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**Combining Novel Simulation Methods and Nucleation Theory to Uncover the
 Secrets of Gas Hydrates**

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Abstract

Conventional computer simulation methods fail for some of the most important problems. With the design and application of innovative algorithms, this project achieved a breakthrough for the case of systems undergoing first-order phase transitions. We gave a complete simulation protocol based upon a well optimized version of our "generalized replica exchange method".

The transition of primary interest was gas hydrate formation, a process of significance for climate science and natural gas retrieval. Since hydrates consist of guest molecules in the cages of a water matrix, β ice, the freezing and melting of water was also studied. New information was uncovered about the transition pathways and thermodynamics. Some highlights are 1. the finding that in a very dilute solution without deep supercooling, representative of real-world conditions and very challenging to conventional algorithms, methane can act as a catalyst to drive the formation of large amounts of β ice with empty cages as metastable intermediates, which might be filled by additional methane in a mechanism for hydrate formation, and 2. illumination of the role of metastable cubic ice in water freezing, with determination of the surface tensions of the cubic, hexagonal, and β ices, and the free energy difference of cubic vs hexagonal ice.

Work was begun on lipid systems, bilayers and nanoreactors promising for energy-related photoreductions, and targets for future research. Our methods yielded what is arguably the most complete description of the composite lipid/water phases and the transition pathways among them.

Accomplishments

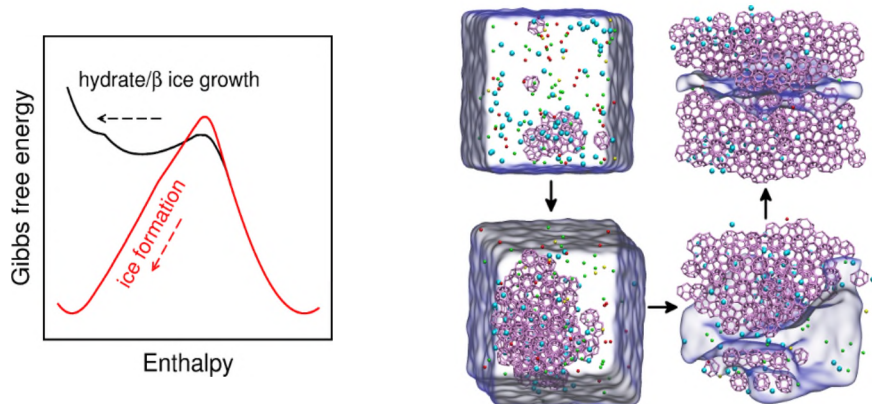


FIG. 1: Right: Dilute methane (cyan) catalyzes conversion of entire box to hydrate matrix with empty cavities, β ice. Individual unorganized water not shown, grey surface is liquid water pool, green is hexagonal ice, red cubic ice, mauve bonds are for water molecules in fully formed hydrate cages. Left: Competing pathways for water/methane system. At 1 atm and equilibrium temperature for freezing, hexagonal ice with pockets of methane is formed in equilibrium (red) but free energy barrier to metastable β ice with full and empty cages is lower and it forms as an intermediate. Methane hydrate will become the stable phase as more methane is available.

Conventional computer simulation methods fail for some of the most interesting contemporary problems. This project addressed that difficulty with the design and application of innovative algorithms, and achieved a breakthrough for the case of systems undergoing first-order phase transitions, where, when using temperature as the control variable, large supercooling or superheating is required to overcome trapping in one phase, making it difficult to learn about the near-equilibrium process proceeding through states with co-existing phases.

The transition of primary interest was gas hydrate formation. Since hydrates consist of guest molecules in the cages of a water matrix (β ice), an understanding of the freezing and melting of water was also sought. Significant new information was uncovered about the transition pathways and thermodynamics. Some highlights are 1. the finding that in a very dilute solution without deep supercooling, representative of real-world conditions and very challenging to conventional algorithms, methane can act as a catalyst to drive the formation of large amounts of β ice with empty cages as metastable intermediates (Fig. 1), which might be filled by additional methane in a mechanism for hydrate formation, and 2. illumination of the role of metastable cubic ice in freezing, with determination of the surface tensions of the cubic, hexagonal, and β ices, and the free energy difference of cubic vs hexagonal ice.

Work was begun on lipid systems, bilayers and nanoreactors promising for energy-related photoreductions, and targets for future research. Our methods yielded what is arguably the most complete description of the composite lipid/water phases and the transition pathways among them. Gold nanoparticles wrapped with lipid layers are virgin territory so all the results are new.

The algorithmic part of the project was primarily based upon our generalized replica exchange method, gREM [1], which was implemented into the powerful simulation package, LAMMPS [2], with many new features and optimizations. As explained in previous reports and in our published papers supported by the grant [3–9], the α replica is a generalized ensemble with an enthalpy-dependent configurational temperature function, $T_\alpha(H) = \lambda + \eta(H - H_0)$, where slope η is negative and H_0 is a reference enthalpy.

The generalized ensemble is especially tailored to sample coexisting states in equilibrium, in sharp contrast to the situation with conventional algorithms, where coexisting states appear transiently in a nonequilibrium process. Parameters are chosen so the most probable enthalpies, H_α^* , span the coexistence range, and we explore it using enthalpy as the control variable. Another method which we have developed, ST-WHAM [10], a non-iterative, faster alternative to conventional WHAM, is used to combine data from all the replicas to obtain the statistical temperature, $T_S(H)$, the basis of the entropic analysis of the transition [11]. The upshot is a complete new procedure for simulation of first order transitions.

1. Method development

The postdoc supported by the grant, Dr. Edyta Malolepsza, wrote a module to support the molecular dynamics (MD) version of the gREM, which had previously been based on the less efficient Monte Carlo, within LAMMPS. The original algorithm was for constant volume. We next developed [5] a theory of constant-pressure MD in generalized ensembles, implemented it in LAMMPS, and thus obtained the isobaric MD gREM. The algorithm was tested [5] on the liquid-vapor transition of the guest molecules [12] for hydrates within the mW water [13] model, with excellent results. Fig. 2 shows the obtained coexistence curves.

We proposed [4, 6] the following procedure for the study of first-order transitions:

- Simulate the system with the isobaric MD gREM.

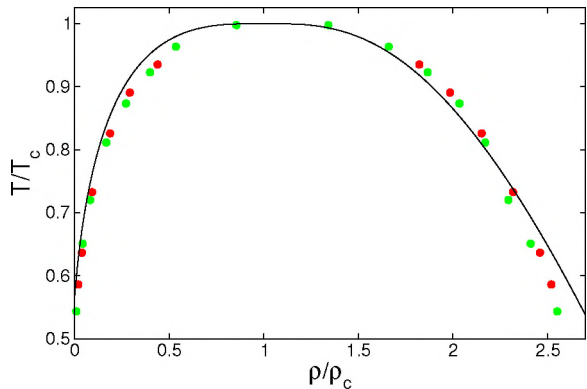


FIG. 2: Liquid-vapor coexistence curves exhibiting the law of corresponding states for small (red) and medium (green) hydrate guest molecules, obtained with the isobaric MD gREM. T_c and ρ_c are the critical temperature and density, respectively.

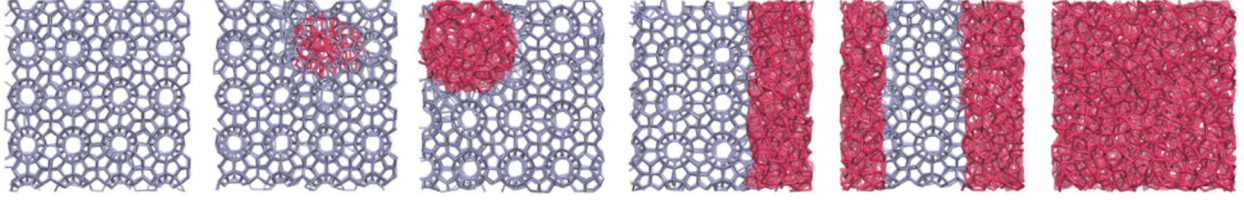


FIG. 3: Coexisting states in melting of β ice. Left to right with increasing enthalpy different "subphases", ice, ice+liquid droplet, ice+liquid cylinder, ice+liquid slab, ice + two liquid slabs, liquid.

- Determine the statistical temperature, $T_S(H)$, from the enthalpy (or energy) histograms in the replicas with ST-WHAM.
- Perform the entropic analysis [11] of phase equilibrium using $S(H) = \int^H dH' \beta_S(H')$, where $\beta_S(H) = 1/T_S(H)$ and S is the entropy.
- Visualize the transition as a function of enthalpy and evaluate order parameters, etc, by following the replicas through the coexisting states, and calculate any constant- T averages by reweighting the configurations.

A Maxwell construction on $\beta_S(H)$ gives the equilibrium transition temperature, T_{eq} . Peaks in the derivative, $d\beta_S(H)/dH$ identify the subphase transitions connecting different structures/topologies of coexisting phases. The statistical temperature alone is extremely informative about phase transformations, as it has a characteristic feature for any significant structural change. When hysteresis is present we proposed that the replicas should be initialized with the low- H phase, as it will not be formed in available CPU following with initialization with the high- H phase, and both phases must be present to get T_{eq} .

We gave a faster method for recognizing water polygons and the cages they form in hydrate growth, both occupied and empty. To distinguish the different phases of water we considered [6] 8 pairs of order parameters and found an optimal pair to characterize molecules as hexagonal ice, cubic ice, or liquid-like.

We began a collaboration with Dr. Chris Knight, Argonne NL, and obtained a Director's Discretionary award for time on the Mira supercomputer, facilitating the development of the LAMMPS isobaric MD gREM. PhD student David Stelter, who received summer support under the grant, has worked with Chris to implement the replica exchange version of our other enhanced sampling algorithm, statistical temperature molecular dynamics, STMD [14], into LAMMPS. STMD samples a flat energy distribution, between upper and lower cutoffs, which facilitates barrier crossing. David has found a promising scheme with one replica handling each phase and a few in the transition enthalpy region, and is currently carrying out RESTMD simulations of lipid vesicles and nanoparticles wrapped in lipid layers that have been proposed for future research, with on the order of a million atoms.

2. Melting of ices and freezing of liquid water

Using the mW model [12, 13], we studied the melting of hexagonal, cubic and β ice, and the freezing of liquid water [3, 4, 6]. Metastable β ice, which holds the guest molecules in hydrates, does not appear in the freezing of pure water, but metastable cubic ice is highly competitive with stable hexagonal ice along the transition pathway.

Fig. 3 shows the progression of coexisting states in melting of β ice, and the other ices show similar patterns. Fig. 4 illustrates our general method for first order transitions, for cubic ice. Having obtained T_S (a), an equal-area construction on β_S (b) gives the equilibrium transition temperature, $T_{eq} = 269$ K (256 K for β ice), and the subphase transitions between different coexisting topologies along the transition pathway are identified by peaks in β'_S (c). $S(H)$ is convex between the enthalpies of the coexisting homogeneous phases, H_1 and H_2 , falling below the double tangent touching $S(H_1)$ and $S(H_2)$, with the difference exaggerated in (d), dashed line. The free energy barrier at T_{eq} (e) allows determination of the surface tension, an essential element of nucleation theory, since the barrier is due to surface effects. At 1 atm, the cubic ice/liquid and β ice/liquid surface tensions, found for the first time, are 23.6 and 26.3 mJ/m², respectively. The hexagonal ice/liquid surface tension is higher, 30.9 mJ/m².

The central plateau in T_S corresponds to the slab configuration, where melting does not change the surface area, so the plateau temperature is not influenced by surface effects. Its coincidence with T_{eq} from the Maxwell construction is an excellent check on the calculations.

The pathways we find for melting are reproducible. The freezing pathways are different and, while broadly reproducible, show run-to-run variations. This makes sense because, with a particular ice already in place, the system is predisposed to that symmetry. In freezing there is no such predisposition. Ultimately one expects hexagonal ice but multiple forms and their composites are possible along the pathway, a subject of intense current interest [15].

Our procedure to classify molecules into hexagonal ice, cubic ice and liquid is based [6] upon the order parameter pair, $(q_3^G, \langle q_6 \rangle)$. Scatterplots for the different types at 290 K define regions for each type, Fig. 5, left. The method is faster than current algorithms as it does not require evaluating the order parameters of the neighbors to classify a molecule. Fig. 5, right, shows distinct mixed cubic/hexagonal/liquid structures in the initial stages of freezing. We discovered a new structure with a pyramidal motif and pentagons reminiscent of hydrate cage faces. Water freezing is a very important process and the participation of multiple competitive structures is well worth future study. We found the prevalence of cubic ice as an intermediate and suggested its low surface tension as the cause.

Statistical temperatures for melting vs freezing are compared in Fig. 5, right. At a given T_S , hexagonal ice has the lowest enthalpy, indicating that it is the stable ice. The maxima of the melting curves give the limit of stability of ice, while the minimum of the freezing curve gives the homogeneous nucleation temperature.

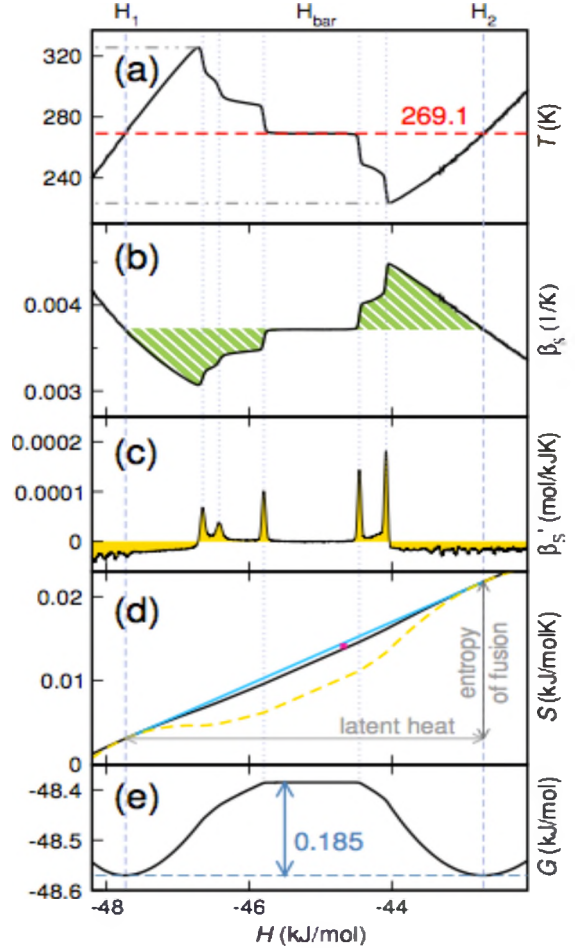


FIG. 4: Entropic analysis of melting of cubic ice. See text for explanation.

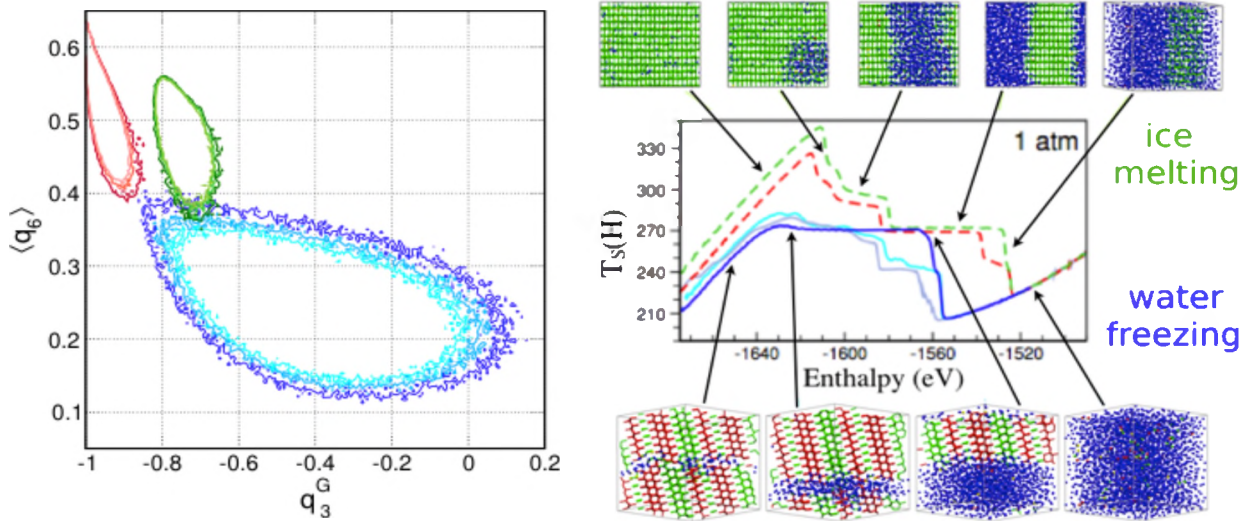


FIG. 5: Left: Regions of $(q_3^G, \langle q_6 \rangle)$ plane for water symmetry types. Blue for liquid, green for hexagonal ice, red for cubic ice. Right: Statistical temperatures for water freezing (solid blue shades) versus melting of hexagonal (dashed green) and cubic (dashed red) ice, with distinctive composite structures of cubic and hexagonal ice illustrated at bottom.

The combined enthalpy distribution of the generalized replicas is almost flat through the transition region for all cases, while it would be almost empty with standard canonical replica exchange. There is some depletion of sampled states around the barriers ($H \approx -45$ and -46 kJ/mol in Fig. 6 for β ice), but exchanges persist.

3. Hydrates

How do hydrophobic guest molecules become surrounded by characteristic water cages with flat pentagonal and hexagonal faces, and self-organize into a crystalline hydrate [12, 16]? By initializing the gREM replicas with water and methane we studied methane hydrate formation [7]. The gREM has a unique ability to sample near-equilibrium pathways, while conventional simulations require large driving forces. Furthermore, low methane concentration, representative of real-world conditions, slows the growth process and makes simulation more difficult. Exploiting the strengths of the gREM, we sought to mimic conditions on the seafloor and to focus on early stage growth without strong driving, simulating a dilute solution with mole fraction ≈ 0.008 . The system is basically water and cannot go to completion as a crystalline hydrate, yet we observed an enormous influence of the methanes.

We found two distinct pathways, formulated within the original context of enhanced sampling. The first pathway occurs when the simulation is started with a set of replicas covering at once the entire interesting range of enthalpy. Then ice forms very quickly in the low-enthalpy replicas, and leads the entire pathway towards ice with methane in bubbles, and the same composite cubic/hexagonal ice structures found in pure water.

We also performed simulations with gradual addition of the low-enthalpy replicas. Each added replica is initialized with the final structure from the previously lowest replica, equilibrated, and so on, until the entire interesting enthalpy region is covered. The second approach allows the rearrangements needed for hydrate formation without interruption by ice formation, and the striking formation of empty cages in intermediate metastable states shown in Fig. 1.

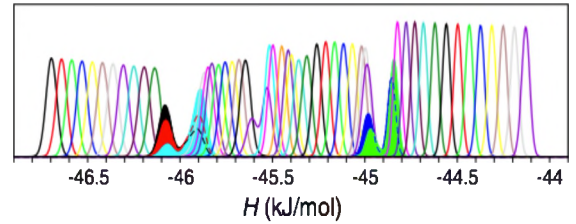


FIG. 6: gREM enthalpy histograms for β ice melting. Color around $H \approx -45$ and -46 highlights sampling of barrier regions.

Our new view of hydrate formation via T_S is summarized in Figs. 1 and 7 [7]. The two statistical temperature functions in Fig. 7 describe the two pathways discussed, and yield the two Gibbs free energy curves in Fig. 1.

The relevant hydrate structures are "sI" and "sII" [16]. They contain three types of cages. Notation is that a cage of type 5^{12} consists of twelve water pentagons, $5^{12}6^2$ means twelve pentagons and two hexagons, while $5^{12}6^4$ means twelve pentagons and four hexagons, etc. The listed cages require 20, 24, and 28 waters, respectively. In a primary cell, sI has 2 5^{12} and 6 $5^{12}6^2$, and sII has 16 5^{12} and 8 $5^{12}6^4$. sI and sII differ not only by cage types, but also by their geometrical arrangement; simple cubic for sI and face centered cubic for sII.

We applied our cage identification algorithm to determine numbers of cage types versus enthalpy along the statistical temperature; results are presented in Fig. 7, bottom. The number of cages found, compared to the number of methanes in the system, establishes that they are predominantly empty, with approximately 10 times more unoccupied than occupied ones.

In each case the most abundant cage was the 20-water 5^{12} , followed by three times fewer 28-water $5^{12}6^4$ cages of sII, and smaller numbers of the 24-water $5^{12}6^2$ of sI (in perfect sI crystal $5^{12}6^2$ is $3\times$ more abundant than 5^{12}) and 26-water $5^{12}6^3$ cages that do not enter any crystal but were proposed [17, 18] as a bridge between $5^{12}6^2$ and $5^{12}6^4$ in early growth. Methane ultimately forms sI, so we confirm [17, 18] that initially elements of both structures co-exist. In our study of early growth, sII is dominant. Cages are arranged in a rhomboidal pattern in contrast to the cubic one for sI. This makes sense with empty cage expansion, since the empty sII lattice is more stable than empty sI [19].

The initial prevalence of kinetically favored sII over the thermodynamically favored sI is analogous to the initial prevalence of cubic ice over hexagonal ice structures in ice nucleation.

We propose that at low methane concentration and with low driving forces, ie real-world conditions, hydrate growth may proceed by the generation of small metastable patches of β ice, with empty cages, that are subsequently filled by an influx of methane, insofar as it is available on the lifetime of the metastable state.

5. Collaboration with the Klein/Gould group

The grant contained minimal funding to formalize the participation of Profs. Klein and Gould, experts on nucleation. We held joint group meetings. and Prof. Klein assigned PhD student Rashi Verma to the project, and she received a small amount of summer support. Her thesis project is characterizing the critical nucleus in phase transitions, exploiting our methods wherever possible.

While the gREM captures coexisting states, it is not possible equilibrate the critical nucleus

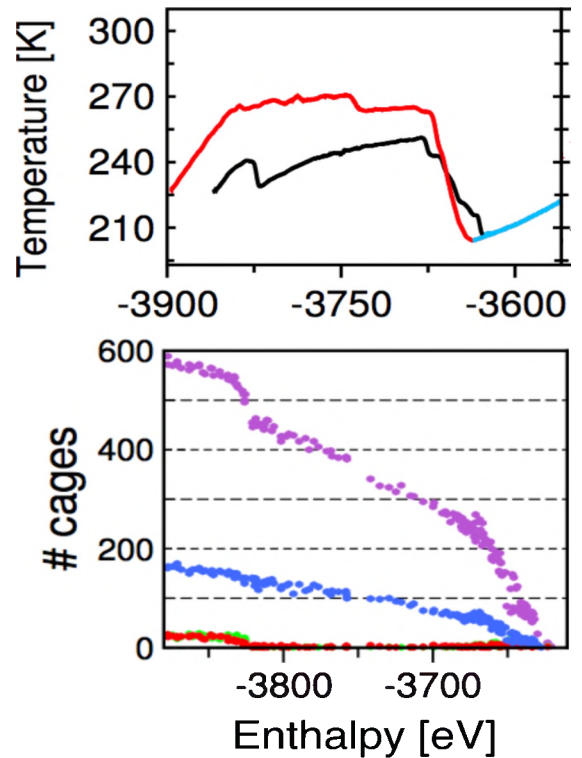


FIG. 7: 64 methanes and 7845 waters at 1 atm. Above: $T_S(H)$ showing two transition pathways. Black lines correspond to regions where methane hydrate was observed, red lines to mixtures of hexagonal and cubic ice plus methane in liquid water, and blue lines to methane solvated in liquid water. Below: Numbers of different cage types vs enthalpy. Right to left is the direction of cage formation. Purple, green, red and blue represents cages with 20, 24, 26 and 28 waters.

in a single replica. So we initially followed the “intervention” [20, 21] approach for water and Lennard-Jones. With canonical MD, the temperature is quenched into the supercooled regime. Configurations along the subsequent trajectory, with randomized velocities, are taken as initial conditions for additional MD runs, which are monitored for nucleation. The probability of nucleation is computed vs time. The critical nucleus has probability of 1/2. Rashi has found that its structure is not described by classical nucleation theory and, as in hydrates and water, intermediates with different structure from the equilibrium final state are important. Rashi and a second Klein student, James Silva, found non-monotonicity of the nucleation probability vs time, increasing with quench depth, apparently caused by a flattening of the free energy barrier as the spinodal is approached, and consistent with critical slowing down.

We began the development of a gREM version of intervention, using configurations from a trajectory in a “generalized quench” in which the parameter λ is decreased instead of the temperature. By exploiting the finding that nucleation occurs in near-vertical sections of $T_S(H)$ (e.g. on the RHS in Fig. 5, right, and 7), we anticipate superior sampling of the critical droplet, even if the gREM alone cannot stabilize it.

4. Lipids

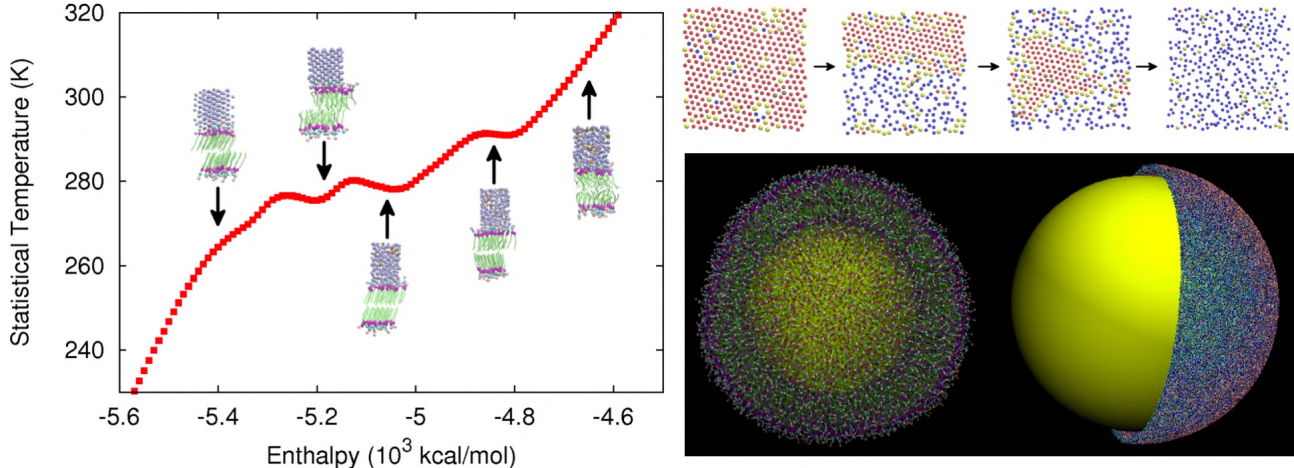


FIG. 8: Left: Statistical temperature from gREM simulation of freezing of the 32 Wet-MARTINI DPPC lipid/water composite system, with phases indicated by arrows. Right to left, fluid lipids with liquid water, gel lipids with liquid water, tilted-gel lipids with liquid water, fluid lipids with ice, gel lipids with ice. Top Right: gREM simulation of melting of a 32 DPPC lipid Dry-MARTINI bilayer showing subphases. Left to right, gel (red beads), gel and fluid (blue beads) slab, circle of fluid in gel, fluid. Bottom Right: STMD simulations of a spherical gold core surrounded by a Wet-MARTINI inner lipid layer and Dry-MARTINI outer layer. Left, 10 nm in diameter. Right, 100 nm, cross-section.

Our methods can make significant advances in the study of phase transitions in lipid systems, which will be the primary area of our future research. Of particular interest are gold nanoparticles wrapped in lipid layers, which we suggest can serve as nanoreactors for photoreduction, eg H_2 production from water, with an electron transfer molecule in the layer. Their function depends on the lipid phase, which may be fluid, or one of several types of gel.

Thus partial summer support was provided for preliminary work on lipids by PhD student David Stelter. Both the explicit solvent Wet-MARTINI [22] and implicit solvent Dry-MARTINI [23] force fields were employed. With gREM [8] David obtained, Fig. 8, left, the statistical temperature, performed the entropic analysis, and characterized the coupled transitions of the lipid and water

subsystems in lamellar Wet-MARTINI DPPC bilayers. Fig. 8, top right, shows the progression of subphases in the melting of Dry-MARTINI gel. All the results mentioned are firsts.

As indicated in "Method Development", David has also worked with Chris Knight to develop LAMMPS RESTMD and apply it, with an innovative selection of replicas, to lipid vesicles and nanosystems. He conceived a computationally efficient approach to lipid-wrapped nanoparticles, using Wet-MARTINI for the inner leaflet and Dry-MARTINI for the outer leaflet, Fig. 8, bottom right. The small system, left, has 1900 inner lipids and 3200 outer lipids, for a total of 61,200 atoms. The larger system, right, is on the scale of nanoparticles synthesized by our collaborator Bjoern Reinhard [24] and has 190,000 inner lipids and 200,000 outer lipids for a total of 4.68 million atoms, representing a "grand challenge" simulation. It is the largest system of this type ever attempted, made possible by our algorithms. The immediate goal is to determine the effect of the nanoparticle on the lipid phase equilibrium.

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