



# Computational Catalysis: A Land of Opportunities

O. Eisenstein<sup>1,2</sup> · S. Shaik<sup>3</sup>

Published online: 24 January 2022

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Theoreticians and computational chemists were always fascinated by the topic of catalysis which has been a major area in chemistry, ever since its recognition by Berzelius in 1836. The present issue entitled “Computational Catalysis: A Land of Opportunities”, presents a panoramic collection of studies on various aspects of computational catalysis, that are told in total of 41 reviews and articles. The contributing authors develop methods and perform theoretical and multiscale calculations to discuss diverse questions relevant to heterogeneous, homogeneous and enzymatic catalytic reactions. In many ways, this is a landmark collection.

## 1 Reviews

There are eleven reviews dedicated to various important topics in catalysis. We start with two reviews which address general principles in computational catalysis.

Computational catalysis can contribute to the determination of catalytic reaction mechanisms and help the understanding and identification of the controlling factors. However, a universal theoretical approach to computational catalysis with widely applicable algorithms is not as yet available. In the first review of this project *Markus Reiher* and *Miguel Steiner* provide a brief overview of the different computational approaches that are available for applications in heterogeneous and homogeneous catalysis. This review

also outlines first-principles modeling of elementary reaction networks.

Electric fields produce a range of effects by interacting with atoms, molecules, and complex matter, and by modifying the activation barriers of chemical reactions. *Giuseppe Cassone* et al. review these effects by means of ab-initio molecular dynamic methods, which include crucial nuclear quantum effects in path-integral ab initio simulations. The authors discuss recent findings on the catalytic effects, which produced by applying strong electric fields on liquids, with implications on technological aspects as well on the “origins of life”.

The next two reviews concern heterogeneous catalysis. Thus, the review by *Sicong Ma* and *Zhi-Pan Liu* deals with zeolites which are key hubs for heterogeneous catalysts. The review examines various types of zeolites which are known and discusses their stabilities including the templating effects. It also addresses the confinement effects of the pores that affect the catalytic conversion of molecules. The review by *Céline Chizallet* is concerned with innovations in heterogeneous catalysts, which are essential to chemical industry. Her review describes how first principle calculations may generate various levels of understanding of catalysts and predicting their actions.

Five reviews are concerned with the improvements of homogeneous catalysts. The review of *Ainara Nova* et al. describes the action of bifunctional catalysts on deaminative amide hydrogenation, a reaction which conveniently yields amines and alcohols using dihydrogen as reducing agent. Until recently, this reaction required extreme conditions. However, thanks to the development of bifunctional catalysts, this field has made major advances towards larger turnovers under milder conditions. Computational studies describe the reasons for these improvements. The next review by *Jeremy Harvey*, *Fahmi Himo* et al. describes how they came to realize during the course of the investigations that the active catalytic species was a bimetallic complex, rather than a monometallic species as was assumed previously. They argue that “two is better than one” turns out to be relevant more often than one might expect. The

✉ O. Eisenstein  
Odile.eisenstein@umontpellier.fr

S. Shaik  
sason@yfaat.ch.huji.ac.il

<sup>1</sup> ICGM, Université de Montpellier, CNRS, ENSCM, Montpellier, France

<sup>2</sup> Department of Chemistry and Hylleraas Centre for Quantum Molecular Sciences, University of Oslo, 0315 Oslo, Norway

<sup>3</sup> Institute of Chemistry, The Hebrew University of Jerusalem, 91904 Jerusalem, Israel

review by *Feliu Maseras* and *Giuseppe Sciortino* deals with a related topic, that of the simultaneous activation of two substrates or functionalities by different catalytic entities. This includes their subsequent coupling, which is responsible for the rate-acceleration and selectivity exhibited by these systems. The review reveals some of the mechanisms of cooperative catalysis, by providing fundamental insights on the substrate activation by metals, as well as on the interactions between the different catalysts. *Gregori Ujaque, Agustí Lledós* et al. review the representations of solvents in catalysis. In homogeneous catalysis, solvent is an inherent part of the catalytic system. As such, they argue, the solvent must be included in the computational modeling. This review describes through selected examples the reasons that urge the authors to go beyond the continuum models and consider micro-solvated (cluster-continuum) models using explicit solvent molecules. The limitations of continuum-solvent usage in computational homogeneous catalysis are thus better appreciated. *Raghavan Sunoj* et al. emphasize the need to properly describe the nature of the chemicals used under experimental conditions. The review focuses on how computational studies have contributed to understand the role of additives, such as Lewis and Brønsted acids or metal salts, in transition-metal catalyzed C–H bond activation.

We close the review section of this issue with two contributions on enzymatic catalysis. *Martin McCullagh, Robert Paton* et al. discuss the modelling of catalysis in allosteric enzymes. The dynamic interconversion of enzyme conformations between active and inactive catalytic forms, involving timescales inaccessible to QM treatments. This presents a formidable challenge for the development of computational models for studying allosterically-modulated enzymes. The review presents an overview of the key concepts underlying multistate models of enzyme catalysis, enzyme allostery, and the challenges that are posed for large-scale QM, QM/MM, and MM methods. Metalloenzymes are essential compounds for oxygen activation, which enables oxidation of a variety of molecules. *Binju Wang* et al. describe the recent computational insights into the oxygen activation by several copper-dependent enzymes; mono-copper enzyme lytic polysaccharide monooxygenase (LPMO), particulate methane monooxygenase (pMMO), and the binuclear copper enzymes; peptidylglycine  $\alpha$ -hydroxylating monooxygenase (PHM) and dopamine beta-monooxygenase (DBM). The authors discuss the structure-function relationships of these enzymes, and generate insight into their future engineering to exhibit new functions.

There are 30 original articles which cover studies in heterogeneous, homogeneous and enzymatic catalysis.

## 2 Heterogeneous, Surface, Supported Catalysis, and Catalysis by Nanoclusters

There are nine contributions in this section. *Lucas Foppa* and *Luca Ghiringhelli* focus on presenting a method for faster evaluation of adsorption energies in heterogeneous catalysis compared the corresponding first-principles calculations. The authors use the subgroup-discovery (SGD) local artificial-intelligence approach to identify the key descriptive parameters and constrain their values. These so-called SG rules describe transition-metal surfaces with outstanding adsorption properties for the oxygen reduction and evolution reactions.

*Yousung Jung* and *Taewon Jin* develop models for determining the structures of Heusler alloys. The work presents simple descriptors, namely, spin moment and occupancy of d-electrons, to predict the stable (tetragonal vs. cubic) phases of all d-metal Heusler alloys. The present phase classification model is expected to reduce the computational cost for the high throughput screening of Heusler compounds in various catalysis applications.

*Yuta Tsuji, Kazunari Yoshizawa* et al. use Swarm intelligence to explore the structure of metal-cluster catalysts which are involved in hydrogen adsorption. Computational chemistry faces difficulties in dealing with the diversity of metal clusters especially in the presence of adsorbates. The authors present a comprehensive, systematic, and efficient search for stable structures of metal nanoclusters with adsorbed hydrogen atom.

*Richard Zare* and *Christian Chamberlayne* report on the chemical reactions arising from static electric charges on insulating surfaces (e.g., charged Teflon) in electrochemical cells. They distinguish between the chemical reactivity of the charge carrying species and the voltage imparted by discharging the electrostatically charged surface. The authors reach the conclusion that the majority of static electricity driven electrode reactions are caused primarily by the chemical reactivity of the charge carrier on the electrode surface and not from discharging the static charge on the electrode.

*Tao Cheng, William Goddard*, et al. show that a single-atom electrocatalyst anchored on MoS<sub>2</sub> for the nitrogen reduction reaction can provide an environmentally green alternative to the Haber–Bosch high-temperature and high-pressure process, replacing the water gas shift production of H<sub>2</sub> with hydrogen atom which is extracted from water. The authors test 23 transition metal elements as the single atom catalyst and identify Ir@MoS<sub>2</sub> as the best catalyst.

*Aleix Comas-Vives* and *CS Praveen* focus on evaluating the catalytic trends in propane dehydrogenation (PDH) for four M<sup>(III)</sup> single-sites (Cr, Mo, Ga and In) on a realistic amorphous model of SiO<sub>2</sub> using DFT-based calculations

and the energy-span model. The calculated catalytic activity for Ga and Cr is comparable to the ones reported at the experimental level, validating the methodology used. Both In<sup>(III)</sup> and Mo<sup>(III)</sup> on SiO<sub>2</sub> are found to be potentially active catalysts for PDH, provided they can be synthesized and prove to be stable under the PDH reaction conditions.

*Egil Skulason, Younes Abghoui* et al. pursue an environmentally-friendly alternative to the Haber–Bosch method. They explore further the merits of transition metal nitride (TMN) surfaces as catalysts for the nitrogen reduction reaction (NRR). The most important outcome of this study is that the presence of the (110) facets of these TMNs in the catalyst will be detrimental to the activity of the catalyst. Investigating the performance of these catalysts by engineering the surface to only include the surface orientation of interest will thus be of great interest.

*Younes Abghoui* provides a continuation of the previous study on the possibility of using the earlier transition metal nitrides for catalyzing hydrogen-evolution reaction. This work analyzes the (111) facets of these surfaces which are as frequent as the (100) facets when a polycrystalline catalyst is manufactured. The outcome of this comprehensive investigation and comparison of activity between the (100) and (111) facets reveal that TaN is the most active surface in both facets with the (100) being more promising with regards to both thermodynamics and kinetics.

*Monica Calatayud and Baohuan Wei* systematically investigate the paths for hydrogen diffusion from the titanium oxide surface into the subsurface, with a focus on the surface topology, the thermal and isotopic effects, and the degree of reduction of the substrate, by means of state of the art periodic DFT calculations.

### 3 Homogeneous Catalysis and its Modelling in Solution

There are sixteen contributions in this section. *Bernd Hartke and Dominik Behrens* employ genetic algorithms and use their GOCAT scheme to find globally optimal embeddings (of partial charges) for exploration of those reaction paths of chemical reactions that lower the respective energy barriers via electric fields. Based on this strategy the authors analyze the Menshutkin S<sub>N</sub>2 reaction and the enzymatic reaction of ketosteroid isomerase.

*Clémence Corminboeuf* and her group have demonstrated earlier that volcano plots, traditionally used in heterogeneous catalysis, can also be used in homogeneous catalysis. In this issue, they demonstrate such usage in the case of catalysis by alkaline earth amides for hydrogenation reaction. The computations highlight that the catalytic activity is by and large determined by the charge and the size of the metal ions.

High-throughput computational studies require fast computational methods such as DFT. The predictive power of this method has been challenged in the case of 3d transition metals. *Heather Kulik* et al. discuss this issue for the conversion of methane to methanol. Importantly, the interplay between spin-state dependent reaction energetics and exchange effects on spin-state ordering means that the choice of DFT functional strongly influences whether the minimum energy pathway is spin-conserved.

Machine learning methods are becoming increasingly attractive in computational catalysis. *David Balcells, Daniel Ess* et al. consider this approach in the case of methane C–H activation and functionalization with Pt<sup>(II)</sup> catalysts. They outline a workflow that combines automated construction of Pt<sup>(II)</sup>–ligand combinations with machine learning and automated transition-state searches that generate fully optimized transition states.

*Julien Panetier and Xiaohui Li* employ DFT calculations to investigate the electronic structure and reactivity in the CO<sub>2</sub> reduction reactions by a series of tungsten electrocatalysts, [W(bpy-R)(CO)<sub>4</sub>] (R=H, CH<sub>3</sub>, <sup>t</sup>Bu, OCH<sub>3</sub>, CF<sub>3</sub>, and CN). Based on the energy-span model and theoretical Tafel plots, the work provides information for designing CO<sub>2</sub> reduction electrocatalysts. Thus, [W(bpy)(CO)<sub>4</sub>] and [W(bpy-<sup>t</sup>Bu)(CO)<sub>4</sub>] are predicted to be better electrocatalysts than [W(bpy-CH<sub>3</sub>)(CO)<sub>4</sub>].

*Samantha Johnson, Simone Raugei*, et al. describe a computational study of the reactivity of metalloporphyrins for NH<sub>3</sub> oxidation. The authors use DFT and molecular dynamics simulations to assess the ability of tetraphenylporphyrin (TPP)M complexes (M=Cr, Mn, Fe, Co, Ni, Mo, Ru, W, and Os) to coordinate and weaken the N–H bonds of ammonia, as well as their propensity for N–N bond formation and N<sub>2</sub> generation.

*Michelle Coote* et al. use high-level quantum chemical calculations to re-examine the proline-catalyzed intermolecular aldol reactions of acetone and *para*-nitrobenzaldehyde in acetone as solvent. Proline catalyzes the aldol reaction according to the enamine mechanism. The authors use the computational results to develop a detailed ab initio kinetic model. They subsequently validate this model by use of kinetic simulations, which include concentration effects and allow for process optimization. This kinetic model is used to predict the optimal concentrations of proline, acetone, aldehyde and water. The authors propose a revised mechanism for enamine formation in which a second proline assists the process which contributes to the enamine formation.

*Sandra Lubner* et al. consider the recently discovered inverse-electron demand Diels–Alder (iEDDA) and nucleophilic (azaphilic) additions on s-tetrazines. In order to have a more realistic dynamic description of this reaction in explicit solution at ambient conditions, the authors use a semiempirical tight-binding method combined with enhanced

sampling techniques to calculate the free energy surfaces of the iEDDA and azaphilic addition reactions. In particular, the authors find that the azaphilic addition is preferred over the iEDDA reaction when the dienophile is substituted by a bulky phenyl group.

*Mårten Ahlquist* and *Juan Angel de Gracia Triviño* describe the role of counterions in intermolecular radical coupling of (Ru-bda) $L_2$  catalysts (bda = 2,2'-bipyridine-6,6'-dicarboxylate, L = pyridine) where the dimerization of the key intermediate [Ru<sup>(VI)</sup>N(bda)(py) $_2$ ]<sup>+</sup> including the counterions is shown to be important. A classical force field is used to simulate the dimerization free energy by calculation of the potential mean force, in both water and acetonitrile.

*Shigeyoshi Sakaki* et al. describe how the heterobimetallic diphosphine-based tridentate pincer-type PAIP ligand bearing an alumanyl moiety at the metal coordination site can be involved in  $\sigma$ -bond activation. The work reports computational studies of the unique Rh–Al direct bond, flexible behavior of Rh(PAIP) towards substrate coordination, and the new catalytic functions of Rh(PAIP) via the C–H and C–F  $\sigma$ -bond activations.

*Djamaladdin Musaev* et al. use calculations to demonstrate the feasibility of a Cu<sup>(I)</sup>-mediated deconstructive fluorination of N-benzoylated cyclic amines with Selectfluor<sup>®</sup> (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate), which contains an N–F bond. The authors propose a mechanism which proceeds through the following steps: (a) substrate coordination to a Cu<sup>(I)</sup> salt, (b) iminium ion formation followed by conversion to a hemiaminal, and (c) fluorination involving C–C cleavage of the hemiaminal, which is a two-state reactivity (TSR) event. Comparison is done with previously published work for analogous Ag<sup>(I)</sup> catalysts.

*Xavier Solans-Monfort* et al. use DFT calculations to study the effect of Lewis acids on the catalytic activity for alkene metathesis, *Z/E*-selectivity and stability of tungsten oxo alkylidenes. It is shown that the Lewis acid increases the reactivity of the catalysts, but this enhancement applies to both the catalytic activity and catalyst deactivation. In addition, the Lewis acid decreases the *Z* selectivity of the catalysts.

*Deryn Fogg* and *Vidar Jensen* et al. present a joint experimental/computational study in search of the highly challenging selective transformation of 1-alkenes into *E*-olefins. Their calculations predict high *E*-selectivity for Ru catalysts incorporating a dianionic thio-indolate ligand. The work reveals the dual challenge which this molecular design faces: (1) Steric pressure must be exerted in opposite directions to closely spaced substituents of the nascent disubstituted olefin. (2) The net steric congestion must be sufficiently low to permit productive metathesis and, in particular, for the product olefin to dissociate from the metal.

*Xiaoguang Bao* et al. present computational studies of the reaction mechanisms of Au<sup>(I)</sup>- and Zn<sup>(II)</sup>-catalyzed cross-coupling of enynones with diazo compounds to produce multi-substituted furylalkenes. Although both enynones and diazo compounds can be converted to the corresponding metal-carbene intermediates, it is more energetically favorable for the enynones to undergo intramolecular nucleophilic cyclization to afford a 2-furyl metal-carbene intermediate for both Au<sup>(I)</sup>- and Zn<sup>(II)</sup>-catalysts. The origin of stereoselectivity in the multi-substituted furylalkenes is also discussed.

*Fu Kit Sheong*, *Zhenyang Lin* et al. describe the Co<sup>(I)</sup>-catalyzed hydrogenation of C=C and C=O substrates to determine whether 1<sup>st</sup> row transition metal elements could be used instead of heavier metals. The study focuses on understanding the reasons why Co-catalyzed hydrogenation was reported to selectively hydrogenate C=C but not C=O. The role of the various ligands in the coordination sphere is analyzed.

*Hélène Gérard* and *Stéphanie Halbert* present DFT calculations which compare the pathways of C–C bond formation involving Cu<sup>(I)</sup> intermediates formed from Zn and Li organometallic species, in catalytic and stoichiometric versions, respectively. The calculations highlight how the solvent and substrate coordination to Li and Zn in the Mixed Aggregates (MAA) manipulate the formation of the most active intermediate.

## 4 Bio and Enzymatic Catalysis

There are five contributions in this section. *Wenzhen Lai* et al. describe the O–O activation in Mn<sup>(IV)</sup>-peroxo corrole to yield Mn<sup>(V)</sup>-oxo corrole. They show that this conversion requires two Mn centers. Thus, in the presence of protonic acids the Mn<sup>(IV)</sup>-peroxo yielded Mn<sup>(III)</sup>-hydroperoxo corrole-radical cation which can produce Mn<sup>(V)</sup>-oxo at the expense of a high barrier and an endothermic reaction. However, the presence of Mn<sup>(III)</sup>-corrole initiates a binuclear O–O cleavage reaction, which is highly exothermic and has a small barrier.

*Katarzyna Świderek*, *Vicent Moliner* et al. address the self-cleavage pistol ribosyme mechanisms, which are formed by RNA and exist in primitive biological systems. The group used multiscale MD simulations and QM/MM calculations, which revealed a unique mechanism by comparison with other ribozymes. Thus, the pistol ribozyme does not require any proton source, and relies on the presence of Mg<sup>2+</sup> ions, which bring about the final P-O5' bond cleavage step. Unveiling the details of this mechanism can contribute not only to the understanding of the origins of life but also to the development of new simplified artificial enzymes.

Rong-Zhen Liao et al. describe QM/M calculations for the action of the SAM enzyme diphthamide biosynthesis protein, that catalyzes the formation of [4Fe–4S]-alkyl complex by cleavage of the S–C $\gamma$  bond in s-adenosylmethionine. The system possesses six potentially active spin states ( $\alpha\alpha\beta\beta$ ,  $\alpha\beta\alpha\beta$ ,  $\alpha\beta\beta\alpha$ ,  $\beta\beta\alpha\alpha$ ,  $\beta\alpha\beta\alpha$ ,  $\beta\alpha\alpha\beta$ ), and the study shows that the reactive state is  $\alpha\beta\alpha\beta$ , which indicates spin-state selectivity. The reaction mechanism is concerted and involves S–C $\gamma$  bond cleavage coupled to Fe–C $\gamma$  bond formation.

Sam de Visser et al. employ the large molecular-cluster approach (212 atoms) to study the biosynthesis of isonitrile substituents in a peptide chain by the nonheme enzyme ScoE. The authors found two consecutive catalytic cycles that use one molecule of dioxygen and  $\alpha$ -ketoglutarate. In both cycles the active species is an Fe<sup>(IV)</sup>-oxo species, which in the first reaction cycle reacts via two consecutive hydrogen atom abstraction (HAT) steps to desaturate the N=C bond. The first HAT occurs from the N–H group and thereafter from the C–H group. The alternative ordering of hydrogen atom abstraction steps was found to be energetically less favorable.

Maria Ramos et al. describe an engineering of polyketide synthase (PKS) mega-enzymes, as potential means for biosynthesis of high-value active molecules. PKS enzymes produce polyketides in bacteria, fungi, plants and certain

animal families. The authors outline the structure, catalysis and machinery of the PKS, as well as their engineering and applications in biotechnology.

## 5 Perspective

We hope that the diversity and scope of these reviews and articles convincingly illustrate that theoretical and computational studies contribute to fundamental understanding of numerous aspects of catalysis. Since the manifold facets of catalysis still constitute a *terra incognita*, which require explorations, computational catalysis is indeed a land of opportunities and will remain so for the years come. The synergy of experiment and theory in catalysis, illustrated in many contributions of this issue, is essential for better control of catalysis. Many more explorations are awaiting the communities of computational and experimental chemists.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.