



Research Article

Modelling metal-organic framework pesticides delivery system using computer simulations

Mohd Hairudin Haryadi¹, Nur Hana Faujan^{1,3} and Muhammad Alif Mohammad Latif^{1,2,3*}

¹Department of Chemistry, Faculty of Science, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

²Nanomaterials Synthesis and Characterization Laboratory, Institute of Nanoscience and Nanotechnology, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

³Centre for Foundation Studies in Science of Universiti Putra Malaysia, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

*Corresponding author: aliflatif@upm.edu.my

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Abstract

The pesticide delivery system is a promising technique that can improve efficiency, reduce environmental impact, and enable controlled release of pesticides. Cyclodextrin Metal-Organic Framework (CD-MOF-1) is a suitable candidate for enhancing pesticide encapsulation and release due to its biocompatibility and porous structure. This study employed computer simulations to analyse the encapsulation and adsorption behaviour of four pesticides: Avermectin (AVM), Dazomet (DAZ), Mancozeb (MAN), and Hexaconazole (HEX). A combination of Density Functional Theory (DFT), Molecular Dynamics (MD), and Grand Canonical Monte Carlo (GCMC) simulations was used to assess their electronic properties, structural stability, diffusion, and adsorption behaviour. Simulation results showed that MAN exhibited the most favourable dynamic delivery system properties, with the smallest HOMO-LUMO gap of 4.37 eV, the highest adsorption capacity, and the highest diffusion coefficient of $3.88 \times 10^{-8} \text{ cm}^2/\text{s}$. In contrast, DAZ showed the lowest root-mean-square deviation (RMSD) of 0.07 nm, indicating excellent structural stability. HEX showed intermediate delivery behaviour with a diffusion coefficient of $1.92 \times 10^{-8} \text{ cm}^2/\text{s}$. AVM showed the highest binding energy of 422.4 kJ/mol and the lowest diffusion coefficient of $2.99 \times 10^{-10} \text{ cm}^2/\text{s}$, making it more suitable for prolonged storage. These findings demonstrate the versatility of CD-MOF-1 as a pesticide delivery system and highlight its potential for sustainable agricultural applications.

Keywords: Adsorption, cyclodextrin-MOF, encapsulation, pesticide delivery, computer simulation

Introduction

The United Nations Sustainable Development Goal 2 (SDG 2 – Zero Hunger) aims “to end hunger, achieve food security and improved nutrition, and promote sustainable agriculture.” Food security is defined as a situation where all people, at all times, have physical, social, and economic access to sufficient, safe, and nutritious food that meets their dietary needs and preferences for an active and healthy life [1]. However, recent data indicate that progress towards achieving this goal has been slow and, in some cases, has even reversed due to lingering effects of the COVID-19 pandemic, climate change, and ongoing conflicts. As of 2022, between 691 and 783 million people were undernourished globally, reflecting an increase in hunger that has brought global food insecurity back to levels seen in 2005. Additionally,

food insecurity affected 29.6% of the global population in 2022, with significant disparities across regions [2]. To address these challenges, it is crucial to promote sustainable agricultural practices and policies that enhance productivity and resilience, particularly amid rising food prices and environmental stressors. Sustainable agriculture is vital for increasing the availability of essential foods, which is essential for achieving global food security.

In plantation agriculture, controlling and reducing the intensive use of pesticides prior to harvesting is a current significant challenge. Pesticides, such as fungicides, herbicides, and insecticides, are well known for their negative environmental impact [3]. A controlled release of these active compounds can increase safety and efficiency while requiring less

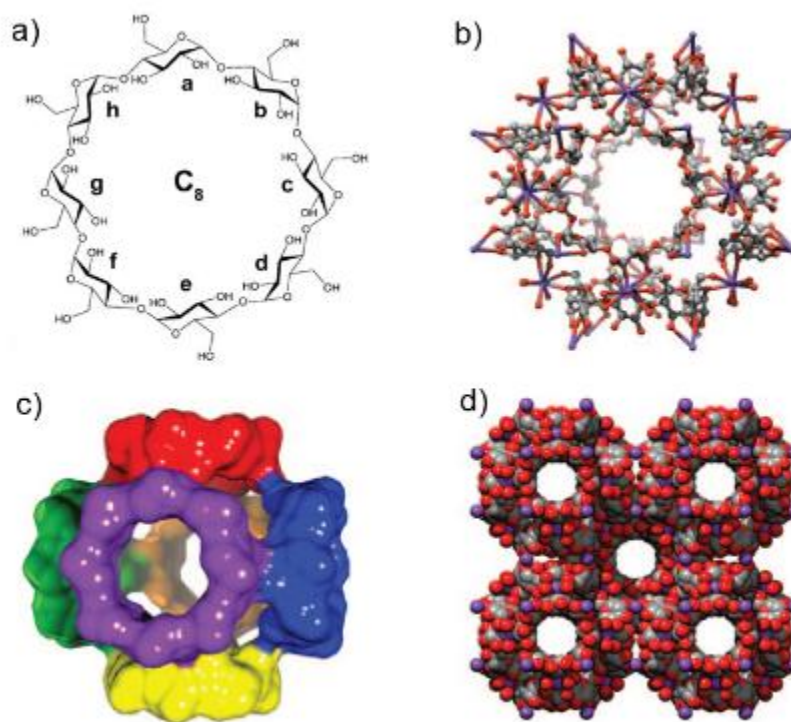


Figure 1: a) Structure of γ -Cyclodextrin, b) Structure of CD-MOF-1 unit cell (Red: Oxygen, Grey: Carbon, White: Hydrogen, Purple: Potassium), c) Surface representation of CD-MOF-1 unit cell, each cyclodextrin represented by different colours, d) Structure of CD-MOF-1 [10]

material in the field of application. Therefore, the development of smart delivery systems, such as stimuli-responsive delivery systems, is crucial for reducing the overuse of pesticides. However, according to Camara et al., only 6% of research on controlled release is related to the agroindustry field. In this area, stimuli-responsive materials only account for 23% of the research. This is a very low number, given the importance of controlling pesticide delivery in plantation agriculture. Stimuli-responsive delivery systems can be made from natural polymers and silica, which are widely available and biodegradable [5]. This study focuses on the stimuli-responsive delivery system based on cyclodextrin (CD) (Figure 1a). Several studies have reported the use of CDs in controlled-release formulations [6–9]. Although these formulations yielded good results in terms of application, the preparation method is neither straightforward nor cost-effective. A computational method for encapsulation and delivery of pesticides was proposed using a metal-organic framework (MOF), specifically CD-MOF-1 (Figure 1b-d).

MOFs are metal ions or clusters coordinated to organic molecules, resulting in a one-, two-, or three-dimensional porous crystalline framework. This unique coordination polymer can be used in a wide range of applications. One of them is serving as a host

for guest molecules. Depending on the MOF's pore aperture, the size of guest molecules can range from simple molecules, such as hydrogen gas [11], to complex structures, such as proteins [12]. It was shown that macromolecular encapsulation, such as enzymes, can be achieved with MOFs, and that improvements in stability under extreme conditions are evident [13]. In 2010, Smaldone et al. successfully synthesised CD-MOF-1 using food-grade γ -CDs and potassium hydroxide [10]. Since then, many researchers have utilised CD-MOF-1 either as is or modified for a target application [14].

In the agricultural field, MOFs have been studied as sorbents for pesticide extraction and sensing [15–17]. There have been reports on the use of cyclodextrin MOF as a pesticide adsorbent and a source of potassium fertilizer [18,19]. However, reports on the application of CD-MOF-1 as a controlled-release medium for pesticides are scarce. In this study, pesticides are encapsulated in CD-MOF-1. However, a potent pesticide such as AVM has a short half-life and is degradable under solar radiation. In addition to its controlled-release properties, encapsulation with CD-MOF-1 should reduce the degradation of pesticides such as AVMs. The proposed release mechanism involves breaking the framework upon γ -CD dissociation in response to stimuli such as pH and

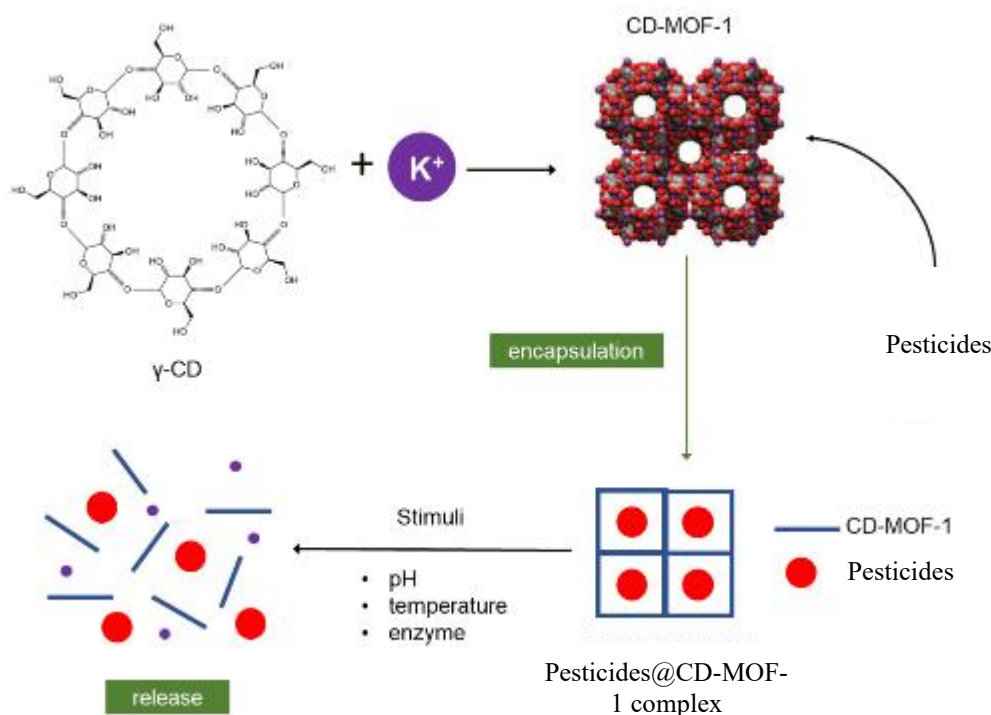


Figure 2. Illustration of the step-by-step preparation and proposed release mechanism of the CD-MOF-1-based stimuli-responsive pesticide delivery system. The diagram outlines the encapsulation of pesticides into CD-MOF-1 and the subsequent release triggered by external stimuli such as pH and temperature

temperature (**Figure 2**). CD-MOF-1 offers an advantage over the currently used support materials such as hollow mesoporous silicas, emulsions, zeolites and others since the pore channels of the framework can serve as a medium for encapsulation while γ -CD act as the trigger for release. Additionally, the mild reaction condition to prepare CD-MOF-1 and the high stability of the framework gives an extra advantage to the stimuli-responsive delivery system.

Materials and Methods

The study of pesticide encapsulation and adsorption within CD-MOF-1 was performed using a combination of computational analysis to analyse the electronic properties, structural stability, and adsorption efficiency. Pesticide molecules of AVM, DAZ, HEX, and MAN were obtained from the PubChem website [20] with CID of 6434889, 10788, 66461, and 3034368, respectively. Meanwhile, the CD-MOF-1 crystal structure was obtained from the CCDC [21] under deposition number 773709 [10].

Ab initio parameterisation

Density Functional Theory (DFT) [22] was used to determine the electronic structure and properties of the

pesticide molecules using Gaussian16 [23]. All geometry optimisation and charge distributions were determined using the function of Becke, Lee, Yang, and Parr (B3LYP) with single-point calculations and a 6-311(d p) basis set that aimed to produce atomic charges aligned with a potential identified based on the Charges from Electrostatic Potentials using a Grid-based (CHelpG) scheme [24]. The charges derived from ab initio calculations improved the accuracy of force-field parameters in MD simulations and provided a basis for analysing adsorption behaviour in GCMC simulations. The molecular electrostatic potential (MEP) mapping was visualised using GaussView. The .fchk file from the CHELPG single-point calculation was used to generate a cube file (.cube) containing the electrostatic potential mapped onto the molecular surface. The resulting MEP surface highlighted electron-rich (red) and electron-deficient (blue) regions, helping to identify potential interaction sites between the pesticides and CD-MOF-1. The electronic property analysis, conducted prior to encapsulation, provided a baseline understanding of the pesticides' stability, reactivity, and interaction potential with CD-MOF-1. These properties informed the parameterisation for MD and adsorption simulations, ensuring accurate modelling of the

encapsulation process. This approach supported predictions of encapsulation efficiency and controlled release behaviour, aligning with the study's objectives.

Molecular packing of pesticides and CD-MOF-1

The initial configuration of the pesticide-CD-MOF-1 complex was built using Packmol software [25]. Packmol was used to position pesticide molecules within the pores of the CD-MOF-1 framework in a defined spatial arrangement. This step was critical to creating a realistic starting structure for subsequent MD simulations. The software ensured that every pair of atoms between pesticides and CD-MOF-1 maintained a minimum distance of 2.0 Å to avoid steric clashes. **Figure 3** displays the initial configuration of encapsulated pesticides within CD-MOF-1 using the input as shown below:

```
tolerance 2.0
filetype pdb
output cd-mof-1_pesticides.pdb
structure CD-MOF-1.pdb
centerofmass
fixed 15.503 15.503 15.503 0. 0. 0.
end structure
structure "pesticide_name".pdb
number 1
inside cube 7.752 7.752 7.752 23.255
end structure
```

The crystal structures of pesticides were retrieved from the PubChem database and inserted into the centre of the simulation box containing CD-MOF-1. The simulation box dimensions were set to $31.006 \times 31.006 \times 31.006$ nm³, providing sufficient space for MD. The final configuration of the composite was saved in the Protein Data Bank (PDB) format for subsequent energy minimisation and MD simulation. This process provided a near-optimal starting point for simulations, minimising computational time during energy minimisation while ensuring realistic spatial arrangements for studying encapsulation and interaction dynamics.

MD Simulations

All MD simulations were performed using GROMACS 2021.1 [26] with the Universal Force Field (UFF) force field [27] and the rigid TIP3P water model [28]. Energy minimisation was performed using the steepest descent algorithm. The new position after each energy minimisation step was calculated. The forces and energy were calculated at each step for the new position. The energy minimisation was repeated until either no change in energy occurred or the convergence criteria were met. These can be either the maximum number of steps or the minimum force defined in the run parameters. The energy of the system was minimised using the steepest descent

technique with a step size capped at 0.01 nm and a force tolerance of 10 kJ mol⁻¹ nm⁻¹.

To study the interaction between CD-MOF-1 and pesticides, a virtual environment was created that included CD-MOF-1, pesticides, and water molecules. CD-MOF-1 was simulated within a container with a boundary of 1.0 nm. All directions had periodic boundary conditions applied. The covalent bonds involving hydrogen atoms were restricted utilising the Linear Constraints Solver (LINCS) algorithm [29]. Electrostatic interactions were calculated using the Particle Mesh Ewald (PME) method [30]. The long-range van der Waals and electrostatic interactions were limited to 1.0 nm, and the leap-frog algorithm was employed to integrate energy every 1 fs. To prepare the system for production simulations, the process began with a canonical (NVT) ensemble MD simulation. Velocities were assigned to atoms according to the Maxwell-Boltzmann distribution at 300 K. The simulation was run for 10 ns, with the temperature controlled using the velocity rescaling technique [31] with a coupling constant of 0.1 ps. The LINCS algorithm was employed to constrain covalent bonds involving hydrogen atoms, while the PME method was used to calculate electrostatic interactions. A cut-off of 1.0 nm was applied to long-range van der Waals and electrostatic interactions. During this phase, the volume was held constant.

Following the NVT equilibration, an isothermal-isobaric (NPT) ensemble MD simulation was performed for 10 ns to allow the system to reach equilibrium under constant temperature and pressure conditions. The pressure was controlled at 1.0 bar using the Parrinello-Rahman barostat [32] with an anisotropic pressure coupling mechanism and a time delay of 10 ns. The MOFs were considered rigid, and atoms within the framework were fixed in place during this phase. The system's potential energy was monitored throughout both equilibration phases to ensure stability. After equilibration, a production MD simulation was performed for 100 ns under the NPT ensemble, maintaining a constant temperature of 300 K and a pressure of 1.0 bar. The production simulation was used to analyse the interactions and dynamics of the CD-MOF-1 and pesticide molecules in the system. MD simulations were carried out to analyse the dynamic interactions, stability, and behaviour of pesticides encapsulated in CD-MOF-1 under realistic conditions (300 K and 1 atm). These simulations provide insights into binding stability, structural flexibility, and molecular movements within the MOF framework. Additionally, MD ensures the optimal arrangement of pesticides, providing a foundation for subsequent analyses, such as GCMC simulations, to evaluate adsorption properties. The total interaction

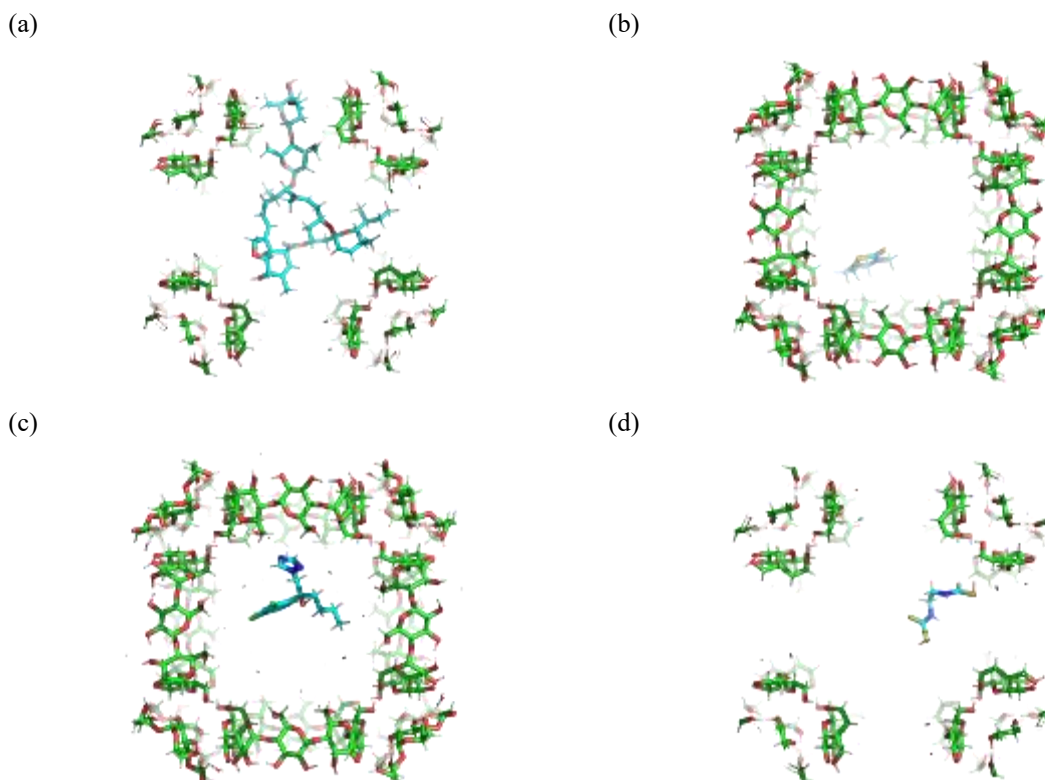


Figure 3. The initial configuration of encapsulated pesticides within CD-MOF-1. (a) AVM@CD-MOF-1 (b) DAZ@CD-MOF-1 (c) HEX@CD-MOF-1 (d) MAN@CD-MOF-1

energy ($E_{interaction}$) between the encapsulated pesticide molecules and CD-MOF-1 was calculated from the MD simulation outputs by summing the short-range non-bonded interaction terms: Lennard-Jones (van der Waals) and Coulombic (electrostatic) energies. These values were extracted using the `gmx energy` command in GROMACS. Before proceeding with packing during MD, it is recommended to eliminate O44 to maintain overall charge stability and ensure uniformity in the simulations. The presence of this atom in DFT calculations primarily introduces targeted reactivity at a localised level within the unit cell, without significantly affecting the overall structural robustness or stability of the final compacted MOFs. To ensure the system is stable and ready, MD requires removing any loose oxygen molecules that could cause unpredictable reactions and undermine the reliability of the results.

Grand Canonical Monte Carlo simulations

Adsorption simulations of CD-MOF-1 filled with pesticides were conducted using Grand Canonical Monte Carlo (GCMC) methodology as outlined by Allen and Tildesley and described by Frekel and Smit [33,34]. The RASPA software package was used for this purpose [35]. The initial step in preparing CD-MOF-1 was to obtain a file from the Cambridge

Structural Database, as suggested by Groom [21]. The research also calculated the helium void fraction within the CD-MOF-1 framework to accurately determine its volume capacity. This task was completed by creating a Monte Carlo simulation in RASPA using helium as the test molecule. The simulation was run for 500,000 cycles at 300 K using the UFF force field. The helium empty space percentage derived from this simulation was then used as a parameter for the following GCMC simulations to guarantee calculation of the void volume within the MOF framework. The pesticides molecular structures were initially fine-tuned using quantum chemistry calculation in Gaussian 16 to determine their optimum conformations. These optimised structures were then converted into RASPA format. The proper format was ensured so that atomic types and charges were accurately assigned in alignment with the force field specific to the MOFs. The UFF was utilised to conduct GCMC simulations on the interactions within both CD-MOF-1 and pesticides. The GCMC simulations were configured with 500,000 Monte Carlo cycles, and the properties were recorded every 10000 cycles. The experiments were carried out at a temperature of 300 K and different pressures between 0.1 to 1.0 bar to construct adsorption isotherm. The resulting adsorption isotherm described the relationship

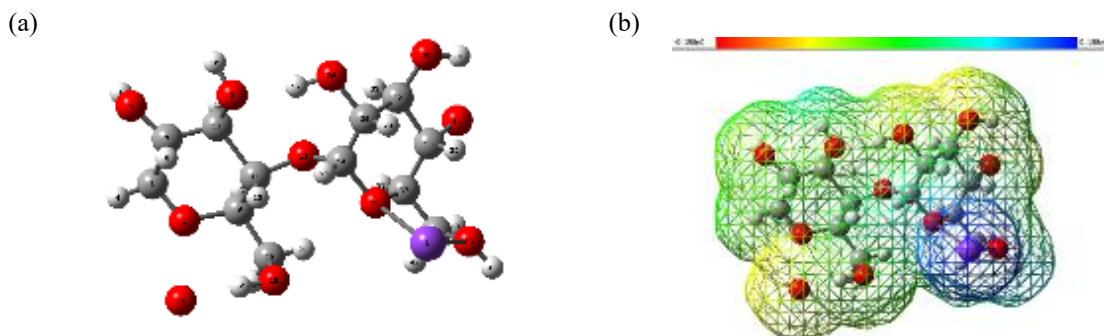


Figure 4. (a) Asymmetric unit of CD-MOF-1 with label. Red = Oxygen, Grey = Carbon, White = Hydrogen, Purple = Potassium. (b) Molecular electrostatic potential (MEP) map of CD-MOF-1 visualised to identify regions of electron-rich (red) and electron-deficient (blue) potential surfaces

between pressure and the amount of pesticide adsorbed into the CD-MOF-1 to evaluate its loading capacity as a delivery system. The helium void fraction determined previously was integrated into the simulation, for volume adjustment. The simulations using GCMC were run on a computing cluster to ensure accuracy and efficiency in monitoring the simulation progress by examining the energy profiles and loading data over Monte Carlo cycles. The results of these simulations were then analysed to gather insights, like the quantity of pesticide molecules absorbed inside the CD-MOF-1 structure at equilibrium state; creating adsorption isotherms that display loading versus pressure relationships within the pores of the MOFs. The adsorption behaviour of pesticides in CD-MOF-1 was determined based on the average number of guest molecules adsorbed per unit cell under each pressure condition. GCMC simulations sample possible molecular insertions and deletions according to statistical thermodynamics in the grand canonical ensemble [34]. This allows direct calculation of equilibrium loading, which is pressure dependent [33]. The resulting data enable the construction of adsorption isotherms and provide insights into the strength of each pesticide's interaction with the framework [36].

Results and Discussion

CD-MOF-1 has shown numerous applications in the encapsulation of small molecules, leveraging its properties and pore size [10]. Thus, CD-MOF-1 was studied as a stimuli-responsive delivery system for pesticides to improve their shelf life and reduce overuse, which can contribute negatively to the environment [37]. Initially, the CD-MOF-1 and pesticide structures were optimised using quantum mechanics. Gaussian 16 was used to analyse their electronic properties and partial charges. To study the behaviour of each pesticide, MD simulations were performed. The structural dynamics properties of

encapsulated pesticides were observed and compared. Finally, the pesticide adsorption behaviour in CD-MOF-1 was investigated using GCMC simulations. These results are significant because they offer new insights into the potential of MOFs for agricultural applications, particularly in improving pesticide delivery systems.

Electronic properties of CD-MOF-1

The DFT calculations on the asymmetric unit (Figure 4a) of CD-MOF-1 revealed a total of 573 molecular orbitals and a doublet spin state, arising from the presence of an oxygen atom no. 44 (O44) with zero net charge. This unpaired electron gives rise to a spin multiplicity of 2 (doublet) [38]. During the packing process, the O44 was removed to stabilise the net charge of the entire structure, ensuring the overall framework has zero net charge. If this oxygen atom had been retained, the packed form would have exhibited a net charge imbalance, making the structure less stable. Since DFT calculations are computationally intensive, they were performed on the asymmetric unit to reduce simulation time and cost. This approach provides accurate insights into the electronic properties while still reasonably representing the behaviour of the entire structure.

The DFT results for the asymmetric unit of CD-MOF-1 reveal essential electronic properties, including spin-dependent stability and reactivity. The larger HOMO-LUMO gap in the alpha (spin-up) state suggests that the unit is stable, while the smaller gap in the beta (spin-down) state indicates areas of reactivity [39]. These insights, while limited to the asymmetric fragment, provide a theoretical basis for understanding how the full CD-MOF-1 might behave. Specifically, they hint at potential reactive sites and charge-stabilising behaviour, which are crucial for interactions in the packed CD-MOF-1, offering a preview of its potential suitability for future

applications, such as pesticide encapsulation. The $E_{HOMO-LUMO}$ can exhibit the chemical stability and reactivity of the molecules, in which molecules that has smaller energy gap tend to exhibit more polarisability and are more reactive [40]. The HOMO-LUMO diagrams (**Table 1**) reveal the distinct roles of different atoms within the asymmetric unit. The K atom in the alpha configuration stabilises the fragment by acting as an electron reservoir, resulting in a larger HOMO-LUMO gap (3.171 eV). Conversely, the O44 in the beta state introduces localised reactivity, contributing to the small HOMO-LUMO gap (0.322 eV) and creating potential reactive sites. Together, these complementary behaviours suggest that the asymmetric unit offers both stability and reactivity, ensuring that the full CD-MOF-1 is effective for adsorption, encapsulation, or chemical interactions.

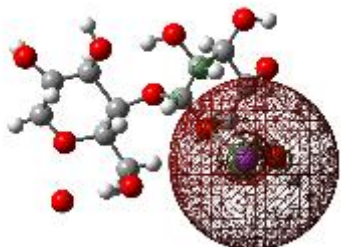
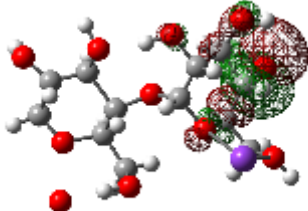
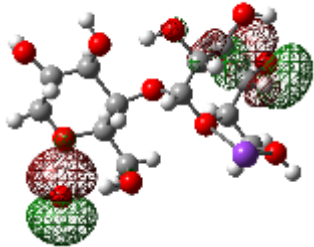
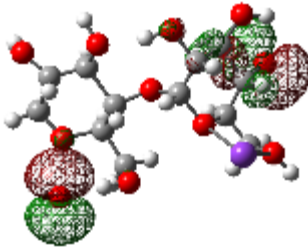
The Molecular Electron Potential (MEP) mapping (**Figure 5**) of the part displays an electronic arrangement consisting of noticeable electron-rich oxygen atoms and a deficient potassium atom, in electrons, which indicates that the unit can engage in both nucleophilic and electrophilic reactions

effectively which makes it suitable for enclosing pesticides, with corresponding charge distributions that complement each other. The existence of the O44 intensifies localised reactivity; however, removing it would enhance system stability for MD simulations. These findings suggest that CD-MOF-1 possesses a balance of strength and adaptability to be considered a potential option, for delivering pesticides effectively.

Electronic properties of pesticides

DFT calculations on the pesticides provide essential insights into their electronic behaviour, and single-point calculations were performed using the 6-311(d,p) basis set. Understanding the HOMO-LUMO gaps and related electronic properties is crucial, as these characteristics influence the adsorption potential and interaction dynamics with the CD-MOF-1 framework. Each pesticide's molecular orbital properties were analysed, focusing on electron density distributions and orbital interactions to predict reactivity and binding behaviour during encapsulation.

Table 1. Electronic properties of the CD-MOF-1 asymmetric unit, including HOMO and LUMO energy levels for alpha (spin-up) and beta (spin-down) states. Numbers in parentheses indicate the molecular orbital indices corresponding to the HOMO and LUMO in each spin state

STATES	HOMO	LUMO	
ALPHA	 (MO: 101) -5.580 eV	 (MO: 100) -2.409 eV	$E_{HOMO-LUMO}$: 3.171 η (eV): 1.585 S (eV ⁻¹): 0.631 χ (eV): 3.994 ω (eV): 5.032
BETA	 (MO: 100) -3.508 eV	 (MO: 99) -3.186 eV	$E_{HOMO-LUMO}$: 0.322 η (eV): 0.161 S (eV ⁻¹): 6.214 χ (eV): 3.347 ω (eV): 34.803

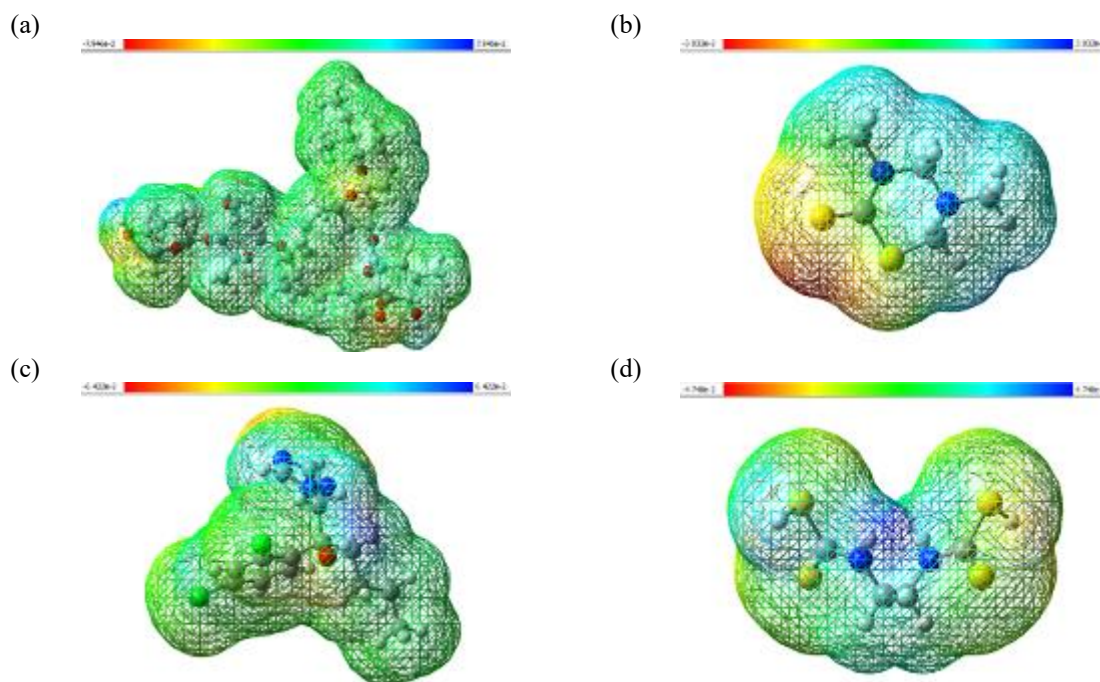


Figure 5. Molecular electrostatic potential (MEP) values of (a) AVM, (b) DAZ, (c) HEX, and (d) MAN calculated using DFT (B3LYP/6-31G(d,p) level)

Electron density

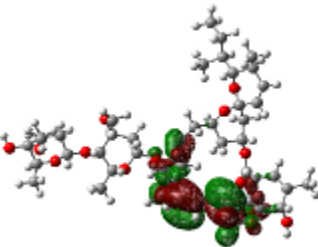
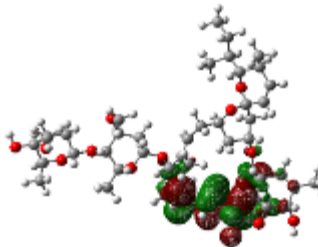
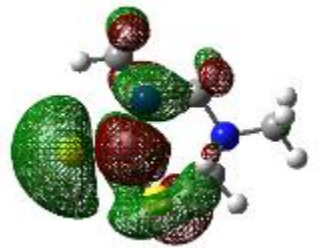
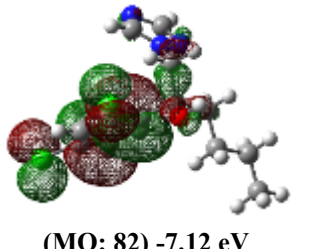
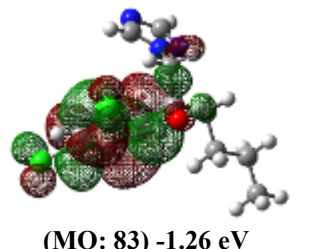
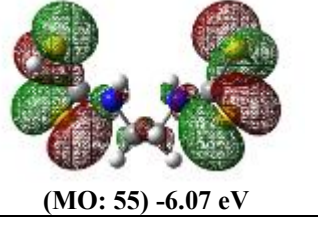
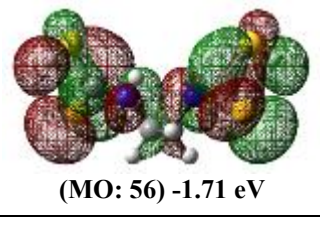
The electron density maps of the pesticides (**Figure 5**) provide essential insights into their charge distributions and potential binding sites. These maps reveal the locations of electron-rich and electron-deficient regions, helping predict how each pesticide interacts with CD-MOF-1 during encapsulation. Colours near red indicate more negative charge, while colours near blue indicate more positive charge. The AVM map displays electron density across areas, with some regions showing high concentrations. The widespread electron distribution in AVM indicates the presence of several binding interaction sites. This could support the formation of a durable encapsulation via point interactions with CD-MOF-1. In contrast to AVMs' distribution pattern, DAZ exhibits a higher electron density, with localised regions of varying density around functional groups. The condensed nature of DAZ suggests that it may engage in targeted interactions with parts of the CD-MOF-1, leading to binding and stable encapsulation. The electron density in HEX mainly clusters around the nitrogen and halogen atoms, with regions suggesting high polarity throughout the structure, hinting at potential interactions with the CD-MOF-1, specifically at electron-deficient sites, which may improve stability upon encapsulation. In contrast to HEX's pattern of electron distribution, MAN exhibits symmetrical electron density throughout its molecule, with

electron-rich regions near the sulphur and nitrogen atoms. The balanced structure and several responsive sites suggest that MAN can also interact with sites within CD-MOF-1.

Molecular orbital and HOMO LUMO gap

The molecular analysis of the HOMO-LUMO diagram is presented in **Table 2**, where the orbital numbers are indicated in parentheses. AVM's HOMO (236), the electron density is distributed across the core molecular backbone, with significant density near the oxygen atoms. The LUMO (237) has a distribution similar to that of the HOMO, with additional density in the central region. AVM's HOMO and LUMO overlap significantly, suggesting moderate reactivity and efficient charge transfer potential. DAZ's HOMO (43) shows electron density concentrated around nitrogen and sulphur atoms, while LUMO (44) shows a slight shift in density, indicating potential reactivity at specific nitrogen sites. This suggests that DAZ's localised HOMO-LUMO distributions indicate selective binding behaviour, favouring interactions with electron-deficient sites in CD-MOF-1. For HEX's HOMO (82), the electron density is heavily localised on nitrogen (N) and chlorine (Cl), suggesting potential nucleophilic behaviour. HEX LUMO (83), the density remains in the same regions, reflecting a localised charge-transfer potential. This shows the concentrated

Table 2. HOMO–LUMO energy levels and orbital diagrams of AVM, DAZ, HEX, and MAN calculated using DFT (B3LYP/6-31G(d,p)). The diagrams show the spatial distribution of the frontier molecular orbitals, with orbital numbers in parentheses

Pesticide	HOMO	LUMO	
AVM	 (MO: 236) -6.02 eV	 (MO: 237) -1.08	$E_{HOMO-LUMO}$: 4.94 η (eV): 2.468 S (eV ⁻¹): 0.405 χ (eV): 3.546 ω (eV): 2.547
DAZ	 (MO: 43) -5.86 eV	 (MO: 44) -0.85 eV	$E_{HOMO-LUMO}$: 5.01 η (eV): 2.504 S (eV ⁻¹): 0.399 χ (eV): 3.354 ω (eV): 2.247
HEX	 (MO: 82) -7.12 eV	 (MO: 83) -1.26 eV	$E_{HOMO-LUMO}$: 5.87 η (eV): 2.931 S (eV ⁻¹): 0.341 χ (eV): 4.187 ω (eV): 2.991
MAN	 (MO: 55) -6.07 eV	 (MO: 56) -1.71 eV	$E_{HOMO-LUMO}$: 4.37 η (eV): 2.184 S (eV ⁻¹): 0.458 χ (eV): 3.890 ω (eV): 3.465

electron density in HEX points to targeted interactions with complementary MOF regions that may contribute to strong encapsulation stability. Next, MAN's HOMO (55) displays symmetrical electron density, particularly around sulphur atoms, as does LUMO (56), which shows a similar distribution to the HOMO, maintaining symmetry. MAN's symmetrical HOMO-LUMO orbitals suggest robust multi-point interactions. The total number of molecular orbitals for each pesticide is 1548 for AVM, 238 for DAZ, 478 for HEX, and 260 for MAN. All molecules of a pesticide consist of a singlet spin-orbital. Exploring the HOMO LUMO diagram offers insights into how pesticides interact within the framework of CD-MOF-1. The diagrams show where electrons are concentrated in the HOMO and LUMO, providing a

glimpse of how each molecule behaves with respect to electron donation or acceptance. The distance between HOMO and LUMO serves as a gauge of the chemical stability and reactivity of the molecules.

The HOMO-LUMO gap provides critical insights into the electronic behaviour of pesticides and their interactions with the CD-MOF-1 framework. Each pesticide exhibits distinct electronic properties that influence its reactivity and stability during encapsulation. AVM, with a moderate HOMO-LUMO gap of 4.94 eV, balances chemical stability and reactivity, enabling dynamic interactions with the MOF and facilitating efficient adsorption. DAZ, with a slightly larger gap of 5.01 eV, exhibits greater stability and reduced electron mobility, suggesting a

lower tendency for dynamic adsorption but a greater potential to maintain structural integrity within the framework. HEX, with the largest HOMO-LUMO gap at 5.87 eV, exhibits high chemical stability and reduced reactivity. While these electronic properties influence molecular behaviour, the encapsulation performance in CD-MOF-1 is more strongly determined by structural compatibility, molecular size, and interaction energy within the framework. In contrast, MAN, with the smallest gap of 4.37 eV, demonstrates the highest reactivity and electron mobility, enabling dynamic adsorption processes that make it effective for rapid release applications. The variations in HOMO-LUMO gaps among the pesticides highlight the relationship between reactivity and stability. Pesticides with smaller gaps, such as AVM and MAN, are predicted to exhibit more dynamic interactions with the MOF framework. Conversely, DAZ and HEX, with larger gaps, prioritise encapsulation stability, making them more suitable for prolonged storage and controlled release. These electronic properties are essential for tailoring MOF-based pesticide delivery systems. By selecting pesticides based on their HOMO-LUMO gaps, it is possible to optimise interactions for specific applications.

Root Mean Square Deviation

The RMSD measures how much a system deviates from its original shape over time. It shows how stable the molecule's structure is over time. The RMSD results provide insights into the movements and bonding characteristics of each pesticide. Figure 6 shows the RMSD of pesticides before and after encapsulation over the simulation. The RMSD plot before AVM encapsulation shows two distinct phases in the molecular dynamic simulation. In the first phase, from 0 to approximately 50 ns, it fluctuates between 0.1 and 0.2 nm, indicating that the system remains relatively stable with minor conformational changes. However, at around 50 ns, a noticeable increase in RMSD occurs, reaching approximately 0.25–0.30 nm. Following this jump, the system stabilises at a higher RMSD, suggesting a significant structural rearrangement. The AVM before encapsulation plot suggests a structural transition mid-simulation, whereas the encapsulated plot shows early stabilisation with no major changes, indicating a more rigid or well-equilibrated system. DAZ's RMSD plot, before and after encapsulation, shows a stable, consistent trend throughout the simulation. The RMSD remains low, fluctuating around 0.1 nm, without any significant jumps or deviations. This suggests that the system is structurally stable and does not undergo major conformational changes over the simulation time, indicating that the molecular system has reached equilibrium early in the simulation and remains in a well-defined state. DAZ, which was

highly rigid in its free form, maintains this stability post-encapsulation, with minimal deviations. HEX's RMSD plot before encapsulation shows an initial structural adjustment (~0–10 ns) followed by stabilisation around 0.1 nm. The early increase suggests equilibration, while the stable fluctuations indicate the system has reached a steady state. Minor variations suggest small conformational relaxations but no major structural changes. HEX's RMSD after encapsulation plot shows that both indicate a stable system after initial adjustment; the encapsulated one shows more frequent temporary decreases in RMSD, possibly due to transient interactions or occasional structural reorientations. MAN's RMSD plot before encapsulation shows consistent fluctuations around 0.0–0.2 nm, indicating a stable system with no major conformational changes. MAN's RMSD plot after encapsulation shows even less structural fluctuation, indicating the system is more stable.

Table 3 presents the average RMSD values for free-form and encapsulated pesticides. Comparing these values supports the finding that encapsulation within CD-MOF-1 consistently reduces structural deviations, highlighting the stabilising influence of the MOF framework. AVM exhibits a significant decrease in average RMSD from 0.167 in its free form to 0.118 upon encapsulation, indicating that while its flexibility is reduced, it still maintains dynamic interactions with the framework. This aligns with its moderate HOMO-LUMO gap, suggesting a balance between reactivity and stability. DAZ, which had the smallest average RMSD in its free form (0.060), shows only a slight increase to 0.074 upon encapsulation. This further confirms its inherent rigidity and high structural stability, even within the MOF framework. HEX and MAN also show increased average RMSD upon encapsulation, but their values indicate greater flexibility than DAZ. HEX's large HOMO-LUMO gap aligns with its stability, while MAN's small gap explains its dynamic flexibility. These results reinforce the conclusion that CD-MOF-1 effectively stabilises pesticides, particularly those with smaller HOMO-LUMO gaps.

Table 3. Comparison of average RMSD for free form and encapsulated pesticides

Pesticides	RMSD (nm)	RMSD (nm)
	Before Encapsulation	After Encapsulation
AVM	0.167	0.118
DAZ	0.060	0.074
HEX	0.095	0.127
MAN	0.080	0.130

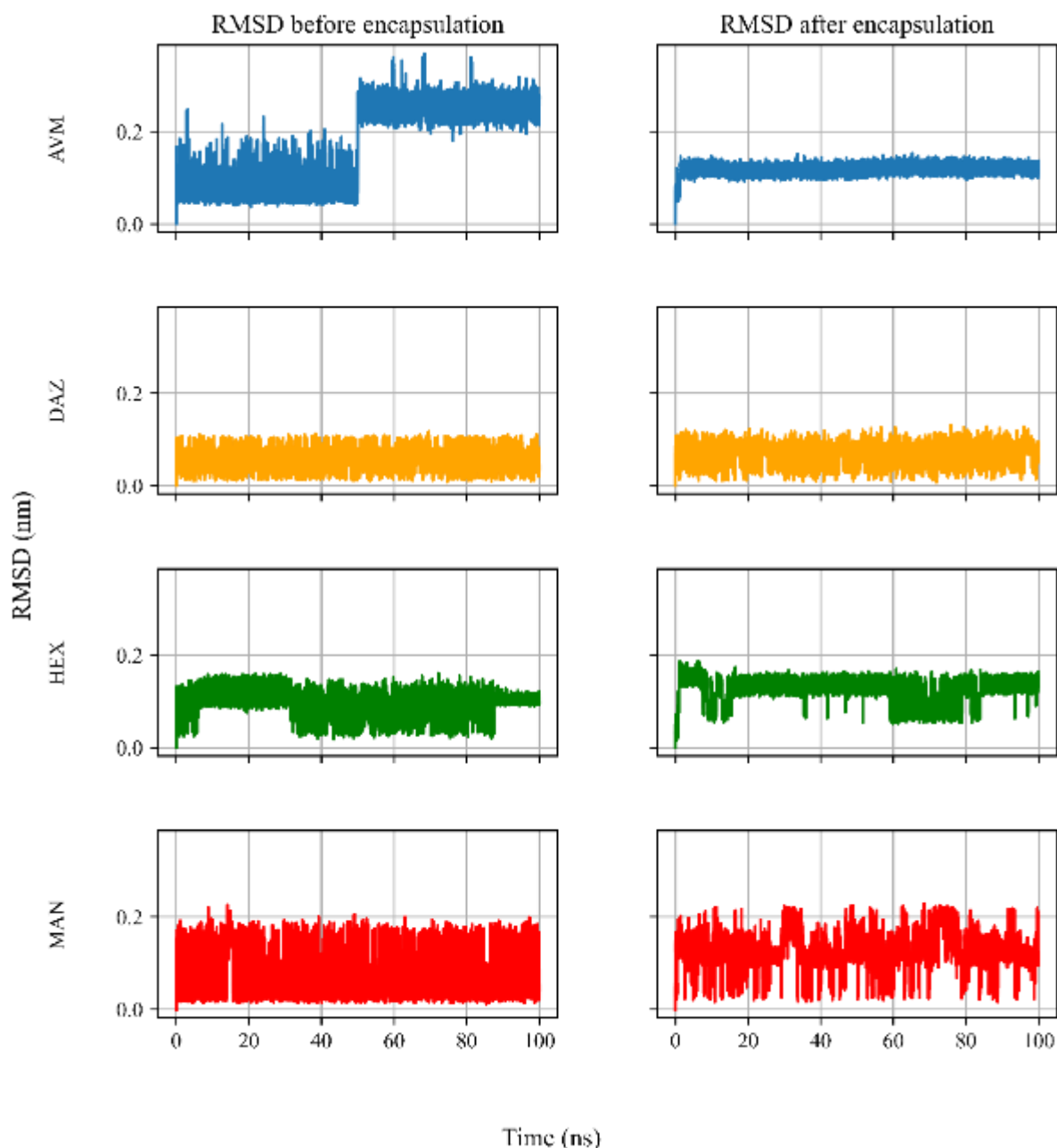


Figure 6. Root Mean Square Deviation (RMSD) profiles for free pesticides (AVM, DAZ, HEX, and MAN) before and after encapsulation with CD-MOF-1 under constant temperature (300 K) and pressure (1 atm) over a 100 ns simulation.

Mean square displacement

Figure 7 shows the mean-squared displacement (MSD) plots for AVM, DAZ, HEX, and MAN encapsulated within CD-MOF-1, illustrating their molecular motion during the simulation. MSD values reflect the molecular mobility of the encapsulated pesticides and their interactions with the MOF framework. Among the pesticides, MAN exhibits the highest MSD, indicating the greatest molecular

motion within the MOF. This behaviour aligns with its smaller HOMO-LUMO gap, which indicates higher reactivity and greater adaptability to the framework. Such mobility suggests that MAN is more suited for applications requiring dynamic adsorption and controlled release. HEX displays moderate MSD values, suggesting balanced mobility and stability. This behaviour aligns with its intermediate HOMO-LUMO gap and structural flexibility, making it a

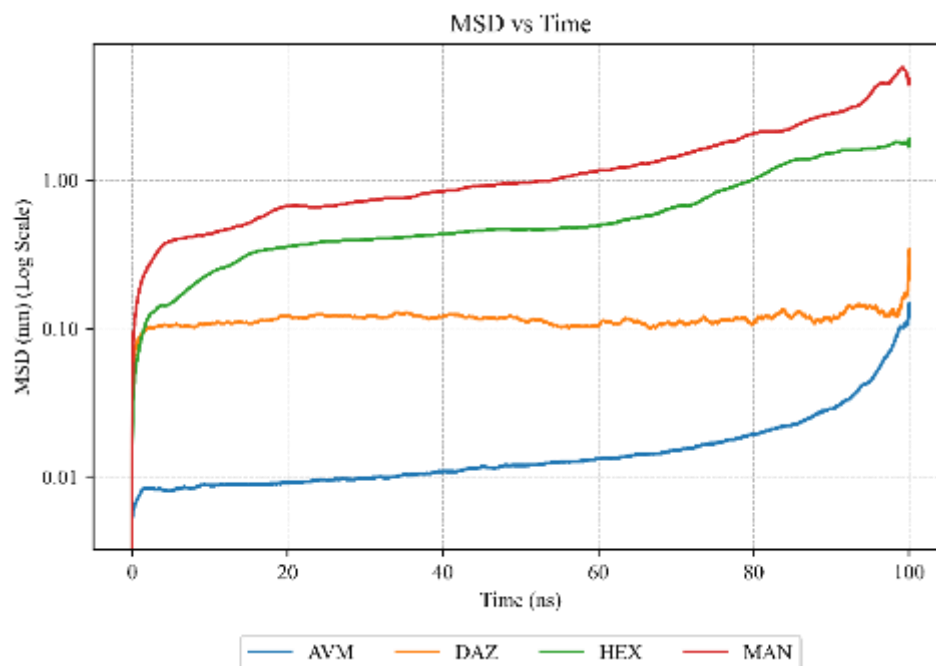


Figure 7. Mean Square Displacement (MSD) analysis of encapsulated pesticides within CD-MOF-1, reflecting their molecular mobility and diffusion behaviour inside the framework throughout the simulation period

candidate for applications that require steady diffusion rates. AVM shows the lowest MSD compared to MAN and HEX, indicating restricted molecular motion. This aligns with its moderate HOMO-LUMO gap, balancing reactivity and stability. Its behaviour reflects a stable interaction with the framework while maintaining limited diffusion. DAZ consistently exhibits the lower MSD, confirming its highly rigid and stable structure. This reduced mobility is associated with its larger HOMO-LUMO gap and structural rigidity, favouring long-term encapsulation and minimal mobility within the MOF framework. These results highlight how electronic properties influence molecular mobility within the MOF framework. Pesticides with greater reactivity, such as MAN, exhibit greater molecular motion, which enhances their adsorption potential. Meanwhile, stable pesticides like DAZ exhibit limited motion, favouring encapsulation stability. Understanding these trends is crucial for designing MOF-based pesticide delivery systems tailored to specific applications, such as controlled release or sustained encapsulation.

Diffusion coefficient

Figure 8 shows the diffusion coefficients of AVM, DAZ, HEX, and MAN encapsulated within CD-MOF-1, providing quantitative insights into their molecular mobility in the MOF framework. The diffusion coefficients indicate how easily each pesticide

molecule moves within the framework over time, which is directly linked to the MSD. MAN exhibits the highest diffusion coefficient ($3.88 \times 10^{-8} \text{ cm}^2/\text{s}$), which aligns with its highest MSD and smallest HOMO-LUMO gap, indicating high reactivity and adaptability [39]. This suggests that MAN has the potential for dynamic adsorption and rapid release from the MOF framework, making it suitable for applications requiring fast pesticide delivery.

HEX has a moderate diffusion coefficient ($1.92 \times 10^{-8} \text{ cm}^2/\text{s}$), reflecting its intermediate mobility observed in the MSD results. This supports the conclusion that HEX balances mobility and stability, which could be advantageous for sustained release applications. AVM shows a significantly lower diffusion coefficient ($2.99 \times 10^{-10} \text{ cm}^2/\text{s}$) compared to MAN and HEX, corresponding to its restricted molecular motion seen in the MSD plot. This indicates a more stable interaction with CD-MOF-1, favouring encapsulation over dynamic mobility. DAZ has observed a negative diffusion coefficient ($-7.83 \times 10^{-11} \text{ cm}^2/\text{s}$) is not physically meaningful and arises from linear-fitting artefacts during the plateau regions of the MSD curve, where molecular displacement becomes negligible. Further analysis revealed that DAZ exhibited minimal movement during the initial 0 to 2 ns (Figure 7), with the MSD increasing only slightly from 0 to 0.1 nm, yielding a diffusion coefficient of $3.70 \times 10^{-8} \text{ cm}^2/\text{s}$. Following this period, the MSD

plateaued, indicating that DAZ remained largely immobile within the CD-MOF-1 structure. Interestingly, a notable increase in MSD was observed between 98 and 100 ns (Figure 7), rising from 1.12 to 3.2 nm, with a diffusion coefficient of $4.03 \times 10^{-8} \text{ cm}^2/\text{s}$, suggesting a noticeable movement of DAZ from the framework. This behaviour implies that DAZ is adsorbed within the pores of CD-MOF-1, resulting in restricted diffusion over extended periods. Such strong host-guest interactions are characteristic of certain MOF systems, in which the encapsulated molecules exhibit limited mobility due to confinement within the porous structure. For instance, a study by Poddar et al. demonstrated that biomolecules encapsulated in zeolitic imidazolate framework-8 (ZIF-8) exhibited restricted movement, which was beneficial for applications like gene delivery [41], and a study demonstrated a novel method to determine diffusion constants of small molecules within highly porous MOFs, highlighting the restricted diffusion behaviour within these structures [42]. Similarly, the strong adsorption of DAZ within CD-MOF-1 could be advantageous for applications requiring controlled release, as the framework can effectively retain the encapsulated molecules until specific conditions trigger their release.

Interaction energy of pesticides and CD-MOF-1

In GROMACS, the total interaction energy encompasses both Coulombic and Lennard-Jones (LJ) interactions. **Figure 9** shows the total interaction energies of AVM, DAZ, HEX, and MAN encapsulated within CD-MOF-1. These values represent the strength and nature of the binding interactions

between the pesticides and the MOF framework, which directly influence the stability and efficiency of the encapsulation process. AVM exhibits the most negative interaction energy (-422.40 kJ/mol), indicating the strongest binding affinity with CD-MOF-1. This suggests that AVM forms highly stable interactions with the MOF framework, likely due to favourable electronic properties and compatibility with the pore environment. This aligns with its relatively restricted mobility, as observed in the diffusion coefficient and MSD results.

HEX shows a moderately negative interaction energy (-140.15 kJ/mol), reflecting stable but less intense binding compared to AVM. This balance between binding strength and mobility supports HEX's suitability for sustained release applications. DAZ and MAN display weaker interaction energies (-104.23 kJ/mol and -106.95 kJ/mol , respectively), indicating lower binding affinities with CD-MOF-1. DAZ's weaker interaction is consistent with its rigid, stable structure, which may limit its ability to form strong contacts with the MOF. In contrast, MAN, despite its high molecular mobility, exhibits weaker binding, suggesting that its high reactivity does not necessarily translate into strong encapsulation stability. These interaction energy trends highlight how the electronic and structural properties of pesticides influence their binding strength with CD-MOF-1. Stronger interactions, as seen in AVM, favour encapsulation stability, whereas weaker interactions, such as those in MAN, may support dynamic adsorption and release [43].

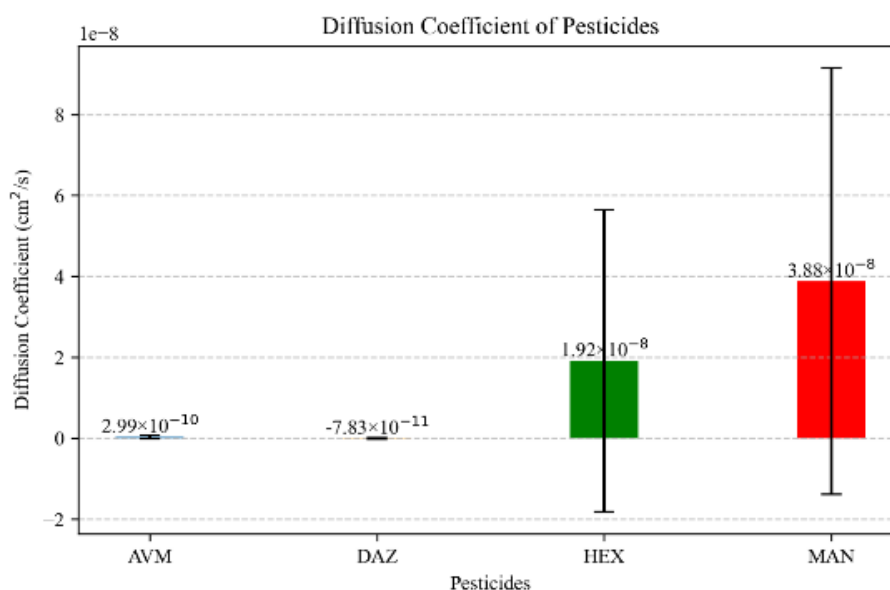


Figure 8. Calculated diffusion coefficients for AVM, DAZ, HEX, and MAN encapsulated in CD-MOF-1

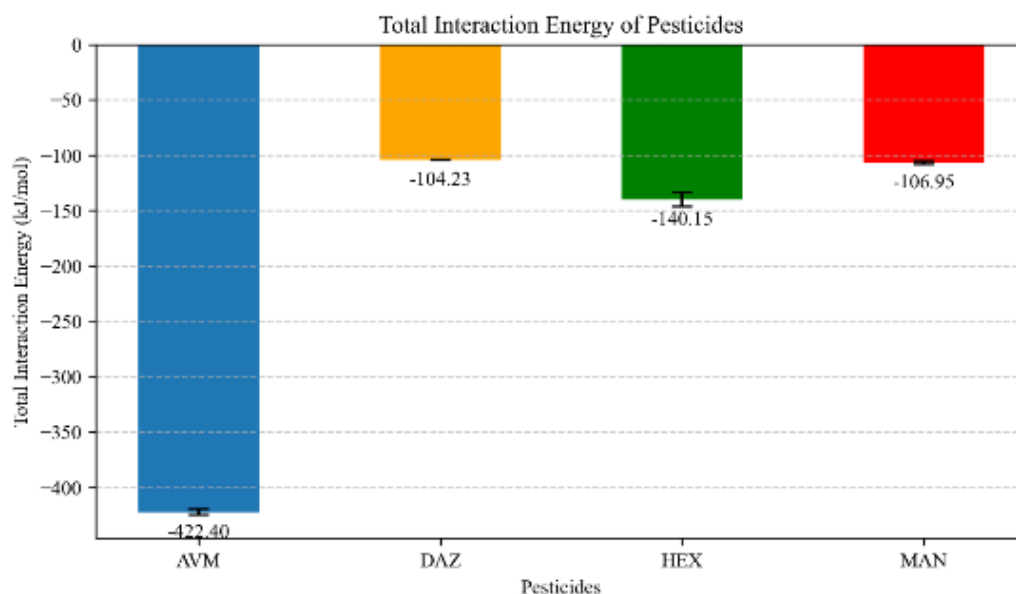


Figure 9. Total interaction energy between CD-MOF-1 and the encapsulated pesticides (AVM, DAZ, HEX, and MAN), illustrating the strength of host–guest binding and encapsulation efficiency.

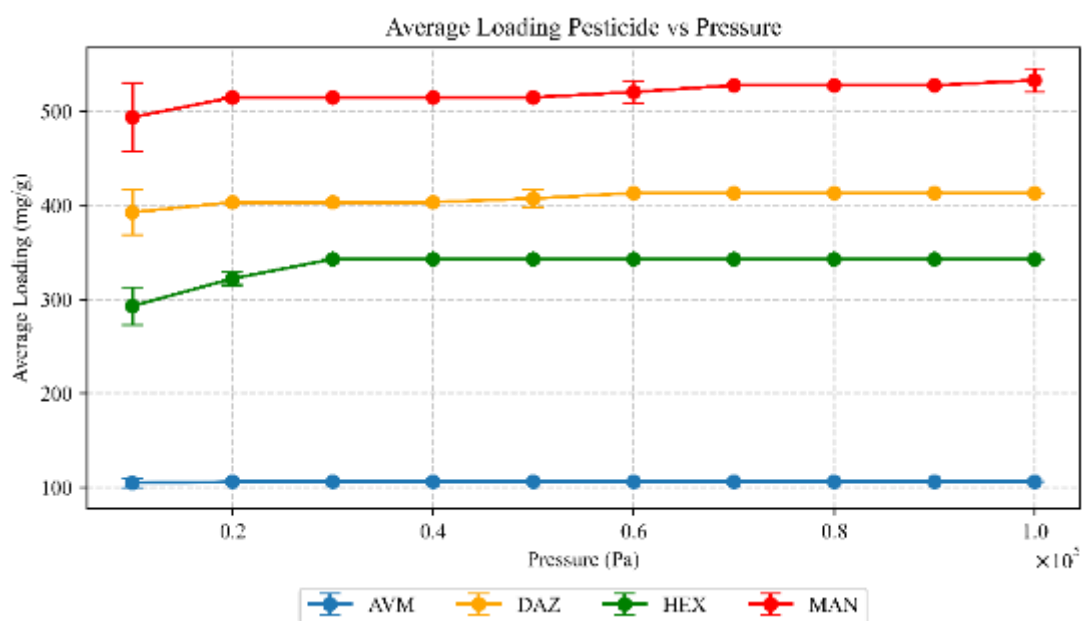


Figure 10. Adsorption isotherms showing average loading capacities of AVM, DAZ, HEX, and MAN into CD-MOF-1 at varying pressure conditions (0.1–1.0 bar), indicating pressure-dependent encapsulation performance

Adsorption behaviour of pesticides in CD-MOF-1

The adsorption behaviour of pesticides in CD-MOF-1 was evaluated using GCMC simulations to examine their behaviour under varying pressure conditions, providing insights into their loading capacities. **Figure 10** illustrates the average loading of AVM, DAZ, HEX, and MAN encapsulated in CD-MOF-1 across varying pressures. The results highlight distinct trends in the adsorption capacities of the pesticides,

influenced by their electronic properties, interaction energies, molecular mobility, and structural properties. MAN achieves the highest average loading at all pressures, with significant increases observed as pressure rises. This behaviour is consistent with its high diffusion coefficient and lower interaction energy, which enable rapid filling of the MOF's available sites. Additionally, MAN's small molecular weight of 212.4 g/mol facilitates its mobility within

the porous structure [44].

Furthermore, MAN's small energy gap (4.37 eV) suggests higher chemical reactivity, further facilitating efficient adsorption processes [45]. Although MAN exhibits a small HOMO–LUMO gap, indicating higher reactivity, its adsorption behaviour is more directly influenced by its smaller molecular size, higher mobility, and favourable interaction energy within the CD-MOF-1 framework. MAN's dynamic adsorption capabilities make it ideal for applications requiring efficient, responsive delivery. Following the highest adsorption, the second most dominant pattern is DAZ, which shows a consistent trend, averaging 407.39 mg/g with minimal variation across pressure ranges. This aligns with its small molecular weight of 162.3 g/mol, energy gap of 5.01 eV, and weaker interaction energy (-104.23 kJ/mol), which increases its adsorption potential and ensures stable encapsulation. HEX demonstrated lower adsorption than MAN and DAZ, with an initial increase from 0.1 to 0.3 bar before reaching equilibrium at higher pressures. Its moderate interaction energy (-140.15 kJ/mol), wider energy gap of 5.89 eV and heavy molecular weight of 314.2 g/mol, allow for low steady adsorption, making it effective for applications requiring balanced loading and release.

AVM exhibits the lowest average loading across all pressures, despite its strong interaction energy (-422.40 kJ/mol) and low energy (4.94 eV). This behaviour can be attributed to its larger molecular weight of 873.1 g/mol, which limits its mobility and diffusion within the MOF's porous structure, reducing its overall adsorption capacity. AVM's low adsorption potential suggests its encapsulation is better suited to long-term stability than to dynamic uptake. These trends highlight the influence of collective properties on adsorption performance in MOF-based systems.

Conclusion

This study successfully modelled and parameterised the CD-MOF-1 structure for use in computational simulations. The force field parameters were developed and validated for accuracy in MD and GCMC simulations. DFT calculations provided insights into the electronic properties of CD-MOF-1 and the selected pesticides, revealing variations in their reactivity and stability. MAN exhibited the smallest HOMO-LUMO gap (4.367 eV), suggesting high reactivity, while DAZ had the largest gap (5.008 eV), indicating greater stability. MD simulations confirmed the structural stability of pesticide encapsulation, with DAZ demonstrating minimal fluctuations (RMSD: 0.074 nm), indicating strong stability, while MAN exhibited more dynamic behaviour (RMSD: 0.130 nm), making it suitable for

responsive delivery applications. Additionally, GCMC simulations revealed that MAN achieved the highest adsorption capacity, while AVM had the lowest due to its high molecular weight and strong interaction energy (-422.40 kJ/mol), which limited diffusion within the framework. These findings highlight the versatility of CD-MOF-1 as a pesticide-delivery platform, demonstrating its ability to accommodate diverse pesticides via tailored encapsulation strategies. The study also identified key factors influencing encapsulation efficiency, including molecular weight and interaction energy, which play a crucial role in adsorption and diffusion behaviour.

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References

- Holleman, C. (2024). The State of Food Security and Nutrition in the World 2024 – Financing to end hunger, food insecurity and malnutrition in all its forms. FAO; IFAD; UNICEF; WFP; WHO.
- Navarro, D., & Gennari, P. (2023). Tracking progress on food and agriculture-related SDG indicators 2023. FAO.
- Mall, D., Larsen, A., & Martin, E. (2018). Investigating the (mis)match between natural pest control knowledge and the intensity of pesticide use. *Insects*, 9(1), 2.
- Camara, M. C., Campos, E. V. R., Monteiro, R. A., Do Espirito Santo Pereira, A., De Freitas Proença, P. L., & Fraceto, L. F. (2019). Development of stimuli-responsive nano-based pesticides: emerging opportunities for agriculture. *Journal of Nanobiotechnology*, 17(1), 100.
- Neri-Badang, M. C., & Chakraborty, S. (2019). Carbohydrate polymers as controlled release devices for pesticides. *Journal of Carbohydrate Chemistry*, 38(1), 67–85.
- Du, L., Liao, S., Khatib, H. A., Stoddart, J. F., & Zink, J. I. (2009). Controlled-access hollow mechanized silica nanocontainers. *Journal of the American Chemical Society*, 131(42), 15136–15142.
- Flaherty, R. J., Nshime, B., DeLaMarre, M., DeJong, S., Scott, P., & Lantz, A. W. (2013). Cyclodextrins as complexation and extraction agents for pesticides from contaminated soil. *Chemosphere*, 91(7), 912–920.
- Kaziem, Amir. E., Gao, Y., Zhang, Y., Qin, X., Xiao, Y., Zhang, Y., You, H., Li, J., & He, S. (2018). α -Amylase triggered carriers based on cyclodextrin anchored hollow mesoporous silica for enhancing insecticidal activity of avermectin

- against *Plutella xylostella*. *Journal of Hazardous Materials*, 359, 213–221.
9. Zhang, X., Liu, J., Hou, W., Tong, J., Ren, L., Sun, G., & Sun, Y. (2016). Preparation and properties of pesticide/cyclodextrin complex intercalated into ZnAl-layered double hydroxide. *Industrial & Engineering Chemistry Research*, 55(6), 1550–1558.
10. Smaldone, R. A., Forgan, R. S., Furukawa, H., Gassensmith, J. J., Slawin, A. M. Z., Yaghi, O. M., & Stoddart, J. F. (2010). Metal–organic frameworks from edible natural products. *Angewandte Chemie International Edition*, 49(46), 8630–8634.
11. Zhou, W., Wu, H., Hartman, M. R., & Yildirim, T. (2007). Hydrogen and methane adsorption in metal–organic frameworks: A high-pressure volumetric study. *The Journal of Physical Chemistry C*, 111(44), 16131–16137.
12. Liang, K., Ricco, R., Doherty, C. M., Styles, M. J., Bell, S., Kirby, N., Mudie, S., Haylock, D., Hill, A. J., Doonan, C. J., & Falcaro, P. (2015). Biomimetic mineralization of metal-organic frameworks as protective coatings for biomacromolecules. *Nature Communications*, 6(1), 7240.
13. Tuan Kob@Yaakub, T. N. A., Abdul Rahman, M. B., Felipe, G., & Mohammad Latif, M. A. (2024). Synthesis and modelling of functionalized UiO-66 metal-organic frameworks for gas adsorption. *Malaysian Journal of Analytical Sciences*, 28(3), 489–499.
14. Rajkumar, T., Kukkar, D., Kim, K.-H., Sohn, J. R., & Deep, A. (2019). Cyclodextrin-metal–organic framework (CD-MOF): From synthesis to applications. *Journal of Industrial and Engineering Chemistry*, 72, 50–66.
15. Huang, Z., & Lee, H. K. (2015). Micro-solid-phase extraction of organochlorine pesticides using porous metal-organic framework MIL-101 as sorbent. *Journal of Chromatography A*, 1401, 9–16.
16. Vikrant, K., Tsang, D. C. W., Raza, N., Giri, B. S., Kukkar, D., & Kim, K.-H. (2018). Potential utility of metal–organic framework-based platform for sensing pesticides. *ACS Applied Materials & Interfaces*, 10(10), 8797–8817.
17. Yang, Q., Wang, J., Zhang, W., Liu, F., Yue, X., Liu, Y., Yang, M., Li, Z., & Wang, J. (2017). Interface engineering of metal organic framework on graphene oxide with enhanced adsorption capacity for organophosphorus pesticide. *Chemical Engineering Journal*, 313, 19–26.
18. Liu, C., Wang, P., Liu, X., Yi, X., Zhou, Z., & Liu, D. (2019). Multifunctional β -cyclodextrin MOF-derived porous carbon as efficient herbicides adsorbent and potassium fertilizer. *ACS Sustainable Chemistry & Engineering*, 7(17), 14479–14489.
19. Liu, G., Li, L., Xu, D., Huang, X., Xu, X., Zheng, S., Zhang, Y., & Lin, H. (2017). Metal–organic framework preparation using magnetic graphene oxide– β -cyclodextrin for neonicotinoid pesticide adsorption and removal. *Carbohydrate Polymers*, 175, 584–591.
20. Kim, S., Chen, J., Cheng, T., Gindulyte, A., He, J., He, S., Li, Q., Shoemaker, B. A., Thiessen, P. A., Yu, B., Zaslavsky, L., Zhang, J., & Bolton, E. E. (2023). PubChem 2023 update. *Nucleic Acids Research*, 51(D1), D1373–D1380.
21. Groom, C. R., Bruno, I. J., Lightfoot, M. P., & Ward, S. C. (2016). The Cambridge Structural Database. *Acta Crystallographica Section B: Structural Science, Crystal Engineering and Materials*, 72(2), 171–179.
22. Makkar, P., & Ghosh, N. N. (2021). A review on the use of DFT for the prediction of the properties of nanomaterials. *RSC Advances*, 11(45), 27897–27924.
23. Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., Scalmani, G., Barone, V., Petersson, G. A., Nakatsuji, H., Li, X., Caricato, M., Marenich, A. V., Bloino, J., Janesko, B. G., Gomperts, R., Mennucci, B., Hratchian, H. P., Ortiz, J. V., Izmaylov, A. F., Sonnenberg, J. L., Williams-Young, D., Ding, F., Lipparini, F., Egidi, F., Goings, J., Peng, B., Petrone, A., Henderson, T., Ranasinghe, D., Zakrzewski, V. G., Gao, J., Rega, N., Zheng, G., Liang, W., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Vreven, T., Throssell, K., Montgomery, J. A., Jr., Peralta, J. E., Ogliaro, F., Bearpark, M. J., Heyd, J. J., Brothers, E. N., Kudin, K. N., Staroverov, V. N., Keith, T. A., Kobayashi, R., Normand, J., Raghavachari, K., Rendell, A. P., Burant, J. C., Iyengar, S. S., Tomasi, J., Cossi, M., Millam, J. M., Klene, M., Adamo, C., Cammi, R., Ochterski, J. W., Martin, R. L., Morokuma, K., Farkas, O., Foresman, J. B., & Fox, D. J. (2016). Gaussian 16 Revision C.01.
24. Breneman, C. M., & Wiberg, K. B. (1990). Determining atom-centered monopoles from molecular electrostatic potentials. The need for high sampling density in formamide conformational analysis. *Journal of Computational Chemistry*, 11(3), 361–373.
25. Martínez, L., Andrade, R., Birgin, E. G., & Martínez, J. M. (2009). PACKMOL: A package for building initial configurations for molecular dynamics simulations. *Journal of Computational Chemistry*, 30(13), 2157–2164.
26. Lindahl, Abraham, Hess, & Spoel, V. D. (2021). GROMACS 2021.1 Source code (Version

- 2021.1) [Computer software]. Zenodo.
27. Rappe, A. K., Casewit, C. J., Colwell, K. S., Goddard, W. A., & Skiff, W. M. (1992). UFF, a full periodic table force field for molecular mechanics and molecular dynamics simulations. *Journal of the American Chemical Society*, 114(25), 10024–10035.
28. Mark, P., & Nilsson, L. (2001). Structure and dynamics of the TIP3P, SPC, and SPC/E water models at 298 K. *The Journal of Physical Chemistry A*, 105(43), 9954–9960.
29. Hess, B. (2008). P-LINCS: A parallel linear constraint solver for molecular simulation. *Journal of Chemical Theory and Computation*, 4(1), 116–122.
30. Essmann, U., Perera, L., Berkowitz, M. L., Darden, T., Lee, H., & Pedersen, L. G. (1995). A smooth particle mesh Ewald method. *The Journal of Chemical Physics*, 103(19), 8577–8593.
31. Bussi, G., Donadio, D., & Parrinello, M. (2007). Canonical sampling through velocity rescaling. *The Journal of Chemical Physics*, 126(1), 014101.
32. Rühle, V. (2008). Pressure coupling/barostats. *Journal Club*, 2008, 1–5.
33. Allen, M. P., & Tildesley, D. J. (2017). *Computer Simulation of Liquids* (2nd edition). Oxford University Press.
34. Frenkel, D., & Smit, B. (2002). *Understanding molecular simulation: From algorithms to applications*. Elsevier Science.
35. Dubbeldam, D., Calero, S., Ellis, D. E., & Snurr, R. Q. (2016). RASPA: Molecular simulation software for adsorption and diffusion in flexible nanoporous materials. *Molecular Simulation*, 42(2), 81–101.
36. Walton, K. S., & Snurr, R. Q. (2017). Applicability of the BET method for determining surface areas of microporous metal-organic frameworks. *Journal of the American Chemical Society*, 129(27), 8552–8556.
37. Hartlieb, K. J., Ferris, D. P., Holcroft, J. M., Kandela, I., Stern, C. L., Nassar, M. S., Botros, Y. Y., & Stoddart, J. F. (2017). Encapsulation of ibuprofen in CD-MOF and related bioavailability studies. *Molecular Pharmaceutics*, 14(5), 1831–1839.
38. Rosen, A. S., Fung, V., Huck, P., O'Donnell, C. T., Horton, M. K., Truhlar, D. G., Persson, K. A., Notestein, J. M., & Snurr, R. Q. (2022). High-throughput predictions of metal-organic framework electronic properties: Theoretical challenges, graph neural networks, and data exploration. *NPJ Computational Materials*, 8(1), 1–10.
39. Mancuso, J. L., Mroz, A. M., Le, K. N., & Hendon, C. H. (2020). Electronic structure modeling of metal-organic frameworks. *Chemical Reviews*, 120(16), 8641–8715.
40. Huang, Y., Rong, C., Zhang, R., & Liu, S. (2017). Evaluating frontier orbital energy and HOMO/LUMO gap with descriptors from density functional reactivity theory. *Journal of Molecular Modeling*, 23, 3715.
41. Poddar, A., Conesa, J. J., Liang, K., Dhakal, S., Reineck, P., Bryant, G., Pereiro, E., Ricco, R., Amenitsch, H., Doonan, C., Mulet, X., Doherty, C. M., Falcaro, P., & Shukla, R. (2019). Encapsulation, visualization and expression of genes with biomimetically mineralized zeolitic imidazolate framework-8 (ZIF-8). *Small (Weinheim an Der Bergstrasse, Germany)*, 15(36), e1902268.
42. Zybaylo, O., Shekhah, O., Wang, H., Tafipolsky, M., Schmid, R., Johannsmann, D., & Wöll, C. (2010). A novel method to measure diffusion coefficients in porous metal-organic frameworks. *Physical Chemistry Chemical Physics*, 12(28), 8093–8098.
43. Li, Z., Sun, Y., Pan, X., Gao, T., He, T., Chen, C., Zhang, B., Fu, X., & Huang, Q. (2022). Controlled release of thymol by cyclodextrin metal-organic frameworks for preservation of cherry tomatoes. *Foods*, 11(23), 3818.
44. Sun, Q., Sheng, J., & Yang, R. (2021). Encapsulation of curcumin in CD-MOFs: promoting its incorporation into water-based products and consumption. *Food & Function*, 12(21), 10795–10805.
45. Zhang, T., Svensson, P. H. W., Brumboiu, I. E., Lanzilotto, V., Grazioli, C., Guarnaccio, A., Johansson, F. O. L., Beranová, K., Coreno, M., de Simone, M., Floreano, L., Cossaro, A., Brena, B., & Puglia, C. (2022). Clarifying the adsorption of triphenylamine on Au(111): Filling the HOMO–LUMO gap. *The Journal of Physical Chemistry C*, 126(3), 1635–1643.