Quo vadis multiscale modeling in reaction engineering? – A perspective

Authors:

Gregor D. Wehinger[1*], Matteo Ambrosetti[2], Raffaele Cheula[2], Zhao-Bin Ding[3], Martin Isoz[4], Bjarne Kreitz[5], Kevin Kuhlmann[6], Martin Kutscherauer[1], Kaustav Niyogi[2], Jeroen Poissonnier[7], Romain Réocreux[8], Dominik Rudolf[9], Janika Wagner[10], Ronny Zimmermann[11], Mauro Bracconi[2*], Hannsjörg Freund[9*], Ulrike Krewer[10*], and Matteo Maestri[2*]

Affiliation:

[1] Institute of Chemical and Electrochemical Process Engineering, Clausthal University of Technology, Clausthal-Zellerfeld, Germany

[2] Laboratory of Catalysis and Catalytic Processes, Dipartimento di Energia, Politecnico di Milano, Milan, Italy

[3] School of Chemical Engineering and Technology, Sun Yat-Sen University, Zhuhai, Guangdong, China

[4] Institute of Thermomechanics of the Czech Academy of Sciences, Prague, Czech Republic

[5] School of Engineering, Brown University, Providence, Rhode Island, USA

[6] Chemical Process Engineering, University of Bremen

[7] Laboratory for Chemical Technology, Ghent University, Ghent, Belgium

[8] Department of Chemical Engineering, University College London, London, United Kingdom

[9] Reaction Engineering and Catalysis, Technical University Dortmund, Dortmund, Germany

[10] Institute for Applied Materials – Electrochemical Technologies, Karlsruhe Institute of Technology, Karlsruhe, Germany

[11] Chair for Process Systems Engineering, Otto von Guericke University Magdeburg, Magdeburg, Germany

[*]**Corresponding authors:**   Gregor D. Wehinger, wehinger@icvt.tu-clausthal.de
Mauro Bracconi, mauro.bracconi@polimi.it
Hannsjörg Freund, hannsjoerg.freund@tu-dortmund.de
Ulrike Krewer, ulrike.krewer@kit.edu
Matteo Maestri, matteo.maestri@polimi.it

Highlights:

- Surface changes are highly dependent on local conditions and require models bridging from molecular to continuum scale.
- Hierarchically-based microkinetic analysis is challenged by the complexity of the material, reaction mechanism, and parameter estimation.
- Coupling kinetic models and CFD simulations must be sped-up with acceleration techniques or surrogate models.
- Catalyst-reactor-plant systems must be based on CFD with which surrogate models should be developed for higher scales.

Abstract

This work reports the results of a perspective workshop held in summer 2021 discussing the current status and future needs for multiscale modeling in reaction engineering. This research topic is one of the most challenging and likewise most interdisciplinary in the chemical engineering community, today. Although it is progressing fast in terms of methods development, it is only slowly applied by most reaction engineers. Therefore, this perspective is aimed to promote this field and facilitate research and a common understanding. It involves the following areas: (1) reactors and cells with surface changes focusing on Density Functional Theory and Monte-Carlo simulations; (2) hierarchically-based microkinetic analysis of heterogeneous catalytic processes including structure sensitivity, microkinetic mechanism development, and parameter estimation; (3) coupling first-principles kinetic models and CFD simulations of catalytic reactors covering chemistry acceleration strategies and surrogate models; and finally (4) catalyst-reactor-plant systems with details on linking CFD with plant simulations, respectively. It therefore highlights recent achievements, challenges, and future needs for fueling this urgent research topic in reaction engineering.

1 Introduction and Motivation

Reaction engineering is the scientific discipline dealing with chemical and electrochemical reactions to meet various business and technical objectives, e.g., high productivity and selectivity, process and product safety, environmentally compatible products, minimization of waste generation, minimization of investment, minimization of energy consumption, and operability and control.[1] In today's global business environment, these objectives are typically included in a framework for chemical product design.[2] One essential part of this framework is the product design model, which comprises model parameter constraints, economic, properties, process, and product performance models, respectively, as well as objective functions with a multitude of constraints.[3] For simultaneous process-product design, the multiscale approach provides opportunities to consider phenomena on different time and length scales of the reaction system basically from the electron level up to the plant level. Figure 1 shows schematically all involved levels for chemical and electrochemical reaction engineering. Inside a reactor, a multitude of different physical and chemical processes occur simultaneously on various time and length scales interacting with each other. The basic idea of multiscale modeling is the computation of information at one scale and passing it to the other scale without losing much of the information. This linkage or coupling between scales is challenging in terms of reducing degrees of freedom (abstraction) and in terms of efficient computing (implementation). In recent years, several comprehensive overviews were published about specific aspects of this rather broad topic, such as e.g., multiscale modeling in computational heterogeneous catalysis,[4] focusing on metal-catalyzed reactions,[5] material-function relationships in heterogeneous catalysis,[6] or computational materials science and process engineering.[7] For a more general view of multiscale modeling covering also generic multiscale computing, the reader is referred to a collection of articles elsewhere.[8]

Since the development of multiscale modeling methods is progressing rapidly and its application is likewise feasible for very different fields, we limit this specific perspective to reaction engineering for chemical and electrochemical applications. In such devices, reactants are converted to (by-)products on a solid interface, i.e., heterogeneous (electro-)chemical reactors. The active sites of the catalyst are typically dispersed on a porous structure, e.g., porous washcoat, catalyst pellet, or electrode, where the gas or liquid phase species has to be transported to or away. Consequently, the intrinsic reaction kinetics is affected by transport phenomena, which can be very different depending on the reactor/cell configuration and operation conditions. The final goal of multiscale modeling in reaction engineering is to describe real reactive systems under industrially relevant reaction conditions. In this manuscript, we briefly introduce the atomic scale aspects, which only recently entered reaction engineering. Most of the well-known concepts of the process simulation/systems engineering scales are not addressed in detail. The basis of this manuscript was developed during an online workshop held in summer 2021. Four main topic areas are discussed thoroughly: (1) reactors and cells with surface changes focusing on Density Functional Theory and Monte-Carlo simulations; (2) hierarchically-based microkinetic analysis of heterogeneous catalytic processes including structure sensitivity, microkinetic mechanism development, and parameter estimation; (3) coupling first-principles kinetic models and CFD simulations of catalytic reactors covering chemistry acceleration strategies and surrogate models; and finally (4) catalyst-reactor-plant systems with details on linking CFD with plant simulations, respectively. The general aim of this perspective is to promote this field and facilitate research as well as application by providing a common understanding between different communities and different applications.
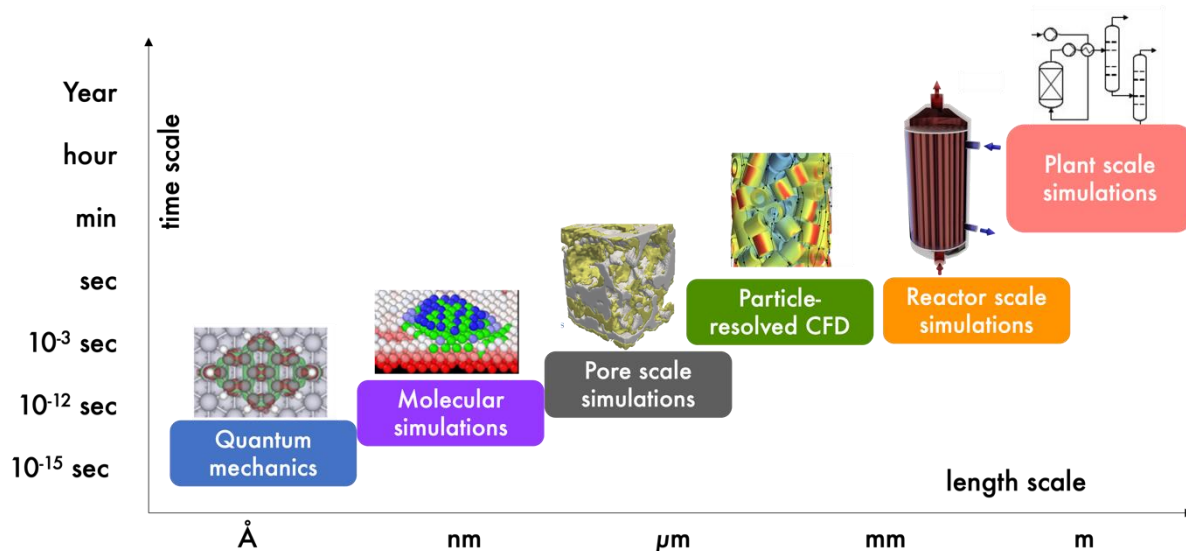

Figure 1: Typical time and length scales in reaction engineering problems. Adapted partly from Ref.[2]

2 Multiscale Modeling in Reaction Engineering

2.1 Reactors and cells with surface changes

Solid/liquid and solid/gas interfaces are ubiquitous in heterogeneous (electro-)chemical systems. Far from being inert, these interfaces host various physical and chemical transformations. They can trigger the precipitation of species and catalyze reactions, which in turn, can affect their structure and chemical compositions. These transformations can be described at different scales ranging from the scale of chemical bonds to that of the solid of interest (shape, crystal structure, …) and can even influence the operation of the whole (electro-)chemical reactor. Here, we discuss the different theories that can be used to model such systems and how the different scales are coupled.

2.1.1 Modeling changes at the atomistic scale with DFT

The atomistic scale is the smallest scale at which one can describe how the surface of a material chemically changes upon given conditions. Albeit not perfect, Density Functional Theory (DFT), which explicitly treats electrons and how they bind atoms together, has become very popular to accurately describe the transformations interfaces may undergo. One approach, usually referred to as 'static DFT', consists in building representative surface models and relaxing their geometric structure until they reach an energy minimum. Because finite temperature effects are not considered during the optimization, these calculations are, in principle, only representative of conditions at 0 K. For uncorrelated systems, i.e., solids and gases, thermal effects can be recovered, from 0 K calculations, using tools of statistical mechanics, such as partition functions. This approach has been applied to predict metal/oxide phase diagrams under varying oxygen atmosphere[9] or electric potential[10]. There is also literature regarding the determination of kinetic parameters for surface restructuration.[11] One success story is the decade-long step-by-step development of a theory-based model for γ-Al$_2$O$_3$ (bulk and then surface) accounting for the changes it undergoes under steam conditions: surface hydroxylation and reorganization of the surface Al network.[12] These models have been key to the understanding of the surface chemistry of this oxide, which is used as a support and a catalyst in industrial processes. However, when dealing with flexible or dynamical systems, such as electrolytes where the dynamics of ions affects that of the solvent molecules, thermal effects cannot be treated as a correction to 'static DFT' calculations as they more drastically influence the structure. In this case, DFT must be coupled with Molecular Dynamics to capture the motion of atoms.[13] As most surface modifications are, even slightly, activated, the so-called *Ab Initio* Molecular Dynamics (AIMD) simulations must be accelerated to make these transformations happen during the simulation. One first way to accelerate AIMD is to bias the simulations using a known constraint (thermodynamic integration or umbrella sampling) or add a known bias potential to help the system cross barriers. For instance, biased AIMD simulations have been used to determine the pK_as of surface hydroxyl,[14] crucial to understanding how pH can alter the surface of a material, and to elucidate the early steps of the chemical weathering of γ-Al$_2$O$_3$, which is associated with the formation of a boehmite layer, in liquid water.[15] One other approach is to use DFT data to train a machine-learning model, which would be able to perform simulations, without biases, but in a considerably faster way. Kozinsky and co-workers recently reported 2μs-long simulations for the study of the alloying mechanism of a Pd island

on an Ag slab using such an approach (Figure 2a).[11] All in all, DFT is good at capturing the energetics of chemical reactions that can induce surface modifications of a solid. The main limitation is that it is borne to study a small portion of the entire system (~nm^2) and to assess the energetics of a few elementary steps leading to surface transformation. Statistical mechanics and transition state theory may translate microscopic data into reliable macroscopic properties. However, this approach is limited to ideal systems.

2.1.2 Monte-Carlo simulations of representative structures

One way forward is to select representative structures and run statistical simulations that can describe larger interfaces and extend the reachable time scale. Monte-Carlo simulations are one example of such an approach. Using a stochastic algorithm, they can sample a large number of configurations, the energetics of which can be assessed from a DFT-parametrized Cluster Expansion (CE) Hamiltonian. For example, such simulations have been used to investigate how adsorbates can affect the aggregation of single atoms to clusters at the surface of Single-Atom-Alloys[16] or the segregation of metals in intermetallics (Figure 2b). Albeit extremely insightful, Monte Carlo simulations can only help identify the most stable phases under given conditions. To get insights into the time evolutions of surface transformation, we need to move to Kinetic Monte Carlo (KMC) simulations, where the transition rate from one state to another is not given by its exothermicity but rather its kinetic rate constant.

KMC models can be set up in different dimensions. In 2D models, the lattice can either represent a smooth surface[9,17,18] or the area above the surface.[19–22] 2D+1 models allow for the diffusion of species on a two-dimensional surface lattice and further enable the accumulation of species in a third dimension. They have been used to study the formation of surface films such as solid electrolyte interphases at carbon electrodes in Li-ion batteries.[23] Eventually, 3D models describe the diffusion and interaction of species in all three dimensions. These models have been used to study crystallization reactions in chemical systems,[24] layer growth in electrochemical systems,[25] and dealloying processes of alloy catalysts.[26]
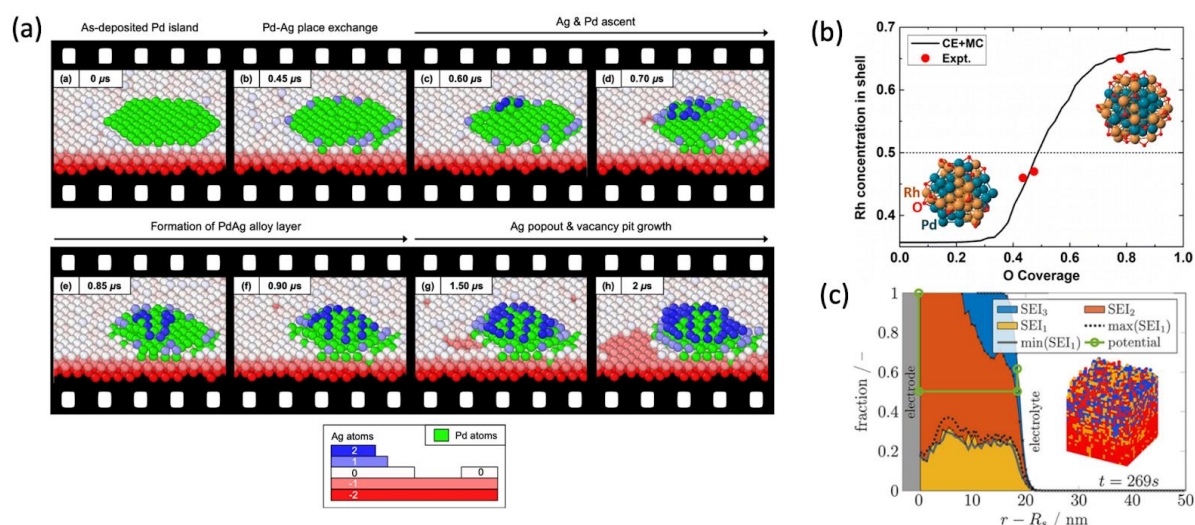

Figure 2: Examples of multi-scale modeling simulations for the investigation of interface modifications. (a) Snapshots of the molecular dynamic simulation performed with the Gaussian process machine learning force field trained on DFT data. The simulation shows the alloying mechanism of a Pd island deposited on Ag.[11] (b) Monte Carlo simulation parameterized with DFT data via a Cluster Expansion Hamiltonian. The simulations identify the alloy surface composition as a function of the

oxygen coverage. (c) Experimentally parameterized Kinetic Monte Carlo - continuum simulation on a 2D+1 lattice reveals the formation of a 20 nm thick solid electrolyte interphase (SEI) consisting of three solid products on graphite electrodes of Li-ion batteries.[27]

One major challenge when setting up a KMC model for surface changes is the adequate selection of the processes that will be included and the parameterization of the related transition rates. The required energy barriers can either be obtained experimentally or by *ab initio* calculations. In the latter case, the lateral interactions between species (intermediates or inert species) can be taken into account so simulations can adapt to experimental conditions.[28] In the past, the *ab initio* parameterization technique was used to study very different systems: the dissolution of NaCl crystals at the NaCl-water interface,[29] the bistability of Pd/PdO under CO oxidation conditions,[9] the formation of coke precursors on metal surfaces,[18] the diffusion of Li ions into the positive Li_xCoO_2-electrode,[30] and the solid electrolyte interphase formation on Li-metal electrodes.[31] However, since the environmental conditions may change during the simulation and since *ab initio* calculations are never perfectly accurate, errors can propagate to larger scales. To prevent this, a stronger coupling between KMC and *ab initio* approaches would be required in the future to correct the energy barriers during the runtime of the simulation. This demands efforts to tackle the computational cost of such an approach and to standardize coupling procedures.

2.1.3 Coupling KMC with continuum models

To investigate the interplay between heterogeneous surface changes and the operation of full-scale (electro-)chemical reactors, a direct coupling of KMC simulations with continuum models can be a suitable approach. This was, for instance, applied to study the growth of a protective solid electrolyte interphase on graphite anodes in Li-ion batteries (Figure 2c) for different battery operating conditions[27,32,33] or to study the Kraft pulping process.[21,34] However, it is important to notice that the integration of the microscopic and macroscopic scales is not straightforward. First, there might be significant time scale disparities between different phenomena. For example, the interphase formation reactions in Li-ion batteries can take place in the nano- to microsecond range while the charging process of the battery, which changes local reaction conditions, may take minutes up to hours. Second, the stochastic fluctuations of the KMC model must be handled during the coupling process, to obtain reliable input parameters for the macroscopic model. Therefore, it is a key challenge to carefully choose a coupling mechanism that allows high-fidelity while keeping the computational cost as low as possible. In this regard, several approaches have been analyzed by Röder et al.[35] For alternatives to the direct coupling of KMC and continuum scale, e.g. by surrogate models, see chapter 2.3.

Many research groups have developed their own KMC software, which they have made publicly available. To name a few, KMCLib provides an on-lattice KMC code that is specifically designed for bulk and surface diffusion processes in complex systems;[36] NASCAM is particularly well-suited for the study of species deposition on substrates;[37] and Zacros provides a very flexible graph-theoretical KMC algorithm to model surface reactions at the solid/gas interface.[38,39] On-lattice codes use a fixed lattice to map coordinates or adsorption sites. But a fixed lattice of adsorption sites can be limiting, especially when the experimental conditions can induce changes of the material's surface (e.g., oxidations, chemical weathering)

and a reorganization of the network of adsorption/diffusion sites. Another limitation is that each software is used for a set of applications and the input files, which are typically large to cover all the possible configurations and elementary events to model, cannot be generated in an automated and software-non-specific way. To make KMC more accessible in the future, it would therefore be essential to have unified tools that are system- and software-independent. A standardized user interface or API would allow researchers to set up new models more easily and efficiently and narrow the gap between atomic and macroscopic techniques.

2.2 Hierarchically-based microkinetic analysis of heterogeneous catalytic processes

Applying molecular simulation methods in heterogeneous catalysis is crucial for the rational understanding of catalysts' functionality with an atomistic level of detail.[5,6] The inclusion of such techniques in the multiscale analysis of catalytic systems faces three main challenges: (i) complexity and dynamic nature of catalyst,[40] (ii) complexity of reaction mechanisms, [6,41,42], and (iii) complication and computational cost of energetic parameter estimation.[43] These challenges must be addressed by an efficient multiscale modeling framework[44] schematically illustrated in Figure 3.
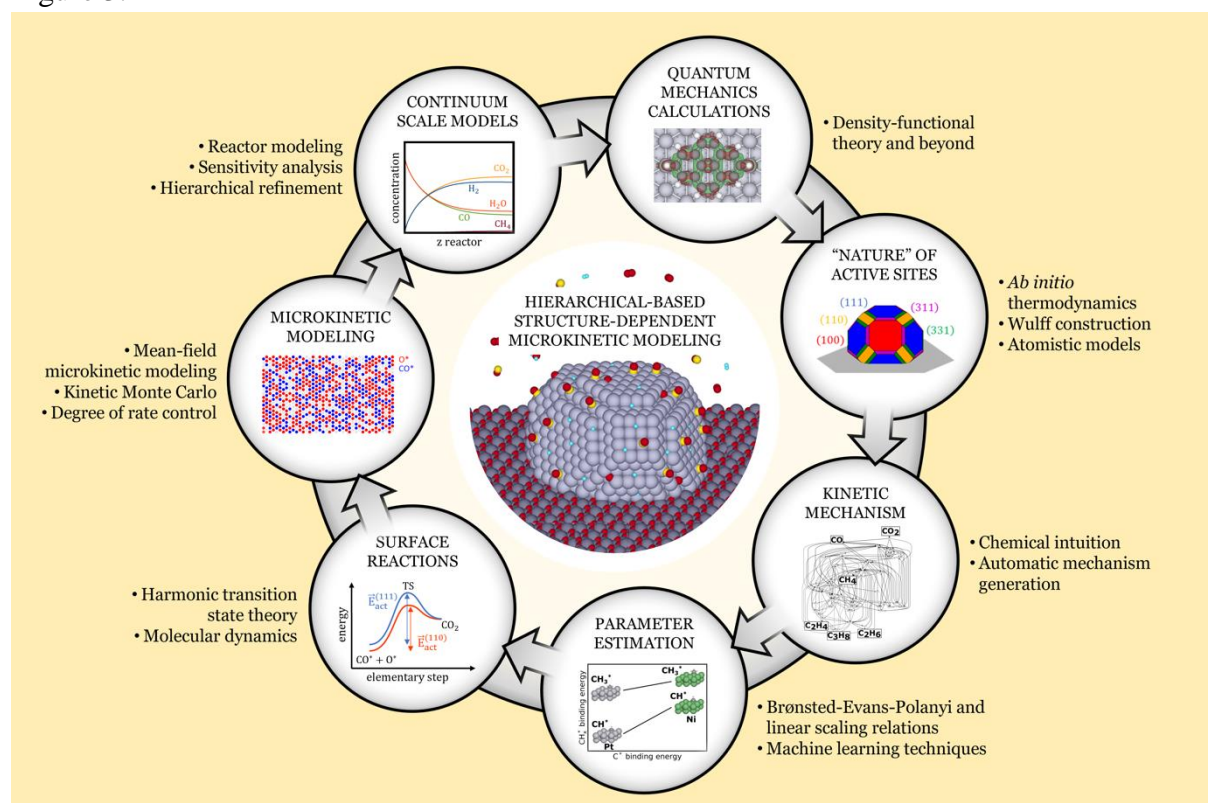

Figure 3: Schematic illustration of the hierarchical-based multiscale modeling approach for catalytic surface reactions.

2.2.1 Catalyst structure and active site

Estimating kinetic and thermodynamic parameters for microkinetics via the application of first-principles electronic structure methods intrinsically requires the knowledge of the catalyst structure in reaction conditions. The surface atoms of heterogeneous catalysts are arranged in diverse geometric configurations, providing numerous active site motifs. Supported catalyst nanoparticles expose different crystal facets, kinks, corners, and edges to the reaction

environment, which establish different interactions with reaction intermediates and transition states, yielding specific catalytic activities.[45] Besides, catalytic particles are dynamic systems and change their size, shape, and composition according to the local chemical environment inside the reactor, as reviewed in chapter 2.1. The local environment and thus the particles dynamically evolve with the proceeding of the reaction.[40,46] Consequently, the amount of the different types of active sites changes during reaction, which translates into a change in the activity of the catalyst. The complex and dynamic nature of catalyst materials in reaction conditions introduces a "material gap"[45] in the modeling of catalytic reactions based on first-principles since extended surface model systems are usually employed due to computational cost. Modeling of the catalyst structure under reaction conditions is needed to overcome this "material" gap. In this view, *ab initio* thermodynamics and Wulff construction can be applied for the description of catalyst nanoparticles under reaction conditions,[47,48] allowing to reveal the "nature" of the active sites, i.e., the configurations of the atoms at the catalyst surface, which potentially give a contribution to the overall reaction rate. The presence of multiple configurations can be also modelled by coupling density functional theory (DFT) calculations with Boltzmann statistics to describe ensembles of nanoparticles obtaining different morphologies under reaction conditions.[49] Other methodologies for the modeling of catalyst materials include molecular dynamics and Monte Carlo techniques,[50] see also chapter 2.1. These methods must be advanced to cope with the challenge of simulation of multi-metallic and metastable nanoparticles. Then, the study of the catalytic activity by simulation of the reaction paths on the available sites can unravel the "identity" of the dominant active sites of the catalyst, i.e., the sites that give a relevant contribution to the macroscopic reaction.[51] Several studies in the literature investigate the structure-sensitivity of reactions by comparing mechanisms on multiple active sites (e.g., different crystal facets) to identify the ones that provide the highest turnover frequency (TOF). A step forward is provided by the methodology of structure-dependent microkinetic modeling,[51] in which both TOF and abundance of the active sites are accounted for by the concerted simulation of catalyst structure and reaction kinetics at the catalyst surfaces. The representation of the active sites, however, is limited by the approximations introduced in models chosen for the analyses. Important aspects that are currently only partially investigated include the characterization of the active sites at the catalyst-support interface, the evaluation of how the sites distribution changes with the particle size (producing experimentally observed particle-size effects), and the analysis of the kinetics of the morphological evolution of the catalysts under reaction conditions. Further studies must concentrate on the analysis of such important aspects to provide a comprehensive description of the dynamic nature of the active sites.

2.2.2 Mikrokinetic mechanism development and parameter estimation

Reaction mechanisms in heterogeneous catalysis can have thousands of possible reaction intermediates and elementary steps,[6,42,52] even when involving only small molecules, e.g., steam reforming of methane[53] or CO_2 methanation.[54] Therefore, constructing the mechanism by hand is a daunting and error-prone task because a researcher needs to rely on his/her chemical intuition to predict species and pathways instead of selecting only the kinetically relevant steps. This adds computational overhead and bias to the mechanism that can result in missing pathways and wrong conclusions. A sophisticated and rate-based network exploration can be processed however with automated mechanism generation tools[55–58] or machine learning (ML)

frameworks.[42,52,59] One example is RMG (reaction mechanism generator),[56] initially developed for combustion processes, which has been successfully used for heterogeneously catalyzed systems.[54,60–62] Only simple terrace facets of pure metals are considered for automated mechanism generation now, which certainly needs to be improved to account for multifaceted crystals, complex catalysts (e.g. multi-metallic, oxides, zeolites) and catalyst/support interactions.[63] However, these are also challenges for manual mechanism development. It is further necessary to directly include uncertainty propagation into the mechanism generation procedures to account for enthalpic and entropic uncertainties.[54,59]

The evaluation of all the parameters of detailed reaction mechanisms from first-principles is not possible due to the size of the networks, especially when different active sites and catalyst compositions are considered. Therefore, (semi) empirical methods are applied, which can be categorized into physics-based and phenomenological correlation. The physics-based correlations like d-band center theory,[64] linear scaling,[65] Brønsted-Evans-Polanyi relations,[66] or the unity bond index-quadratic exponential potential method[67] are developed based on the common physics behind the targeting surface processes. However, these methods are not always universal.[68] An inaccurate empirical or semi-empirical method can lead to a misinterpretation of key elementary steps and, consequently, slow down the iteration of model refinements. Protocols to assess the accuracy of an empirical method are demanded to facilitate the selection of proper methods. New correlations are also required to accurately describe complex active site motifs such as coked or oxidized surfaces or phenomena like coverage effects. The construction of these correlations requests a more thorough understanding of physical essentials of those phenomena. The second category are phenomenology-based methods. These methods do not require the descriptor linking to the fundamental physics of the targeting reactions. Instead, they map the targeting parameters to the input parameter through a "black box" via usage of ML.[69] Available approaches are compressed sensing methods,[70] gaussian process regression, and graph neural networks.[71] The development of ML methods in catalysis is also accompanied by the release of open-source databases of DFT-calculated data, which are stimulating the scientific community to produce increasingly more accurate models. However, up to now, ML models have been applied mainly to calculate binding energies for catalyst screening. The extension to the modeling of kinetic parameters and the inclusion of the catalyst materials' whole complexity represents an important step toward the efficient estimation of parameters needed for microkinetic modeling. A proper combination of physics-based correlations and phenomenology-based may further improve the applicability and accuracy.

2.2.3 Hierarchical multiscale modelling

Software tools for mean-field models are already well established,[5,6] but these must be revisited to handle the increasing complexity and stiffness of the microkinetics. KMC simulations capture the effect of the surface diffusion kinetics and local concentration of reaction intermediates, but their high computational cost calls for the development of techniques for their speed-up.[72] A further challenge is the thermodynamically consistent implementation of coverage effects on kinetics and thermodynamics, as well as the multifaceted nature of real catalysts. Identifying important reaction pathways has been mostly done via local sensitivity analyses, especially with the degree of rate control concept.[73,74] In these methods, it is necessary

to correctly quantify the correlation among the parameters since this significantly affects the outcome.[75] However, especially with regard to the uncertainty in DFT-based energetic parameters, there is currently a lack of global sensitivity methods even though they provide useful insights into the mechanism.[54] Further, the uncertainty in the microkinetic model parameters has to be propagated to the results to avoid over-interpretation.[76] It is still computationally demanding to include the microkinetics into multiscale simulation frameworks on the reactor scale, like CFD models. An advance in the usage of ML tools to build surrogate models that will enable a speed-up of the simulation is necessary to bridge this gap. New methods for microkinetic modeling need to be developed to describe the effect of electromagnetic fields such as plasma- and photocatalysis.[77–80] In contrast, microkinetic modeling has only begun to be used more frequently for electrocatalytic systems.[81,82] While the complex effects of potential on the energetic parameters are already considered, there are still difficult obstacles to overcome, such as modeling of the electrode-electrolyte interface and solvent effects.[83,84] The use of detailed microkinetic models for reactor scale simulations with e.g. CFD codes is still computationally demanding. Hierarchical microkinetic modeling can be used to derive physically sound global rate expressions for computationally efficient reactor simulations.[53] Another option is the usage of ML tools to build surrogate microkinetic models that will enable a speed-up of the simulation and allow to bridge this gap.[85]

The proposed advancements of the hierarchical-based multiscale modeling approach provide new opportunities to improve our understanding of the complexity of heterogeneous catalysis at the atomic level. In the years to come, it will be possible to screen for catalyst materials using structure-dependent multiscale models instead of simplified microkinetics for single crystal facets. Moreover, with the exploitation of parameter estimation methods, mechanisms can be automatically generated on the fly for all catalytic materials. This procedure will help to identify catalytic materials and intensify reactors for crucial processes for this century, such as the production of synthetic fuels, abatement of pollutions, and the catalytic upcycling of plastic waste just to name a few.

2.3 Coupling first-principles kinetic models and CFD simulations of catalytic reactors

Catalytic reactors are generally characterized by complex interactions of various physical and chemical processes ranging from the reactor's macro-scale to the active site's micro-scale (see Figure 4a-e). An ideal multi-scale model should be (i) general with respect to the studied system and process conditions, (ii) accurate, (iii) strongly linked to the fundamental mechanisms of all the occurring phenomena (i.e., explainable), and (iv) computationally feasible, as shown in Figure 4f. However, such a model is not attainable and a trade-off between the multi-scale model resolution and computational costs is required. Such a trade-off should be made based on the model primary application, e.g., improving fundamental understanding, parametric studies and optimization, or system control and monitoring.
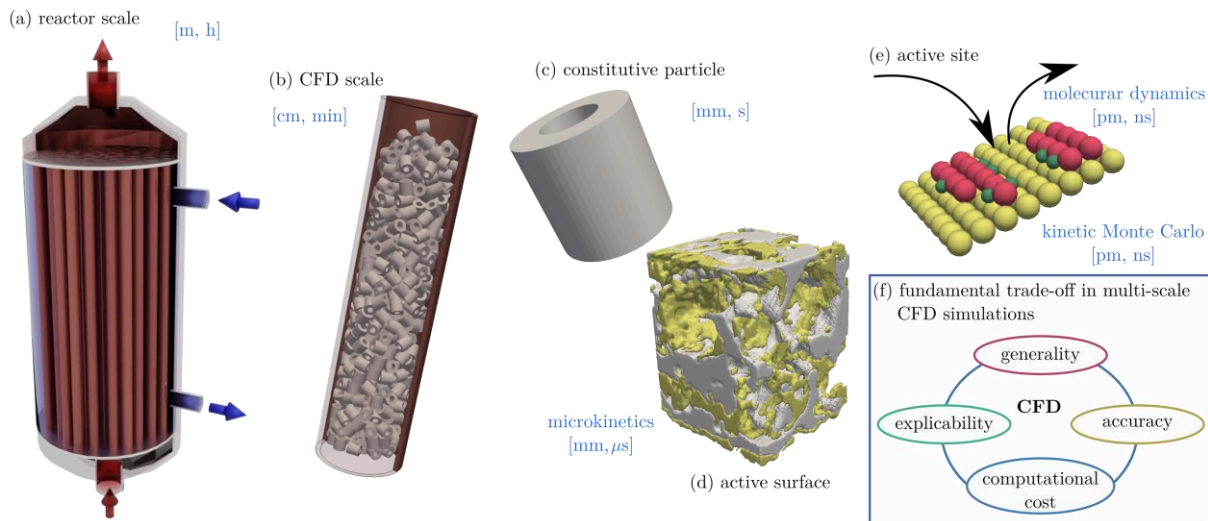
Figure 4: (a)-(e) Different scales in multi-scale modeling in reactor engineering. The scales of interest in the present section are (c)-(e). (f) General trade-off to be considered in multi-scale CFD modeling.

The observed macro-scale reactor functionality is usually strongly dependent on the scale-to-scale interactions.[86,87] Thus, understanding not only the mechanisms relevant to each scale, but also the mutual interactions between the scales is of utmost importance to create more efficient chemical technologies. To achieve this, it is necessary to adopt a first-principle approach at each scale based on the fundamental governing equations, e.g., microkinetic modeling based on electronic structure theory calculations and Navier–Stokes equations at the macroscale. The macro-scales ranging from the reactor down to the pellet scale (see Figure 4a-d) are governed by the transport phenomena and can be described, according to the first-principles approach, by the means of the CFD. However, in heterogeneous reacting systems, the governing equations are influenced by the source terms either in the volume or at the boundaries stemming from the micro- and meso-scale chemical interactions (see Figure 4e).[88–91] Ideally, the problem should be tackled by a seamless and full coupling across all the scales, from the reactor to the electrons, by an intimate connection of Direct Numerical Simulation (DNS) at the macro-scales, detailed microkinetic models or KMC simulations at the meso scale and electronic structure calculation at the microscale.[85,87] Unfortunately, the simultaneous and coupled solution of the characteristic equations at each scale is and, for a foreseeable future, will be, far from computationally feasible due to the required bridging of phenomena spanning on a broad range of different time and length scales. However, depending on the required level of accuracy, it is possible to couple continuum models with detailed description of the surface reactivity. For instance, Maestri et al. coupled detailed microkinetic models with 1D reactor model for describing the catalytic partial oxidation of methane.[92] Deutchmann and coworkers coupled detailed microkinetic models with 2D and 3D models for the analysis of structured reactors.[86,93,94] Wehinger and coworkers coupled 3D CFD simulations of packed-bed reactors with detailed microkinetic models.[89,95,96] Röder et al. achieved a complete coupling even with KMC simulations in the context of Li-ion batteries[35], as discussed in chapter 2.1.3. The coupling of first principles based reactivity in CFD calculation is, however, even more complex and requires specific methodology to be achieve. In this view, the most severe bottleneck preventing computationally efficient first-principles-based multi-scale modelling of heterogeneous reactors is the coupling

between CFD and first-principles kinetic models itself,[97] i.e., bridging the scales (c), (d) and (e) as shown in Figure 4.

2.3.1 Coupling strategies with CFD and speed-up techniques

An accurate coupling of microkinetics and CFD is essential to improve the understanding of the interactions between surface reactivity and fluid flow. Coupling the different scales get computational manageable by solving the equations for the first principle microkinetics and the fluid flow separately and transferring the required information between the scales. Different strategies for this information transfer can be considered.

In case of microkinetic models, the analytical expression of the elementary rates allows for their direct inclusion into the reactor models.[98–100] Consequently, the relevant computational burden can be alleviated by considering on-the-fly methodologies like in-situ Adaptive Tabulation (ISAT),[101–103] Cell Agglomeration,[104–107] dynamic adaptive chemistry,[108,109] and the Reaction-Diffusion Manifold (REDIM) reduced kinetic model.[110,111] Collectively, these methods are often termed chemical acceleration and were developed primarily in the combustion community.[112] KMC simulations can be included in CFD by an effective decoupling between the scales due to the overwhelming computational cost of the single calculation. Doing so, it is assumed that the catalyst surface instantaneously adapts and relaxes to a new steady-state catalytic activity when new local fluid phase conditions are experienced. This enables to the adoption of pre-computed production rates properly tabulated to reproduce the chemical behavior of the system.[113] The possibility to employ pre-calculated rate data properly tabulated paves the way for a new paradigm for the coupling which is the adoption of surrogate models of the first-principles detailed kinetic model, which has been applied first for combustion of fuels.[114,115] Currently, the construction of suitable surrogates for chemistry models in CFD simulations is one of the most active research areas in multi-scale modelling in reaction engineering. Thus, the complete next section is devoted to its description and discussion of potential research perspectives.

2.3.2 Surrogate models and future research directions

Replacing the first principles chemistry model by a suitable surrogate can significantly reduce the computational cost. However, the quality of the surrogate model becomes a critical factor in this case, as it significantly affects the accuracy of the overall multi-scale simulation. The derivation of simplified kinetic models such as the macroscopic and power-law kinetics from microkinetic models can be considered an attempt of the generation of surrogate models and it has been widely employed in the past.[88] Recently, the breakthroughs in Machine learning (ML), a subset of Artificial Intelligence (AI), proved to be extremely promising in developing efficient surrogates of the detailed chemistry. Due to their nonlinear and non-parametric structures, such models can retain detailed information of lower-scale system dynamics and can be applied across different systems.[52,85] One way such ML techniques can be used is to surrogate the entire chemistry time-integration step.[116] In such an approach, the ML model learns the direct mapping between the meso-scale inputs (such as current local chemical composition, operating conditions) and the final states of the meso-scale processes (Figure 4d). This eliminates the need to compute the time-evolution of the meso-scale chemistry and significantly accelerating the computational runs. Another approach that has gained recent attention is to use ML models

such as Artificial Neural Networks[117], Gaussian Process modeling[118], and Random Forests[119] to surrogate the source terms like the net reaction rate. This approach is particularly beneficial for systems with detailed/large microkinetics or KMC models. Therefore, the ML techniques can both be used to surrogate the chemical step as well as approximating directly the source terms like the net reaction rate[85,119].

However, the application of ML techniques in the multi-scale modeling of heterogeneous catalysis is still in a nascent stage and further research is needed on several fronts. One of the primary challenges associated with ML is that the quality of such black box model predictions is heavily dependent on the quality of the training data.[120] Therefore, to efficiently train ML models, high quality training data needs to be generated from lower-scale first-principles simulations. Even for highly accurate first-principles simulations, some modeling discrepancies will be present based on the modeling assumptions influencing the results and propagate across the scale affecting the accuracy of the entire process.[121] Another challenge in building accurate ML models as surrogates is the amount of training data needed to learn the true internal dynamics.[122] Since the training data is primarily generated through computational runs of lower-scale physics, generating a sufficiently large data set for model learning can be computationally unfeasible. Moreover, in physical systems the underlying dynamics is often nonlinear and space filling sampling methods may be insufficient for model learning.[123] Recent advances in the paradigm of physics-guided machine learning techniques can prove useful in this regard, as in such methods the exploration space for data-point selection is not only based on statistical sampling techniques, but also constrained by the physical governing equations of the system.[85,124]

Applying machine learning in system design also suffers from the lack of physical or chemical relationships, due to the black box form of such models. However, for multi-scale simulations, understanding the underlying relationship and coupling of inter-scale phenomena is equally important as the prediction accuracy. Traditional ML models such as neural networks and ensemble models are limited in this sense and a shift is needed to more sophisticated symbolic AI techniques.[125,126] Such techniques are capable of revealing the internal governing equations of the system, thereby increasing the explainability of the model predictions. As surrogate models replace the first-principles kinetics, care should be taken to estimate the modeling uncertainties that may arise as a result of the lower-scale information transformation, averaging and coarse-graining.[127] Therefore, surrogate modeling should go hand-in-hand with rigorous uncertainty quantification techniques, an emerging research area in general, almost completely unexplored with respect to the multi-scale modeling in reaction engineering.

Finally, despite the large impact that is expected by surrogate models, methodologies that effectively combine surrogate models and full coupling can be suitable to further mitigate the computational cost without penalization on the accuracy. For instance, zonal approaches can be considered. They have been proposed in cold fluid dynamics as detached eddy simulations, which switches between Reynolds averaging and large eddy simulation to resolve turbulence.[128] A reactive zonal approach is deemed to distinguish simulation areas (zones) where a direct coupling to first-principles kinetic models is necessary, and zones where a description via

simpler surrogated kinetic models is sufficiently accurate. However, finding reasonable criteria for the definition of the zones requires further research.

2.4 Catalyst-reactor-plant systems

Especially for technically relevant systems, such as catalytic fixed-bed or structured reactors, it is necessary to bridge scales from the catalyst particle/pellet over the reactor to the plant scale, as shown in Figure 5. The purpose for such technical systems is not necessarily a most detailed simulation of the given system; the describing model should rather be as simple as possible, but as exact as necessary. For optimization purposes, further model reduction is often required to account for numerical feasibility, while the validity range of a model must still be complied. Therefore, an adequate degree of abstraction is required, while addressing equal basic assumptions and uncertainty levels on each of the bridged model scales. The three levels of reaction engineering modeling and simulation discussed hereafter are (i) particle, (ii) reactor, and (iii) plant scale, respectively.
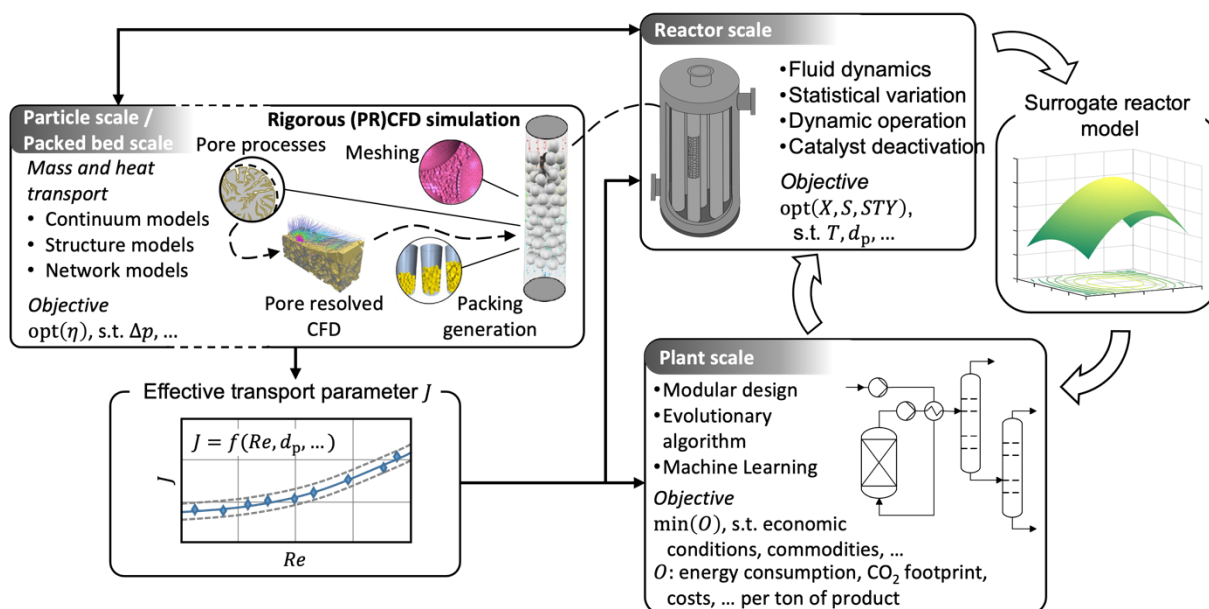

Figure 5:Multiscale modeling of catalyst-reactor-plant systems. Full arrows represent the current state of the art and are still subject of ongoing research. Dashed or blank arrows address hot or future research topics, e.g., including resolved catalyst pellet pores in PRCFD simulation, further coupled with reactor simulation at industrial scale. Partly adopted from.[88,129]

2.4.1 Particle-scale simulations

In most cases, powder materials, which are often used for lab-scale intrinsic reaction kinetics acquisition, are not used in industrial scale catalytic reactors, as the pressure drop in the catalyst bed would be too high. Consequently, catalyst pellets with a size of at least a few millimeters, or structured packings are applied, typically in reactor tubes of length of a few meters and a diameter >20 mm. Concentration and temperatures gradients inside these pellets are present, which affect the overall performance of the system, due to complex interplay of reaction kinetics with mass and energy transport phenomena.

The quickly growing field of (particle-resolved) computational fluid dynamics (PRCFD) will play a major role towards understanding the interaction of these phenomena.[90] PRCFD allows

for detailed simulations of flow within complex geometries. Coupled with microkinetic models, a non-intrusive, invaluable tool is given to investigate heterogeneous (fluid-solid) reaction systems and understand the underlying complexities. Today, PRCFD can be considered state-of-the-art, as technical issues are widely addressed. Although, drawbacks still arise from limited computational power, which hinder the full-scale simulation of industrial scale fixed beds with thousands of pellets, besides that the numerical generation of such large packed beds is challenging. Especially for random beds of non-spherical particles – e.g., hollow cylinders are often used in industry – the most challenging part is the volumetric mesh generation of contact areas of particles among each other and of particles and reactor wall, that strongly influences the heat transport in the system.[130–133] Combined with the development of powerful 3D imaging techniques, such as X-Ray tomography and electron tomography, PRCFD will enable going beyond conventional engineering approaches. As an example, Koči and coworkers investigated the detailed reaction-transport in gasoline catalytic filters, where several portions of the material were investigated to extract average properties of the system (e.g., porosity, pore diameter), correlate these to the macroscopic features (e.g., permeability) of the support and use the latter to estimate the catalyst effectiveness more accurately.[129,134–136]

Nevertheless, as pore diameters in catalyst materials can span several orders of magnitude, from nanometers to micrometers, resolving every single pore in an entire fixed-bed reactor is computationally out of reach in the near future. Therefore, the conventional modelling approach, which treats the catalyst moldings as a homogeneous medium with effective/lumped parameters for reaction and transport phenomena, will continue to be developed, e.g., for application in reactor optimization and control.[137,138] A pertinent example is the literature of multi-component mass transport models in porous media. The Dusty Gas Model,[139] the Binary Friction Model,[140] the Capillary Interpolation Model,[141] the Modified Binary Friction Model,[142] and the Adaptive Binary Friction Model[143] were each designed as an improvement of their predecessor. One possible research direction will be the inclusion of network effects, such as pore size, length, and connectivity distributions, as it was done for the Dusty Gas Model[144] as well as anisotropic catalyst pellet properties, which can be of significance as shown more recently.[145] Compared to mass transport models, heat transport models for porous media are scarcer in literature, which is most likely due to the large number of possible structures in solids and absence of experimental data to validate these models. In this context, the development of spatially distributed probing techniques will give rise to new possibilities for generating experimental data for model validation.[146] The future application of these techniques in other reactors of recent interest is expected, such as lab-scale reactors like Temkin[147] and single pellet string reactors,[148] respectively.

2.4.2 Industrial reactor-scale simulations

Industrial reactors are characterized by a scale in the range of 0.1-10 m in both axial and radial direction. These systems can be distinguished in fixed bed reactors (i.e., pellets or structured supports are not moving with the flow) or moving bed reactors (i.e., fluid flow and solid flow coexist), reactants and products can be present in a single or in different phases and finally systems can be adiabatic or can exchange energy with the environment (i.e., multi-tubular externally heated/cooled reactors). In the following, the focus is on two-phase fluid-solid

applications, while it can be extended to three-phase gas-liquid-solid application, e.g., trickle bed reactors, where also particle wetting should be assessed.[149]

The change of the representative scale required to move from particle scale to industrial reactor scale requires the use of different mathematical approaches to maintain a sufficiently 'low' computational cost. In the early 1970's, continuum reactor models with resolution in 1D or 2D, considering temporal evolution of the system and considering kinetics with different orders of complexity were already proposed.[150] In the basic 1D models the different phases are either treated as a single, pseudo-homogeneous continuum or as two heterogeneous phases and are based on a multitude of engineering closure correlations.[151] To account for radial gradients, two-dimensional models were developed. These models may also include mass transport limitations and non-isothermal conditions in catalyst pellets.

Recent advances in computer science have led to possible improvements in these approaches. On the one hand, detailed PRCFD and CFD simulations of different structured supports can be used, as already discussed in chapter 2.4.1, to provide a one-to-one comparison with the experimental data. Moreover, PRCFD can be used as cost-efficient studies for investigations of novel reactor concepts for process intensification.[95,152,153] On the other hand, rigorous CFD simulations are at the basis of the hierarchical approach. These simulations can be used as well to perform in-silico experiments: diverse parameters and process conditions can be finely adjusted towards the derivation of descriptive, physically driven correlations, describing the transport properties that can be included in conventional reactor models.[154,106,96,155] Thus, PRCFD is a reliable means to assess engineering correlations for estimation of transport properties (i.e., pressure drop, heat and mass transfer coefficients), to bridge the gap between the scales towards (industrial) reactor and process simulations.

In order to reduce the computational burden of PRCFD simulations, some authors proposed a hybrid modeling approach to be promising: areas in the reactor of steep temperature or concentration gradients, e.g., hot spots, are modeled by PRCFD, whereas the remainder is covered by a porous medium models. Meinicke et al. introduced a hybrid scale CFD approach, first of all to suppress entrance effects to the fully resolved simulation zone of perfused solid sponges (this corresponds to the particle scale).[156] The main purpose is to guarantee reasonable boundary conditions for the rigorously simulated zone, while it is surrounded by the embedding zone, handled with an effective porous medium approach (macro scale). Elegantly, to avoid artificial jumps at the interface between those zones, a transition zone was introduced.[156] A similar approach should be developed and applied for catalytic fixed-bed or structured reactors.

Nevertheless, even though effective medium models are computationally much less expensive than PRCFD, they might still be too extensive for answering recent questions at the reactor scale. e.g., the design of reactors, which can be operated dynamically depending on the given reactant load, which is a focus of research in the context of Power-to-X applications. This adds an additional level of complexity to the reactor design.[157,158] For such cases, computationally efficient models with discontinuity are necessary. Machine learning tools can be applied for such cases for reducing the model complexity at reactor scale, see also the discussion on modelling at the plant scale below. For example, a neural network can be trained to calculate

the catalyst effectiveness factor depending on the present and past process conditions, based on experimental data or simulation results. Nevertheless, the full potential of machine learning tools has not yet been explored in depth. Schweidtmann et al. identify six key challenges for upcoming research work in this respect.[159] Therefore, another approach is dedicated to tailored model reduction approaches, which are based on approximate solutions of the underlying mass and energy balance equations. So far, most of the literature approaches deal with the steady-state problem, but advances for dynamic scenarios[160] are necessary for future considerations.

Considering reactor-scale simulations for fluidized beds, the tracking of single particles in the system and their evolution in time and space is computationally demanding. Therefore, to enable industrial scale simulations of fluidized bed reactors, approaches to reduce computational costs are required. One option is the coarse grain model,[161] where different particles are grouped in virtual grains with bigger size that are then solved considering possible interactions and real motion of the particles. Contrarily, the Euler-Euler approach models the solid phase as a homogeneous phase and effective transport properties of the solid are considered, for which the energy and mass balances are solved while accounting for the interplay between the different phases. In particular, continuity at the boundary between gas and average solid phases are imposed. This approach has been successfully adopted to analyze reactors with intra-phase mass and heat transfer resistances including microkinetics descriptions.[91,162] Especially, the coarse grain model seems promising for future reactive fluidized beds including multi-scale modeling considerations.

Finally, other relevant approaches have been introduced in the last years to introduce effects of non-idealities and statistical variations in idealized reactor simulations, that can have a strong impact on local and overall properties of the system. As an example, Freund and coworkers studied the effect of a statistical variation of the activity of the catalyst bed on local temperatures inside the reactor. For an exothermic reaction, with respect to the ideal case (i.e., averagely distributed catalyst), nonideal dilution may lead to temperature deviations in the range of ± 10 °C, which are considered significant with respect to reactor design under safe operation.[163] PRCFD could give even more detailed insights into diluted fixed-bed reactors, where active and inert particles are spatially resolved. Another aspect to be considered in multi-tubular reactor models is the multiplicity of possible operating conditions inside the single tubes and non-idealities. In multi-tubular reactors, in fact, pellet distribution cannot be equal, and also the cooling/heating tubes.[164] Additionally, the integration of catalyst deactivation (a phenomenon that typically takes place on a long-time scale) in model-based reactor design and optimization has recently been shown,[165] where possible strategies for operations with deactivating catalysts were compared. Consequently, very different requirements are formulated for industrial reactor-scale simulations: computationally efficient models, transient formulation, flexible consideration or omittance of phenomena based on pre-defined criteria.

2.4.3 Plant-scale simulations

Including detailed industrial reactor models in process scale simulations is challenging as the computational cost of the reactor block should remain limited. Therefore, a small number of contributions incorporating industrial reactor models in a process simulator (e.g., Aspen Plus) include user-defined 1D reactor models.[166,167] Thereby, the model detail goes beyond built-in

power law or LHHW type kinetics in ideal and isothermal reactors and beyond intrinsic kinetics as mass and heat transfer on the particle scale are accounted for. Yet, 2D or PRCFD simulations remain computationally too expensive, despite the continuous increase in availability of computational power. Another, less detailed and physically meaningful approach for process simulation is the use of response surface models (RSM), which are constructed from lab-scale experiments or data available in the open literature.[168,169] To achieve an optimal balance between model accuracy and computational cost, such RSM models are, however, relevant. The data to train the model can be envisaged to be obtained from PRCFD simulations, or 2D simulations if the former would still be too computationally expensive. A simulation design, i.e., the equivalent to a design of experiments, can then be developed and the corresponding simulations can be run with the very detailed model, as demonstrated during the optimization of the oxidative coupling of methane.[170] After development of the multiparametric equations constituting the RSM model, some validation simulations could be performed with the detailed PRCFD model to finally verify the accuracy of the reduced model. Upon successful validation, the RSM model can be then used for the coupling with a process simulator. Along similar lines, machine learning techniques, such as artificial neural networks, can be applied to obtain mathematically inexpensive models. While these are black box models and interpretation thereof is dangerous[171], such tools are envisaged to be useful on the process scale, as the need for fundamental information on the reactor level during process simulation is limited. Most important is to retain the accuracy on the model simulations, as e.g., successfully demonstrated for the Fischer-Tropsch synthesis using a ML model trained using data generated from a microkinetic model.[172] Interpretability techniques have been used to demonstrate that the trends predicted as a function of the operating variables is indeed present in the ML model, albeit that no fundamental relationship can be formulated. Nevertheless, as ML model simulated outlet values closely correspond to the ones simulated with detailed models, ML models can be envisaged as a potential tool for upscaling purposes. The reasoning followed for the reactor can also be expanded to other unit operations and coupled to multi-objective evolutionary algorithms for optimal equipment sizing.[173] This implies that for each unit operation multiple (sets of) equipment modules are iteratively evaluated, aiming at the development of a process with a low minimal capacity, high maximal capacity and low capital investment for maximal process flexibility. The set of equipment modules is thereby treated as a genetic strain, which is subject to single-point crossover (of two parent sets) and/or mutation. The offspring are simulated in Aspen Plus and added to the module set if they converge properly. The sequence is repeated until a stopping criterion is achieved, e.g., no successful offsprings are generated in an iteration. In order to obtain reliable lumped models on the plant-scale simulations, physical and chemical constraints[174] should be incorporated, and the data used should follow the FAIR principles, i.e., findable, accessible, interoperable, reusable.[175]

3   Conclusions

Multiscale modeling in reaction engineering is highly important and powerful. It is surely one of the most challenging and likewise most interdisciplinary research topics in the chemical engineering community, today. Although it is progressing fast in terms of methods development, it is only slowly applied by most reaction engineers. Based on the discussion given above, we summarize the main trends and fields of actions as follows:

- Surface changes in reactors and cells, whether due to aging or dynamic operation, are gaining increasing attention. Understanding and controlling their inherent multiscale nature in reactors requires coupling of molecular surface models on different levels with continuum models. Attention needs to be given to implement realistic, local conditions in DFT or AIMD models for parameterization of KMC; here, stronger coupling of the scales seems promising. Further, bidirectional, direct coupling of KMC and continuum scale simulations have been shown to reach the scales from ns to hours, and nm to cm. Methods to reduce complexity and computational cost are welcome.
- Three main challenges are connected with hierarchically-based microkinetic analysis of heterogeneous catalytic processes: the complexity of the material and the reaction mechanism as well as the parameter estimation.
- Coupling CFD with detailed reaction mechanisms is especially computational demanding. Although several acceleration methods already exist, speed-up factors are typically below 100. Therefore, surrogate models, especially those derived with ML, are very promising.
- Multiscale modeling of catalyst-reactor-plant systems should be based on PRCFD. Huge progress has been achieved in the last decade. However, the description of the transport phenomena considering the complex porous structures coupled with heterogeneous reaction inside porous catalyst particles is still not well elaborated. Since PRCFD simulations are computationally demanding, process and plant level models can only consider a portion of information from the PRCFD level. Recent applications, especially for optimization purposes, make use of ML to develop surrogate models on the plant level.
- For coupling purposes between scales, surrogate models based on ML techniques seem to be very promising and have only begun to be applied. Similar research questions address appropriate training sets, incorporation of physical laws in the surrogate model, as well as transferability between codes.
- In addition, FAIR principles are needed for scientific data stewardship and management in reaction engineering in order to facilitate model development across the disciplines and scales.
- Uncertainties at all scales should be quantified thoroughly, since their propagation could lead to severe errors at larger scales. As uncertainty quantification is computationally costly, use of efficient methods is crucial.
- Many research groups have developed their specific code for a subset of applications. This leads to difficulties for incorporation of this code into existing or new ones. Hence, it is indispensable to have unified tools that are operating-system- and software-independent. Standardized graphical user interfaces (GUI) or application programming interfaces (API) would allow researchers to set up new models more quickly and efficiently and narrow the gap between scales.

This perspective paper is meant to promote the field of multiscale modeling in reaction engineering and facilitate research and a common understanding. While much of the highlighted research needs address theoretical aspects, especially for coupling between different scales, it must be emphasized that also experimental insights are very much needed on the corresponding scales.[40] To achieve the above mentioned ambitious future goals, scientists from different research communities, like data science, mathematics, chemistry, chemical engineering, and physics, have to work collaboratively. Therefore, we invite researchers to join our mission and discuss methodologies and concrete applications in the community.

Acknowledgments

References

(1) Lerou, J. J.; Ng, K. M. Chemical Reaction Engineering: A Multiscale Approach to a Multiobjective Task. *Chem. Eng. Sci.* **1996**, *51* (10), 1595–1614. https://doi.org/10.1016/0009-2509(96)00022-X.

(2) Uhlemann, J.; Costa, R.; Charpentier, J.-C. Product Design and Engineering in Chemical Engineering: Past, Present State, and Future. *Chem. Eng. Technol.* **2019**, *42* (11), 2258–2274. https://doi.org/10.1002/ceat.201900236.

(3) Zhang, L.; Mao, H.; Liu, Q.; Gani, R. Chemical Product Design – Recent Advances and Perspectives. *Curr. Opin. Chem. Eng.* **2020**, *27*, 22–34. https://doi.org/10.1016/j.coche.2019.10.005.

(4) Keil, F. Diffusion and Reaction in Porous Networks. *Catal. Today* **1999**, *53* (2), 245–258. https://doi.org/10.1016/S0920-5861(99)00119-4.

(5) Salciccioli, M.; Stamatakis, M.; Caratzoulas, S.; Vlachos, D. G. A Review of Multiscale Modeling of Metal-Catalyzed Reactions: Mechanism Development for Complexity and Emergent Behavior. *Chem. Eng. Sci.* **2011**, *66* (19), 4319–4355. https://doi.org/10.1016/j.ces.2011.05.050.

(6) Bruix, A.; Margraf, J. T.; Andersen, M.; Reuter, K. First-Principles-Based Multiscale Modelling of Heterogeneous Catalysis. *Nat. Catal.* **2019**, *2* (8), 659–670. https://doi.org/10.1038/s41929-019-0298-3.

(7) Cheimarios, N.; Kokkoris, G.; Boudouvis, A. G. Multiscale Modeling in Chemical Vapor Deposition Processes: Models and Methodologies. *Arch. Comput. Methods Eng.* **2021**, *28* (2), 637–672. https://doi.org/10.1007/s11831-019-09398-w.

(8) Hoekstra, A. G.; Portegies Zwart, S.; Coveney, P. V. Multiscale Modelling, Simulation and Computing: From the Desktop to the Exascale. *Philos. Trans. R. Soc. Math. Phys. Eng. Sci.* **2019**, *377* (2142), 20180355. https://doi.org/10.1098/rsta.2018.0355.

(9) Rogal, J.; Reuter, K.; Scheffler, M. First-Principles Statistical Mechanics Study of the Stability of a Subnanometer Thin Surface Oxide in Reactive Environments: CO Oxidation at Pd(100). *Phys. Rev. Lett.* **2007**, *98* (4), 046101. https://doi.org/10.1103/PhysRevLett.98.046101.

(10) Panaritis, C.; Hajar, Y. M.; Treps, L.; Michel, C.; Baranova, E. A.; Steinmann, S. N. Demystifying the Atomistic Origin of the Electric Field Effect on Methane Oxidation. *J. Phys. Chem. Lett.* **2020**, *11* (17), 6976–6981. https://doi.org/10.1021/acs.jpclett.0c01485.

(11) Lim, J. S.; Vandermause, J.; van Spronsen, M. A.; Musaelian, A.; Xie, Y.; Sun, L.; O'Connor, C. R.; Egle, T.; Molinari, N.; Florian, J.; Duanmu, K.; Madix, R. J.; Sautet, P.; Friend, C. M.; Kozinsky, B. Evolution of Metastable Structures at Bimetallic Surfaces from Microscopy and Machine-Learning Molecular Dynamics. *J. Am. Chem. Soc.* **2020**, *142* (37), 15907–15916. https://doi.org/10.1021/jacs.0c06401.

(12) Digne, M. Use of DFT to Achieve a Rational Understanding of Acid?Basic Properties of ?-Alumina Surfaces. *J. Catal.* **2004**, *226* (1), 54–68. https://doi.org/10.1016/j.jcat.2004.04.020.

(13) Réocreux, R.; Jiang, T.; Iannuzzi, M.; Michel, C.; Sautet, P. Structuration and Dynamics of Interfacial Liquid Water at Hydrated γ-Alumina Determined by Ab Initio Molecular

Simulations: Implications for Nanoparticle Stability. *ACS Appl. Nano Mater.* **2018**, *1* (1), 191–199. https://doi.org/10.1021/acsanm.7b00100.

(14)   Gaigeot, M.-P.; Sprik, M.; Sulpizi, M. Oxide/Water Interfaces: How the Surface Chemistry Modifies Interfacial Water Properties. *J. Phys. Condens. Matter* **2012**, *24* (12), 124106. https://doi.org/10.1088/0953-8984/24/12/124106.

(15)   Réocreux, R.; Girel, É.; Clabaut, P.; Tuel, A.; Besson, M.; Chaumonnot, A.; Cabiac, A.; Sautet, P.; Michel, C. Reactivity of Shape-Controlled Crystals and Metadynamics Simulations Locate the Weak Spots of Alumina in Water. *Nat. Commun.* **2019**, *10* (1), 3139. https://doi.org/10.1038/s41467-019-10981-9.

(16)   Papanikolaou, K. G.; Darby, M. T.; Stamatakis, M. Engineering the Surface Architecture of Highly Dilute Alloys: An Ab Initio Monte Carlo Approach. *ACS Catal.* **2020**, *10* (2), 1224–1236. https://doi.org/10.1021/acscatal.9b04029.

(17)   Varshney, A.; Armaou, A. Multiscale Optimization Using Hybrid PDE/KMC Process Systems with Application to Thin Film Growth. *Chem. Eng. Sci.* **2005**, *60* (23), 6780–6794. https://doi.org/10.1016/j.ces.2005.05.055.

(18)   Lian, Z.; Ali, S.; Liu, T.; Si, C.; Li, B.; Su, D. S. Revealing the Janus Character of the Coke Precursor in the Propane Direct Dehydrogenation on Pt Catalysts from a KMC Simulation. *ACS Catal.* **2018**, *8* (5), 4694–4704. https://doi.org/10.1021/acscatal.8b00107.

(19)   Sitapure, N.; Lee, H.; Ospina-Acevedo, F.; Balbuena, P. B.; Hwang, S.; Kwon, J. S. A Computational Approach to Characterize Formation of a Passivation Layer in Lithium Metal Anodes. *AIChE J.* **2021**, *67* (1). https://doi.org/10.1002/aic.17073.

(20)   Blanquer, G.; Yin, Y.; Quiroga, M. A.; Franco, A. A. Modeling Investigation of the Local Electrochemistry in Lithium-O $_2$ Batteries: A Kinetic Monte Carlo Approach. *J. Electrochem. Soc.* **2016**, *163* (3), A329–337. https://doi.org/10.1149/2.0841602jes.

(21)   Choi, H.; Kwon, J. S. Multiscale Modeling and Control of Kappa Number and Porosity in a Batch-type Pulp Digester. *AIChE J.* **2019**, *65* (6). https://doi.org/10.1002/aic.16589.

(22)   Rasoulian, S.; Ricardez-Sandoval, L. A. A Robust Nonlinear Model Predictive Controller for a Multiscale Thin Film Deposition Process. *Chem. Eng. Sci.* **2015**, *136*, 38–49. https://doi.org/10.1016/j.ces.2015.02.002.

(23)   Hao, F.; Liu, Z.; Balbuena, P. B.; Mukherjee, P. P. Mesoscale Elucidation of Solid Electrolyte Interphase Layer Formation in Li-Ion Battery Anode. *J. Phys. Chem. C* **2017**, *121* (47), 26233–26240. https://doi.org/10.1021/acs.jpcc.7b09465.

(24)   Kwon, J. S.-I.; Nayhouse, M.; Christofides, P. D.; Orkoulas, G. Modeling and Control of Crystal Shape in Continuous Protein Crystallization. *Chem. Eng. Sci.* **2014**, *107*, 47–57. https://doi.org/10.1016/j.ces.2013.12.005.

(25)   Thangavel, V.; Guerrero, O. X.; Quiroga, M.; Mikala, A. M.; Rucci, A.; Franco, A. A. A Three Dimensional Kinetic Monte Carlo Model for Simulating the Carbon/Sulfur Mesostructural Evolutions of Discharging Lithium Sulfur Batteries. *Energy Storage Mater.* **2020**, *24*, 472–485. https://doi.org/10.1016/j.ensm.2019.07.011.

(26)   Callejas-Tovar, R.; Diaz, C. A.; de la Hoz, J. M. M.; Balbuena, P. B. Dealloying of Platinum-Based Alloy Catalysts: Kinetic Monte Carlo Simulations. *Electrochimica Acta* **2013**, *101*, 326–333. https://doi.org/10.1016/j.electacta.2013.01.053.

(27)   Röder, F.; Laue, V.; Krewer, U. Model Based Multiscale Analysis of Film Formation in Lithium-Ion Batteries. *Batter. Supercaps* **2019**, *2* (3), 248–265. https://doi.org/10.1002/batt.201800107.

(28)   Papanikolaou, K. G.; Darby, M. T.; Stamatakis, M. Adlayer Structure and Lattice Size Effects on Catalytic Rates Predicted from KMC Simulations: NO Oxidation on Pt(111). *J. Chem. Phys.* **2018**, *149* (18), 184701. https://doi.org/10.1063/1.5048787.

(29)   Chen, J.-C.; Reischl, B.; Spijker, P.; Holmberg, N.; Laasonen, K.; Foster, A. S. Ab Initio Kinetic Monte Carlo Simulations of Dissolution at the NaCl–Water Interface. *Phys Chem Chem Phys* **2014**, *16* (41), 22545–22554. https://doi.org/10.1039/C4CP02375G.

(30)   Van der Ven, A.; Ceder, G.; Asta, M.; Tepesch, P. D. First-Principles Theory of Ionic Diffusion with Nondilute Carriers. *Phys. Rev. B* **2001**, *64* (18), 184307. https://doi.org/10.1103/PhysRevB.64.184307.

(31)   Ramos-Sanchez, G.; Soto, F. A.; Martinez de la Hoz, J. M.; Liu, Z.; Mukherjee, P. P.; El-Mellouhi, F.; Seminario, J. M.; Balbuena, P. B. Computational Studies of Interfacial Reactions at Anode Materials: Initial Stages of the Solid-Electrolyte-Interphase Layer Formation. *J. Electrochem. Energy Convers. Storage* **2016**, *13* (3), 031002. https://doi.org/10.1115/1.4034412.

(32)   Röder, F.; Braatz, R. D.; Krewer, U. Multi-Scale Simulation of Heterogeneous Surface Film Growth Mechanisms in Lithium-Ion Batteries. *J. Electrochem. Soc.* **2017**, *164* (11), E3335–E3344. https://doi.org/10.1149/2.0241711jes.

(33)   Shinagawa, C.; Ushiyama, H.; Yamashita, K. Multiscale Simulations for Lithium-Ion Batteries: SEI Film Growth and Capacity Fading. *J. Electrochem. Soc.* **2017**, *164* (13), A3018–A3024. https://doi.org/10.1149/2.0381713jes.

(34)   Choi, H.-K.; Kwon, J. S.-I. Modeling and Control of Cell Wall Thickness in Batch Delignification. *Comput. Chem. Eng.* **2019**, *128*, 512–523. https://doi.org/10.1016/j.compchemeng.2019.06.025.

(35)   Röder, F.; Braatz, R. D.; Krewer, U. Direct Coupling of Continuum and Kinetic Monte Carlo Models for Multiscale Simulation of Electrochemical Systems. *Comput. Chem. Eng.* **2019**, *121*, 722–735. https://doi.org/10.1016/j.compchemeng.2018.12.016.

(36)   Leetmaa, M.; Skorodumova, N. V. KMCLib: A General Framework for Lattice Kinetic Monte Carlo (KMC) Simulations. *Comput. Phys. Commun.* **2014**, *185* (9), 2340–2349. https://doi.org/10.1016/j.cpc.2014.04.017.

(37)   Lucas, S.; Moskovkin, P. Simulation at High Temperature of Atomic Deposition, Islands Coalescence, Ostwald and Inverse Ostwald Ripening with a General Simple Kinetic Monte Carlo Code. *Thin Solid Films* **2010**, *518* (18), 5355–5361. https://doi.org/10.1016/j.tsf.2010.04.064.

(38)   Stamatakis, M.; Vlachos, D. G. A Graph-Theoretical Kinetic Monte Carlo Framework for on-Lattice Chemical Kinetics. *J. Chem. Phys.* **2011**, *134* (21), 214115. https://doi.org/10.1063/1.3596751.

(39)   Nielsen, J.; d'Avezac, M.; Hetherington, J.; Stamatakis, M. Parallel Kinetic Monte Carlo Simulation Framework Incorporating Accurate Models of Adsorbate Lateral Interactions. *J. Chem. Phys.* **2013**, *139* (22), 224706. https://doi.org/10.1063/1.4840395.

(40)   Kalz, K. F.; Kraehnert, R.; Dvoyashkin, M.; Dittmeyer, R.; Gläser, R.; Krewer, U.; Reuter, K.; Grunwaldt, J.-D. Future Challenges in Heterogeneous Catalysis: Understanding Catalysts under Dynamic Reaction Conditions. *ChemCatChem* **2017**, *9* (1), 17–29. https://doi.org/10.1002/cctc.201600996.

(41)   Lu, T.; Law, C. K. Toward Accommodating Realistic Fuel Chemistry in Large-Scale Computations. *Prog. Energy Combust. Sci.* **2009**, *35* (2), 192–215. https://doi.org/10.1016/j.pecs.2008.10.002.

(42)   Margraf, J. T.; Reuter, K. Systematic Enumeration of Elementary Reaction Steps in Surface Catalysis. *ACS Omega* **2019**, *4* (2), 3370–3379. https://doi.org/10.1021/acsomega.8b03200.

(43)   Chen, B. W. J.; Xu, L.; Mavrikakis, M. Computational Methods in Heterogeneous Catalysis. *Chem. Rev.* **2021**, *121* (2), 1007–1048. https://doi.org/10.1021/acs.chemrev.0c01060.

(44)   Maestri, M. Escaping the Trap of Complication and Complexity in Multiscale Microkinetic Modelling of Heterogeneous Catalytic Processes. *Chem. Commun.* **2017**, *53* (74), 10244–10254. https://doi.org/10.1039/C7CC05740G.

(45)   Schlögl, R. Heterogeneous Catalysis. *Angew. Chem. Int. Ed.* **2015**, *54* (11), 3465–3520. https://doi.org/10.1002/anie.201410738.

(46)   Maurer, F.; Gänzler, A.; Lott, P.; Betz, B.; Votsmeier, M.; Loridant, S.; Vernoux, P.; Murzin, V.; Bornmann, B.; Frahm, R.; Deutschmann, O.; Casapu, M.; Grunwaldt, J.-D. Spatiotemporal Investigation of the Temperature and Structure of a Pt/CeO$_2$ Oxidation Catalyst for CO and Hydrocarbon Oxidation during Pulse Activation. *Ind. Eng. Chem. Res.* **2021**, *60* (18), 6662–6675. https://doi.org/10.1021/acs.iecr.0c05798.

(47)   Cheula, R.; Soon, A.; Maestri, M. Prediction of Morphological Changes of Catalyst Materials under Reaction Conditions by Combined *Ab Initio* Thermodynamics and Microkinetic Modelling. *Catal. Sci. Technol.* **2018**, *8* (14), 3493–3503. https://doi.org/10.1039/C8CY00583D.

(48)   Kreitz, B.; Wehinger, G. D.; Goldsmith, C. F.; Turek, T. Microkinetic Modeling of the CO$_2$ Desorption from Supported Multifaceted Ni Catalysts. *J. Phys. Chem. C* **2021**, *125* (5), 2984–3000. https://doi.org/10.1021/acs.jpcc.0c09985.

(49)   Cheula, R.; Maestri, M.; Mpourmpakis, G. Modeling Morphology and Catalytic Activity of Nanoparticle Ensembles Under Reaction Conditions. *ACS Catal.* **2020**, *10* (11), 6149–6158. https://doi.org/10.1021/acscatal.0c01005.

(50)   van Etten, M. P. C.; Zijlstra, B.; Hensen, E. J. M.; Filot, I. A. W. Enumerating Active Sites on Metal Nanoparticles: Understanding the Size Dependence of Cobalt Particles for CO Dissociation. *ACS Catal.* **2021**, *11* (14), 8484–8492. https://doi.org/10.1021/acscatal.1c00651.

(51)   Cheula, R.; Maestri, M. Nature and Identity of the Active Site via Structure-Dependent Microkinetic Modeling: An Application to WGS and Reverse WGS Reactions on Rh. *Catal. Today* **2021**, S0920586121002261. https://doi.org/10.1016/j.cattod.2021.05.016.

(52)   Stocker, S.; Csányi, G.; Reuter, K.; Margraf, J. T. Machine Learning in Chemical Reaction Space. *Nat. Commun.* **2020**, *11* (1), 5505. https://doi.org/10.1038/s41467-020-19267-x.

(53)   Maestri, M.; Vlachos, D.; Beretta, A.; Groppi, G.; Tronconi, E. Steam and Dry Reforming of Methane on Rh: Microkinetic Analysis and Hierarchy of Kinetic Models. *J. Catal.* **2008**, *259* (2), 211–222. https://doi.org/10.1016/j.jcat.2008.08.008.

(54)   Kreitz, B.; Sargsyan, K.; Blöndal, K.; Mazeau, E. J.; West, R. H.; Wehinger, G. D.; Turek, T.; Goldsmith, C. F. Quantifying the Impact of Parametric Uncertainty on Automatic Mechanism Generation for CO$_2$ Hydrogenation on Ni(111). *JACS Au* **2021**, *1* (10), 1656–1673. https://doi.org/10.1021/jacsau.1c00276.

(55)   Vernuccio, S.; Broadbelt, L. J. Discerning Complex Reaction Networks Using Automated Generators. *AIChE J.* **2019**, *65* (8). https://doi.org/10.1002/aic.16663.

(56)   Liu, M.; Grinberg Dana, A.; Johnson, M. S.; Goldman, M. J.; Jocher, A.; Payne, A. M.; Grambow, C. A.; Han, K.; Yee, N. W.; Mazeau, E. J.; Blondal, K.; West, R. H.; Goldsmith, C. F.; Green, W. H. Reaction Mechanism Generator v3.0: Advances in Automatic Mechanism Generation. *J. Chem. Inf. Model.* **2021**, *61* (6), 2686–2696. https://doi.org/10.1021/acs.jcim.0c01480.

(57)   Gao, C. W.; Allen, J. W.; Green, W. H.; West, R. H. Reaction Mechanism Generator: Automatic Construction of Chemical Kinetic Mechanisms. *Comput. Phys. Commun.* **2016**, *203*, 212–225. https://doi.org/10.1016/j.cpc.2016.02.013.

(58)   Gupta, U.; Vlachos, D. G. Learning Chemistry of Complex Reaction Systems via a Python First-Principles Reaction Rule Stencil (PReSt) Generator. *J. Chem. Inf. Model.* **2021**, *61* (7), 3431–3441. https://doi.org/10.1021/acs.jcim.1c00297.

(59)   Ulissi, Z. W.; Medford, A. J.; Bligaard, T.; Nørskov, J. K. To Address Surface Reaction Network Complexity Using Scaling Relations Machine Learning and DFT Calculations. *Nat. Commun.* **2017**, *8* (1), 14621. https://doi.org/10.1038/ncomms14621.

(60)   Goldsmith, C. F.; West, R. H. Automatic Generation of Microkinetic Mechanisms for Heterogeneous Catalysis. *J. Phys. Chem. C* **2017**, *121* (18), 9970–9981. https://doi.org/10.1021/acs.jpcc.7b02133.

(61)   Mazeau, E. J.; Satpute, P.; Blöndal, K.; Goldsmith, C. F.; West, R. H. Automated

Mechanism Generation Using Linear Scaling Relationships and Sensitivity Analyses Applied to Catalytic Partial Oxidation of Methane. *ACS Catal.* **2021**, *11* (12), 7114–7125. https://doi.org/10.1021/acscatal.0c04100.

(62)   Blondal, K.; Jelic, J.; Mazeau, E.; Studt, F.; West, R. H.; Goldsmith, C. F. Computer-Generated Kinetics for Coupled Heterogeneous/Homogeneous Systems: A Case Study in Catalytic Combustion of Methane on Platinum. *Ind. Eng. Chem. Res.* **2019**, *58* (38), 17682–17691. https://doi.org/10.1021/acs.iecr.9b01464.

(63)   Kauppinen, M. M.; Melander, M. M.; Bazhenov, A. S.; Honkala, K. Unraveling the Role of the Rh–ZrO $_2$ Interface in the Water–Gas-Shift Reaction via a First-Principles Microkinetic Study. *ACS Catal.* **2018**, *8* (12), 11633–11647. https://doi.org/10.1021/acscatal.8b02596.

(64)   Hammer, B.; Nørskov, J. K. Theoretical Surface Science and Catalysis—Calculations and Concepts. In *Advances in Catalysis*; Elsevier, 2000; Vol. 45, pp 71–129. https://doi.org/10.1016/S0360-0564(02)45013-4.

(65)   Abild-Pedersen, F.; Greeley, J.; Studt, F.; Rossmeisl, J.; Munter, T. R.; Moses, P. G.; Skúlason, E.; Bligaard, T.; Nørskov, J. K. Scaling Properties of Adsorption Energies for Hydrogen-Containing Molecules on Transition-Metal Surfaces. *Phys. Rev. Lett.* **2007**, *99* (1), 016105. https://doi.org/10.1103/PhysRevLett.99.016105.

(66)   Bligaard, T.; Nørskov, J. K.; Dahl, S.; Matthiesen, J.; Christensen, C. H.; Sehested, J. The Brønsted–Evans–Polanyi Relation and the Volcano Curve in Heterogeneous Catalysis. *J. Catal.* **2004**, *224* (1), 206–217. https://doi.org/10.1016/j.jcat.2004.02.034.

(67)   Shustorovich, E. The UBI-QEP Method: A Practical Theoretical Approach to Understanding Chemistry on Transition Metal Surfaces. *Surf. Sci. Rep.* **1998**, *31* (1–3), 1–119. https://doi.org/10.1016/S0167-5729(97)00016-2.

(68)   Ding, Z.-B.; Maestri, M. Development and Assessment of a Criterion for the Application of Brønsted–Evans–Polanyi Relations for Dissociation Catalytic Reactions at Surfaces. *Ind. Eng. Chem. Res.* **2019**, *58* (23), 9864–9874. https://doi.org/10.1021/acs.iecr.9b01628.

(69)   Chanussot, L.; Das, A.; Goyal, S.; Lavril, T.; Shuaibi, M.; Riviere, M.; Tran, K.; Heras-Domingo, J.; Ho, C.; Hu, W.; Palizhati, A.; Sriram, A.; Wood, B.; Yoon, J.; Parikh, D.; Zitnick, C. L.; Ulissi, Z. Open Catalyst 2020 (OC20) Dataset and Community Challenges. *ACS Catal.* **2021**, *11* (10), 6059–6072. https://doi.org/10.1021/acscatal.0c04525.

(70)   Deimel, M.; Reuter, K.; Andersen, M. Active Site Representation in First-Principles Microkinetic Models: Data-Enhanced Computational Screening for Improved Methanation Catalysts. *ACS Catal.* **2020**, *10* (22), 13729–13736. https://doi.org/10.1021/acscatal.0c04045.

(71)   Back, S.; Yoon, J.; Tian, N.; Zhong, W.; Tran, K.; Ulissi, Z. W. Convolutional Neural Network of Atomic Surface Structures To Predict Binding Energies for High-Throughput Screening of Catalysts. *J. Phys. Chem. Lett.* **2019**, *10* (15), 4401–4408. https://doi.org/10.1021/acs.jpclett.9b01428.

(72)   Ravipati, S.; Savva, G. D.; Christidi, I.-A.; Guichard, R.; Nielsen, J.; Réocreux, R.; Stamatakis, M. Coupling the Time-Warp Algorithm with the Graph-Theoretical Kinetic Monte Carlo Framework for Distributed Simulations of Heterogeneous Catalysts. *Comput. Phys. Commun.* **2022**, *270*, 108148. https://doi.org/10.1016/j.cpc.2021.108148.

(73)   Stegelmann, C.; Andreasen, A.; Campbell, C. T. Degree of Rate Control: How Much the Energies of Intermediates and Transition States Control Rates. *J. Am. Chem. Soc.* **2009**, *131* (23), 8077–8082. https://doi.org/10.1021/ja9000097.

(74)   Campbell, C. T. The Degree of Rate Control: A Powerful Tool for Catalysis Research. *ACS Catal.* **2017**, *7* (4), 2770–2779. https://doi.org/10.1021/acscatal.7b00115.

(75)   Sutton, J. E.; Guo, W.; Katsoulakis, M. A.; Vlachos, D. G. Effects of Correlated Parameters and Uncertainty in Electronic-Structure-Based Chemical Kinetic Modelling. *Nat. Chem.* **2016**, *8* (4), 331–337. https://doi.org/10.1038/nchem.2454.

(76)   Medford, A. J.; Wellendorff, J.; Vojvodic, A.; Studt, F.; Abild-Pedersen, F.; Jacobsen, K. W.; Bligaard, T.; Nørskov, J. K. Assessing the Reliability of Calculated Catalytic Ammonia Synthesis Rates. *Science* **2014**, *345* (6193), 197–200. https://doi.org/10.1126/science.1253486.

(77)   Nottoli, M.; Cupellini, L.; Lipparini, F.; Granucci, G.; Mennucci, B. Multiscale Models for Light-Driven Processes. *Annu. Rev. Phys. Chem.* **2021**, *72* (1), 489–513. https://doi.org/10.1146/annurev-physchem-090419-104031.

(78)   Brault, P. Multiscale Molecular Dynamics Simulation of Plasma Processing: Application to Plasma Sputtering. *Front. Phys.* **2018**, *6*, 59. https://doi.org/10.3389/fphy.2018.00059.

(79)   Bogaerts, A.; Tu, X.; Whitehead, J. C.; Centi, G.; Lefferts, L.; Guaitella, O.; Azzolina-Jury, F.; Kim, H.-H.; Murphy, A. B.; Schneider, W. F.; Nozaki, T.; Hicks, J. C.; Rousseau, A.; Thevenet, F.; Khacef, A.; Carreon, M. The 2020 Plasma Catalysis Roadmap. *J. Phys. Appl. Phys.* **2020**, *53* (44), 443001. https://doi.org/10.1088/1361-6463/ab9048.

(80)   Kovačič, Ž.; Likozar, B.; Huš, M. Photocatalytic CO_2 Reduction: A Review of Ab Initio Mechanism, Kinetics, and Multiscale Modeling Simulations. *ACS Catal.* **2020**, *10* (24), 14984–15007. https://doi.org/10.1021/acscatal.0c02557.

(81)   Geppert, J.; Kubannek, F.; Röse, P.; Krewer, U. Identifying the Oxygen Evolution Mechanism by Microkinetic Modelling of Cyclic Voltammograms. *Electrochimica Acta* **2021**, *380*, 137902. https://doi.org/10.1016/j.electacta.2021.137902.

(82)   Zijlstra, B.; Zhang, X.; Liu, J.-X.; Filot, I. A. W.; Zhou, Z.; Sun, S.; Hensen, E. J. M. First-Principles Microkinetics Simulations of Electrochemical Reduction of CO2 over Cu Catalysts. *Electrochimica Acta* **2020**, *335*, 135665. https://doi.org/10.1016/j.electacta.2020.135665.

(83)   Baz, A.; Dix, S. T.; Holewinski, A.; Linic, S. Microkinetic Modeling in Electrocatalysis: Applications, Limitations, and Recommendations for Reliable Mechanistic Insights. *J. Catal.* **2021**, *404*, 864–872. https://doi.org/10.1016/j.jcat.2021.08.043.

(84)   Studt, F. Grand Challenges in Computational Catalysis. *Front. Catal.* **2021**, *1*, 658965. https://doi.org/10.3389/fctls.2021.658965.

(85)   Bracconi, M.; Maestri, M. Training Set Design for Machine Learning Techniques Applied to the Approximation of Computationally Intensive First-Principles Kinetic Models. *Chem. Eng. J.* **2020**, *400*, 125469. https://doi.org/10.1016/j.cej.2020.125469.

(86)   Hettel, M.; Wörner, M.; Deutschmann, O. Computational Fluid Dynamics of Catalytic Reactors. In *Handbook of Materials Modeling*; Andreoni, W., Yip, S., Eds.; Springer International Publishing: Cham, 2018; pp 1–34. https://doi.org/10.1007/978-3-319-50257-1_6-1.

(87)   Matera, S.; Maestri, M.; Cuoci, A.; Reuter, K. Predictive-Quality Surface Reaction Chemistry in Real Reactor Models: Integrating First-Principles Kinetic Monte Carlo Simulations into Computational Fluid Dynamics. *ACS Catal.* **2014**, *4* (11), 4081–4092. https://doi.org/10.1021/cs501154e.

(88)   Jurtz, N.; Kraume, M.; Wehinger, G. D. Advances in Fixed-Bed Reactor Modeling Using Particle-Resolved Computational Fluid Dynamics (CFD). *Rev. Chem. Eng.* **2019**, *35* (2), 139–190. https://doi.org/10.1515/revce-2017-0059.

(89)   Wehinger, G. D.; Eppinger, T.; Kraume, M. Detailed Numerical Simulations of Catalytic Fixed-Bed Reactors: Heterogeneous Dry Reforming of Methane. *Chem. Eng. Sci.* **2015**, *122*, 197–209. https://doi.org/10.1016/j.ces.2014.09.007.

(90)   Dixon, A. G.; Partopour, B. Computational Fluid Dynamics for Fixed Bed Reactor Design. *Annu. Rev. Chem. Biomol. Eng.* **2020**, *11* (1), 109–130. https://doi.org/10.1146/annurev-chembioeng-092319-075328.

(91)   Micale, D.; Uglietti, R.; Bracconi, M.; Maestri, M. Coupling Euler–Euler and Microkinetic Modeling for the Simulation of Fluidized Bed Reactors: An Application to the Oxidative Coupling of Methane. *Ind. Eng. Chem. Res.* **2021**, *60* (18), 6687–6697.

https://doi.org/10.1021/acs.iecr.0c05845.

(92)   Maestri, M.; Beretta, A.; Faravelli, T.; Groppi, G.; Tronconi, E.; Vlachos, D. G. Two-Dimensional Detailed Modeling of Fuel-Rich H2 Combustion over Rh/Al2O3 Catalyst. *Chem. Eng. Sci.* **2008**, *63* (10), 2657–2669. https://doi.org/10.1016/j.ces.2008.02.024.

(93)   Deutschmann, O.; Schwiedemoch, R.; Maier, L. I.; Chatterjee, D. Natural Gas Conversion in Monolithic Catalysts: Interaction of Chemical Reactions and Transport Phenomena. In *Studies in Surface Science and Catalysis*; Elsevier, 2001; Vol. 136, pp 251–258. https://doi.org/10.1016/S0167-2991(01)80312-8.

(94)   Tischer, S.; Deutschmann, O. Recent Advances in Numerical Modeling of Catalytic Monolith Reactors. *Catal. Today* **2005**, *105* (3–4), 407–413. https://doi.org/10.1016/j.cattod.2005.06.061.

(95)   Wehinger, G. D.; Eppinger, T.; Kraume, M. Evaluating Catalytic Fixed-Bed Reactors for Dry Reforming of Methane with Detailed CFD. *Chem. Ing. Tech.* **2015**, *87* (6), 734–745. https://doi.org/10.1002/cite.201400153.

(96)   Wehinger, G. D.; Flaischlen, S. Computational Fluid Dynamics Modeling of Radiation in a Steam Methane Reforming Fixed-Bed Reactor. *Ind Eng Chem Res* **2019**, *58* (31), 14410–14423. https://doi.org/10.1021/acs.iecr.9b01265.

(97)   Wehinger, G. D.; Flaischlen, S. Computational Fluid Dynamics Modeling of Radiation in a Steam Methane Reforming Fixed-Bed Reactor. *Ind. Eng. Chem. Res.* **2019**, *58* (31), 14410–14423. https://doi.org/10.1021/acs.iecr.9b01265.

(98)   Maestri, M.; Cuoci, A. Coupling CFD with Detailed Microkinetic Modeling in Heterogeneous Catalysis. *Chem. Eng. Sci.* **2013**, *96*, 106–117. https://doi.org/10.1016/j.ces.2013.03.048.

(99)   Maffei, T.; Gentile, G.; Rebughini, S.; Bracconi, M.; Manelli, F.; Lipp, S.; Cuoci, A.; Maestri, M. A Multiregion Operator-Splitting CFD Approach for Coupling Microkinetic Modeling with Internal Porous Transport in Heterogeneous Catalytic Reactors. *Chem. Eng. J.* **2016**, *283*, 1392–1404. https://doi.org/10.1016/j.cej.2015.08.080.

(100)   Uglietti, R.; Bracconi, M.; Maestri, M. Coupling CFD–DEM and Microkinetic Modeling of Surface Chemistry for the Simulation of Catalytic Fluidized Systems. *React. Chem. Eng.* **2018**, *3* (4), 527–539. https://doi.org/10.1039/C8RE00050F.

(101)   Pope, S. B. Computationally Efficient Implementation of Combustion Chemistry Using **in Situ** Adaptive Tabulation. *Combust. Theory Model.* **1997**, *1* (1), 41–63. https://doi.org/10.1080/713665229.

(102)   Blasi, J. M.; Kee, R. J. In Situ Adaptive Tabulation (ISAT) to Accelerate Transient Computational Fluid Dynamics with Complex Heterogeneous Chemical Kinetics. *Comput. Chem. Eng.* **2016**, *84*, 36–42. https://doi.org/10.1016/j.compchemeng.2015.08.020.

(103)   Bracconi, M.; Maestri, M.; Cuoci, A. *In Situ* Adaptive Tabulation for the CFD Simulation of Heterogeneous Reactors Based on Operator-Splitting Algorithm. *AIChE J.* **2017**, *63* (1), 95–104. https://doi.org/10.1002/aic.15441.

(104)   Babajimopoulos, A.; Assanis, D. N.; Flowers, D. L.; Aceves, S. M.; Hessel, R. P. A Fully Coupled Computational Fluid Dynamics and Multi-Zone Model with Detailed Chemical Kinetics for the Simulation of Premixed Charge Compression Ignition Engines. *Int. J. Engine Res.* **2005**, *6* (5), 497–512. https://doi.org/10.1243/146808705X30503.

(105)   Goldin, G. M.; Ren, Z.; Zahirovic, S. A Cell Agglomeration Algorithm for Accelerating Detailed Chemistry in CFD. *Combust. Theory Model.* **2009**, *13* (4), 721–739. https://doi.org/10.1080/13647830903154542.

(106)   Rebughini, S.; Bracconi, M.; Dixon, A. G.; Maestri, M. A Hierarchical Approach to Chemical Reactor Engineering: An Application to Micro Packed Bed Reactors. *React. Chem. Eng.* **2018**, *3* (1), 25–33. https://doi.org/10.1039/C7RE00195A.

(107)   Uglietti, R.; Bracconi, M.; Maestri, M. Development and Assessment of Speed-up Algorithms for the Reactive CFD–DEM Simulation of Fluidized Bed Reactors. *React. Chem.*

Eng. **2020**, *5* (2), 278–288. https://doi.org/10.1039/C9RE00440H.

(108) Liang, L.; Stevens, J. G.; Farrell, J. T. A Dynamic Adaptive Chemistry Scheme for Reactive Flow Computations. *Proc. Combust. Inst.* **2009**, *32* (1), 527–534. https://doi.org/10.1016/j.proci.2008.05.073.

(109) Ren, Z.; Liu, Y.; Lu, T.; Lu, L.; Oluwole, O. O.; Goldin, G. M. The Use of Dynamic Adaptive Chemistry and Tabulation in Reactive Flow Simulations. *Combust. Flame* **2014**, *161* (1), 127–137. https://doi.org/10.1016/j.combustflame.2013.08.018.

(110) Strassacker, C.; Bykov, V.; Maas, U. REDIM Reduced Modeling of Quenching at a Cold Wall Including Heterogeneous Wall Reactions. *Int. J. Heat Fluid Flow* **2018**, *69*, 185–193. https://doi.org/10.1016/j.ijheatfluidflow.2017.12.011.

(111) Strassacker, C.; Bykov, V.; Maas, U. Reduced Modeling of Flame-Wall-Interactions of Premixed Isooctane-Air Systems Including Detailed Transport and Surface Reactions. *Proc. Combust. Inst.* **2021**, *38* (1), 1063–1070. https://doi.org/10.1016/j.proci.2020.07.040.

(112) Law, C. K. Combustion at a Crossroads: Status and Prospects. *Proc. Combust. Inst.* **2007**, *31* (1), 1–29. https://doi.org/10.1016/j.proci.2006.08.124.

(113) Matera, S.; Schneider, W. F.; Heyden, A.; Savara, A. Progress in Accurate Chemical Kinetic Modeling, Simulations, and Parameter Estimation for Heterogeneous Catalysis. *ACS Catal.* **2019**, *9* (8), 6624–6647. https://doi.org/10.1021/acscatal.9b01234.

(114) Dagaut, P.; El Bakali, A.; Ristori, A. The Combustion of Kerosene: Experimental Results and Kinetic Modelling Using 1- to 3-Component Surrogate Model Fuels. *Fuel* **2006**, *85* (7–8), 944–956. https://doi.org/10.1016/j.fuel.2005.10.008.

(115) Wang, J.; Li, S.; Yang, B. Combustion Kinetic Model Development Using Surrogate Model Similarity Method. *Combust. Theory Model.* **2018**, *22* (4), 777–794. https://doi.org/10.1080/13647830.2018.1454607.

(116) Blasco, J.; Fueyo, N.; Dopazo, C.; Chen, J.-Y. A Self-Organizing-Map Approach to Chemistry Representation in Combustion Applications. *Combust. Theory Model.* **2000**, *4* (1), 61–76. https://doi.org/10.1088/1364-7830/4/1/304.

(117) Ouyang, Y.; Vandewalle, L. A.; Chen, L.; Plehiers, P. P.; Dobbelaere, M. R.; Heynderickx, G. J.; Marin, G. B.; Van Geem, K. M. Speeding up Turbulent Reactive Flow Simulation via a Deep Artificial Neural Network: A Methodology Study. *Chem. Eng. J.* **2022**, *429*, 132442. https://doi.org/10.1016/j.cej.2021.132442.

(118) Stephenson, D.; Kermode, J. R.; Lockerby, D. A. Accelerating Multiscale Modelling of Fluids with On-the-Fly Gaussian Process Regression. *Microfluid. Nanofluidics* **2018**, *22* (12), 139. https://doi.org/10.1007/s10404-018-2164-z.

(119) Partopour, B.; Paffenroth, R. C.; Dixon, A. G. Random Forests for Mapping and Analysis of Microkinetics Models. *Comput. Chem. Eng.* **2018**, *115*, 286–294. https://doi.org/10.1016/j.compchemeng.2018.04.019.

(120) Rupp, M.; von Lilienfeld, O. A.; Burke, K. Guest Editorial: Special Topic on Data-Enabled Theoretical Chemistry. *J. Chem. Phys.* **2018**, *148* (24), 241401. https://doi.org/10.1063/1.5043213.

(121) Tran, A. V.; Wang, Y. Reliable Molecular Dynamics: Uncertainty Quantification Using Interval Analysis in Molecular Dynamics Simulation. *Comput. Mater. Sci.* **2017**, *127*, 141–160. https://doi.org/10.1016/j.commatsci.2016.10.021.

(122) Brunton, S. L.; Proctor, J. L.; Kutz, J. N. Discovering Governing Equations from Data by Sparse Identification of Nonlinear Dynamical Systems. *Proc. Natl. Acad. Sci.* **2016**, *113* (15), 3932–3937. https://doi.org/10.1073/pnas.1517384113.

(123) McBride, K.; Sundmacher, K. Overview of Surrogate Modeling in Chemical Process Engineering. *Chem. Ing. Tech.* **2019**, *91* (3), 228–239. https://doi.org/10.1002/cite.201800091.

(124) Ji, W.; Zanders, J.; Park, J.-W.; Deng, S. Machine Learning Approaches to Learn HyChem Models. *ArXiv210407875 Phys.* **2021**.

(125) Champion, K.; Lusch, B.; Kutz, J. N.; Brunton, S. L. Data-Driven Discovery of

Coordinates and Governing Equations. *Proc. Natl. Acad. Sci.* **2019**, *116* (45), 22445–22451. https://doi.org/10.1073/pnas.1906995116.

(126) Hvatov, A.; Maslyaev, M. The Data-Driven Physical-Based Equations Discovery Using Evolutionary Approach. In *Proceedings of the 2020 Genetic and Evolutionary Computation Conference Companion*; ACM: Cancún Mexico, 2020; pp 129–130. https://doi.org/10.1145/3377929.3389943.

(127) van der Giessen, E.; Schultz, P. A.; Bertin, N.; Bulatov, V. V.; Cai, W.; Csányi, G.; Foiles, S. M.; Geers, M. G. D.; González, C.; Hütter, M.; Kim, W. K.; Kochmann, D. M.; LLorca, J.; Mattsson, A. E.; Rottler, J.; Shluger, A.; Sills, R. B.; Steinbach, I.; Strachan, A.; Tadmor, E. B. Roadmap on Multiscale Materials Modeling. *Model. Simul. Mater. Sci. Eng.* **2020**, *28* (4), 043001. https://doi.org/10.1088/1361-651X/ab7150.

(128) Spalart, P. R. Detached-Eddy Simulation. *Annu. Rev. Fluid Mech.* **2009**, *41* (1), 181–202. https://doi.org/10.1146/annurev.fluid.010908.165130.

(129) Kočí, P.; Isoz, M.; Plachá, M.; Arvajová, A.; Václavík, M.; Svoboda, M.; Price, E.; Novák, V.; Thompsett, D. 3D Reconstruction and Pore-Scale Modeling of Coated Catalytic Filters for Automotive Exhaust Gas Aftertreatment. *Catal. Today* **2019**, *320*, 165–174. https://doi.org/10.1016/j.cattod.2017.12.025.

(130) Wehinger, G. D.; Fütterer, C.; Kraume, M. Contact Modifications for CFD Simulations of Fixed-Bed Reactors: Cylindrical Particles. *Ind. Eng. Chem. Res.* **2017**, *56* (1), 87–99. https://doi.org/10.1021/acs.iecr.6b03596.

(131) Eppinger, T.; Seidler, K.; Kraume, M. DEM-CFD Simulations of Fixed Bed Reactors with Small Tube to Particle Diameter Ratios. *Chem Eng J* **2011**, *166* (1), 324–331. https://doi.org/10.1016/j.cej.2010.10.053.

(132) Partopour, B.; Dixon, A. G. 110th Anniversary: Commentary: CFD as a Modeling Tool for Fixed Bed Reactors. *Ind. Eng. Chem. Res.* **2019**, *58* (14), 5733–5736. https://doi.org/10.1021/acs.iecr.8b06380.

(133) Kutscherauer, M.; Böcklein, S.; Mestl, G.; Turek, T.; Wehinger, G. D. An Improved Contact Modification Routine for a Computationally Efficient CFD Simulation of Packed Beds. *Chem. Eng. J. Adv.* **2022**, *9*, 100197. https://doi.org/10.1016/j.ceja.2021.100197.

(134) Weber, S.; Abel, K. L.; Zimmermann, R. T.; Huang, X.; Bremer, J.; Rihko-Struckmann, L. K.; Batey, D.; Cipiccia, S.; Titus, J.; Poppitz, D.; Kübel, C.; Sundmacher, K.; Gläser, R.; Sheppard, T. L. Porosity and Structure of Hierarchically Porous Ni/Al2O3 Catalysts for CO2 Methanation. *Catalysts* **2020**, *10* (12), 1471. https://doi.org/10.3390/catal10121471.

(135) Belot, I.; Vidal, D.; Greiner, R.; Votsmeier, M.; Hayes, R. E.; Bertrand, F. Impact of Washcoat Distribution on the Catalytic Performance of Gasoline Particulate Filters as Predicted by Lattice Boltzmann Simulations. *Chem. Eng. J.* **2021**, *406*, 127040. https://doi.org/10.1016/j.cej.2020.127040.

(136) Coppens, M.; Weissenberger, T.; Zhang, Q.; Ye, G. Nature-Inspired, Computer-Assisted Optimization of Hierarchically Structured Zeolites. *Adv. Mater. Interfaces* **2021**, *8* (4), 2001409. https://doi.org/10.1002/admi.202001409.

(137) Pietschak, A.; Kaiser, M.; Freund, H. Tailored Catalyst Pellet Specification for Improved Fixed-Bed Transport Characteristics: A Shortcut Method for the Model-Based Reactor Design. *Chem. Eng. Res. Des.* **2018**, *137*, 60–74. https://doi.org/10.1016/j.cherd.2018.06.043.

(138) Kaiser, M.; Freund, H. A Multimodular Pseudoheterogeneous Model Framework for Optimal Design of Catalytic Reactors Exemplified by Methanol Synthesis. *Chem. Eng. Sci.* **2019**, *206*, 401–423. https://doi.org/10.1016/j.ces.2019.04.036.

(139) Davies, C. N. Gas Transport in Porous Media: The Dusty-Gas Model. *J. Aerosol Sci.* **1984**, *15* (1), 81. https://doi.org/10.1016/0021-8502(84)90058-2.

(140) Kerkhof, P. J. A. M. A Modified Maxwell-Stefan Model for Transport through Inert Membranes: The Binary Friction Model. *Chem. Eng. J. Biochem. Eng. J.* **1996**, *64* (3), 319–

343. https://doi.org/10.1016/S0923-0467(96)03134-X.

(141) Young, J. B.; Todd, B. Modelling of Multi-Component Gas Flows in Capillaries and Porous Solids. *Int. J. Heat Mass Transf.* **2005**, *48* (25–26), 5338–5353. https://doi.org/10.1016/j.ijheatmasstransfer.2005.07.034.

(142) Pant, L. M.; Mitra, S. K.; Secanell, M. A Generalized Mathematical Model to Study Gas Transport in PEMFC Porous Media. *Int. J. Heat Mass Transf.* **2013**, *58* (1–2), 70–79. https://doi.org/10.1016/j.ijheatmasstransfer.2012.11.023.

(143) Ren, W.; Duan, Y.; Guo, J.; Wang, T. An Adaptive Binary Friction Model for Multicomponent Gas Transport in Tight Porous Media. *J. Appl. Phys.* **2021**, *129* (9), 094701. https://doi.org/10.1063/5.0042709.

(144) Feng, C.; Stewart, W. E. Practical Models for Isothermal Diffusion and Flow of Gases in Porous Solids. *Ind. Eng. Chem. Fundam.* **1973**, *12* (2), 143–147. https://doi.org/10.1021/i160046a001.

(145) Partopour, B.; Troupel, A.; Dixon, A. G. Flux-Dependent Anisotropic Pellet Diffusivity in Particle-Resolved CFD Simulations of Fixed Beds. *Chem. Eng. Sci.* **2019**, *198*, 224–234. https://doi.org/10.1016/j.ces.2018.10.005.

(146) Sosna, B.; Korup, O.; Horn, R. Probing Local Diffusion and Reaction in a Porous Catalyst Pellet. *J. Catal.* **2020**, *381*, 285–294. https://doi.org/10.1016/j.jcat.2019.11.005.

(147) Wehinger, G. D.; Kreitz, B.; Nagy, A.; Turek, T. Characterization of a Modular Temkin Reactor with Experiments and Computational Fluid Dynamics Simulations. *Chem. Eng. J.* **2020**, *389*, 124342. https://doi.org/10.1016/j.cej.2020.124342.

(148) Fernengel, J.; Bolton, L.; Hinrichsen, O. Numerical Investigation of Pressure Drop in Single Pellet String Reactors. *Chem. Eng. Technol.* **2020**, *43* (1), 172–178. https://doi.org/10.1002/ceat.201900372.

(149) Bouras, H.; Haroun, Y.; Fortunato Bodziony, F.; Philippe, R.; Fongarland, P.; Augier, F. Use of CFD for Pressure Drop, Liquid Saturation and Wetting Predictions in Trickle Bed Reactors for Different Catalyst Particle Shapes. *Chem. Eng. Sci.* **2022**, *249*, 117315. https://doi.org/10.1016/j.ces.2021.117315.

(150) Froment, G. F.; De Wilde, J.; Bischoff, K. B. *Chemical Reactor Analysis and Design*, 3rd ed.; Wiley: Hoboken, N.J, 2011.

(151) Stegehake, C.; Riese, J.; Grünewald, M. Modeling and Validating Fixed-Bed Reactors: A State-of-the-Art Review. *ChemBioEng Rev.* **2019**, *6* (2), 28–44. https://doi.org/10.1002/cben.201900002.

(152) Jurtz, N.; Flaischlen, S.; Scherf, S. C.; Kraume, M.; Wehinger, G. D. Enhancing the Thermal Performance of Slender Packed Beds through Internal Heat Fins. *Processes* **2020**, *8* (12), 1528. https://doi.org/10.3390/pr8121528.

(153) Jurtz, N.; Srivastava, U.; Moghaddam, A. A.; Kraume, M. Particle-Resolved Computational Fluid Dynamics as the Basis for Thermal Process Intensification of Fixed-Bed Reactors on Multiple Scales. *Energies* **2021**, *14* (10), 2913. https://doi.org/10.3390/en14102913.

(154) Bracconi, M.; Ambrosetti, M.; Maestri, M.; Groppi, G.; Tronconi, E. A Fundamental Investigation of Gas/Solid Mass Transfer in Open-Cell Foams Using a Combined Experimental and CFD Approach. *Chem. Eng. J.* **2018**, *352*, 558–571. https://doi.org/10.1016/j.cej.2018.07.023.

(155) Ferroni, C.; Bracconi, M.; Ambrosetti, M.; Maestri, M.; Groppi, G.; Tronconi, E. A Fundamental Investigation of Gas/Solid Heat and Mass Transfer in Structured Catalysts Based on Periodic Open Cellular Structures (POCS). *Ind. Eng. Chem. Res.* **2021**, *60* (29), 10522–10538. https://doi.org/10.1021/acs.iecr.1c00215.

(156) Meinicke, S.; Dubil, K.; Wetzel, T.; Dietrich, B. Characterization of Heat Transfer in Consolidated, Highly Porous Media Using a Hybrid-Scale CFD Approach. *Int. J. Heat Mass Transf.* **2020**, *149*, 119201. https://doi.org/10.1016/j.ijheatmasstransfer.2019.119201.

(157) Fischer, K. L.; Freund, H. Intensification of Load Flexible Fixed Bed Reactors by Optimal Design of Staged Reactor Setups. *Chem. Eng. Process. - Process Intensif.* **2021**, *159*, 108183. https://doi.org/10.1016/j.cep.2020.108183.

(158) Zimmermann, R. T.; Bremer, J.; Sundmacher, K. Load-Flexible Fixed-Bed Reactors by Multi-Period Design Optimization. *Chem. Eng. J.* **2022**, *428*, 130771. https://doi.org/10.1016/j.cej.2021.130771.

(159) Schweidtmann, A. M.; Esche, E.; Fischer, A.; Kloft, M.; Repke, J.; Sager, S.; Mitsos, A. Machine Learning in Chemical Engineering: A Perspective. *Chem. Ing. Tech.* **2021**, *93* (12), 2029–2039. https://doi.org/10.1002/cite.202100083.

(160) Ratnakar, R. R.; Dadi, R. K.; Balakotaiah, V. Multi-Scale Reduced Order Models for Transient Simulation of Multi-Layered Monolith Reactors. *Chem. Eng. J.* **2018**, *352*, 293–305. https://doi.org/10.1016/j.cej.2018.04.053.

(161) Di Renzo, A.; Napolitano, E.; Di Maio, F. Coarse-Grain DEM Modelling in Fluidized Bed Simulation: A Review. *Processes* **2021**, *9* (2), 279. https://doi.org/10.3390/pr9020279.

(162) Vandewalle, L. A.; Marin, G. B.; Van Geem, K. M. CatchyFOAM: Euler–Euler CFD Simulations of Fluidized Bed Reactors with Microkinetic Modeling of Gas-Phase and Catalytic Surface Chemistry. *Energy Fuels* **2021**, *35* (3), 2545–2561. https://doi.org/10.1021/acs.energyfuels.0c02824.

(163) Ganzer, G.; Freund, H. Influence of Statistical Activity Variations in Diluted Catalyst Beds on the Thermal Reactor Behavior: Derivation of an a Priori Criterion. *Chem. Eng. Sci.* **2020**, *220*, 115607. https://doi.org/10.1016/j.ces.2020.115607.

(164) Müller, M.; Kutscherauer, M.; Böcklein, S.; Wehinger, G. D.; Turek, T.; Mestl, G. Modeling the Selective Oxidation of N-Butane to Maleic Anhydride: From Active Site to Industrial Reactor. *Catal. Today* **2021**, S0920586121001577. https://doi.org/10.1016/j.cattod.2021.04.009.

(165) Xie, M.; Freund, H. Optimal Reactor Design and Operation Taking Catalyst Deactivation into Account. *Chem. Eng. Sci.* **2018**, *175*, 405–415. https://doi.org/10.1016/j.ces.2017.10.010.

(166) Cruellas, A.; Heezius, J.; Spallina, V.; van Sint Annaland, M.; Medrano, J. A.; Gallucci, F. Oxidative Coupling of Methane in Membrane Reactors; A Techno-Economic Assessment. *Processes* **2020**, *8* (3), 274. https://doi.org/10.3390/pr8030274.

(167) Pirro, L.; Mendes, P. S. F.; Kemseke, B.; Vandegehuchte, B. D.; Marin, G. B.; Thybaut, J. W. From Catalyst to Process: Bridging the Scales in Modeling the OCM Reaction. *Catal. Today* **2021**, *365*, 35–45. https://doi.org/10.1016/j.cattod.2020.06.084.

(168) Zaman, S. A.; Roy, D.; Ghosh, S. Process Modeling and Optimization for Biomass Steam-Gasification Employing Response Surface Methodology. *Biomass Bioenergy* **2020**, *143*, 105847. https://doi.org/10.1016/j.biombioe.2020.105847.

(169) Singh, D. K.; Tirkey, J. V. Modeling and Multi-Objective Optimization of Variable Air Gasification Performance Parameters Using Syzygium Cumini Biomass by Integrating ASPEN Plus with Response Surface Methodology (RSM). *Int. J. Hydrog. Energy* **2021**, *46* (36), 18816–18831. https://doi.org/10.1016/j.ijhydene.2021.03.054.

(170) Eppinger, T.; Wehinger, G.; Kraume, M. Parameter Optimization for the Oxidative Coupling of Methane in a Fixed Bed Reactor by Combination of Response Surface Methodology and Computational Fluid Dynamics. *Chem. Eng. Res. Des.* **2014**, *92* (9), 1693–1703. https://doi.org/10.1016/j.cherd.2013.12.017.

(171) Dobbelaere, M. R.; Plehiers, P. P.; Van de Vijver, R.; Stevens, C. V.; Van Geem, K. M. Machine Learning in Chemical Engineering: Strengths, Weaknesses, Opportunities, and Threats. *Engineering* **2021**, *7* (9), 1201–1211. https://doi.org/10.1016/j.eng.2021.03.019.

(172) Chakkingal, A.; Janssens, P.; Poissonnier, J.; Barrios, A. J.; Virginie, M.; Khodakov, A. Y.; Thybaut, J. W. Machine Learning Based Interpretation of Microkinetic Data: A Fischer–Tropsch Synthesis Case Study. *React. Chem. Eng.* **2022**, 10.1039.D1RE00351H.

https://doi.org/10.1039/D1RE00351H.

(173) Radatz, H.; Schröder, M.; Becker, C.; Bramsiepe, C.; Schembecker, G. Selection of Equipment Modules for a Flexible Modular Production Plant by a Multi-Objective Evolutionary Algorithm. *Comput. Chem. Eng.* **2019**, *123*, 196–221. https://doi.org/10.1016/j.compchemeng.2018.12.009.

(174) Mohan, A. T.; Lubbers, N.; Livescu, D.; Chertkov, M. Embedding Hard Physical Constraints in Neural Network Coarse-Graining of 3D Turbulence. *ArXiv200200021 Phys.* **2020**.

(175) Wilkinson, M. D.; Dumontier, M.; Aalbersberg, Ij. J.; Appleton, G.; Axton, M.; Baak, A.; Blomberg, N.; Boiten, J.-W.; da Silva Santos, L. B.; Bourne, P. E.; Bouwman, J.; Brookes, A. J.; Clark, T.; Crosas, M.; Dillo, I.; Dumon, O.; Edmunds, S.; Evelo, C. T.; Finkers, R.; Gonzalez-Beltran, A.; Gray, A. J. G.; Groth, P.; Goble, C.; Grethe, J. S.; Heringa, J.; 't Hoen, P. A. C.; Hooft, R.; Kuhn, T.; Kok, R.; Kok, J.; Lusher, S. J.; Martone, M. E.; Mons, A.; Packer, A. L.; Persson, B.; Rocca-Serra, P.; Roos, M.; van Schaik, R.; Sansone, S.-A.; Schultes, E.; Sengstag, T.; Slater, T.; Strawn, G.; Swertz, M. A.; Thompson, M.; van der Lei, J.; van Mulligen, E.; Velterop, J.; Waagmeester, A.; Wittenburg, P.; Wolstencroft, K.; Zhao, J.; Mons, B. The FAIR Guiding Principles for Scientific Data Management and Stewardship. *Sci. Data* **2016**, *3* (1), 160018. https://doi.org/10.1038/sdata.2016.18.