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Molecular dynamics insights into tetrahydrofuran-assisted formation of CH₄, CO₂, and H₂ gas hydrates

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Gas hydrates, also known as clathrate hydrates, are crystalline compounds formed when water molecules organize into cage-like structures that encapsulate gas molecules under conditions of high pressure and low temperature. These hydrates occur naturally in permafrost regions and deep-sea sediments and have gained significant interest as potential energy sources and for applications in gas storage, transportation, and sequestration. Here, we deploy molecular dynamics (MD) simulations to investigate the molecular-level mechanisms governing the formation and stabilization of CH₄, CO₂, and H₂ hydrates in the presence of tetrahydrofuran (THF). We analyze key structural and energetic properties, including tetrahedral order parameters, cage dynamics, and gas uptake throughout different hydrate formation stages: pre-nucleation, nucleation (induction), growth, and saturation. Our findings provide insights into the role of THF concentration in altering hydrate phase behavior, as well as kinetic and gas occupancy preferences within hydrate cages. The study offers a comprehensive understanding of hydrate nucleation mechanisms and thermodynamic stability, contributing to advancements in gas hydrate applications for energy and environmental technologies.

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1. Introduction

Gas hydrates, also known as clathrate hydrates, are solid crystalline compounds in which water molecules, bonded through hydrogen bonds, form polyhedral cages that encapsulate various gas molecules such as carbon dioxide (CO₂), methane (CH₄), hydrogen (H₂), nitrogen (N₂), hydrogen sulfide (H₂S), ethane, propane, and butane under high-pressure and low-temperature conditions.^{1–4} Substantial deposits of gas hydrates are naturally found in permafrost regions and deep-sea sediments, which has led to significant interest in their potential as major energy sources.^{5,6} Meanwhile, clathrate hydrate-based technologies are increasingly being employed in diverse, innovative applications, including the separation, storage, transportation, and sequestration of natural gases and greenhouse gases, wastewater treatment and desalination, oil, and gas flow assurance due to their

complete recovery of environmental friendliness, and non-explosive nature, which make them particularly attractive.^{7,8}

In general, there are three widely recognized hydrate crystalline structures (see Scheme 1): structure I (SI), structure II (SII), and structure H (sH).^{9,10} These structures are made by various combinations of cages, including the pentagonal dodecahedron, tetrakaidecahedron, hexakaidecahedron, pentagonal irregular dodecahedron, and icosahedron.^{11–13} The formation of these structures seems strongly depend on the size and shape of the guest molecules involved, as well as the conditions present during gas hydrate formation.¹⁴ Furthermore, in our earlier studies, we have shown that the composition of a gas mixture dictates the crystallinity of the gas hydrate structures.¹⁵

Several strategies have been employed to promote hydrate nucleation and enhance gas content in clathrate hydrates, including stirring or mixing, reactor design, and the addition of additives.^{16,17} Different types of promoters have diverse impacts on hydrate formation and are typically classified as kinetic and thermodynamic promoters.¹⁸ Kinetic promoters, such as surfactants, polymers, amino acids, and nanofluids, improve the kinetics of hydrate formation by increasing the solubility of the gas in the solution, thereby accelerating the formation rate.^{19,20} For example, sodium dodecyl sulfate (SDS) surfactant molecule has displayed a remarkable impact on the rate of formation of the gas hydrates.²¹ On the other hand, thermodynamic promoters

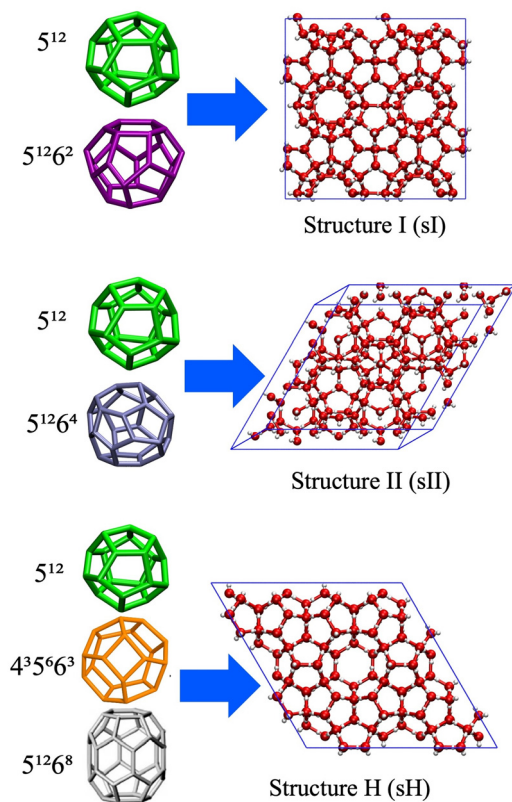
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Scheme 1 Schematic representation of different clathrate hydrate structures and their constituent building cages.

modulate the hydrate equilibrium conditions to more favorable reaction conditions (*i.e.*, lower pressure and higher temperature) by increasing gas–liquid contact and stabilizing the hydrate cage structure through their presence in the cavity.²² Several thermodynamic promoters, including tetrahydrofuran (THF), cyclopentane (CP), methylcyclohexane (MCH), neohexane, tetrabutylammonium chloride (TBAC), tetra-*n*-butylammonium chloride (TBAC), and tetrabutylammonium bromide (TBAB), have been identified and examined for their effects on gas hydrate formation.^{19,20} Especially it is well known from previous studies that tetrahydrofuran (THF), which forms an sII type of hydrate structure, is an excellent thermodynamic promoter that significantly affects gas hydrate nucleation and growth by moderating equilibrium conditions, reducing nucleation induction time, and enhancing the formation rate.^{23,24}

Lee *et al.*²⁵ investigated the phase equilibrium behavior of gas hydrates in the presence of THF and found that the dissociation conditions of the hydrates shifted to higher temperatures and lower pressures than those of pure hydrates. Additionally, they observed that the dissociation conditions of CH₄ and CO₂ gas hydrates depend on the THF concentration, identifying an optimal stoichiometric concentration of 5.56 mol% THF in the aqueous solution. Wang *et al.* investigated the effect of THF and THF/SDS on CO₂ hydrate formation and reported that THF significantly reduces the induction time. Furthermore, the combined use of THF and SDS enhances the gas storage density compared to systems containing only THF or no

additives.²⁶ Phan *et al.* recently studied the effect of THF on the kinetics of CO₂ hydrate growth and dissociation using molecular dynamics and demonstrating that THF facilitates CO₂ diffusion and shifts the favorable conditions for hydrate formation and stability to lower pressures and higher temperatures compared to systems without THF.²⁷

Kumar *et al.*²⁸ demonstrated a two-step hydrate formation mechanism in a 5.56 mol% THF solution and elucidated the synergistic effect between CH₄ and THF in forming mixed CH₄–THF hydrates. Recently, Ge *et al.*²⁹ reported that CH₄ gas molecules occupy the small cavities of the sII hydrate structure, with their occupancy increasing with the THF concentration, while THF molecules preferentially enter the large cavities, as determined through *in situ* Raman spectroscopy measurements. Furthermore, they found that CH₄ and CH₄–THF hydrates coexist at 2.78 and 4.17 mol% THF, with gas consumption being 2.2 times greater compared to hydrate formation at 5.56 mol% THF. Strobel *et al.*³⁰ developed a thermodynamics model to capture the phase behavior of various gas hydrates in the presence of THF and provide insights into hydrogen filling in hydrate cavities, which largely depend on the pressure. Khurana *et al.* proposed a mass transfer-based model for the CH₄–THF system, where methane diffuses through a THF hydrate layer and becomes encapsulated in hydrate cages.³¹ Jiyang *et al.* demonstrated that CH₄–THF hydrates can form under milder conditions, enabling efficient gas storage.³² Mahant *et al.* reported the first measurements of CH₄–THF hydrate nucleation rates and formation probability using a high-pressure automated reactor, providing valuable insights into phase equilibria and nucleation behavior.³³

Hashimoto *et al.*³⁴ studied the phase equilibrium of mixed H₂–THF hydrate systems with varying THF concentrations and found the three-phase line shifted to lower pressure or higher temperature compared to pure stoichiometric THF solutions. Zhang *et al.* reported that THF effectively promotes H₂ clathrate hydrate formation under milder conditions, with optimal concentrations enhancing formation kinetics, making it a promising route for safe and efficient hydrogen storage.³⁵ Experimental studies using high-pressure differential scanning calorimetry have explored the formation and dissociation of H₂ hydrates in the presence of THF, emphasizing the crucial influence of operating pressure on hydrate stability.^{36–38} Although several studies have investigated the kinetics of CO₂ and CH₄ hydrate formation and a few experimental studies have explored H₂ hydrates in the presence of THF, a systematic investigation examining the effect of increasing THF concentration (from 0 to 5.56 mol%) and comparing different gas hydrates remains lacking.

In our recent studies, we report how surfactants control the CH₄ hydrate growth,³⁹ The impact of additives on the growth of binary mixture gas hydrates.⁴⁰ Here, we ask the question whether the hydrate growth depends on the characteristics of gas molecules. Towards this end, we examine the molecular dynamics of hydrate growth for three gas molecules, *viz.*, CH₄, CO₂, and H₂ independently. Further, we study how these growth profiles of single-component gas hydrates are impacted by the presence of a thermodynamic promoter such as THF. The key molecular mechanisms for hydrate nucleation and growth are based on



water–gas coordinated structuring (tetrahedral order parameter, cage dynamics, and number of gas molecules in the hydrate region). The examined system properties are given the entire spectrum from pre-nucleation stage, nucleation (induction), growth, and saturation, as well as how properties are influenced by types of gas and varying amounts of THF. The CH₄ hydrate is found to grow faster than the CO₂ hydrate at the same thermodynamic conditions. However, the H₂ hydrate growth is extremely slow compared to CH₄ and CO₂ hydrate cases under quiescent conditions. These guest molecule-dependent hydrate growth profiles seem to overlap in the presence of a small amount of THF. The work provides molecular mechanisms of hydrate growth and how it is impacted by the presence of a thermodynamic promoter *viz.*, THF.

2. Simulation model and methodology

Water is modelled using the TIP4P/ice force field.⁴¹ We employ the EPM2⁴² to model CO₂, and the OPLS-AA force field is used for methane⁴³ and hydrogen.⁴⁴ The AMBER⁴⁵ forcefield is used THF. The Lennard-Jones interaction between the cross-species is determined using the geometric mean combination rule. Each system contains 384 gas molecules and 2944 water molecules. The number of THF molecules in the systems is 0, 30, 48, 114, and 196, corresponding to 0, 0.90, 1.42, 3.40, and 5.56 mol% of THF in the solutions, respectively. The initial systems are prepared by randomly inserting molecules into a cubic box with dimensions of 5 × 5 × 5 nm³, as shown in Fig. 1.

Water molecules are treated as rigid, and the LINCS algorithm⁴⁶ was used to maintain their rigid geometry. The short-range non-bonded interactions (van der Waals and Coulombic interactions) were truncated at 1.2 nm. The long-range electrostatic interactions were computed using the particle mesh Ewald (PME) summation method with a grid spacing of 0.1 nm and 1.2 nm real-space cutoff.⁴⁷ Periodic boundary conditions were applied in all three directions. The leapfrog integration scheme⁴⁸ with a time step of 2 fs was used to solve the equations of motion. The systems were initially energy-minimized using the

steepest descent method.⁴⁹ After that, it was subjected to an equilibration run in an isothermal–isobaric ensemble (NPT) for 5 ns at 300 K and 10 MPa. In the NVT equilibration, the temperature was controlled using the Berendsen thermostat⁵⁰ with a relaxation time of 0.2 ps. In the NPT equilibration, temperature was controlled using the Nose–Hoover thermostat^{51,52} with a relaxation time of 0.5 ps, and pressure was controlled using the Parrinello–Rahman barostat⁵³ with a relaxation time of 2 ps. Finally, the gas hydrate simulations were carried out at 240 K and 50 MPa for 1 microsecond using the NPT ensemble. All simulations were conducted using GROMACS v.2023.⁵⁴ All the properties are averaged over three independent simulations

The order parameter, F_4 is calculated to quantify the hydrate formation for all the cases. The F_4 is defined as⁵⁵

$$F_4 = \frac{1}{k} \sum \cos 3\phi_i$$

where, ϕ_i is the H–O–O–H torsional angle and k is the number of oxygen–oxygen pairs within 0.35 nm of the selected molecule. The F_4 parameter was computed for the entire trajectory of production runs.

3. Results and discussion

All the systems are equilibrated in an isothermal–isobaric ensemble at 300 K and 10 MPa for 5 ns. These pre-nucleation simulations generate gas nanobubbles in water, as shown in Fig. 2. The shape of the bubbles appears to be spherical for CH₄ and CO₂, however, it is cylindrical for H₂. This is due to the inherent lower density of H₂, which corresponds to the higher volume fraction when they aggregate in the simulation box. The gas molecule pair correlation function suggests that the correlation is strongest for CH₄, CO₂, and H₂ correlations are of similar strength. The correlation does not change significantly in the presence of THF. Prior works reported that methane forms a quasi-spherical bubble during methane hydrate dissociation, which then transforms into a cylindrical-shaped nanobubble due to the effect of interfacial tension⁵⁶ Furthermore, the formation of spherical and cylindrical nanobubbles has been observed in an aqueous solution of CH₄/CO₂ mixed gases during the initial simulation at a temperature of 300 K and a pressure of 10 MPa.⁵⁷ Recently, experimental measurements and simulation studies have confirmed the coexistence of CO₂ nanobubbles and droplets during gas–hydrate dissociation.⁵⁸ Our results confirm the formation of nanobubbles during pre-equilibration. These gas–water two – phase systems obtained after pre-equilibration at 300 K and 10 MPa are then quenched to 240 K and 50 MPa. Under these conditions, simulations are run for 1000 ns, during which hydrates nucleate, grow, and reach a saturation.

We compare the F_4 order parameter at various THF concentrations to assess its influence on the formation of gas hydrates. The F_4 value is known to be around –0.04 for liquid water, –0.4 for ice, and approximately 0.7 for hydrate structure.⁵⁵ These distinct values allow for the differentiation between the aqueous and hydrate phases.

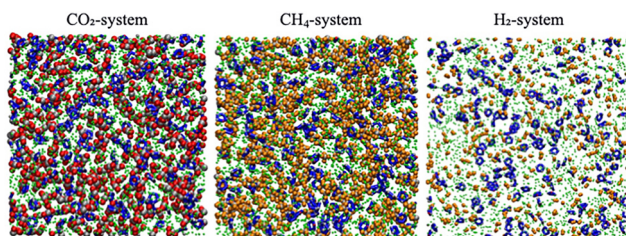


Fig. 1 The initial configurations of the gas–water mixtures in the presence of THF molecules. Each system contains 2944 water molecules and 196 THF (*i.e.*, 5.56 mol%). The left, middle, and right panels correspond to CO₂, CH₄, and H₂ gas systems, respectively. Small green spheres represent the oxygen atoms of water molecules. The carbon and oxygen atoms of CO₂ molecules are depicted as grey and red large spheres, respectively. Orange spheres represent the hydrogen atoms of CH₄ and H₂ molecules, while grey spheres denote the carbon atoms of CH₄. THF molecules are represented by blue sticks. For clarity, the hydrogen atoms of both water and THF molecules are not shown.



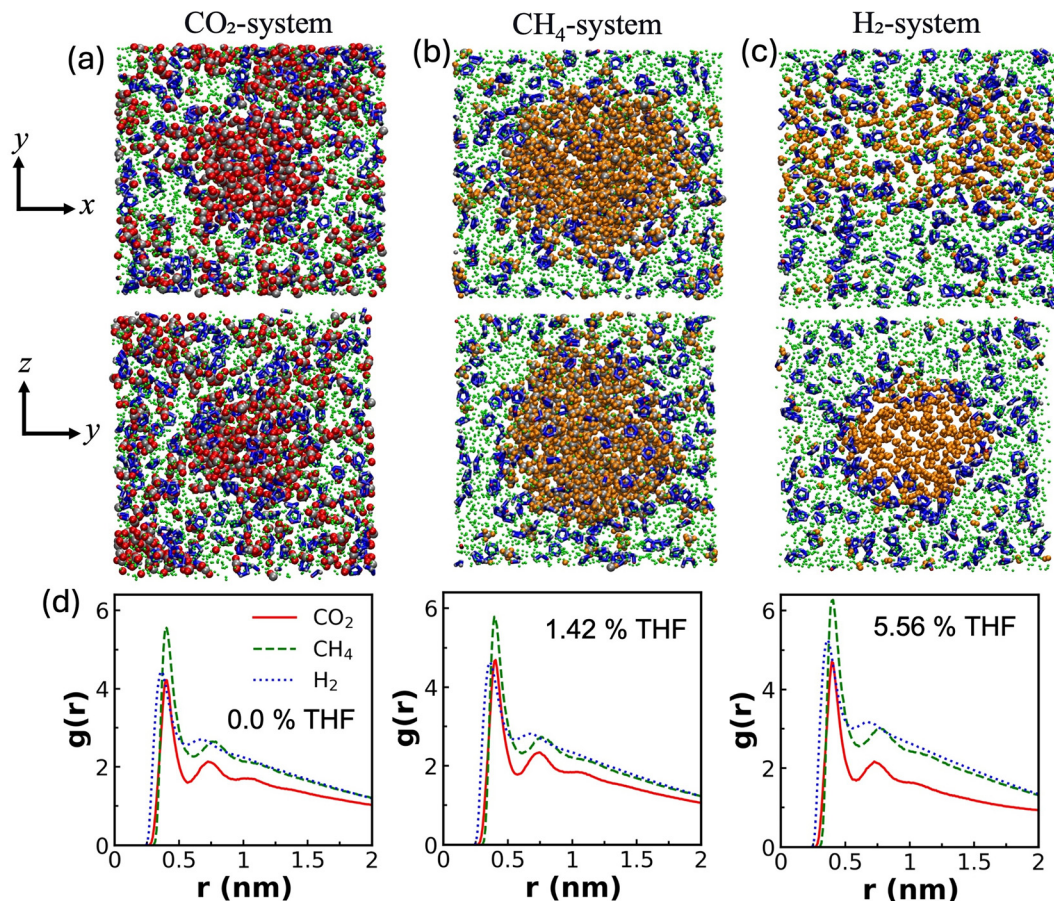


Fig. 2 Side views of MD snapshots captured at the end of 5 ns of initial equilibration at 300 K and 10 MPa in the presence of 5.56 mol% THF for gas systems: (a) CO₂, (b) CH₄, and (c) H₂. Atom colors are the same as those denoted in Fig. 1. Panel (d) shows the radial distribution function of gas molecules computed over the 5–10 ns interval at 300 K and 10 MPa for THF concentrations of 0 (left), 1.42 (middle), and 5.56% (right).

Fig. 3a shows representative snapshots of the nucleation and growth processes during the simulation at THF concentrations of 0.9% and 5.56%, comparing systems containing different gases. During the nucleation phase, relatively stable clusters of 5¹² cages form, which subsequently promote the development and expansion of additional hydrate cages in the growth stage. Additionally, small gas molecules are initially encapsulated within the 5¹² cages in the early stages of hydrate formation. As hydrate nucleation begins, the F_4 parameter increases (see Fig. 3), reflecting the progressive ordering of water molecules around guest species. In the early stages, water forms transient, hydrate-like structures around gas molecules (CO₂, CH₄, or H₂), occasionally giving rise to short-lived 5¹² and 5¹²6² cages. These intermediate structures contribute to an increase in the F_4 value from its baseline (−0.04 for liquid water), even though the number of fully formed hydrate cages remains limited due to repeated formation and dissociation. After a sufficient induction period, a stable number of cages form, marking the onset of nucleation. The corresponding F_4 value at this point is dependent on the size and compactness of the nucleus. Typically, F_4 values range between 0.1 and 0.2 during this transition. The shift from nucleation to growth is defined by the formation of a critical nucleus – a stable cluster of hydrate cages that can grow further. Following

nucleation, the system enters the growth phase, during which the size of the hydrate cluster increases, and the structure becomes more stable. This leads to a continued rise in the F_4 parameter until it eventually plateaus, indicating the saturation of hydrate growth within the simulation timeframe.

Fig. 3b illustrates the F_4 order parameter for THF concentrations of 0%, 0.9%, 1.42%, 3.4%, and 5.56% in the solutions. In the absence of THF, the F_4 order parameter gradually increases with time for CO₂ gas and CH₄ gas, suggesting the gas hydrate formation, whereas the F_4 value remains below 0.05 for the H₂ system, suggesting no hydrate formation within the nucleation timeframe. Even after extending the H₂–water system simulation to 2 μ s, no nucleation was observed. At the pre-nucleation stage, the F_4 value for CO₂ is slightly higher than that for CH₄, indicating early ordering; however, as time progresses, the F_4 value for CH₄ eventually surpasses that of CO₂, reflecting a faster transition into the growth phase. We find that the F_4 values are higher in the presence of THF compared to its absence, indicating that THF promotes faster gas hydrate formation. This finding is consistent with previous studies reporting that THF enhances the kinetics of gas hydrate formation.^{59–61}

At low THF concentrations (0.9 and 1.42 mol%), the F_4 values for the CH₄–water and H₂–water systems show minimal



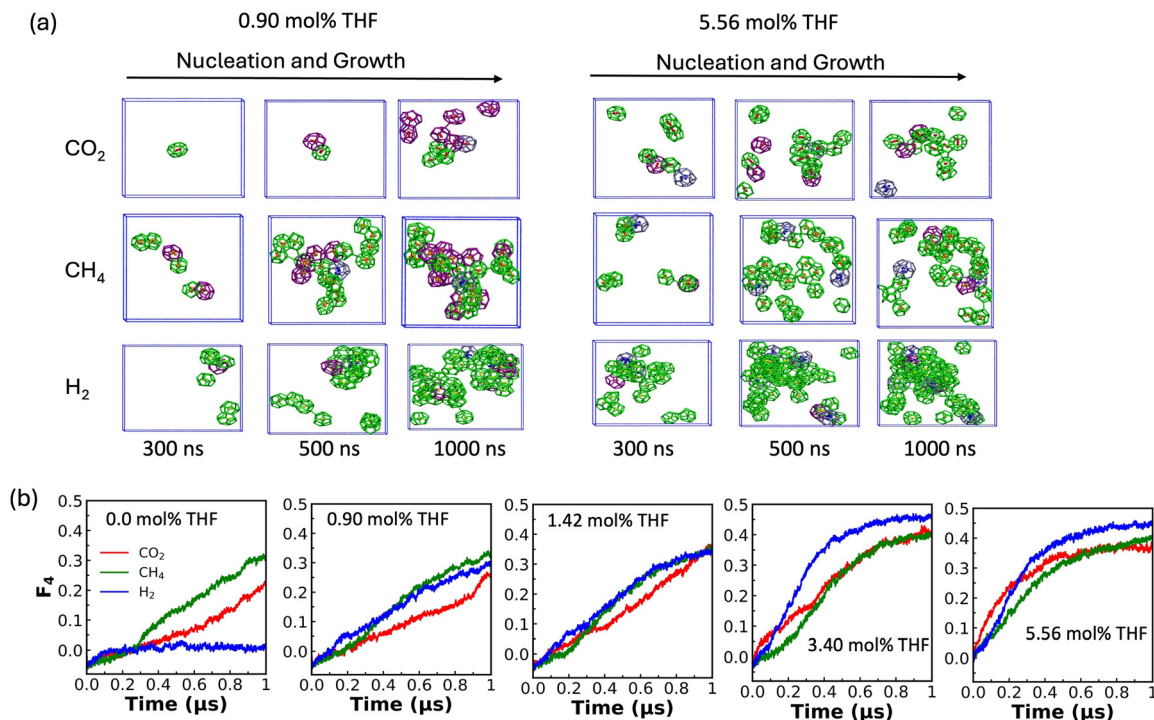


Fig. 3 (a) Snapshots illustrate the nucleation and growth process of gas hydrate formation with 0.9 mol% (left panel) and 5.56 mol% (right panel) THF in solution. Water molecules in the 5¹², 6²5¹², and 6⁴5¹² cages are connected by green, purple, and ice blue lines, respectively. (b) Evaluation of F_4 order parameter is plotted as a function of time for three gas hydrates H₂ (blue), CH₄ (green), and CO₂ (red) with THF concentration of 0, 0.9, 1.42, 3.4, and 5.56 mol% in the solution, respectively.

variation, suggesting that the impact of THF on gas hydrate formation is less pronounced at lower concentrations. In contrast, at higher concentrations of THF, a significant difference in the F_4 values is observed across the gas systems. As shown in Fig. 3, during the nucleation stage of gas hydrate formation, the F_4 parameter trends as follows: CO₂ > H₂ > CH₄, indicating that CO₂ hydrates nucleate earlier than H₂, while CH₄ hydrates exhibit the slowest nucleation among the three gases. Nevertheless, the greater F_4 value for H₂ at the end of the simulation period suggests a higher growth rate of H₂ hydrate formation compared to CO₂ and CH₄ gas hydrates. Thus, these results suggest that THF strongly affects gas hydrate nucleation and growth processes when its concentration exceeds 1.42%.

Next, we analyze cages that are formed in our simulations. The three most abundant cages in clathrate hydrate structures are identified through the connectivity of five- and six-membered rings formed by the first-neighbor water molecules, considering the atomic coordinates of the oxygen atoms in water. In this study, we employ the GRADE code developed by Mahmoudinobar and Dias⁶² to identify three main types of cages: 5¹², 5¹²6², and 5¹²6⁴, which consist of 20, 24, and 28 water molecules, respectively. Fig. 4 illustrates the variation in the number of different types of cages over simulation time during the formation of CO₂, CH₄, and H₂ gas hydrates, both in the presence and absence of the THF in the solutions. The results indicate that hydrate-like ordering of water molecules first forms small 5¹² cages, which initiate gas hydrate formation

during the nucleation stage of all gas hydrates, while a few large 5¹²6² and 5¹²6⁴ cages are formed during the growth process.

We find that a greater number of small 5¹² cages are formed compared to large 5¹²6² and 5¹²6⁴ cages, and the total number of cages increases as the concentration of the promoter THF in the solution increases, indicating a strong influence of THF concentration on gas hydrate formation. Interestingly, the number of 5¹²6² cages increases as the THF concentration rises to 1.42% for CO₂ gas hydrate, while for CH₄ gas hydrate, the number of 5¹²6² cages decreases with increasing THF concentrations. On the other hand, there is an insignificant effect of THF concentration on the formation of large cages for H₂ gas hydrate. At 0% THF concentration, 1–3 small 5¹² cages form during prenucleation, however, there is no H₂ clathrate formation within the 1 ns simulation time. Fig. 5 shows the total average number of cage (5¹², 5¹²6², and 5¹²6⁴) formations with varying THF concentrations in the solutions for the last 100 ns of the simulations. We find that the total number of cages increases with increasing THF concentration up to 3.4%. However, beyond this concentration, there is a noticeable decline in cage formation. Furthermore, within the 0.9–3.4% THF concentration, the number of cages formed in CH₄ and H₂ gas hydrates is approximately twice that observed in CO₂ gas hydrate. These findings indicate that THF has a strong influence on gas hydrate formation and that the extent of cage formation is strongly dependent on THF concentration. Moreover, the variations in cage structures suggest the potential



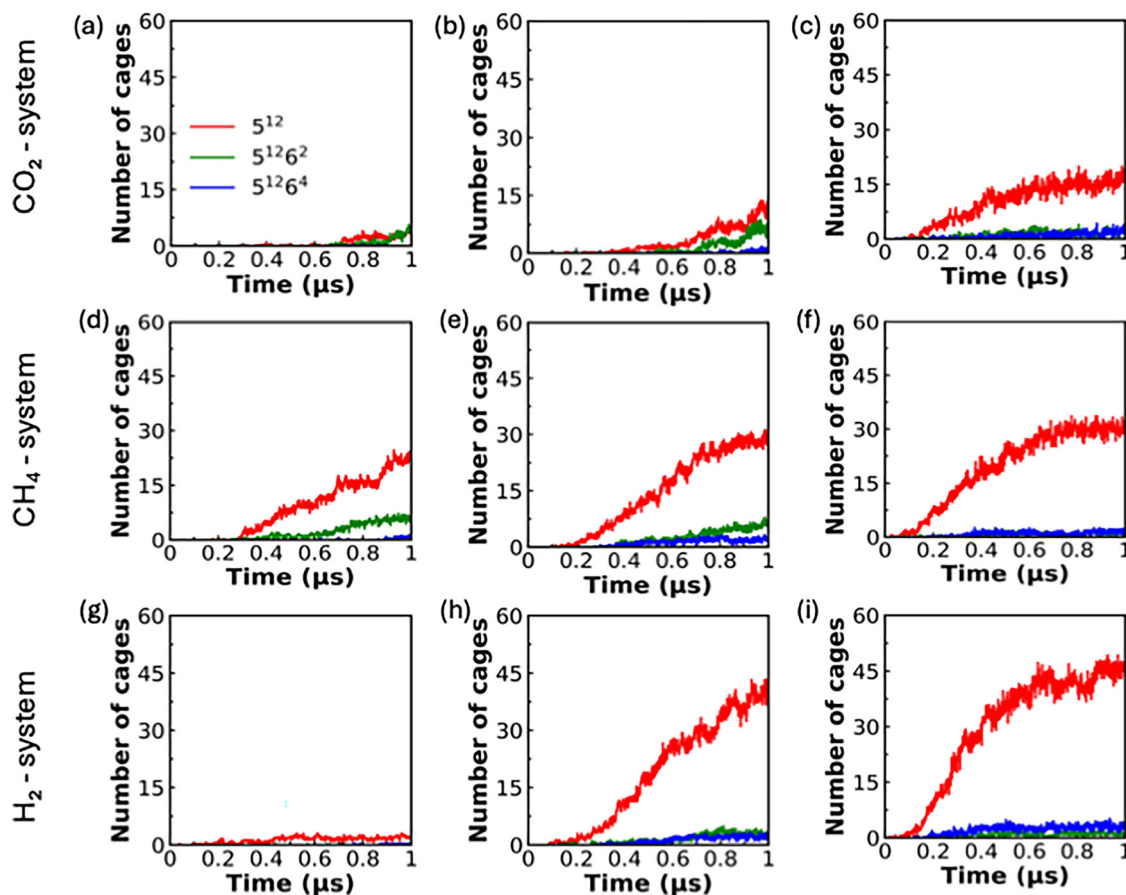


Fig. 4 Time evolution of the number of hydrate cages – 5^{12} , $5^{12}6^2$, and $5^{12}6^4$ – formed in (a)–(c) the CO₂ system, (d)–(f) the CH₄ system, and (g)–(i) the H₂ system at THF concentrations of 0% (left panels), 1.42% (middle panels), and 5.56% (right panels).

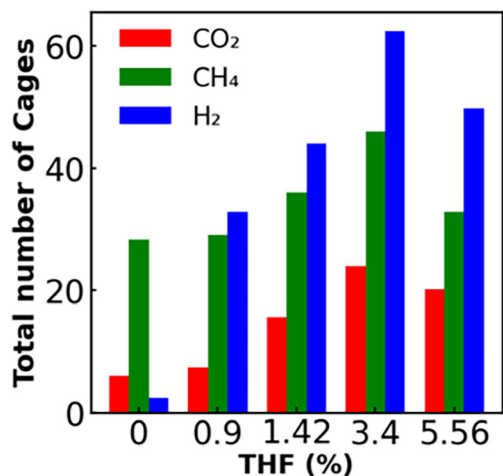


Fig. 5 The total average number of cages (5^{12} , $5^{12}6^2$, and $5^{12}6^4$) for the last 100 ns of the simulation for all the systems for different percentages of THF.

formation of amorphous hydrate phases during the nucleation and growth process.

Finally, we evaluate the number of gas molecules in the gas hydrates with different THF concentrations to reveal the gas uptake kinetics of CO₂, CH₄, and H₂ into clathrates. Fig. 6

shows the number of gas molecules in the hydrate at different concentrations of THF in solution for the system with CO₂, CH₄, and H₂ gases. The gas molecules trapped inside the cages are considered based on the center of mass distances between the cages and the gas molecules being less than 0.2 nm.⁶² The results indicate that the number of gas molecules encapsulated within the hydrate cages increases with rising THF concentration during the early stages of gas hydrate formation. Specifically, gas uptake continues to increase up to a THF concentration of 3.4%. However, beyond this concentration, a noticeable decrease in CO₂ occupancy within the hydrate cages is observed during the growth stage of hydrate formation. Additionally, our results reveal that, in the presence of THF, the overall gas uptake follows the order: H₂ > CH₄ > CO₂. These findings suggest that the optimal gas storage capacity is both gas-specific and dependent on the concentration of THF in the system.

Our results are consistent with experimental findings on CO₂ gas hydrate formation from flue gas in the presence of THF, where the induction time decreases and gas uptake increases as the THF concentration increases from 1 mol% to 1.5 mol% in the solution.⁶³ Furthermore, our findings align with previous simulation studies, which demonstrate that the presence of THF significantly accelerates the rate of CO₂



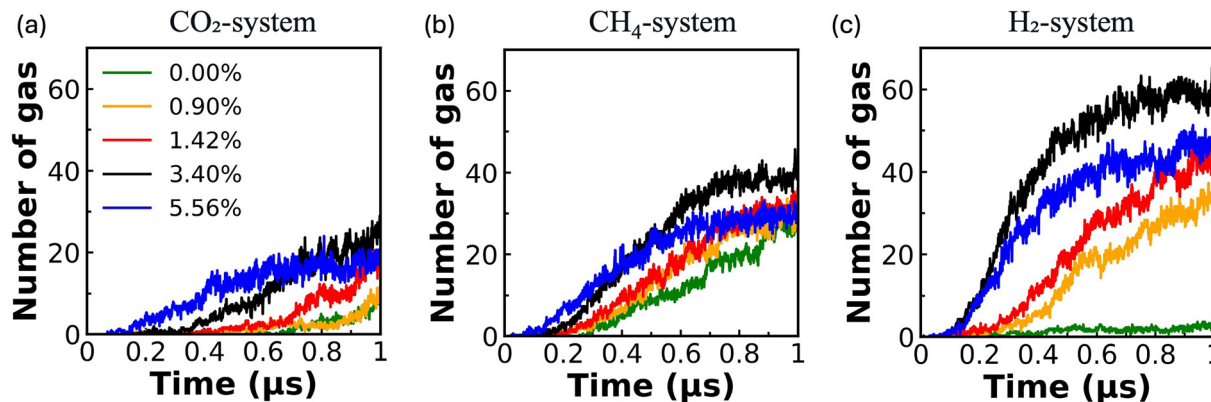


Fig. 6 The number of gas molecules encapsulated within the hydrate cages as a function of time at different THF concentrations for (a) the CO₂ system, (b) the CH₄ system, and (c) the H₂ system.

hydrate formation compared to systems without THF.^{64,65} It has also been reported that the storage stability and gas uptake capacity of THF-CH₄ hydrates are strongly influenced by process conditions. For H₂ hydrate formation, no hydrate structures are observed in the absence of THF within the simulation timeframe, supporting the notion that THF stabilizes H₂ clathrate hydrates by occupying large water cages.^{66,67} Overall, the gas uptake and growth behavior of CO₂, CH₄, and H₂ hydrates in the presence of THF observed in this study are in good agreement with previously reported trends from both simulation and experimental investigations.

4. Conclusions

This study provides a comprehensive molecular-level understanding of the formation and stabilization mechanisms of CO₂, CH₄, and H₂ gas hydrates in the presence of THF using extensive MD simulations. By systematically varying THF concentrations, we elucidate how THF acts as a thermodynamic promoter, significantly influencing the nucleation, growth, and structural characteristics of gas hydrates. THF concentration above 1.42% markedly accelerates the nucleation of gas hydrates, with CO₂ hydrates nucleating fastest, followed by H₂ and CH₄. However, at higher THF concentrations, H₂ hydrates exhibit the highest growth rate, as indicated by the F_4 order parameter. The presence of THF increases the total number of hydrate cages, particularly up to a concentration of 3.4%, after which the effect plateaus for CO₂ and H₂ hydrates but leads to a decrease in cage formation for CH₄ hydrates at even higher THF content. The initial nucleation predominantly involves the formation of small 5¹² cages, while larger 5¹²6² and 5¹²6⁴ cages emerge during the growth phase, with their abundance and distribution being sensitive to both the gas type and THF concentration. Gas uptake analysis demonstrates that the number of guest molecules encapsulated within hydrate cages increases with THF concentration up to an optimal point, beyond which the effect varies by gas type. At higher THF concentrations, H₂ shows the greatest uptake, followed by CH₄ and CO₂, highlighting the tunable nature of gas storage capacity via THF concentration. Collectively, these insights advance our

understanding of the molecular dynamics governing gas hydrate nucleation and growth in mixed systems. The results underscore the important role of THF as a promoter, not only in modulating hydrate phase behavior and cage architecture but also in optimizing gas storage and sequestration strategies. The work will have fundamental implications in designing efficient gas hydrate-based technologies for energy storage, transportation, and environmental applications.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article are available upon reasonable request from the corresponding authors.

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