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Review

Toward Realistic Simulations of Zeolite Catalytic Processes: A Mini Review

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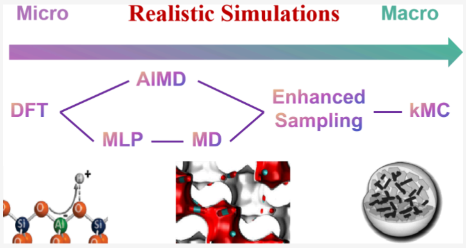
ABSTRACT: Zeolites are crucial in industrial catalysis, renowned for their unique microporous structures and versatile catalytic properties. However, accurately simulating zeolite-catalyzed processes poses significant challenges due to their spatiotemporal complexity, which requires capturing both atomic-level interactions and macroscopic phenomena. This review examines recent advancements in realistic simulations of zeolite catalytic processes, focusing on techniques such as machine learning potentials (MLPs), enhanced sampling methods, and kinetic Monte Carlo (KMC) simulations. These computational strategies have substantially improved the accuracy and efficiency of catalytic reaction simulations, addressing the traditional limitations associated with complex systems like zeolites. MLPs offer precise potential energy surfaces at lower computational costs, enabling extended molecular dynamics simulations. Enhanced sampling techniques, including umbrella sampling and metadynamics, effectively explore rare events and complex energy landscapes, although their success depends on the careful selection of collective variables (CVs). KMC simulations further enhance our understanding by modeling long-term molecular events, such as diffusion and reaction kinetics, at larger spatial and temporal scales. Despite notable progress, challenges remain, particularly regarding CV selection and KMC's reliance on accurate first-principles data. The integration of machine learning approaches, such as automated CV selection and transfer learning for MLP refinement, presents promising solutions to these issues. This review highlights these advancements and their potential to revolutionize the study of zeolite catalytic processes, bridging the gap between theoretical modeling and experimental observations and contributing to the design of more effective and sustainable catalysts.



INTRODUCTION

Zeolites are integral to many chemical researches due to their complex structures and diverse applications.[1,2] These crystalline aluminosilicates possess unique microporous frameworks, formed from corner-sharing [TO_4] tetrahedral units, which create channels, cages, and acidic sites. This distinctive architecture allows zeolites to serve as highly effective molecular sieves and catalysts, making them essential in industries like petrochemicals and environmental protection.

However, understanding the intricate chemical reactions and dynamic processes within zeolites presents considerable challenges, primarily due to their spatial and temporal complexity. Under reaction conditions, numerous experiments have shown that zeolites exhibit significant flexibility—meaning their structures cannot be assumed as fixed or rigid—along with heterogeneity, where active sites and defects are unevenly distributed, and dynamic behavior, as these properties evolve over time. This demands first-principles-based simulations capable of spanning extended time scales and large spatial dimensions to capture the true nature of chemical reactions within zeolites.[3] Such an approach bridges the gap between microscopic theoretical models and macroscopic experimental observations, providing a more comprehensive and accurate understanding of zeolite catalysis in real-world applications.

As shown in Figure 1, this review aims to explore the recent advancements in computational methods that address these challenges. Specifically, we examine state-of-the-art techniques that integrate both quantum mechanical accuracy and practical scalability, bridging the gap between atomic-level interactions and macroscopic catalytic behaviors. Traditional quantum mechanical approaches, such as Density Functional Theory (DFT), have been pivotal in elucidating reaction mechanisms within zeolites, yet they are constrained by high computational demands, which limit their applicability to smaller systems and shorter time scales. In light of these limitations, this review

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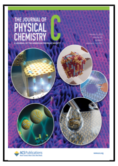

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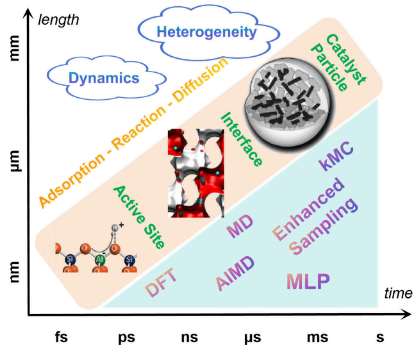

Figure 1. Schematic representation of the key topics in this review. This figure highlights the adsorption-reaction-diffusion processes in zeolite catalysis. State-of-the-art computational methods are illustrated, including Density Functional Theory (DFT) for atomic-level insights, Machine Learning Potentials (MLPs) that enable large-scale molecular dynamics (MD) simulations, and enhanced sampling techniques for exploring complex free energy landscapes. Additionally, kinetic Monte Carlo (KMC) simulations are shown as powerful tools to model long-time scale phenomena.

highlights alternative methods, including machine learning-based potentials, enhanced sampling molecular dynamics, and kinetic Monte Carlo (KMC) simulations, that enable multiscale simulations with efficiency and accuracy.

Recent advancements in computational methods have expanded the potential for realistic simulations[3−6] in zeolite catalysis. Machine learning techniques, especially neural network potentials, have proven valuable for accurately constructing potential energy surfaces (PES) while significantly reducing computational expenses.[7] These ML-driven PES models enable molecular dynamics (MD) simulations to be conducted over longer time scales and larger system sizes compared to conventional DFT approaches.

In addition to ML-driven PES, enhanced sampling methods like umbrella sampling (US), metadynamics (MTD) have been developed to probe rare events and complex free energy landscapes in catalytic processes.[8] These techniques effectively navigate energy barriers, allowing for the exploration of various reaction pathways. When combined with ML-driven PES models, enhanced sampling can better capture the intricate dynamics of zeolite catalysis under realistic conditions.

Kinetic Monte Carlo (KMC) simulations offer another significant advancement by modeling events as discrete transitions between states.[9,10] This approach allows for the simulation of processes over much longer time scales without the need to resolve atomic vibrations in detail, making KMC particularly effective for studying mass transport, diffusion, and reaction kinetics in porous materials like zeolites.

Despite these progressions, challenges persist, such as the reliance on human intuition for selecting collective variables (CVs) in enhanced sampling methods and the dependence of KMC on precise first-principles data. To address these challenges, researchers are increasingly leveraging advanced machine learning techniques, including automated CV selection and transfer learning for MLP refinement.[5,11]

This review explores these recent advancements, highlighting their potential to transform the study of zeolite catalytic processes. By providing an in-depth overview of machine learning potentials, enhanced sampling methods, and kinetic Monte Carlo simulations, this paper outlines pathways toward more accurate, efficient, and practical realistic simulations. While the focus of this review is on catalytic reaction and diffusion processes, it is worth noting that these simulation techniques are also theoretically applicable to other areas of zeolite science, such as nucleation, crystallization, and crystal growth.[12,13] The integration of these innovative computational approaches aims to bridge the gap between theoretical modeling and experimental observations, ultimately aiding in the design of more effective and sustainable catalysts.

■ SPATIOTEMPORAL COMPLEXITY IN REALISTIC ZEOLITE CATALYSIS

Zeolite catalytic processes are characterized by significant spatiotemporal complexity. A primary challenge in zeolite catalysis is the inherent heterogeneity of the system. Buurmans and Weckhuysen have noted that catalyst particles exhibit both spatial and temporal heterogeneity,[14] a trait that is particularly pronounced in zeolite systems. Variations in pore size, shape, and active site distribution create diverse reaction environments within individual catalyst particles, influencing reaction rates and molecular behavior, and resulting in nonuniform catalytic performance.

Recent studies that combine AIMD (Ab Initio Molecular Dynamics) simulations with advanced spectroscopic techniques have significantly advanced our understanding of the intricate catalytic behavior of zeolites.[15−19] These efforts underscore the crucial role of zeolite confinement effects in stabilizing short-lived, highly reactive intermediates such as nonclassical carbocations and acylium ions.[15,17] AIMD simulations have provided valuable insights into the formation, migration, and transformation of these intermediates under realistic reaction conditions, thereby offering a more detailed perspective on zeolite catalysis.[18,19] For example, the stabilization of acylium ions and other reactive species within the confined zeolite environment plays a pivotal role in determining reaction pathways, reactivity, and selectivity.[16,19] These findings highlight the indispensable role of realistic simulations in elucidating the dynamics of active species and their interactions within the zeolite framework, as well as the influence of structural and environmental factors on catalytic performance.[16,18]

Beyond molecular interactions, macroscopic variations within the catalyst also contribute to overall system heterogeneity. For example, during hydrocarbon conversion processes, Brønsted acid sites (BAS) and carbonaceous intermediates are unevenly distributed within zeolite crystals. This heterogeneity is further complicated by variations in temperature, guest molecule concentration, and heat transfer, all of which affect reaction dynamics. Advanced imaging techniques, such as infrared microscopy (IRM), confocal fluorescence microscopy (CFM), and interference microscopy, have been instrumental in visualizing these variations within individual particles.[23−25]

In addition, recent studies by Weckhuysen's group have uncovered temperature differences between the external surfaces of catalyst particles and the reactor bed. Local surface temperatures can increase by as much as +16 K during methane oxychlorination[26] and +40 K during syngas conversion.[27] Additionally, research by Ye et al. showed that factors like particle size and zeolite density can create significant temperature gradients within a single catalyst particle (Figure 2a).[20] These temperature heterogeneities critically influence the reactivity and diffusion of guest molecules, necessitating their consideration in simulation models.

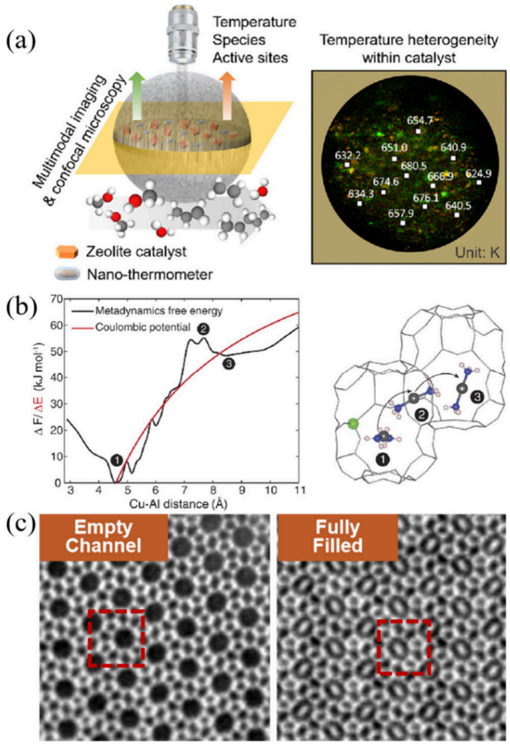

Figure 2. Representative cases of spatiotemporal complexity in zeolite catalysis. (a) Temperature distribution within a single catalyst particle, as measured by nanoscale temperature probes, illustrating the thermal gradients present during reaction processes.[20] Reproduced from ref 20. Copyright 2024 ACS. (b) Migration of active sites throughout the catalytic process, highlighting dynamic changes in reactivity and efficiency.[21] Reproduced with permission from ref 21. Copyright 2017 AAAS. (c) Comparison of the zeolite structure before and after molecular filling, demonstrating the extensibility and adaptability of the molecular sieve framework in response to adsorbate interaction.[22] Reproduced with permission from ref 22. Copyright 2022 AAAS.

The dynamic nature of catalytic processes adds another layer of complexity.[28,29] Reactants, intermediates, and products within zeolite pores are in constant motion, influenced by environmental factors such as temperature, pressure, and the presence of other adsorbed molecules. The mobility of these species directly impacts catalytic efficiency and reaction rates. For instance, Paolucci and colleagues[21] found that under certain reaction conditions, copper ions can become mobile within the zeolite framework, forming transient ion pairs that move through the zeolite's windows (Figure 2b). This mobility alters reaction rates, particularly at low temperatures, where the behavior of these transient species diverges from that of reactions occurring at fixed sites. Similarly, Wei et al. demonstrated that zeolite pores can expand by up to 15% when interacting with confined benzene molecules, allowing larger molecules to diffuse through the material (Figure 2c).[22] This challenges the assumption that pore sizes remain constant during reactions.

These dynamic behaviors significantly influence molecular diffusion and reaction kinetics within zeolites. Therefore, realistic simulation models of zeolite catalysis must account for structural fluctuations and the mobility of active sites to accurately predict catalytic performance. Zeolite catalysis, like many real-world chemical processes, involves reactions that span multiple scales. Chemical bond vibrations occur on the femtosecond scale, which is markedly different from the longer time scales of molecular diffusion. Capturing the entirety of the catalytic process requires simulations that encompass these diverse time and spatial scales, necessitating a combination of various computational methods.

In summary, realistic simulations of zeolite catalytic processes must address the inherent spatiotemporal complexity of these systems, including their heterogeneity and dynamic behavior, and must be conducted from a macroscopic, dynamic perspective.[10] Understanding these processes requires a multiscale approach that integrates various simulation techniques. At the atomic level, bond vibrations happen on femtosecond (fs) and Ångström (Å) scales, while molecular diffusion occurs over microsecond (μs) and micrometer (μm) scales. To effectively capture the full catalytic process in zeolites, a robust workflow that combines Density Functional Theory (DFT), machine learning-based potential energy surfaces, molecular dynamics (MD), and kinetic Monte Carlo (KMC) simulations is essential. Given the complexities of zeolite catalysis—ranging from atomic-level bond vibrations to diffusion processes spanning microseconds and micrometers—it is evident that no single simulation method can fully capture the entire process. A multiscale approach is necessary to create a unified molecular description of the catalytic process that encompasses reaction, diffusion, and adsorption/desorption, which will enhance our understanding of the interactions that govern catalytic performance and provide insights crucial for the design and optimization of industrial catalytic systems.

■ ON-THE-FLY SIMULATIONS WITH FIRST-PRINCIPLES ACCURACY

Density Functional Theory (DFT). Density Functional Theory (DFT) serves as a foundational tool in computational catalysis, balancing accuracy with computational efficiency. In realistic simulations, DFT provides vital insights into the electronic structures of active sites in zeolites, including the adsorption and activation of reactants. These calculations are essential for understanding reaction mechanisms, particularly in processes like methanol-to-olefins (MTO) conversion.

Recent advancements in DFT have improved its accuracy, especially regarding long-range dispersion interactions. The DFT-D method, which incorporates dispersion corrections into standard Kohn−Sham DFT, has notably progressed. The DFT-D3 approach developed by Grimme and colleagues achieves accuracy within 10% of the coupled-cluster single, double, and perturbative triple (CCSD(T)) method for van der Waals complexes and noncovalent interactions.[30] This enhancement is critical for studying the conformations and stability of adsorbed molecules within zeolite frameworks. However, it is worth noting that the Grimme group has recently introduced the successor DFT-D4, which further improves the model by making the atomic reference polarizabilities charge-dependent. While its application to zeolite catalysis remains an area for further exploration, the D4 version holds significant potential for more accurate simulations in zeolite catalysis.[31,32]

Despite significant advancements, challenges remain in accurately modeling complex catalytic processes. For instance, conventional DFT methods often underestimate energy barriers in acid-catalyzed reactions. Goncalves et al. highlighted

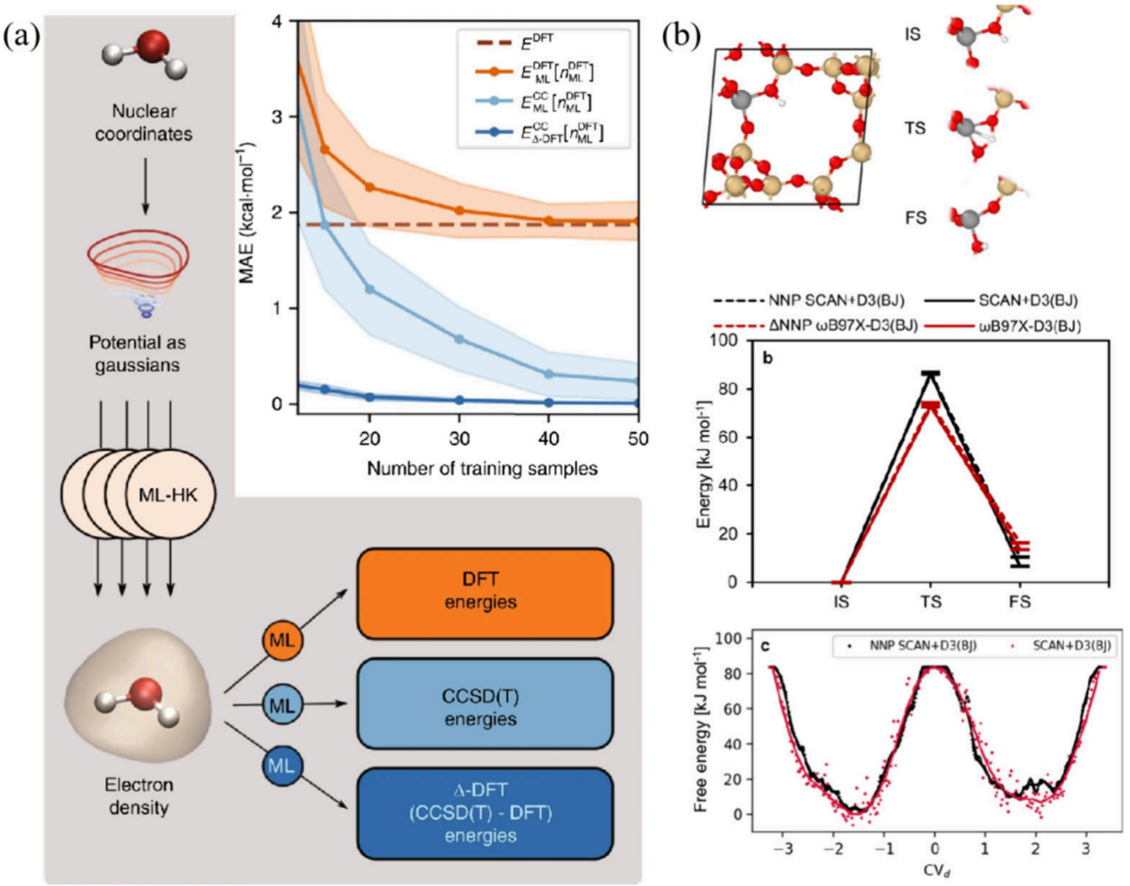

Figure 3. Enhancement of DFT accuracy through Delta-Learning. (a) Schematic of the Delta-Learning approach, showing the interaction among three models: a lower-level method (DFT), a higher-level method (CCSD(T)), and a Delta model, applied to the water system.[39] Reproduced from ref 39. Copyright 2020 The Authors. (b) Use of Delta-Learning with higher-level references to analyze a proton jump behavior in acidic CHA zeolites.[40] Reproduced from ref 40. Copyright 2024 The Authors.

that the commonly used PBE-D3 functional can exhibit mean absolute errors exceeding 40 kJ/mol for reaction barrier heights.[33] The benchmark hierarchical cluster approach[34−38] developed by Sauer and Plessow, which combines PBE-D3 for cluster optimization with DLPNO−CCSD(T) for single-point calculations, offers a highly accurate description of reaction barriers and energies in zeolite-catalyzed reactions. This approach allows for a detailed comparison of the performance of various density functionals, including M06 and PBE-D3. In contrast, hybrid functionals such as M06 demonstrate improved reliability, reducing errors to as low as 7 kJ/mol compared to the DLPNO−CCSD(T) benchmark, thereby providing a more precise representation of zeolite-catalyzed reactions.

While higher-level ab initio methods, such as coupled-cluster theory, provide superior accuracy, their high computational costs limit their application to small systems. To overcome this constraint, researchers like Bogojeski et al. have explored machine learning techniques, including Δ-learning (Figure 3a).[39] This method applies corrections to standard DFT calculations using data from high-level methods like CCSD(T), allowing for quantum-chemical accuracy in larger systems. Erlebach et al. successfully applied this approach in zeolite catalysis, achieving hybrid-level accuracy using the SCAN+D3(BJ) model (Figure 3b).[40]

In summary, advancements in DFT—through improved functionals and dispersion corrections—have significantly enhanced the modeling of zeolite catalysis. These developments deepen our understanding of reaction energetics and mechanisms, ultimately facilitating more effective prediction and optimization of catalytic performance.

Ab Initio Molecular Dynamics (AIMD). Ab initio molecular dynamics (AIMD) simulations extend the capabilities of static DFT by revealing the dynamic behavior of catalytic systems under realistic conditions.[41] Unlike static DFT, which provides a fixed view of the reaction landscape, AIMD incorporates thermal fluctuations and dynamic effects. This enables the investigation of how temperature, pressure, and molecular diffusion influence catalytic activity. AIMD is particularly effective for studying the movement of reactants and products within zeolite pores and the stability of reaction intermediates.

In AIMD, nuclei are treated as classical particles moving on a potential energy surface (PES) calculated from the electronic structure at each time step. The system evolves according to Newtonian equations of motion, with the PES guiding the nuclei's movement. This method offers a more dynamic and realistic perspective on catalytic processes, uncovering phenomena that static models may overlook. For instance, Hack et al. combined ultrafast two-dimensional infrared (2D IR) spectroscopy with AIMD to study water confined within the pores of highly hydrated zeolite HZSM-5. Their research provided quantitative insights into the molecular environments and hydrogen-bonding structures of protonated water clusters

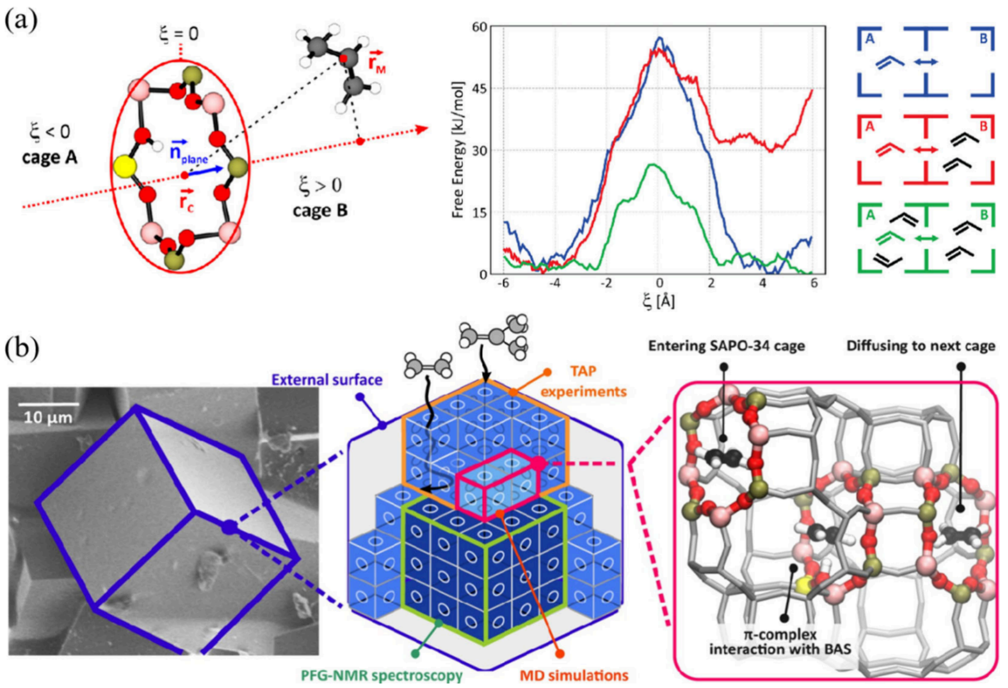

Figure 4. First-principles MD simulations with enhanced sampling are used to study hopping events between adjacent cages. (a) Schematic representation of collective variables used in light olefin diffusion through an 8-ring of H-SAPO-34. The free energy profiles show propene diffusion through a type 0 ring at 600 K with varying propene loadings in the cages.[44] Reproduced from ref 44. Copyright 2020 The Authors. This article is published under an ACS Author Choice License. (b) Combination of PFG-NMR spectroscopy and TAP experiments: PFG-NMR is used to estimate intracrystalline diffusivities, while TAP experiments explore diffusion at the outer layers of the zeolite crystal, offering a complementary understanding of diffusion dynamics.[45] Reproduced with permission from ref 45. Copyright 2021 The Authors. Published by Wiley-VCH GmbH in Angewandte Chemie International Edition.

under extreme confinement conditions.[42] Similarly, Hutton et al. employed AIMD simulations to investigate the adsorption of methane, ethane, and propane onto purely siliceous and protonated SSZ-13 zeolites.[43] Their results were compared to static calculation methods, which typically assume that molecules completely lose their translational degrees of freedom upon adsorption and leads to an overestimation of the adsorption free energy relative to the results of AIMD.

However, AIMD simulations are typically limited to short time scales, often in the range of hundreds of picoseconds, particularly in zeolite systems. Since catalytic processes often involve rare events, such as activated transitions, these time limitations restrict AIMD's ability to capture the full scope of reaction dynamics. To mitigate this, enhanced sampling techniques are being developed to broaden the applicability of AIMD, enabling the study of rare events that occur over longer time scales.

The integration of AIMD with enhanced sampling methods holds promise for revealing critical dynamic features of catalytic processes, contributing to a more comprehensive understanding of zeolite catalysis.[46] For instance, research from Veronique Van Speybroeck's group employed enhanced sampling molecular dynamics to examine how molecular factors affect the diffusion of light olefins through the 8-ring windows of H-SAPO-34 (Figure 4a).[44] Their findings indicate that Brønsted acid sites significantly enhance diffusion, while aromatic hydrocarbons may hinder it. Additionally, studies in the same group that use AIMD simulations alongside experimental techniques, such as Pulsed Field Gradient Nuclear Magnetic Resonance (PFG-NMR) and pulse-response temporal analysis (TAP), have provided insights into the diffusion of light olefins and paraffins through zeolite SAPO-34 (Figure 4b).[45] AIMD simulations examine interactions at the nanometer scale, while PFG-NMR experiments, conducted on large zeolite crystals (20−30 mm), measure intracrystalline diffusivities over milliseconds. TAP experiments on micron-sized H-SAPO-34 crystals probe surface barrier resistances and diffusion characteristics. These methods, though separate, complement each other, with AIMD helping to interpret the experimental data and revealing how Brønsted acid sites affect the diffusion of ethene and propene, but not alkanes. In another notable study, Xu and Liu et al. used a combination of metadynamics and AIMD simulations to show that water molecules can participate in catalytic reactions through a proton transfer mechanism. They revealed that a water-mediated proton transfer bridge enhances the continuous oxidation of methane to methanol over Cu-BEA zeolite.[47] These findings highlight the potential of enhanced AIMD approaches to uncover previously unknown pathways in catalytic processes.

In conclusion, recent advancements in both DFT and AIMD have greatly enhanced our capacity to simulate catalytic processes with first-principles accuracy. Although challenges remain—particularly concerning time scale limitations in AIMD and energy barrier accuracy in DFT—ongoing developments in hybrid functionals, machine learning corrections, and enhanced sampling techniques are paving the way for more accurate and efficient realistic simulations of zeolite catalysis.

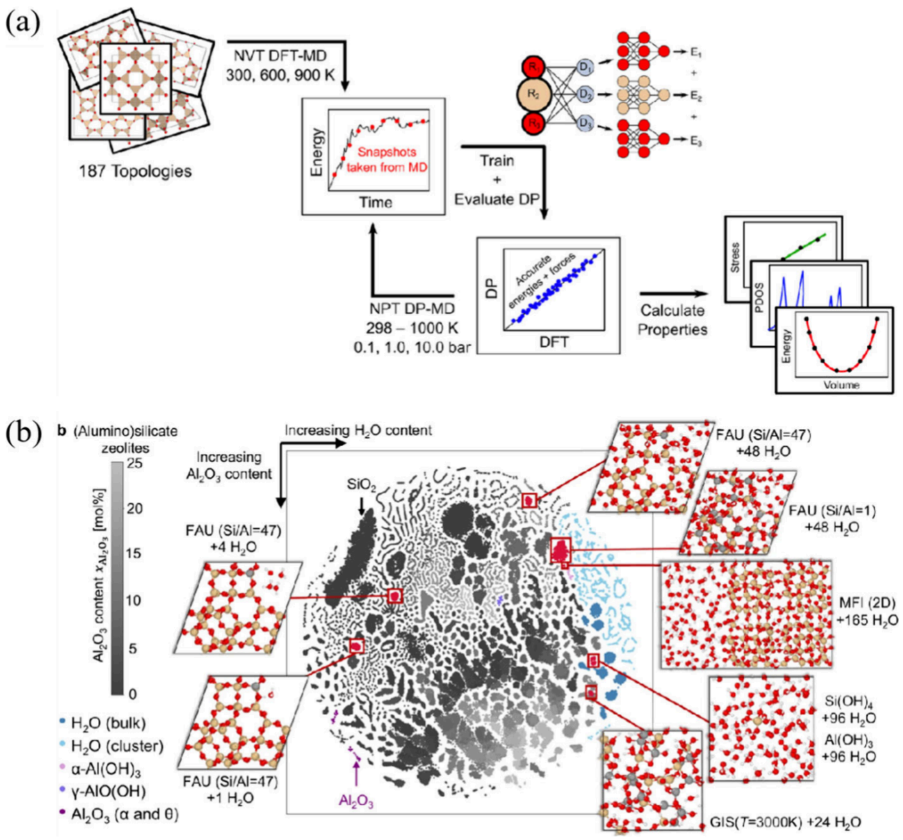

Figure 5. Representative cases for MLPs developed for zeolites. (a)Schematic illustration of the MLP training process for predicting structural properties of silica zeolites. The initial model was trained on configurations obtained from multiple AIMD simulations, and this trained MLP was further used to generate extensive MLP-MD trajectories to obtain new uncorrelated configurations for training the final model.[63] Reproduced from ref 63. Copyright 2023 The Authors. Published by ACS. (b) Data set designed to cover the full spectrum of acidic zeolites, incorporating a wide range of experimentally relevant water concentrations and Si/Al ratios.[40] Reproduced with permission from ref 40. Copyright 2024 The Authors.

■ MOVING TOWARD REALISTIC SIMULATION WITH MACHINE LEARNING POTENTIAL ENERGY SURFACES

Machine Learning Potential Energy Surfaces. In molecular dynamics and quantum chemistry, the Born–Oppenheimer (BO) approximation simplifies the study of molecular systems by separating the motions of nuclei and electrons. This separation allows researchers to focus on electronic structures while treating the nuclei as relatively fixed. However, exploring intricate potential energy surfaces (PES) for complex molecules often requires numerous quantum mechanical calculations, which can be prohibitively expensive.

Recent advancements in machine learning (ML) offer efficient alternatives for calculating PES.[48−50,7,51,52] Leveraging extensive existing quantum mechanical data, ML models such as neural network (NN) potentials, Gaussian approximation potentials (GAP) can accurately approximate PES while significantly reducing computational costs. These ML-driven PES models can effectively capture molecular interactions across diverse chemical environments, making them suitable for studying complex systems in catalysis and materials science. Among these, NN PES has garnered significant attention in the field of zeolite catalysis due to its exceptional prediction speed, making it particularly advantageous for large-scale molecular dynamics simulations. Other methods, such as GAP, are more suitable for smaller systems or those requiring higher interpretability, but they tend to be more computationally expensive when predicting energy and forces.[53]

A key challenge in developing ML potentials lies in accurately representing atomic configurations through structural descriptors. These descriptors transform raw atomic coordinates into features interpretable by ML models. After selecting appropriate descriptors, they are linked to the system's total energy using either a many-body expansion or an atomic energy summation approach.

The many-body expansion method decomposes the total energy into interaction terms, accounting for one-, two-, and three-body interactions. While precise, this method becomes impractical for large molecular systems due to the exponential increase in interaction terms with system size. Conversely, the atomic energy summation method, as utilized in the high-dimensional neural network (HDNN) model developed by Behler and Parrinello,[54] scales more efficiently by associating each atom's energy with its local chemical environment, making it better suited for complex systems.

Choosing suitable structural descriptors is critical for the accuracy of ML potentials. Various descriptor types are employed, including Gaussian-type symmetry functions (GTF), power-type structure descriptors (PTSD), and smooth overlap of atomic positions (SOAP).[55] These descriptors are designed to be invariant to atomic permutations, translations, and rotations, ensuring that ML models accurately reflect the system's physics. The quality of these descriptors directly affects the performance of ML potentials, particularly when extrapolating to new molecular configurations. Self-learning methods, where ML models refine their training sets with new

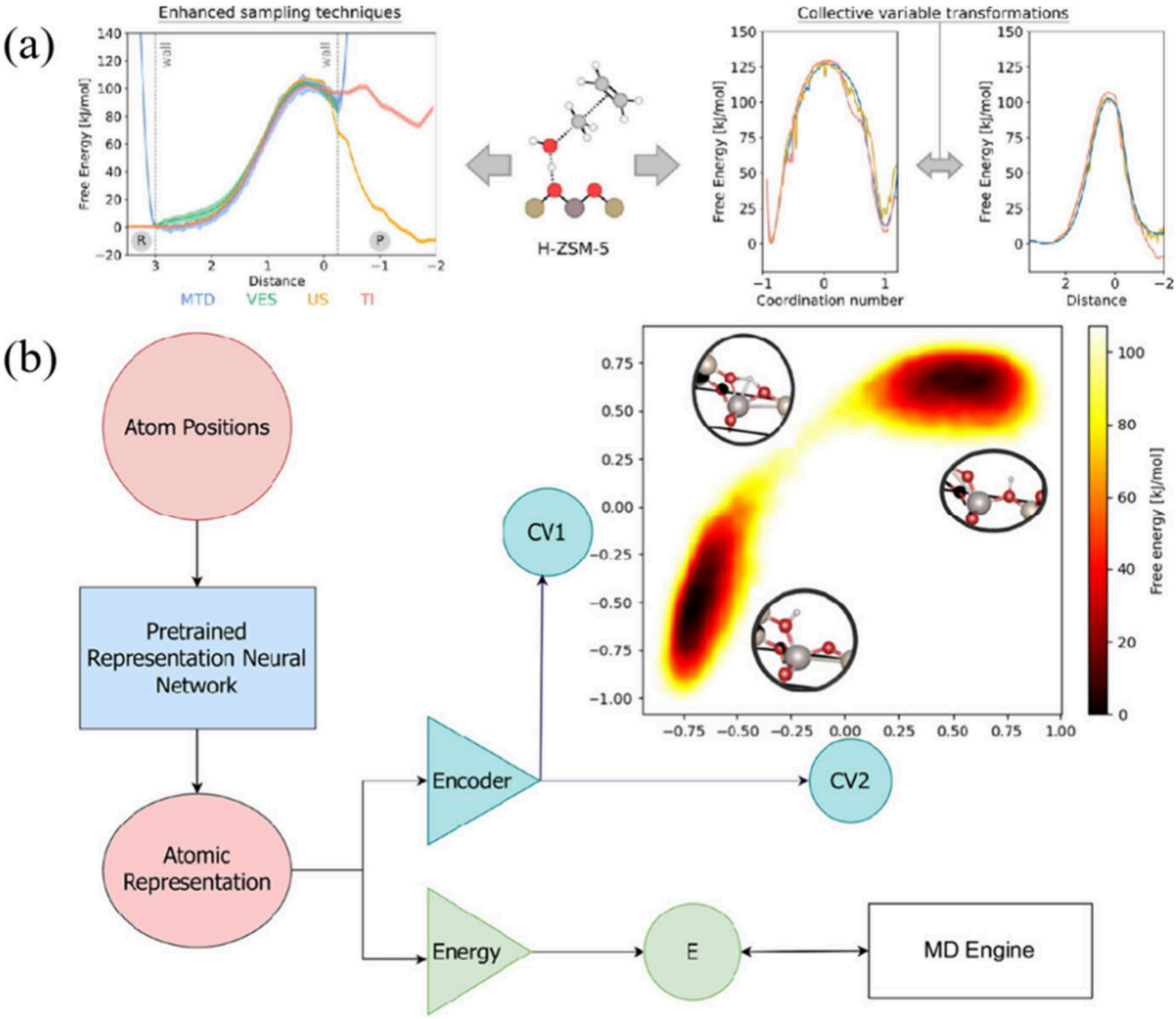

Figure 6. Protocol for describing reaction kinetics and an example of collective variable discovery with the machine-learning method. (a) A general protocol for determining reaction kinetics, independent of the collective variables (CVs) used to represent the reaction coordinate or the specific enhanced sampling technique.[46] Reproduced with permission from ref 46. Copyright 2020 Elsevier Inc. (b) Collective variable discovery through dimensionality reduction of atomic representation vectors. These representations, which are linear-scaling and invariant, can be either fixed (untrained) or optimized through supervised training in an end-to-end machine learning potential, enhancing the efficiency of CV selection for complex reactions.[11] Reproduced from ref 11. Copyright 2023 ACS.

data, are being explored to improve the robustness and accuracy of ML potentials.[56,57]

ML potentials have shown considerable success in modeling gas or surface small-molecule reactions. For instance, neural network-fitted PES models have been applied to reactions such as H_2 on Ag(111),[58] O + CH_4,[59] and F^- + $(CH_3)_3Cl$,[60] producing results that closely align with experimental observations and quantum mechanical simulations. These models effectively capture essential PES features, providing detailed insights into reaction pathways and energy barriers while offering substantial speed improvements over traditional quantum mechanical methods.

As ML-driven potentials gain traction, their application to more complex environments, such as zeolite-catalyzed reactions, has emerged as a significant research area.[61] Traditional quantum mechanical methods struggle to handle the large system sizes and complex interactions inherent in zeolite-catalyzed reactions. Recently, neural network potentials have successfully simulated proton hopping in H−CHA zeolites, reproducing DFT-calculated PES and enabling molecular dynamics simulations over longer time scales than typically allowed by DFT. These simulations provide valuable insights into reaction kinetics, diffusion processes, and nuclear quantum effects, particularly at elevated temperatures (around 473 K).[62] In another significant study, Kulkarni et al. leveraged an extensive DFT data set, comprising 219 unique zeolite topologies and over 350,000 DFT calculations from the International Zeolite Association (IZA) database, to train a machine learning potential (MLP) (Figure 5a). This MLP demonstrated strong agreement with DFT predictions for various zeolite properties, including structural characteristics, energy-volume relationships, and phonon density of states.[63]

Utilizing ML potentials in molecular dynamics simulations significantly enhances computational efficiency. For example, recent studies demonstrated that simulations of CHA zeolite using the same NN potentials showed a significant speedup, with the time per MD-simulation step reduced from ∼8.3 s on 56 Xeon E5 cores to ∼0.01 s on a single NVIDIA V100 GPU.[62] This improvement allows researchers to explore a broader range of conditions, including longer time scales and larger system sizes previously constrained by computational limitations. As a result, ML potentials are increasingly employed to investigate complex chemical processes relevant to industrial catalysis and material design.

Despite their successes, challenges remain in applying ML potentials to realistic studies of catalytic systems. Realistic simulations aim to capture catalytic processes in real-time, requiring efficient sampling of diverse chemical environments, including various reactant and product states. Reactive neural network potentials (NNPs), developed specifically for reactions in acidic zeolites, have shown promise in overcoming these challenges. For instance, NNPs accounting for varying water concentrations and Si/Al ratios in zeolites have maintained DFT-level accuracy while sampling a much broader range of configurations (Figure 5b). This has led to the identification of previously unknown reaction mechanisms, such as surface defect formation, which traditional computational methods could not access.[40]

Looking ahead, integrating machine learning techniques with traditional quantum mechanical methods is poised to transform the study of PES in complex systems. One promising avenue is transfer learning,[5,40] wherein models trained on lower-level quantum mechanical data (e.g., DFT) are fine-tuned with a smaller set of high-level data (e.g., post-Hartree–Fock or coupled-cluster). This strategy allows researchers to benefit from the efficiency of ML potentials while preserving the accuracy of high-level quantum mechanical calculations. Additionally, employing graph neural networks (GNNs) to learn PES representations shows potential for enhancing the scalability and accuracy of ML models.[64,65] GNNs can effectively capture both local and global atomic interactions, making them particularly suitable for modeling complex chemical environments in catalysis and materials science.

Adsorption, diffusion, and reaction are three fundamental processes of zeolite catatic reactions, and an integrated free energy surface of a complete catalytic cycle (including all these three processes) at the realistic reaction conditions should be one of the ultimate goal for zeolite catalytic reactions,[3,66] and AIMD simulations with enhanced sampling methods can realize the establishment of this kind of free energy surface in a small spatiotemporal scale, but the combination between MLP and enhanced sampling methods will greatly increase this scale (longer time scale, larger zeolite lattice, more reaction conditions, etc.), therefore greatly bridging the gap between theoretical modeling and experimental observations.

Enhanced Sampling Techniques. A significant challenge in molecular simulations is the identification of suitable collective variables (CVs), which are essential for enhanced sampling techniques.[67,68] Methods such as umbrella sampling (US), metadynamics (MTD) rely on well-chosen CVs to bias the system's dynamics and efficiently sample the free energy landscape. An effective CV should be dependent solely on the system's configuration, vary consistently along the reaction coordinate, and reduce the dimensionality of the free energy surface (FES) to a manageable number of degrees of freedom. However, finding appropriate CVs can be difficult, particularly in complex systems with multiple competing reaction pathways.

Umbrella sampling (US), one of the earliest enhanced sampling methods, is widely used to calculate free energy profiles along a reaction coordinate. In US, the system is biased to explore specific regions of the reaction coordinate, and the FES is reconstructed by combining results from multiple biased simulations. The accuracy of the reconstructed FES depends heavily on the chosen reaction coordinate, highlighting the importance of selecting an appropriate CV for the method's success.

Metadynamics (MTD) is another popular enhanced sampling technique that addresses some limitations of US by constructing a dynamic bias potential during the simulation. In MTD, Gaussian "hills" are periodically added to the bias potential, encouraging the system to escape energy minima and explore new regions of the FES. While MTD offers more flexibility than US, the choice of CV remains crucial, especially in complex systems like zeolite catalysis, where multiple reaction pathways may coexist, necessitating the use of multiple CVs to adequately describe reaction dynamics.

An illustrative example of the importance of CV selection is the methylation of ethene in H-ZSM-5 zeolites,[46] a key step in the methanol-to-olefins (MTO) process (Figure 6a). Different CVs can describe this reaction, each providing unique insights into the reaction dynamics and free energy barriers. Researchers have employed enhanced sampling methods to examine how various CVs influence the calculated FES, comparing these results with static DFT calculations and experimental data. Such studies underscore the necessity of careful CV selection, as even minor differences can lead to significant variations in predicted reaction kinetics.

To address the challenge of CV selection, researchers are increasingly turning to machine learning (ML) techniques.[11,68,69] ML methods, including dimensionality reduction techniques like principal component analysis (PCA) and advanced approaches such as variational autoencoders (VAEs), can automatically identify optimal CVs by analyzing atomic configurations (Figure 6b). These approaches are particularly beneficial in complex systems where manually defining CVs is impractical. ML-based methods can capture both structural and energetic features of the system, systematically selecting CVs that accurately represent underlying reaction mechanisms. Additionally, neural networks can be trained to learn the most relevant CVs from input data, enhancing the applicability of enhanced sampling methods in complex scenarios.

While these machine learning-driven approaches show promise, many enhanced sampling simulations in zeolite catalysis still rely on manually defined CVs. As machine learning techniques advance, they are expected to play a more significant role in the automated selection of reaction coordinates, reducing reliance on human intuition and broadening the applicability of enhanced sampling methods.

Advancements in enhanced sampling techniques have greatly improved our ability to explore complex free energy landscapes in zeolite catalysis. By effectively identifying and utilizing appropriate CVs, these methods provide deeper insights into reaction mechanisms and energetics. However, to fully capture the long-time scale dynamics and rare events critical in catalytic processes, it is essential to integrate enhanced sampling techniques with other simulation methodologies. The following section explores kinetic Monte Carlo

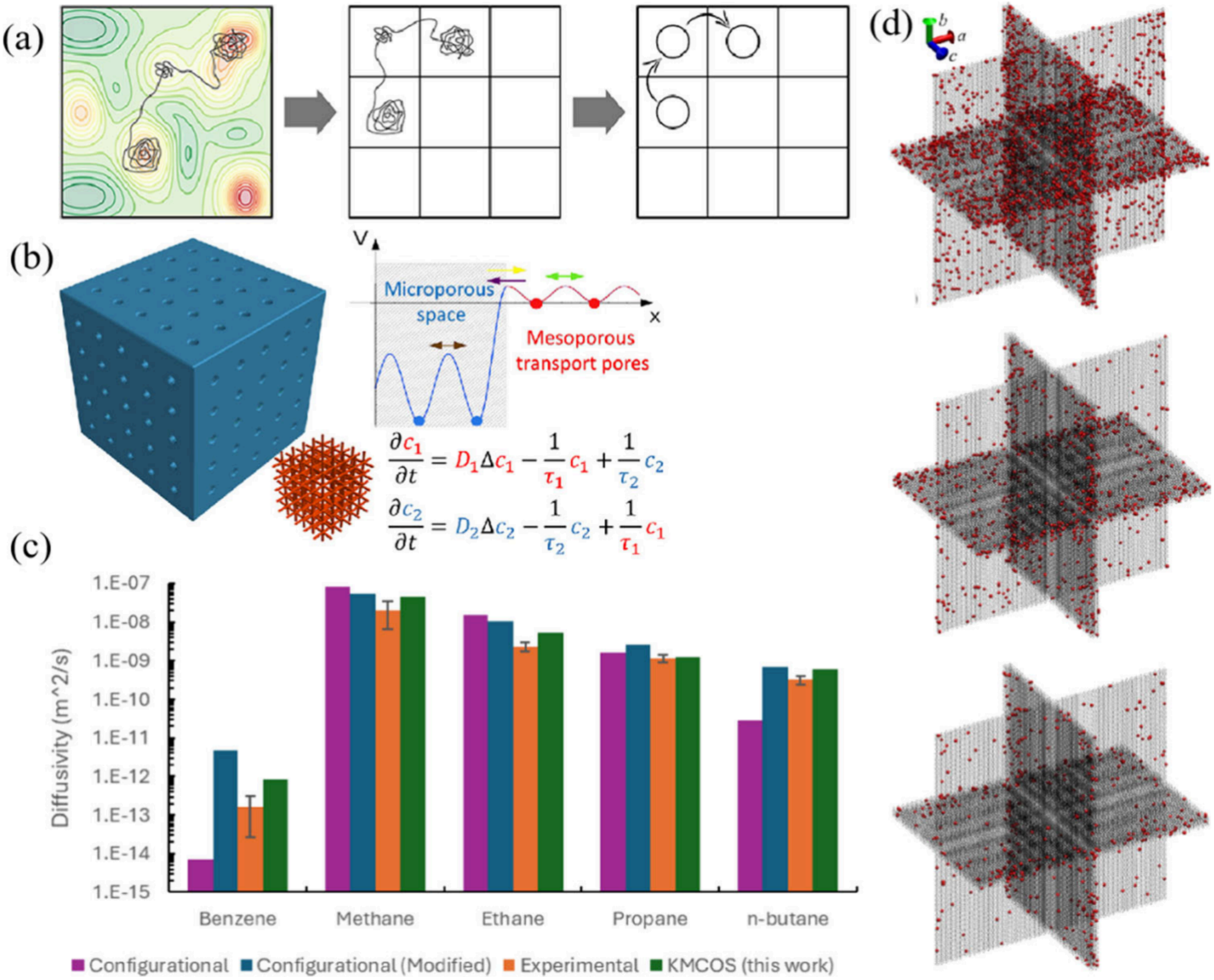

Figure 7. KMC application in accelerating molecular simulations for zeolite diffusion-reaction. (a) Comparison of KMC and MD: KMC filters out inefficient molecular motions by converting an MD trajectory into a Markov chain for more efficient dynamics exploration.[70] Reproduced from ref 70. Copyright 2019 The Authors. (b) Transient molecular uptake profiles from KMC simulations align well with the two-region Kärger model for diffusion.[79] Reproduced with permission from ref 79. Copyright 2022 ACS. (c) Diffusion coefficients of various hydrocarbons in ZSM-5 zeolite at 300 K, as obtained from KMC and other methods.[80] Reproduced with permission from ref 80. Copyright 2024 AIChE. (d) Snapshots of adsorbate distributions in the ZSM-5 zeolite supercell (two unit cells thick) at steady state under increasing reaction frequencies from top to bottom.[81] Reproduced with permission from ref 81. Copyright 2018 Elsevier Ltd.

(KMC) simulations, which complement enhanced sampling methods by offering insights into the temporal evolution of catalytic systems over extended periods. Together, these approaches create a comprehensive framework for modeling the intricate dynamics of zeolite-catalyzed reactions.

Kinetic Monte Carlo (KMC) Simulations. Kinetic Monte Carlo (KMC) simulations are vital for studying stochastic processes in systems where molecular events—such as adsorption, desorption, diffusion, and chemical reactions—occur over extended time scales.[64,70−76] Unlike molecular dynamics (MD) simulations that track atomic trajectories through interatomic potentials, KMC models events as discrete transitions between states.[73] Each state in the system represents a specific configuration, and transitions between states occur with probabilities determined by reaction rates or diffusion coefficients. These transition rates are derived from rate constants, which can be obtained either from experimental data, first-principles calculations, or enhanced sampling methods. Enhanced sampling techniques provide free energy profiles and activation barriers for key molecular events, especially those involving slow processes such as cage-to-cage diffusion. Conversely, MD simulations using MLP offer a reliable approach to capture fast processes, such as chemical reactions. By combining these methods, KMC simulations can accurately capture the intricate dynamics of zeolite catalytic processes under realistic conditions. KMC allows for the simulation of processes over significantly longer time frames without the need for detailed atomic vibration resolution which represents a significant computational bottleneck in MD simulations, making the method particularly useful for exploring phenomena like mass transport in zeolite materials.[77,78]

One notable application of KMC simulations is in the study of molecular diffusion within zeolites. Kärger group utilized KMC to generate transient molecular uptake profiles for adsorbates in zeolites, comparing the results with those from the two-region diffusion model (Karger model) (Figure 7b).[79] The KMC-generated profiles aligned well with the Karger model, demonstrating KMC's effectiveness in capturing molecular diffusion in porous materials. These findings highlight KMC's potential to optimize mass transfer in zeolite-based catalytic processes and offer valuable insights into the efficiency of industrial catalysts. Similarly, Paschek et al. reported KMC simulations of self-diffusion of a methane/perfluoromethane mixture in silicalite.[75] Their relatively simple KMC model successfully reproduced key features of the mixture's diffusion behavior and supported the validity of a logarithmic interpolation rule for mixture self-diffusion coefficients, findings that were recently observed in MD simulations. In a related study, Babu Joseph et al. used KMC to investigate the diffusion behaviors of binary mixtures of alkanes and aromatics through ZSM-5 zeolite (Figure 7c).[80] The KMC simulations showed reasonable agreement with experimental data. This further highlights KMC's ability to model complex diffusion phenomena and its relevance to industrial applications involving zeolite-based catalysts.

In addition to diffusion studies, KMC simulations have been employed to investigate the effects of adsorption, desorption, and chemical reactions on adsorbate distribution in zeolites. For instance, Huang et.al modeled the distribution of adsorbates in ZSM-5 zeolites using KMC,[81] revealing complex spatial patterns such as nonlinear concentration gradients and adsorbate shell formation (Figure 7d). These insights are crucial for understanding catalytic efficiency, as they illustrate how adsorbates interact with the zeolite framework and how these interactions affect overall reaction rates.

A key advantage of KMC simulations is their ability to bridge the gap between atomic-level insights and larger-scale phenomena. While MD simulations excel at detailing atomic-scale processes, they are less efficient for simulating long-term events like diffusion and reaction kinetics in porous materials. In contrast, KMC models these processes as random jumps between adsorption sites, providing a more computationally efficient method for studying long-term dynamics in systems such as zeolites.

KMC simulations are also highly adaptable and can be integrated with other methodologies, including Transition State Theory (TST) and temperature-accelerated molecular dynamics, to enhance accuracy while maintaining computational efficiency. This versatility makes KMC a valuable tool for investigating dynamic systems, including amorphous materials where atomic environments evolve continuously under reaction conditions. In zeolite catalysis, where adsorption sites and reaction pathways frequently change, KMC offers a robust framework for modeling complex catalytic processes over extended time scales.[82−85]

Despite their advantages, KMC simulations face challenges, particularly in integrating first-principles data. The accuracy of KMC relies heavily on the quality of the input data, often sourced from methods like Density Functional Theory (DFT). Ensuring that DFT calculations accurately capture the relevant potential energy surfaces (PES) for adsorption and reaction events is crucial for KMC's success. However, as DFT data becomes more accessible and machine learning-based potentials improve, these challenges are being addressed, positioning KMC simulations as an increasingly important tool in catalytic research.

In conclusion, KMC simulations provide a versatile and powerful method for studying zeolite catalytic systems. By bridging the gap between atomistic and macroscopic phenomena, KMC yields valuable insights into the processes influencing catalytic efficiency, from molecular diffusion to chemical reactions. As computational techniques advance, KMC is expected to play an even more integral role in catalytic research, especially when combined with methods like enhanced sampling and machine learning-driven potentials.

Conclusions and Outlook In this review, we explored recent advancements in realistic simulations of zeolite catalytic processes, with a focus on machine learning potentials (MLPs), enhanced sampling methods, and kinetic Monte Carlo (KMC) simulations. These approaches have significantly improved the accuracy and efficiency of catalytic reaction simulations by overcoming traditional computational limitations, particularly in complex systems like zeolites. MLPs offer precise descriptions of potential energy surfaces while reducing computational costs, enabling molecular dynamics simulations to extend over longer time scales. Enhanced sampling techniques address the challenge of exploring rare events in catalytic processes, although their success is still heavily reliant on the appropriate selection of collective variables (CVs). KMC simulations complement these methods by modeling long-term molecular events, such as diffusion and reaction kinetics, across micron and microsecond time scales.

Despite these advancements, several challenges remain. The selection of CVs for enhanced sampling often depends on human intuition, and KMC simulations require accurate first-principles data. However, the integration of machine learning (ML) techniques, including automated CV selection and transfer learning for refining MLPs, shows great potential for addressing these challenges. Additionally, innovations in graph neural networks (GNNs) and multiscale simulation frameworks are expected to significantly enhance realistic simulations.

Looking forward, the combination of these advanced techniques could yield transformative insights into catalytic processes, paving the way for more efficient and sustainable industrial applications. Ongoing improvements in ML-driven potentials, enhanced sampling methods, and hybrid simulation approaches are likely to expand the horizons of catalyst design and optimization, fueling innovation in chemical engineering and materials science. In summary, the integration of these advanced simulation techniques is set to revolutionize the field of zeolite catalysis. By bridging the gap between atomistic interactions and macroscopic behavior, these methods offer unprecedented opportunities for understanding and optimizing catalytic processes. As computational capabilities and algorithms continue to progress, we anticipate further significant advancements in the design of highly efficient and sustainable catalysts, ultimately contributing to improvements in chemical manufacturing and environmental sustainability.

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