data may have a strong impact on the enthalpic terms, that is most of the time unknown *a priori*. Most data are currently obtained at the DFT level, that might not be sufficient to reach chemical accuracy in many cases.[187-190] This is a crucial question when the integration of first principles rate constants into higher scale models is aimed at: the propagation of errors may have tremendous impact on the predicted performances.[18] However, combining *ab initio* molecular dynamics and high level of theory, for complex catalytic site models, is currently not realistic with the usual implementations of AIMD.

Thus, all these challenges raise the question of how to simulate larger and larger models, doing ab initio molecular dynamics, at the optimal level of theory. The growth of computational resources is key, but the impact of it will be maximal if we have codes available, that scale well with increasing resources. This is usually not the case of most DFT codes. Linear scaling approaches, such as the one developed in ONETEP,[191] CONQUEST[192] or BigDFT,[193] inter alia, are highly interesting in that respect.

As a corollary, big data and artificial intelligence have already impacted computational heterogeneous catalysis, as attested by the already huge number of reviews published in that field over the past three years (see for example refs. [7, 194-199]). The reader will find in these reviews a large set of domains linked to atomic scale simulations, that already benefit from the developments in this domain. Notably, developments at all scales depicted in Figure 1 are concerned by improvements proposed by Machine Learning approaches (including microkinetics, reactor design, computational fluid dynamics). Regarding atomic scale simulations, a strong benefit may first be found for catalyst design, in the spirit of section 5, thanks to data hosted on computational materials databases that have flourished over the years.[200] Machine learning schemes have already provided new descriptors for the prediction of the performances of monometallic, [201] multimetallic[160, 162, 202, 203] and oxide[161] catalysts, inter alia, combining structural, electronic and energetic parameters. Supervised machine learning methods were successful in the extraction of morphological information from XANES spectra, thanks to ab initio calculations for platinum particles.[204]

Machine Learning interatomic potentials (in some cases, reactive forcefields[205]) are also highly promising for speeding-up tremendously evolution algorithm search,[206] transition state search [207, 208] and ab initio molecular dynamic calculations.[125, 209-211] They are built upon training on DFT calculations, sometimes thanks to active learning schemes (for example, along a molecular dynamic run). They show high accuracy even for systems (e.g.

metallic) for which accurate traditional forcefields are not available, but their transferability is still an open question. So far, they have opened the door to much quicker and longer molecular dynamic runs than in traditional AIMD (by several orders of magnitude), or to large scale Monte-Carlo simulations, or to the simulation of very large systems (e.g. thousands of metallic atoms) with close to DFT accuracy, for example for N<sub>2</sub> dissociation on Ru(0001),<sup>[212]</sup> phase transition in perovskites,<sup>[210]</sup> bulk properties of alloys,<sup>[213]</sup> alloy segregation and reactivity in water, with particles containing up to 3915 atoms,<sup>[214]</sup> to name a few. Machine Learning schemes are also relevant options to improve the level of theory along a MD trajectory for a moderate computational cost,<sup>[215-217]</sup> and for the finding of relevant collective variables before running constrained ab initio molecular dynamics runs.<sup>[218, 219]</sup>

All this suggests that we currently arrive at a turning point in terms of methodologies, with an expected deep transformation of the practices of computational heterogeneous catalysis (among other branches of atomic scale simulations), likely to enhance drastically the impact it will have on industry and, consequently, on society.

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