Review

by Dr. Vesselin Tonchev, Associate Professor in Faculty of Physics, Sofia University

on

doctoral dissertation titled:

"Molecular Modeling of Phase Transitions at the Water-Alkane Interface: The Role of Surfactants and Curvature"

by

Stoyan Iliyanov Iliev

in partial fulfillment of the requirements for obtaining a PhD degree

Professional field

4.2. Chemical sciences (Theoretical Chemistry / Computational Chemistry)

I. General Information about the Doctoral Candidate

Stoyan Iliev, MSc is a young scientist who graduated with distinction the master degree program in Computational Chemistry at the Faculty of Chemistry and Pharmacy of the Sofia University in 2020 and demonstrates a pronounced interest in the interdisciplinary aspects of computational chemistry and materials science. His research in molecular modeling demonstrates both maturity and methodological competence.

I will sequentially review the documents provided for the defence and comment on them only where there is something noteworthy to address.

0. **Application**

   Stoyan Iliev submitted his application along with documents numbered from 1 to 14.

1. **Rector's Order for Admission**

   Issued on July 9, 2020, admitting Stoyan Iliev as a full-time doctoral student.

2. **Rector's Order for Clearance for Defence**

   Issued on July 10, 2023, allowing the candidate to defend his dissertation. After that period, Iliev worked as an R1-level researcher at Sofia University, as detailed in the next document—his CV (in European format).

3. **Curriculum Vitae (CV)**

The CV confirms that Iliev has maintained an excellent academic and professional record.

4. **Bachelor's Degree Diploma**

   Issued on February 13, 2019, confirming that Iliev performed well as an undergraduate student in Chemistry.

5. **Master's Degree Diploma**

   Awarded on February 1, 2021, reflecting outstanding academic performance throughout the Master's program in Computational Chemistry.

6. **Dissertation**

   This will be discussed in detail below.

7-8. Author's Abstracts (Bulgarian and English)

Both abstracts will be addressed briefly. There is a growing sense in me that the relevance of this document type has diminished in recent years, especially since another candidate combined his abstract with his paperss to produce an innovative dissertation format (and still defended successfully!).

9. Certificate of Exam Result

The document indicates that the candidate performed well (with a grade 4/6) on two specialized exams during the doctoral program.

10. Publications

The three articles supporting the dissertation are all published in Q1-ranked journals. This provides significant assurance regarding the quality and relevance of the work. For a particularly meticulous reviewer, evaluating how well these articles are reflected in the dissertation, and identifying any additional material present, he might want to suggest whether further articles could be published or whether the two realities—articles and dissertation—are stylistically harmonized. I will not delve into such meticulous detail but will briefly address the articles after discussing the dissertation itself.

11. Compliance Report

The document confirms that S.Iliev either meets or exceeds the minimum academic requirements under Article 2b of the Bulgarian Law on the

Development of Academic Staff. Notably, Iliev has achieved an h-index of 5, which surpasses the requirements for higher academic positions.

12. Declaration of Authorship

This declaration has been completed and signed by both doctoral advisors as well as the candidate.

13. Plagiarism Report

The report and its two appendices confirm that no plagiarism was found.

14. Pre-Defense Protocol

Summarizes the feedback from the extended departmental council of the Department of Physical Chemistry at the Faculty of Chemistry and Pharmacy, Sofia University. My comments during the pre-defense are accurately reflected, together with the responses of the two co-advisors provided immediately.

After this detailed enumeration, I can only conclude that even the preparation of all these documents requires significant effort, organization, and coordination, especially when there are two thesis advisors. Let us now examine the content of the dissertation.

II. Dissertation

The dissertation of Stoyan Iliev represents a serious and result-rich collective effort, with fundamental and methodological contributions related to phase transitions in water-alkane systems, emphasizing the influence of surfactants (SAA) and interface curvature—a term that could perhaps extend the title, which currently stops at curvature. In any case, the title introduces another uncertainty—on which side of the interface the study's focus lies. To get ahead, I will say that the "water side" has not only remained outside the main focus but also somewhat outside the scope of development, as seen in the dissertation—water is modeled using a force field from 1985. At the same time, the main "actor" among the alkanes in the dissertation is hexadecane, and this could be reflected in the title instead of the rather general term "alkane."

It is also important to note here that this research builds upon a tradition established over decades in two different departments at the Faculty of Chemistry and Pharmacy, which have not always been in close collaboration, especially during the time when I was making

my professional choices. In addition to growing on this fertile ground, a modern study like the present one may also bear some negative traits, such as the inevitable "omission" of certain important and fundamental elements of the "craft," which were central to the work of previous generations. To avoid being unsubstantiated, I will mention the "coincidence" in the length of the hydrophobic tail of the surfactant used—16 carbon atoms—with the length of the hexadecane studied, which is unlikely to be accidental. This is not explained, i.e., it is taken as self-evident, but this choice is surely based on careful prior analyses. As the text progresses, the attentive reader will observe that the tradition of the two departments is enriched before their eyes—the text becomes context.

For me, the dissertation is a lively and engaging narrative, though uneven in places and slightly more detailed than necessary in others. It is an open-ended story about how structured knowledge is derived from a fundamental problem, initially observed in systematic experiments and about which little—if anything—was known at the outset. This structured knowledge emerges through effort and thought. And this story is the doctoral candidate's own.

The dissertation consists of seven parts (chapters): Introduction, Literature Review, Computational Methods, Results and Discussion, Conclusion, Contributions (how many are needed to merit a separate chapter?!), and References. There are no explicit conclusions, and the term "conclusions" appears only once—in Chapter 4.

The text of the dissertation spans 113 (114) pages, which might seem modest if one does not consider that it is formatted with single-line spacing. I will not count the figures, as the last figure is numbered 62, but rarely does a figure consist of a single panel (e.g., Figures 52, 53, and 59). For example, Figure 57 includes eight graphs, and the last figure, 62, contains eight visualizations arranged in a 4x2 layout, generated from numerical experiments. In other words, calculations underpin each of the four configurations. Not all the figures are the author's original work, but for the "borrowed" ones, the sources are duly cited.

The last equation is numbered 49, but this does not fully reflect the total number of equations—there are three equations each for numbers 40 and 41, with suffixes a, b, and c added to the numbering. To me, this suggests that Stoyan did not use specialized software for numbering the equations but instead numbered them manually and later needed to renumber them, resolving the issue by adding letters. Equation 43, which

provides the expression for the covariance matrix, is so concise that it borders on incomprehensibility; it simply reads $\mathbf{M}\mathbf{M}^T$ and is not even a proper equation, as it lacks an equals sign. I would have placed it within the main text rather than presenting it as a standalone equation.

The list of references includes 72 entries, which do not adhere to a consistent bibliographic standard—toward the end, the publication year is often bolded, whereas at the beginning, the journal volume is bolded, with the year placed in parentheses. I did not have the patience to check whether all the references are cited within the body of the dissertation. Interestingly, even the popular AI bot ChatGPT failed to complete this task—perhaps I did not phrase my query correctly!

Before recommending how to approach reading the dissertation, I would like to highlight two points about the introduction, which spans one and a half pages:

- The term "supramolecular formulations" is used only once in the dissertation and seems out of place in the context of the text, as it refers to "the possible phase transitions between them." To me, the term "formulation" is more associated with pharmacy, though I am unsure of its connection for Stoyan.
- In this brief introduction, the four objectives of the dissertation are outlined as follows:
    1. Development of a computational protocol for molecular modeling of the phase transition from isotropic liquid to solid in hexadecane-containing systems, applicable to other alkanes.
    2. Elucidation of the mechanism behind the observed transition from liquid to solid through an analysis of the thermodynamic and structural characteristics of the systems.
    3. Creation of a methodology for analyzing the structure of the resulting solid phases.
    4. Identification of the type of solid phases (crystalline or rotator).

Empirical experience suggests that the objectives of a dissertation are often formulated after identifying its contributions. However, to the author's credit, this is not evident, at least not overtly. Knowing the team, I can assume that the objectives were established at

the outset, and Stoyan diligently worked to fulfill them, which ultimately led to the more substantial contributions observed.

Now, if I were to traditionally recommend how to approach reading the dissertation, I would suggest that an unbiased reader begin directly with Chapter 4 – **Results and Discussion** – referring to Chapter 3 – **Methods** – as needed, and turning to the literature review only when absolutely necessary. Perhaps this is because the inaccuracies are most noticeable in the review.

In the review, terms like " oversaturation " instead of "supersaturation" and "the energetic barrier" instead of "the energy barrier," or statements like, "The driving force responsible for the stability of these ordered states remains to be explained" (if they are stable → d.f. = 0!), do not detract from the overall excellent impression but might irritate perfectionists. For me, these are more a reflection of the candidate's independence.

In any case, the reader will not find an answer to the question of why the presentation of Gibbs' theory of phase formation is not accompanied by a reference to a source. Meanwhile, the late Ivan Markov's book *Crystal Growth for Beginners* has already undergone three editions (plus one in Chinese). Additionally, the reader might wonder why "4.10. Nucleation Analysis" contains virtually nothing from the apparatus presented in "2.1.2.1. Classical Nucleation Theory."

At the same time, there is no mention of studies on two-step nucleation, for which Prof. Peter Vekilov from the University of Houston received the Sir Frank Award from the International Organization for Crystal Growth last year. These concepts resonate most strongly with the formation of so-called rotator phases—intermediate, metastable phases initially introduced in Section 2.1.3 and described using four order parameters.

In total, the phases (or transition states) amount to five, which remains one of the unresolved mysteries left for the open-ended nature of this narrative. Are they truly phases, or are they short-lived states along the kinetic pathways between the initial and final phases?

Based on further reading, particularly of the results, I would have expected the literature review to include a brief overview of the concepts and theories of Ostwald ripening. However, this would first require identifying such phenomena, particularly in cases where

small crystallites form, followed by the growth of one dominant crystal while the others disappear.

Still, it should be noted that in the literature review, Section 2.1.4. **Crystalline Phases in Alkane Systems**, important concepts about the crystalline state, which will be further investigated, are introduced. Additionally, Section 2.2. presents theoretical studies on alkanes.

However, the authorship of Figures 12–14 remains unclear, as they are not linked to any sources, nor are Tables 4–11. It seems that time may have accelerated in this part of the dissertation.

Moving on, I will briefly touch upon the methodological part, Chapter 3, merely to note that for one side of the interface, as well as for the bulk alkanes, the CHARMM36 force field was chosen. It should be explicitly noted that this force field was not calibrated for a specific temperature (such as the melting point) but was validated across an entire temperature range (as stated in Section 4.8), which may be more convincing. However, I cannot help but point out that the force field was selected in such a way as to produce the desired phase transitions within the range of 273–300 K, and it was subsequently used to study these transitions.

The most convincing part of the validation is undoubtedly the quantitative reproduction of experimental density values, as shown in Figure 28. For the other side of the interface—water—when included in the numerical experiment, the TIP4P model was chosen, despite being validated back in 1985 using the Monte Carlo method.

Attention is also given to the "tricks of the trade" (in Section 3.3)—how constant temperature and pressure (T and p) are maintained. Following this, a set of methods for analyzing the results is presented.

I will move directly to the results section and will highlight the monitoring of the calculations where relevant. However, I would already like to emphasize, purely subjectively, the determination of the crystallite plane (Section 4.5) and the Voronoi tessellation (Section 4.6).

Within Chapter 4, the reading could likely begin with **Section 4.12, "Determination of the Type of Solid Phases Formed at Different Cooling Rates,"** and, more specifically, with Section 4.12.2. Here, I would highlight a convincing result that confirms previous

experimental findings—namely, that a significant portion of the transition enthalpy is due to the formation of the rotator phase. Everything built so far contributes to this result.

Admittedly, the reported R^2 values from this study (ranging from 0.93 to 0.96) appear significant in some areas but questionable in others. However, it is quite evident that the measured transition enthalpy and final density are correlated. Perhaps Figure 51A shows this correlation less clearly, as the author did not include a guide-to-the-eye line.

Before concluding this section, I should also mention the analysis of the radial distribution functions for the model and reference systems (these references were introduced unobtrusively towards the end of page 72) in Section 4.12.4. I expect that the other reviewer will delve into this part in greater detail.

Towards the end of this chapter, the dissertation accelerates, and results accumulate rapidly. The effort invested thus far begins to pay off. In the final section, **4.13**, a spherical droplet is constructed with hexadecane inside, surfactant ($C_{16}EO_2$—note the chain length!) at the interface, and water (TIP4P) outside. It is worth noting that this section corresponds directly to the dissertation title.

The construction process is described: Monte Carlo methods were used for hexadecane and maximally dense packing for the surfactant, plus the water model (TIP4P). The system contains approximately 2 million atoms. In Figures 62B and 62D, the onset of crystallization is clearly visible at 278 K, initiated from 350 K and 300 K, respectively. It would be interesting to understand precisely what the colors in these visualizations encode.

At an accelerating pace, this chapter concludes, somewhat unexpectedly but not illogically, with a technological recommendation. The recommendation appears easily digestible for technologists, should there be any interested in crystallizing alkane/surfactant systems. It certainly seems much simpler than heavy industrial crystallization methods like the Czochralski process:

"The described differences in the two systems allow for the development of technological strategies by which alkane/surfactant droplets can be directed along different crystallization pathways by varying the initial temperature before cooling" (p. 104).

This brings us to the conclusion in Chapter 5, where the achievements of this work are systematically summarized without introducing new findings compared to the previous

chapter. Expectations for this chapter may be high, given the absence of a separate section for listed conclusions earlier in the dissertation.

At the end, we come to the contributions, which I fully acknowledge as comprehensive yet free from excessive claims:

1. A new computational protocol has been proposed for conducting classical atomistic molecular dynamics (MD) simulations of hexadecane-containing systems. This protocol successfully reproduces transitions from the regular lattice of hexadecane to an isotropic liquid (melting) and from an isotropic liquid to an ordered state (freezing).
2. Using the proposed protocol, the molecular-level mechanism of freezing has been traced for bulk hexadecane, as well as for hexadecane in contact with water at an interface stabilized by long-chain surfactants. During the freezing process, the formation of intermediate, polycrystalline rotator phases was observed, consistent with experimental data from other authors.
3. A set of specialized procedures has been developed for the structural analysis of polycrystalline model phases composed of quasi-linear molecules.
4. Using these procedures, a structural analysis of crystallites formed by hexadecane molecules in frozen model systems was performed. The type of solid phases was identified, and possible sequences of interfacial transitions during the crystallization of hexadecane were proposed.

Before moving on to the articles supporting the dissertation, I will briefly address the author's abstracts. Both are of similar length—the Bulgarian version spans 58 pages, while the English version covers 55. It is easy to identify what was omitted to achieve this reduction in length—Chapter 3 of the dissertation is entirely absent, reduced to a single sentence in the abstract that refers to the dissertation itself.

Otherwise, the final figure remains numbered 62, and there does not appear to be a reduction in the multiple panels within some of the figures. It is assumed that the English version of the abstract is merely a translation of the Bulgarian one, but I would not venture to comment on the accuracy of the translation. The number of figures is the same in both versions.

III. The Papers

There are three articles supporting the dissertation, all of which are in Q1 journals, and, logically, have high impact factors (IF). Among them, the most recent article also has the highest IF. These three publications would suffice for a successful defense almost anywhere in the world.

If I were to highlight one article that most fully represents the candidate's contributions—and even one figure within it—it would be **Fig. 5. Summary of the analyses done to determine the onset of freezing and the location of the nucleation site** from Iliev et al., *Journal of Colloid and Interface Science* 638 (2023) 743–757.

At the time of their publication, these articles underwent rigorous peer review, and I would not presume to re-review them here. However, they provide a direct pathway for understanding the work accomplished and the findings reported in the dissertation. Together, the three articles amount to 40 pages, albeit formatted in smaller font sizes.

I cannot help but note the unusual structure of the abstract in the JCIS article, which follows an explicit **Hypothesis-Simulations-Findings** template. I would be curious to know who the innovator behind this structure was—after reviewing other related articles from the same journal, I discovered that this is not a mandatory template for the journal.

In summary, the methods described in the three articles are also detailed in the dissertation, but the dissertation itself contains additional results.

I am expected to pose questions, and I am certain I will have more after the defense. For now, however, I will ask just one:

On the infamous page 10, the one with "oversaturation," there is the following statement:

"In the second case, a metastable new phase forms, where the nuclei are in equilibrium with the old phase."

If it is metastable, it can only be in equilibrium with itself, at the bottom of a local minimum. Is that correct?

At the conclusion of this review, I must provide an explicit opinion on the originality of the dissertation and its qualification as a doctoral thesis. I am convinced that doctoral candidate Stoyan Iliev is at the center of the research described in his dissertation and has made a significant contribution to the overall success of the strategy outlined by his

advisors. I have no doubt that they have not left him alone on this path and have been delicately present whenever he needed them.

I have already mentioned that three Q1 articles are a strong foundation for doctoral success almost anywhere. I believe this also applies to the specific dissertation of Stoyan Iliev, which demonstrates a high level of methodological and theoretical maturity.

Despite the minor weaknesses noted, the scientific contributions are significant and original. Hoping that the defense will be at the same level, I confidently recommend that the esteemed academic jury award Stoyan Iliyanov Iliev the educational and scientific degree of "Doctor." I will personally vote "FOR" such a decision.

Sofia, 4.12.2024

Digitally signed by Veselin Tonchev
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