

# Quo vadis multiscale modeling in reaction engineering? – A perspective

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## 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.

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## 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 (Lerou and Ng, 1996). In today's global business environment, these objectives are typically included in a framework for chemical product design (Uhlemann et al., 2019). 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 (Zhang et al., 2020a). 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. Fig. 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 multi-scale modeling is the computation of relevant information at multiple scales of time and/or space. The 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, (Keil, 1999, 2013; Hoekstra et al., 2021; Keil, 2018; Chizallet, 2022) focusing on metal-catalyzed reactions, (Saliccioli et al., 2011) material-function relationships in heterogeneous catalysis, (Bruix et al., 2019) or computational materials science and process engineering (Cheimarios et al., 2021). For a more general view

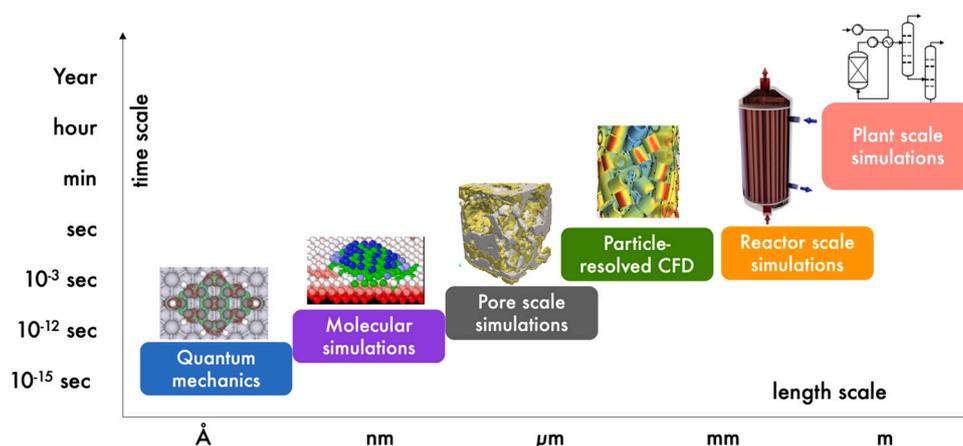


Fig. 1 - Typical time and length scales in reaction engineering problems. Adapted partly from Ref (Uhlemann et al., 2019).

of multiscale modeling covering also generic multiscale computing, the reader is referred to a collection of articles elsewhere (Hoekstra et al., 2019).

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 atomistic 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.

## 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.

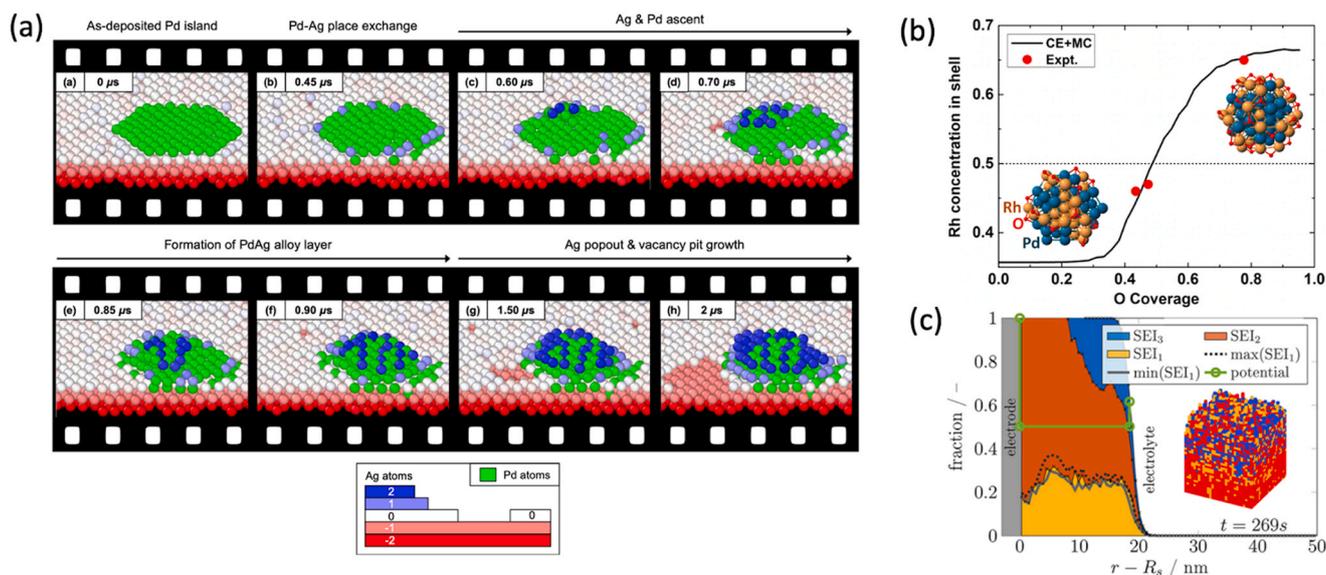
#### 2.1.1. Modeling changes at the atomistic scale with DFT

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 ideal systems (the dynamic of which can be treated as the superposition of the uncorrelated dynamics of its constituents) such as gases and solids, thermal effects can be recovered at almost no cost using the translational, rotational and vibrational partition functions. This approach has been applied to predict metal/oxide phase diagrams under varying oxygen atmosphere (Rogal et al., 2007) or electric potential (Panaritis et al., 2020). There is also literature regarding the determination of kinetic parameters for surface reconstruction (Lim et al., 2020). One success story is the decade-long step-by-step development of a theory-based model for  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (bulk and then surface) accounting for the changes it undergoes under steam conditions: surface hydroxylation and reorganization of the surface Al network (Digne, 2004). 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 (Réocreux et al., 2018). 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 (Piccini et al., 2022). 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<sub>AS</sub> of surface hydroxyl, (Gaigeot et al., 2012) crucial to understanding how pH can alter the surface of a material, and to elucidate the early steps of the chemical weathering of  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, which is associated with the formation of a boehmite layer, in liquid water (Réocreux et al., 2019). 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 2  $\mu$ s-long simulations for the study of the alloying mechanism of a Pd island on an Ag slab using such an approach (Fig. 2a) (Lim et al., 2020). 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 ( $\sim$ nm<sup>2</sup>) and to assess the energetics of a few elementary steps leading to surface transformation.

#### 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 (Hess, 2019). For example, such simulations have been used



**Fig. 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 (Lim et al., 2020). (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 (Röder et al., 2019a).

to investigate how adsorbates can affect the aggregation of single atoms to clusters at the surface of Single-Atom-Alloys (Papanikolaou et al., 2020) or the segregation of metals in intermetallics (Fig. 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, (Stamatakis, 2015; Andersen et al., 2019) 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 (Rogal et al., 2007; Varshney and Armaou, 2005; Lian et al., 2018) or the area above the surface (Sitapure et al., 2021; Blanquer et al., 2016; Choi and Kwon, 2019a; Rasouljan and Ricardez-Sandoval, 2015). 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 (Hao et al., 2017). 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, (Kwon et al., 2014) layer growth in electrochemical systems, (Thangavel et al., 2020) and dealloying processes of alloy catalysts (Callejas-Tovar et al., 2013).

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

(Papanikolaou et al., 2018). 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, (Chen et al., 2014) the bistability of Pd/PdO under CO oxidation conditions, (Rogal et al., 2007) the formation of coke precursors on metal surfaces, (Lian et al., 2018) the diffusion of Li ions into the positive  $\text{Li}_x\text{CO}_2$ -electrode, (Van der Ven et al., 2001) and the solid electrolyte interphase formation on Li-metal electrodes (Ramos-Sanchez et al., 2016). However, since the environmental conditions may change during the simulation and since ab initio calculations are never perfectly accurate, (Hansen et al., 2010) 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 (Fig. 2c) for different battery operating conditions (Röder et al., 2019a, 2017; Shinagawa et al., 2017) or to study the Kraft pulping process (Choi and Kwon, 2019a, 2019b). 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 (Röder et al., 2019b), showing that correction loops for estimated parameters can increase the accuracy of the multi-scale simulation up to one order of magnitude at the cost of a significant decrease in computational efficiency. They further provide guidance for the selection and tuning of accurate and efficient coupling algorithms. 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; (Leetmaa and Skorodumova, 2014) NASCAM is particularly well-suited for the study of species deposition on substrates; (Lucas and Moskovkin, 2010) and Zacros provides a very flexible graph-theoretical KMC algorithm to model surface reactions at the solid/gas interface (Stamatakis and Vlachos, 2011; Nielsen et al., 2013). 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 atomistic and macroscopic techniques.

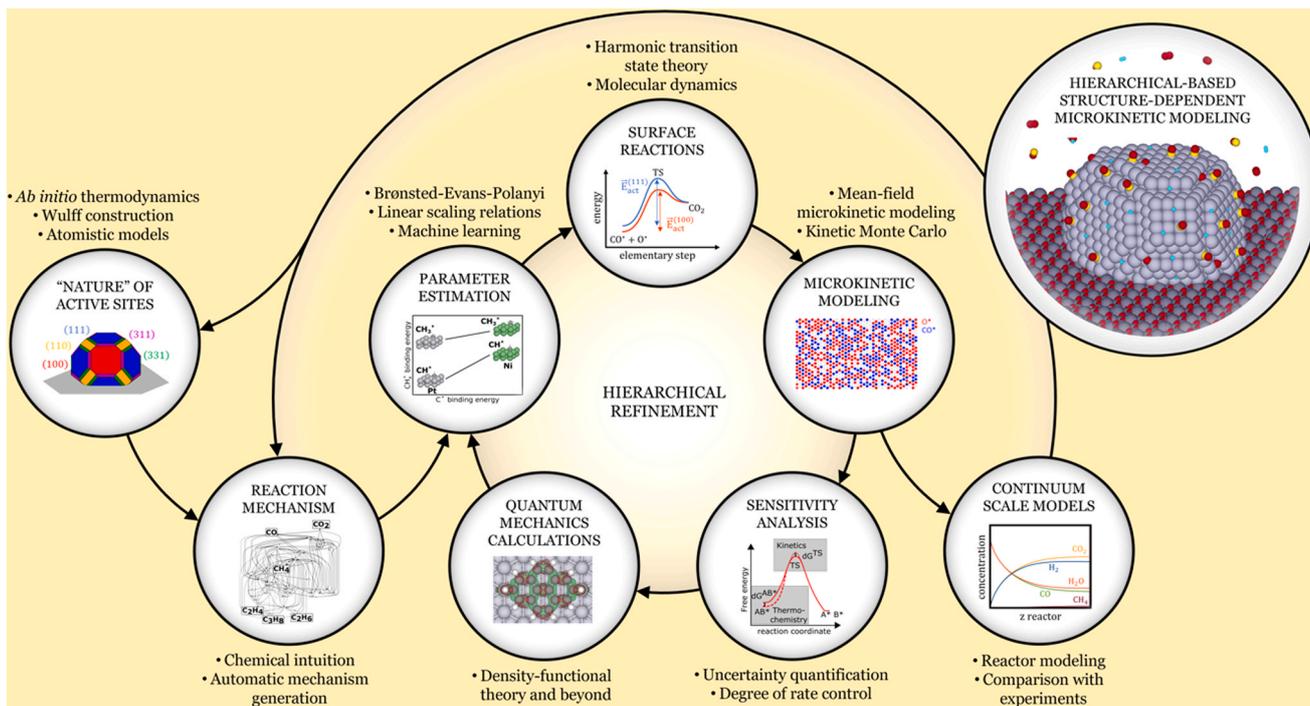
## 2.2. Hierarchical microkinetic analysis of heterogeneous catalytic processes

Applying molecular simulation methods in heterogeneous catalysis is crucial for the rational understanding of catalysts' functionality with an atomistic level of detail (Saliccioli et al., 2011; Bruix et al., 2019). The inclusion of such techniques in the multiscale analysis of catalytic systems faces three main challenges: (i) complexity and dynamic nature of catalyst, (Kalz et al., 2017) (ii) complexity of reaction mechanisms, (Bruix et al., 2019; Lu and Law, 2009; Margraf and Reuter, 2019; Matera et al., 2019; Motagamwala and Dumesic, 2021), and (iii) complication and computational cost of energetic parameter estimation (Chen et al., 2021). These challenges must be addressed by an efficient multi-scale modeling framework (Maestri, 2017) schematically illustrated in Fig. 3.

### 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 (Schlögl, 2015). 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 (Kalz et al., 2017; Zhang et al., 2020b; Maurer et al., 2021). 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" (Schlögl, 2015) 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, (Cheula et al., 2018; Kreitz et al., 2021a) 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 modeled by coupling density functional theory (DFT) calculations with Boltzmann statistics to describe ensembles of nanoparticles obtaining different morphologies under reaction conditions (Cheula et al., 2020). Other methodologies for the modeling of catalyst materials include molecular dynamics and Monte Carlo techniques, (van Etten et al., 2021) 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 (Cheula and Maestri, 2021). 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, (Cheula and Maestri, 2021) 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, (Ewing et al., 2016; van Deelen et al., 2019) 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.



**Fig. 3 – Schematic illustration of the hierarchical-based multiscale modeling approach for catalytic surface reactions. The complexity of catalytic systems is tackled with a hierarchical refinement procedure: (i) microkinetic simulations are performed with low-accuracy parameters, (ii) the most relevant parameters are identified by sensitivity analysis techniques, and (iii) those parameters are refined with high-accuracy quantum mechanical calculations (Mhadeshwar and Vlachos, 2005; Maestri et al., 2014). These microkinetic simulations must be included in a multiscale framework, in which the effect of the reaction environment on the catalyst structure and the reaction mechanism is accounted for (Cheula and Maestri, 2021).**

### 2.2.2. Mikrokinetic mechanism development and parameter estimation

Reaction mechanisms in heterogeneous catalysis can have thousands of possible reaction intermediates and elementary steps, (Bruix et al., 2019; Margraf and Reuter, 2019; Stocker et al., 2020) even when involving only small molecules, e.g., steam reforming of methane (Maestri et al., 2008a) or CO<sub>2</sub> methanation (Kreitz et al., 2021b). 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 (Motagamwala and Dumesic, 2021; Gao et al., 2016; Plehiers et al., 2018; Dewyer et al., 2018; Vernuccio and Broadbelt, 2019; Zeng et al., 2020; Gupta and Vlachos, 2021; Liu et al., 2021) or machine learning (ML) frameworks (Margraf and Reuter, 2019; Stocker et al., 2020; Ulissi et al., 2017). One example is RMG (reaction mechanism generator), (Liu et al., 2021) initially developed for combustion processes, which has been successfully used for heterogeneously catalyzed systems (Kreitz et al., 2021b; Goldsmith and West, 2017; Mazeau et al., 2021; Blondal et al., 2019). 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 (Kauppinen et al., 2018). 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 (Kreitz et al., 2021b; Ulissi et al., 2017).

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, (Hammer and Nørskov, 2000) linear scaling, (Abild-Pedersen et al., 2007) Brønsted-Evans-Polanyi relations, (Bligaard et al., 2004) or the unity bond index-quadratic exponential potential method (Shustorovich, 1998) are developed based on the common physics behind the targeting surface processes. However, these methods are not always universal (Ding and Maestri, 2019). 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 (Chanussot et al., 2021). Available approaches are compressed sensing methods, (Deimel et al., 2020) gaussian process regression, and graph neural

networks (Back et al., 2019). 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 (Zeng et al., 2020; Kim et al., 2021; Xu et al., 2021; Schlexer Lamoureux et al., 2019; Noé et al., 2020; Guan et al., 2022; Erdem Günay and Yıldırım, 2021; Ma and Liu, 2020). A proper combination of physics-based correlations and phenomenology-based may further improve the applicability and accuracy.

### 2.2.3. Hierarchical multiscale modeling

Software tools for mean-field models are already well established, (Saliccioli et al., 2011; Bruix et al., 2019) 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, such as scaling the rate constants of quasi-equilibrated steps (Dybeck et al., 2017; Ravipati et al., 2022). A further challenge is the thermodynamically consistent implementation of coverage effects on kinetics and thermodynamics, (Mhadeshwar et al., 2003; Mitrichev et al., 2017) 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 (Stegelmann et al., 2009; Campbell, 2017). In these methods, it is necessary to correctly quantify the correlation among the parameters since this significantly affects the outcome (Sutton et al., 2016). 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 (Kreitz et al., 2021b). Further, the uncertainty in the microkinetic model parameters has to be propagated to the results to avoid over-interpretation (Medford et al., 2014). 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 (Nottoli et al., 2021; Brault, 2018; Bogaerts et al., 2020; Kovačič et al., 2020). This necessitates development on the quantum chemistry scale to describe the electronically excited states accurately and efficiently (Neyts, 2018; Ghosh et al., 2018) as well as advancing methods to incorporate the complex phenomena into macroscopic models (Ma and Schneider, 2021). In contrast, microkinetic modeling has only begun to be used more frequently for electrocatalytic systems (Shinagawa et al., 2015; Maheshwari et al., 2018; Marshall, 2018; Zijlstra et al., 2020; Geppert et al., 2021). 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 (Saleheen and Heyden, 2018;

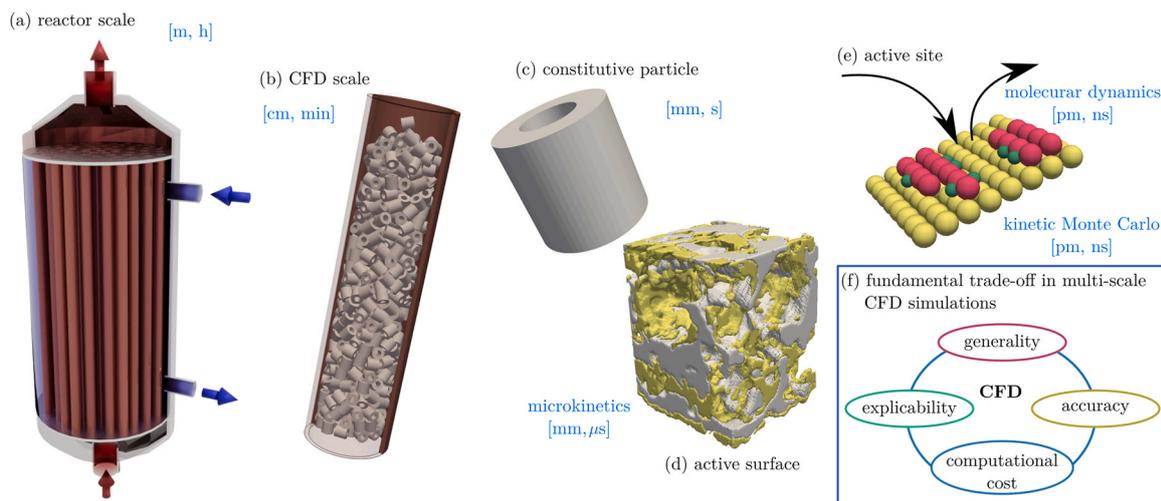
Saleheen et al., 2019; Baz et al., 2021; Studt, 2021). The use of detailed microkinetic models for reactor scale simulations with e.g. CFD codes is still computationally demanding. Hierarchical microkinetic modeling can be used to derive physically sound global rate expressions for computationally efficient reactor simulations (Maestri et al., 2008a). 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 (Bracconi and Maestri, 2020).

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 atomistic 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 Fig. 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 Fig. 4 f. 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.

The observed macro-scale reactor functionality is usually strongly dependent on the scale-to-scale interactions (Hettel et al., 2018; Matera et al., 2014). 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 Fig. 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 Fig. 4e) (Jurtz et al., 2019; Wehinger et al., 2015a; Dixon and Partopour, 2020; Micale et al., 2021). 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



**Fig. 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. Please note that for (c) and (d) pore diffusion effects are of importance and further discussed in Section 2.4.1.**

models or KMC simulations at the meso scale and electronic structure calculation at the microscale (Bracconi and Maestri, 2020; Matera et al., 2014). 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 (Bukowski et al., 2021). 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 (Maestri et al., 2008b). Deutschmann and coworkers coupled detailed microkinetic models with 2D and 3D models for the analysis of structured reactors (Hettel et al., 2018; Deutschmann et al., 2001; Tischer and Deutschmann, 2005). Wehinger and coworkers coupled 3D CFD simulations of packed-bed reactors with detailed microkinetic models (Wehinger et al., 2015a, 2015b). Röder et al. achieved a complete coupling even with KMC simulations in the context of Li-ion batteries (Röder et al., 2019b), 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 achieved. In this view, the most severe bottleneck preventing computationally efficient first-principles-based multi-scale modeling of heterogeneous reactors is the coupling between CFD and first-principles kinetic models itself, (Wehinger and Fleischlen, 2019) i.e., bridging the scales (c), (d) and (e) as shown in Fig. 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 gets computationally 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 (Maestri and Cuoci, 2013; Maffei et al., 2016; Uglietti et al., 2018). Consequently, the relevant computational burden can be alleviated by considering on-the-fly methodologies like in-situ Adaptive Tabulation (ISAT), (Pope, 1997; Blasi and Kee, 2016; Bracconi et al., 2017) Cell Agglomeration, (Babajimopoulos et al., 2005; Goldin et al., 2009; Rebughini et al., 2018; Uglietti et al., 2020) dynamic adaptive chemistry, (Liang et al., 2009; Ren et al., 2014) and the Reaction-Diffusion Manifold (REDIM) reduced kinetic model (Strassacker et al., 2018, 2021). Collectively, these methods are often termed chemical acceleration and were developed primarily in the combustion community (Law, 2007). 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 (Matera et al., 2019). 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 (Dagaut et al., 2006; Wang et al., 2018). Currently, the construction of suitable surrogates for chemistry models in CFD simulations is one of the most active research areas in multi-scale modeling 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 (Jurtz et al., 2019). Recently,

the breakthroughs in Machine learning (ML), (Jablonka et al., 2020) 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 (Stocker et al., 2020; Bracconi and Maestri, 2020). One way such ML techniques can be used is to surrogate the entire chemistry time-integration step (Blasco et al., 2000). In such an approach, the ML model learns the direct mapping between the meso-scale inputs and outputs represented in both cases by the local chemical composition, temperature and pressure which evolve due to the effect of the chemical reactions. 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 (Ouyang et al., 2022), Gaussian Process modeling (Stephenson et al., 2018), and Random Forests (Partopour et al., 2018) 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 (Bracconi and Maestri, 2020; Partopour et al., 2018).

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 (Rupp et al., 2018). 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 (Tran and Wang, 2017). Another challenge in building accurate ML models as surrogates is the amount of training data needed to learn the true internal dynamics (Brunton et al., 2016). 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 (McBride and Sundmacher, 2019). 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 (Bracconi and Maestri, 2020; Ji et al., 2021).

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 (Champion et al., 2019; Hvatov and Maslyayev, 2020). 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 (van der Giessen et al., 2020). 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 (Spalart, 2009). 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.

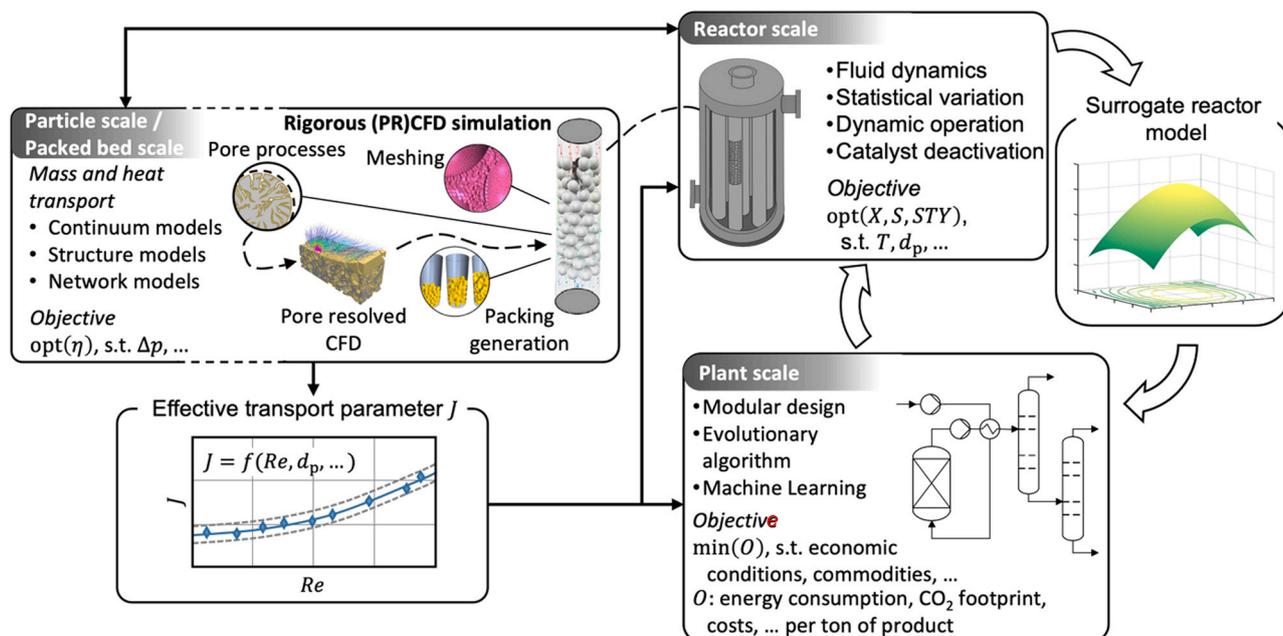
## 2.4. Catalyst-reactor-plant systems

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 Fig. 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.

### 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 (Dixon and Partopour, 2020). 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



**Fig. 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 (Jurtz et al., 2019; Kočí et al., 2019).

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 (Wehinger et al., 2017; Eppinger et al., 2011; Partopour and Dixon, 2019; Kutscherauer et al., 2022). 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, Kočí 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 (Kočí et al., 2019; Weber et al., 2020; Belot et al., 2021; Coppens et al., 2021).

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 (Bukowski et al., 2021; Hansen and Keil, 2012). Therefore, the conventional modeling 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 (Pietschak et al., 2018; Kaiser and Freund, 2019). A pertinent example is the literature of multi-component mass transport models in porous media. The Dusty Gas Model, (Davies, 1984) the Binary Friction Model, (Kerkhof, 1996) the Capillary Interpolation Model, (Young and

Todd, 2005) the Modified Binary Friction Model, (Pant et al., 2013) and the Adaptive Binary Friction Model (Ren et al., 2021) 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 (Feng and Stewart, 1973) as well as anisotropic catalyst pellet properties, which can be of significance as shown more recently (Partopour et al., 2019). 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 (Sosna et al., 2020). The future application of these techniques in other reactors of recent interest is expected, such as lab-scale reactors like Temkin (Wehinger et al., 2020) and single pellet string reactors, (Fernengel et al., 2020) 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 (Bouras et al., 2022).

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 (Froment et al., 2011). 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 (Stegehake et al., 2019). 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 and to identify strategies for reactor optimization (Dong et al., 2018). Moreover, PRCFD can be used as cost-efficient studies for investigations of novel reactor concepts for process intensification (Wehinger et al., 2015b; Jurtz et al., 2020, 2021). 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 (Rebughini et al., 2018; Bracconi et al., 2018; Wehinger and Flaischlen, 2019; Ferroni et al., 2021). 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) (Meinicke et al., 2020). 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 (Meinicke et al., 2020). 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 (Fischer and Freund, 2021; Zimmermann et al., 2022). For such cases, computationally efficient models without discontinuity are necessary (Pietschak et al., 2020). Machine learning (ML) tools can be applied for such cases for reducing the model complexity at reactor scale, see also the

discussion on modeling at the plant scale below. For example, a neural network can be trained to calculate the catalyst effectiveness factors 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. In general, Schweidtmann et al. identify six key challenges for upcoming research work in this respect (Schweidtmann et al., 2021). In short, these can be summarized to: optimal decision making from data-driven models, the physicality of ML models, the latter leading beyond towards issues of safety and trust in ML applications as well as the respective validity ranges, data handling and extraction of information from diverse sources and creativity, for instance regarding novel process designs or catalyst material (Schweidtmann et al., 2021). Moreover, 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 (Ratnakar et al., 2018) 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 (Deen et al., 2007; Lu et al., 2017). The validation of these models can be provided, as an example, by comparing the obtained transport properties against cold-flow or reactive experiments as described by Diez et al (Diez et al., 2019). One option is the coarse grain model, (Di Renzo et al., 2021) 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. 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 (Micale et al., 2021; Vandewalle et al., 2021). 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  $\pm 10^\circ\text{C}$ , which are considered significant with respect to reactor design under safe operation (Ganzer and Freund, 2020). 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, the pellet distribution in the individual tubes cannot be exactly identical, which inevitably has an impact on the individual temperature and pressure profiles (Müller et al., 2021). Moreover, a completely identical and uniform heating/cooling of all individual tubes in systems that comprise hundreds or thousands of tubes is hard to realize (Engel et al., 2020). 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, (Xie and Freund, 2018) 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 omission 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 (Cruellas et al., 2020; Pirro et al., 2021). Thereby, the model detail goes beyond built-in power law or Langmuir-Hinshelwood-Hougen-Watson (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 (Khuri and Mukhopadhyay, 2010; de Oliveira et al., 2019; Zaman et al., 2020; Singh and Tirkey, 2021). 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 (Eppinger et al., 2014). 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 (Dobbelaere et al., 2021), 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 (Chakkingal et al., 2022). 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 (Radatz et al., 2019). 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 (Mohan et al., 2020) should be incorporated, and the data used should follow the FAIR principles, i.e., findable, accessible, interoperable, reusable (Wilkinson et al., 2016).

### 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 relate to hierarchical 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 computationally demanding. Although several acceleration methods already exist, speed-up factors are typically below 100 (Bracconi et al., 2017; Rebughini et al., 2017; Daymo et al., 2022). 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 (Kalz et al., 2017). 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.

## Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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