

Excerpts From Reviewer Comments

53161-ND6

David A. Kofke

This is a very nice proposal looking at the thermodynamics of clathrate hydrates. The methods to be applied to determine the phase equilibrium conditions have been well studied by the PI for other systems and it would be a great contribution to see those methods applied for clathrate hydrates, which are much more complex systems. The PI has a strong record in free energy calculation methods and this proposal has a very high probability of success. The proposed work is much needed in the field of clathrate hydrates. The PI has given significant thought on the problems that may arise with the calculations as well as the different contributions that may contribute to the stability of clathrate hydrates (e.g., nuclear quantum effects).

One aspect that the PI may need to give further consideration is the actual process for determining the coexistence conditions of the clathrate hydrates in equilibrium with liquid water and gas. The important component here is the composition and cage occupancy of the clathrate hydrate.

The systems to be studied are very relevant and once this is well demonstrated for the proposed system, this will provide a well established way to determine the phase coexistence conditions for any other system.

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The proposed research is both fundamental and related to the petroleum field. The author proposes to perform a comprehensive and rigorous molecular simulation study of gas hydrate phase equilibria for a wide range of conditions, including pressure, temperature, solute concentration and distribution, solute type, hydrate structure, and will also investigate nuclear quantum effects, especially for hydrogen hydrates. A harmonically targeted temperature perturbation (HTTP) method will be applied to calculate free energy as a function of temperature. An interesting feature of this proposed method is that it is not so dependent on system size, thereby allowing a smaller numbers of unit cells to be used in the calculations and reducing the computational expense.

The proposed research is important as there is a need to develop more accurate and reliable thermodynamic simulation models for gas hydrates. The fundamental thermodynamic behavior of the simulation models are required to provide confidence in dynamic and mechanistic studies of gas hydrate nucleation and growth.

The PI is very well qualified in the different computational methods to be applied in the proposed studies. This is a new area of research for the PI, as he has not worked previously in gas clathrate hydrate research. He appears to have a reasonable grasp of the

literature related to the proposed research. Comparisons of the calculated phase diagrams with experimental data (which are well established, e.g. for methane and carbon dioxide hydrates and methane-carbon dioxide and H₂-THF mixed hydrates) should be included in the proposed studies. A major concern of the proposal is that it lacks focus and seems too ambitious, with several different aspects and systems of gas hydrates to be investigated, including studying the stability of sI/sII methane hydrate, CO₂ hydrate hydrates, CO₂-CH₄ sequestration, hydrogen storage, and design of stabilizing/destabilizing guest molecules. With such a broad scope of research, the details of the proposed approach and questions to be addressed for a specific application are somewhat unclear. It appears unrealistic that all of these proposed objectives could be achieved in the timeframe of the project and with the resources requested. Even just 1-2 of the proposed studies described in further detail would make a stronger proposal, and should be worthy of study.

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The proposal addresses a very important fundamental problem of determining the coexistence lines between the solid clathrate hydrate phase and liquid / gas phases. Many molecular dynamics and Monte Carlo simulation studies have appeared in which the properties of the hydrate phase have been simulated under different pressure / temperature conditions. It becomes very important to know where in the phase diagram these simulation studies are performed. This is particularly important since it is well known that many water models do not predict the correct melting point of ice and are thus also not expected to correctly predict the decomposition temperature of the clathrate hydrate phases. The expertise and research accomplishments of the PI strongly suggest he will succeed in achieving the goals set out in this proposal. The time frame and suggested funding are appropriate and the nature of the proposal is such that it would be appropriate for a combination of graduate student and post-doctoral associate work.

However, I would also state that a number of the applications described by the PI are somewhat outdated and the literature search misses many relevant references which may have impact on the research described and proposed. As a result, I believe a revision of the goals of the proposal is in order. In particular, attention should be paid to the following points:

- Due to the non-spherical nature of the CO₂ molecule, the Monte Carlo scheme for CO₂ placement in the oblate sI clathrate hydrate large cages will not be straightforward as the placement of the spherical methane molecules in the same cages. Modifications of the spatial sampling of the CO₂ in the cage will be needed to make the calculations feasible. The complex shape of guests placed in the cages by the Monte Carlo routine something the PI should pay mention to as some biased sampling methods may be required in implementing the proposed methodology.
- The section on H₂ hydrates is somewhat dated and superseded by subsequent work. For example, quantum chemical calculations (Alavi, Ripmeester, Angew. Chem. Inter. Ed., 46, 6102 (2007)) show that H₂ molecules can diffuse through the clathrate hydrate cage faces with barriers that may be accessible under pressure / temperature conditions of stability of the hydrate. My opinion is that H₂ storage in the canonical clathrate hydrate phases will not be feasible under conditions of practical interest.
- Last section, Okano and Yasuoka (J. Chem. Phys. 124, 024510 (2006)) have performed free energy calculations of sH clathrate hydrate guests of different size. These calculations overlap with those suggested in this proposal and at the least may be used as a reference for the suggested calculations in Section 4.4 of the proposal.
- A set of guests of importance not included in the proposal are those which interact directly with the water cages to form hydrogen bonds. The methods suggested by the PI seem to exclude this type of guest from the study. The hydrogen bonding of the guests with the cage waters are different from the anharmonic effects mentioned by the PI in the

introduction and previous work. Some aspects of the guest water hydrogen bonding are discussed in Buch et al. (PCCP 11, 10245 (2009)) and Alavi et al. (J. Chem. Phys. 130, 174501 (2009)).

- There are some correlations between guests in the small and large cages and the stability of the clathrate hydrate phases. How would these effects be incorporated in the proposed Monte Carlo simulations? The most obvious example of this is the sH clathrate hydrates where the presence of the small help gas molecules are required before the large guests will form the hydrate phase.
- The nature of the intermolecular potentials chosen and their affect on the phase diagram should also be acknowledged.
- While nuclear quantum effects can be important at low temperatures, these effects will likely not play a major role in determining the solid-gas or solid-liquid phase boundaries of the hydrate systems and the transitions between phases and coexistence lines occur at higher temperatures. Therefore, it is not clear if the study of quantum effects has relevance to the proposal.

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The PI proposes to study the thermodynamic stability of clathrate hydrate phases using molecular simulations. These phases are solid H₂O cage-like structures with solute molecules (eg, methane, CO₂) incorporated in the cages. These phases arise in a number of natural and technological contexts, and so knowledge of their thermodynamic stability is important. The clathrates could be described as 'complex' structures because they are not perfect crystals, and the occupancy of the cages (and thus solute composition) can vary -- thus understanding the thermodynamic stability of these phases is a challenge. The molecular simulation approach presents further challenges because the phases are somewhere between crystals (with long-range order) and liquids (eg, the solutes in the cages will have much mobility within the cages).

The PI is well positioned to overcome these challenges. He is a world leader in using molecular simulations to calculate free energy and phase stability, and had developed some of the pioneering methods in this area. His plan is well thought out, with particular attention paid to details including the most appropriate free energy methods and force fields.