Response Letter

Dear Editor

We hereby submit the revised manuscript entitled:

"Stability and Composition of Large SA–MSA–Base Molecular Clusters"

for publication in *Aerosol Research*. We sincerely thank the editor and the reviewers for their careful evaluation of our manuscript and for their constructive comments. The reviewers' comments are reproduced in blue below, followed by our point-by-point replies. Page and line numbers in our responses refer to the revised manuscript.

Sincerely

Galib Hasan, on behalf of all authors

Response to Referee #1

General assessment

This manuscript presents a computational investigation of large neutral clusters containing sulfuric acid (SA), methanesulfonic acid (MSA), and amine bases (AM, MA, DMA), extending the cluster size up to 10 acid–base pairs (20 molecules). The study addresses an important topic in aerosol formation, and the reported structural and thermochemical data for large mixed-acid clusters could constitute a valuable contribution to the field, consistent with the scope of Aerosol Research. The manuscript addresses a timely and interesting topic, and the generation of large-cluster data is potentially valuable. However, the current version has substantial gaps in literature coverage, compositional sampling and data accessibility. A major revision is required to address these points. After thorough revision and careful technical editing, the manuscript could become a worthy contribution to Aerosol Research.

Author reply:

We sincerely thank and appreciate the reviewer for his constructive comments. The manuscript has been revised accordingly.

Major Comments

Major Comment 1. Lines 78–83 state that the synergistic effects of mixed acids remain poorly understood, but the manuscript does not cite or discuss the directly relevant work by Elm, 2022, Clusteromics III, which specifically reports that MSA can enhance cluster formation potential by up to approximately 20-fold and explicitly identifies the SA–MSA–DMA system as the most promising candidate for extension to larger sizes. This omission is critical and must be rectified. Johnson and Jen, 2023 provides experimental evidence for SA–MSA–base co-condensation and observes enhanced pathways involving SA–MSA–MA. This work should be incorporated as a benchmark for the chosen base systems. Baalbaki et al., Nature, 2026 reports that below -10 °C, MSA–NH_3 nucleation can rival SA–NH_3, with clear SA–MSA synergy, and that under humid conditions MSA can drive growth near the kinetic limit. Even if this paper appeared after the current submission, it is highly relevant and must be discussed in the revised manuscript to situate the findings within the most recent experimental context.

Author reply:

We sincerely thank the reviewer for pointing out these highly relevant studies. We agree that these works provide important context for the present manuscript and that they should be discussed to better position our work within the existing computational and experimental literature on mixed SA–MSA systems.

Following the reviewer's suggestion, we have revised both the Introduction and the Discussion to include the computational study by Elm (2022), which demonstrated that the incorporation of MSA can enhance the cluster formation potential by up to approximately 20-fold and identified the SA–MSA–DMA system as a particularly promising candidate for extending investigations to larger cluster sizes. We have also included the experimental work of Johnson and Jen (2023), which reported co-condensation of SA, MSA, and atmospheric bases, providing important experimental support for mixed-acid systems involving methylamine. In addition, we have incorporated a discussion of the

recent study by Baalbaki *et al.* (2026), which demonstrated strong SA–MSA synergy and efficient MSA-driven nucleation and particle growth under cold marine conditions.

The following paragraph has been added to the Introduction.

Added paragraph (Introduction, Lines 78–84):
Despite significant recent progress, several important questions regarding mixed SA–MSA systems remain unresolved. Previous computational work has demonstrated that incorporating MSA into SA clusters can substantially enhance cluster formation potential by up to approximately 20-fold and identified the SA–MSA–DMA system as a particularly promising candidate for extending investigations to larger cluster sizes (Elm, 2022). Experimental studies have likewise demonstrated co-condensation of SA, MSA, and atmospheric bases, providing direct evidence for the formation of mixed-acid clusters under laboratory conditions (Johnson and Jen, 2023). More recently, Baalbaki *et al.*, (2026) reported that MSA can substantially enhance both nucleation and particle growth through synergistic interactions with SA under cold marine conditions.

Major Comment 2. The methodology only considers pure SA, pure MSA, and mixed clusters of the form $(MSA)_1(SA)_{n-1}(base)_n$. As n increases from 2 to 10, the MSA mole fraction automatically decreases from 1/2 to 1/10. Under atmospherically relevant MSA:SA ratios of 100:1 or 1000:1, this single-MSA substitution path cannot represent the likely cluster compositions that would dominate. More critically, it cannot answer whether acid synergy exists or what the preferred compositions are.

Author reply:

We thank the reviewer for this valuable comment. We agree that investigating a wider range of mixed-acid compositions would provide a more comprehensive picture of the preferred cluster compositions under different atmospheric conditions. However, such an investigation would be computationally very expensive.

However, the objective of the present work was not to determine the globally preferred cluster composition, but rather to systematically investigate how the incorporation of a single MSA molecule influences the stability and structural evolution of increasingly larger SA–base clusters. Besides we found in our previous work (Rasmussen *et al.*, 2022) that a single MSA was the most likely composition under most conditions. We have revised the manuscript to clarify this point and explicitly state that the present calculations provide molecular-level insight into the effect of MSA incorporation, rather than predicting the equilibrium distribution of atmospheric mixed-acid cluster compositions.

The following paragraph has been added to the Discussion.

Added Paragraph (Discussion, Lines 173–178):
The mixed-acid clusters investigated in this work represent a systematic substitution pathway designed to isolate the effect of incorporating a single MSA molecule into growing SA clusters. In our previous work (Rasmussen *et al.*, 2022), we found that clusters containing a single MSA molecule represented the most likely composition under most conditions. Consequently, the present calculations provide molecular-level insight into the thermodynamic role of MSA incorporation rather than predicting the most abundant mixed-acid cluster compositions under atmospheric conditions.

Major Comment 3. Lines 124–136 report training and validation set sizes and state "validation errors below 0.012 kcal mol^{-1}" without specifying whether this is MAE or RMSE, per-cluster or per-atom, and whether it applies to energies, forces, or both. No force error is given. This value is notably lower. The authors must clarify the metric and units, and verify that the reported accuracy

is consistent with the referenced methodology.

Author reply:

We agree that the meaning of this value was unclear. The validation error refers to the loss function defined in the reference methodology, which combines the mean absolute errors (MAEs) of the binding electronic energies and forces. We have revised this section to report the final validation of MAE and RMSE for the per-cluster binding electronic energies and the force-components.

Added lines (Subsection 2.3, Lines 140–148):

The models were trained for 600 epochs using the loss function as given in Kubecka *et al.* 2024. which yielded the validation metrics given in Table 1.

Table 1: The mean absolute errors (MAE) and root mean squared errors (RMSE) of the validation set in the final epoch. ΔE are the per-cluster binding electronic energies [kcal/mol] and F are the force-components [kcal/mol/Å].

System	MAE(ΔE)	RMSE(ΔE)	MAE(F)	RMSE(F)
SA-MSA-AM	0.12	0.15	0.08	0.14
SA-MSA-MA	0.10	0.19	0.10	0.15
SA-MSA-DMA	0.07	0.15	0.08	0.11

Major Comment 4. The phrase "atmospherically relevant" requires more careful justification. The introduction cites typical MSA concentrations of 10^5–10^7 molecules cm^{-3}, yet Figure 7 uses 10^9 molecules cm^{-3}. Similarly, AM at 10 ppb may be high for cold, pristine marine or polar environments. Provide explicit references for the chosen concentration ranges and include a sensitivity analysis or at least a discussion of how results would change under lower, more pristine conditions.

Author reply:

We thank the reviewer for this important comment. We agree that the highest MSA concentration considered (10^9 molecules cm^{-3}) exceeds typical atmospheric ranges. However, the purpose of this calculation was not to represent a realistic atmospheric scenario but rather to perform a sensitivity analysis to identify the conditions under which MSA begins to significantly influence cluster stability. We have revised the manuscript to clarify this motivation supporting the concentration ranges used for SA, MSA, and the base species. Furthermore, we now explicitly discuss that under lower and more representative atmospheric concentrations, the influence of MSA is expected to be weaker, consistent with the trends observed in our calculations.

Added sentence (Lines 301–305):
However, the highest MSA concentration considered in this work (10^9 molecules cm^{-3}) was intentionally chosen as a sensitivity test rather than to represent a typical atmospheric condition. This allows us to identify the concentration regime at which MSA begins to noticeably influence cluster stability and to better understand its potential thermodynamic role. Under more representative atmospheric MSA concentrations, the effect of MSA is expected to be correspondingly smaller.

Major Comment 5. The Data Availability statement points only to the ACDB Articles/ root directory, without providing a dedicated subdirectory, version, submission hash, or DOI. Upon verification, the link does not uniquely identify the new structures and thermochemical data reported

in this study. A direct, versioned dataset link with a citation is required.

Author reply:

The final data have now been updated in the ACDB database and can be found at the following link: https://github.com/elmjonas/ACDB/tree/master/Articles/hasan_2026_msa_fnp

Major Comment 6. The study does not directly compute particle sizes, formation rates, or observable particle numbers; it focuses on thermochemical properties of clusters up to 20 molecules. If the title emphasising "Formation and Growth" is retained, the manuscript should include size indicators (e.g., diameters) and some kinetic or dynamic support (e.g., evaporation rates, growth pathways). Alternatively, the title should be narrowed to reflect the actual content, such as "Stability and Composition of Large SA–MSA–Base Molecular Clusters".

Author reply:

We thank the reviewer for this valuable comment. We agree that particle sizes, formation rates, evaporation rates, and particle number concentrations are important quantities for assessing atmospheric new particle formation. However, the primary objective of the present study is to investigate the thermodynamic stability, composition, and structural evolution of large SA–MSA–base molecular clusters.

A quantitative prediction of cluster formation and growth kinetics would require a comprehensive kinetic treatment incorporating collision and evaporation rate coefficients for all relevant cluster compositions and growth pathways. This would roughly require at least three times the current work. Such calculations would constitute a separate kinetic study and are beyond the scope of the present thermochemical investigation. We have clarified this limitation in the revised manuscript and have avoided drawing conclusions regarding particle formation rates or observable particle number concentrations.

Following the recommendation of the reviewer, we have narrowed the title to better reflect the scope and principal findings of the study. The title has been changed to

"Stability and Composition of Large SA–MSA–Base Molecular Clusters"

Added sentence (Conclusion, Lines 347–349):
While these Gibbs free energies provide important thermodynamical insight into the potential role of MSA during cluster formation and early growth, quantitative predictions of atmospheric formation rates and particle growth kinetics require comprehensive kinetic modelling, which is beyond the scope of the present work.

Technical Corrections

Technical Correction 1. Abstract, line 7: "methane sulfonic acid" → "methanesulfonic acid".

Author reply:

Corrected as suggested.

Technical Correction 2. Abstract, line 16: "a secondary species that participate" → "a secondary species that participates".

Author reply:

Corrected as suggested.

Technical Correction 3. Line 41: "2nm" → "2 nm".

Author reply:

Corrected as suggested.

Technical Correction 4. Line 43: "around approximately 1.5 nm" – use either "around 1.5 nm" or "approximately 1.5 nm" (redundant).

Author reply:

Corrected, thanks for the suggestions.

Technical Correction 5. Lines 47–48: Add parentheses before and after "Almeida et al. (2013)" and clarify whether "ten acid and base molecules" means ten molecules total or ten acid–base pairs.

Author reply:

Corrected as suggested. Parentheses have been added around the citation, and the text has been clarified to specify that the clusters contain **ten acid–base pairs (20 molecules)**.

Technical Correction 6. Line 57: "marine environment" → "marine environments".

Author reply:

corrected

Technical Correction 7. Line 83: "up to n=10 acid-base molecules" → "up to n=10 acid–base pairs (20 molecules)".

Author reply:

corrected

Technical Correction 8. Lines 97–98: Revise "clusters of 1 to n=5" for clarity (e.g., "clusters with n = 1 to 5").

Author reply:

corrected

Technical Correction 9. Line 102: "improves finding global minimum" → "improves the likelihood of finding the global minimum"; use "global minima" when referring to several clusters.

Author reply:

corrected

Technical Correction 10. Line 120: "as implement in SchNetPack" → "as implemented in SchNetPack".

Author reply:

corrected

Technical Correction 11. Lines 122–124: "model to performed excellently" → "model to perform well"; "structures ... was used" → "structures ... were used".

Author reply:

corrected

Technical Correction 12. Line 132: "as following" → "as follows".

Author reply:

corrected

Technical Correction 13. Line 145: "Equation (1) ... describe" → "describes"; remove the comma in "with a 100 cm^{-1}, threshold".

Author reply:

corrected

Technical Correction 14. Line 158: "as a function of molecules in the cluster" → "as a function of the number of molecules in the cluster".

Author reply:

corrected

Technical Correction 15. Lines 169–171 and throughout: Standardise spacing in kcal mol^{-1} and all units (e.g., use non-breaking thin spaces where appropriate).

Author reply:

corrected throughout the manuscript

Technical Correction 16. Line 222: "MSA only affect" → "MSA only affects".

Author reply:

corrected

Technical Correction 17. Line 231: Remove "the" from "the our calculations".

Author reply:

corrected

Technical Correction 18. Figure 4: Reconcile 298Lmsa in the panels with 298Hmsa in the caption/text.

Author reply:

Corrected as suggested. They have now been corrected to "298Lmsa" to be consistent with the caption and main text.

Technical Correction 19. Line 246: "we see now role of MSA" – ambiguous; revise for clarity (likely a typo).

Author reply:

corrected

Technical Correction 20. Line 252: "the DMA-containing cluster remain" → "clusters remain" (or "the DMA-containing clusters remain").

Author reply:

corrected

Technical Correction 21. Section 3.2.4 heading: Standardise capitalization and spacing in "High MSA–high SA".

Author reply:

corrected

Technical Correction 22. Figure 7 caption: Remove the comma in "molec., cm^{-3}" and use "molecules cm^{-3}" consistently.

Author reply:

corrected

Technical Correction 23. Data availability: Replace the ACDB root link with a direct, versioned dataset link and citation.

Author reply:

The final data have now been updated at the following link: https://github.com/elmjonas/ACDB/tree/master/Articles/hasan_2026_msa_fnp

Technical Correction 24. References: Kirkby et al. (2011a, 2011b) appear to duplicate the same Nature article; Nadykto et al. (2014a, 2014b) also appear duplicated. Remove duplicates and retain single entries.

Author reply:

corrected

Technical Correction 25. References: Cooley et al. (2023) and Cromar and Lazrak (2023) lack complete bibliographic information (e.g., volume, page numbers, or DOI); provide full details.

Author reply:

corrected

Response to Referee #2

General assessment

Hasan et al. employed quantum chemical calculations, configurational sampling, and machine learning to investigate the role of methanesulfonic acid (MSA) in sulfuric acid (SA)–base clusters containing up to 20 monomers. The comparison among AM, MA, and DMA systems provides useful information on the thermodynamic difference between SA- and MSA-containing clusters. However, I have several concerns about whether the present calculations are sufficient to support the conclusions regarding nucleation and growth. In particular, the mixed-acid calculations include only one MSA molecule, while several conclusions are drawn for MSA-rich conditions. Hence, I recommend a major revision for this manuscript. The critical questions below need to be adequately addressed before the manuscript can be accepted.

Author reply:

Thank you for your comments. We will address all the comments as suggested.

Specific Comments

Comment 1. Page 3, lines 82–84: "Specifically, we perform quantum chemical calculations on clusters of the form $(\mathrm{MSA})_n(\mathrm{base})_n$ and $(\mathrm{SA})_{n-1}(\mathrm{MSA})_1(\mathrm{base})_n$, considering systems up to $n = 10$ acid-base molecules."

The mixed-acid series contains only one MSA molecule at every cluster size. Thus, the calculations compare pure SA, pure MSA, and a single-MSA substitution, but do not examine mixed-acid clusters containing two or more MSA molecules. The manuscript does not explain why this composition was selected. Considering that the MSA concentration is much higher than the SA concentration under some of the investigated conditions, could neglecting mixed-acid clusters containing more MSA molecules lead to an underestimation of the contribution of MSA to nucleation? I believe that this issue needs further discussion.

Author reply:

We thank the reviewer for raising this important point. This concern overlaps with Major Comment 2 raised by Reviewer 1. We agree that the original manuscript did not sufficiently explain the rationale for selecting the single-MSA mixed-acid series or the limitations associated with this compositional restriction.

The investigated systems include the two pure-acid endpoints, $(\mathrm{SA})_n(\mathrm{base})_n$ and $(\mathrm{MSA})_n(\mathrm{base})_n$, together with the single-substitution series $(\mathrm{SA})_{n-1}(\mathrm{MSA})_1(\mathrm{base})_n$. The latter was selected to isolate systematically the thermodynamic and structural effects of replacing one SA molecule with MSA in otherwise SA-rich clusters as the cluster size increases. This choice was also motivated by our previous study, in which clusters containing a single MSA molecule were predicted to represent the most likely mixed-acid compositions under most of the conditions examined (Rasmussen *et al.*, 2022).

However, we agree that mixed clusters containing two or more MSA molecules may become increasingly relevant when the gas-phase MSA:SA concentration ratio is very high. Although the gas-phase concentration ratio does not translate directly into the cluster composition, because incorporation

also depends on the relative binding free energies and evaporation tendencies of SA and MSA, excluding intermediate compositions of the form $(SA)_{n-m}(MSA)_m(base)_n$, where $2 \leq m \leq n-1$, could lead to an underestimation of MSA incorporation under strongly MSA-rich conditions.

The present calculations therefore cannot provide a complete prediction of the preferred atmospheric cluster compositions or quantify the overall contribution of MSA to nucleation. Such an assessment would require broader compositional sampling combined with kinetic modelling of cluster formation and evaporation. Besides, this would be very expensive to calculate. We have now clarified the rationale for selecting the single-MSA series and have explicitly discussed this limitation in the revised Discussion.

The following paragraph has been added to the Discussion.

Added Paragraph (Discussion, Lines 172–177):
The mixed-acid clusters investigated in this work represent a systematic substitution pathway designed to isolate the effect of incorporating a single MSA molecule into growing SA clusters. In our previous work (Rasmussen *et al.*, 2022), we found that clusters containing a single MSA molecule represented the most likely composition under most conditions. Consequently, the present calculations provide molecular-level insight into the thermodynamic role of MSA incorporation rather than predicting the most abundant mixed-acid cluster compositions under atmospheric conditions.

Comment 2. Page 6, lines 155–159: "The SA–base clusters were taken from Wu et al. (2024)."

The three types of clusters compared in Figure 1 were not obtained through the same configurational-sampling procedure. Pure MSA clusters were sampled with the full workflow, large mixed-acid clusters were treated using ML-assisted optimization, and pure SA clusters were taken from a previous study. Since configurational sampling can influence the identification of low-energy structures, these methodological differences may affect the comparison of relative cluster stability. The authors are encouraged to provide further details on how the structures in the three series were obtained and discuss the possible influence of using different sampling methods on the results.

Author reply:

We thank the reviewer for raising this important point. The differences among the sampling procedures reflect the chronological development of our computational workflow and the increasing computational cost associated with the larger mixed-acid clusters. The pure SA–base clusters were taken from Wu *et al.* (2024), where extensive configurational sampling and quantum-chemical evaluation had already been performed. The pure MSA–base clusters were generated using the same systematic configurational-sampling strategy. For the larger, mixed SA–MSA–base clusters, we employed our recently developed machine-learning-assisted optimization workflow to explore the configurational space more efficiently.

Importantly, the ML model was used solely to guide structural optimization, steering candidate conformers toward low-energy regions of the reference potential energy surface; it was not used as the basis for selecting the final structures or for determining the reported electronic energies. Every candidate conformer retained through the ML-assisted workflow was subsequently re-evaluated with quantum-chemical single-point calculations at the reference level. The final energy ranking was therefore based entirely on these quantum-chemical calculations rather than on the ML-predicted energies, and the relative binding energies reported for all three cluster series were evaluated consistently at the same quantum-chemical level.

We nevertheless acknowledge that no configurational-sampling procedure can guarantee identification

of the global-minimum structure, and that the use of different sampling strategies may introduce some uncertainty into comparisons across the three cluster series. We expect this effect to be limited, however, since all three series underwent extensive configurational exploration and the final candidate structures were evaluated consistently at the reference quantum-chemical level. Moreover, the ML-assisted optimization is expected to improve the candidate geometries relative to those obtained from the initial xTB sampling, bringing them closer to low-energy regions of the reference potential-energy surface.

We have revised the text to describe how the three cluster series were obtained and to discuss the possible influence of the different sampling procedures. The following paragraph has been added to the discussion.

Added paragraph (Discussion, Lines 150–154):
The SA–base clusters were taken from Wu *et al.* (2024). Nevertheless, all three cluster series underwent extensive configurational sampling protocol, and the final selected candidate structures were optimized consistently at the reference quantum-chemical level. Moreover, the ML-assisted optimization is expected to improve the candidate geometries relative to those obtained from the initial xTB sampling, bringing them closer to low-energy regions of the reference potential energy surface.

Comment 3. Sections 3.2 and 4: "both systems still exhibit an initial nucleation barrier," "MSA can influence the growth trajectory," and "the strong SA–DMA interaction leads to nearly barrierless cluster growth."

The manuscript evaluates the nucleation behavior mainly based on the concentration-dependent Gibbs free-energy profiles. However, when molecular clusters become sufficiently stable against evaporation, collisions between clusters may contribute significantly to their subsequent growth, in addition to cluster–monomer collisions. Under such conditions, a lower free-energy barrier does not necessarily indicate a larger contribution to actual particle formation, because the dominant growth pathway also depends on cluster concentrations and collision frequencies. Olenius et al. demonstrated that the main clustering pathways do not necessarily follow the lowest-free-energy route and that collisions between stable small clusters can contribute significantly to the growth of SA–DMA clusters (https://doi.org/10.1063/1.4819024). Therefore, I suggest that the authors supplement the thermodynamic analysis with a kinetic analysis that considers cluster–cluster collisions and evaporation processes to support their conclusions regarding the nucleation barriers and the contribution of MSA to particle formation.

Author reply:

We thank the reviewer for this valuable suggestion. This also aligns with Reviewer 1's Comment 6. We agree that kinetic modelling provides a more complete description of atmospheric particle formation. However, the primary objective of the present study is to investigate the thermodynamic stability of large mixed-acid clusters using quantum chemical calculations. A quantitative kinetic analysis would require collision and evaporation rate constants for all "off-diagonal" structures, together with comprehensive cluster-dynamics simulations, essentially tripling the required work. This would be computationally heavy expensive and beyond the scope of the present work. We have clarified this limitation in the revised manuscript and explicitly state that our conclusions are based on thermodynamic stability rather than kinetic particle formation rates.

We also narrowed the title to better reflect the scope and principal findings of the study. The title has been changed to

Added sentence (Conclusion, Lines 347–349):
While these Gibbs free energies provide important thermodynamical insight into the potential role of MSA during cluster formation and early growth, quantitative predictions of atmospheric formation rates and particle growth kinetics require comprehensive kinetic modelling, which is beyond the scope of the present work.

Comment 4. Page 9, lines 203–212: "Figures 3–7 present the binding Gibbs free energies... under four representative concentration regimes... These conditions were chosen to mimic typical chamber and atmospheric environments."

The MSA concentration of 10^9 molecules cm^{-3} represents a relatively extreme condition. Although an AM concentration of 10 ppb may occur in certain regions, it is unclear whether such a high AM concentration can coexist with low temperature, extremely high MSA concentrations, and 5 ppt MA or DMA under the atmospheric conditions discussed in this manuscript. Therefore, these favorable combinations should not simply be described as "atmospherically relevant" without observational support. The authors should relate the selected concentrations to specific atmospheric environments and discuss the results within the corresponding environmental context.

Author reply:

We thank the reviewer for this important comment. This also aligns with Reviewer 1's Comment 4. We agree that the highest MSA concentration considered exceeds typical atmospheric range. The purpose of this calculation was not to represent a realistic atmospheric environment but rather to perform a sensitivity analysis to identify the concentration regime at which MSA begins to noticeably influence cluster stability. We have revised the manuscript to clarify this motivation, included additional references for the selected concentration ranges, and explicitly discuss that under lower atmospheric MSA concentrations the influence of MSA is expected to be correspondingly weaker.

Added sentence (Lines 301–305):
However, the highest MSA concentration considered in this work (10^9 molecules cm^{-3}) was intentionally chosen as a sensitivity test rather than to represent a typical atmospheric condition. This allows us to identify the concentration regime at which MSA begins to noticeably influence cluster stability and to better understand its potential thermodynamic role. Under more representative atmospheric MSA concentrations, the effect of MSA is expected to be correspondingly smaller.

Comment 5. Page 14, line 303 to page 15, line 325: "MSA contributes primarily during the early growth regime rather than the initial nucleation step itself."

The authors conclude that MSA contributes primarily to cluster growth rather than the initial nucleation process. However, this conclusion appears inconsistent with recent experimental and modeling evidence obtained under cold atmospheric conditions. Baalbaki et al. experimentally demonstrated that MSA nucleates together with NH_3 below -10 °C at rates comparable to SA–NH_3, and that MSA and SA can act synergistically in multi-acid nucleation (https://doi.org/10.1038/s41586-026-10810-2). Consistently, Ning et al. showed through quantum-chemical calculations, cluster-dynamics simulations, and global modeling that MSA can enhance SA–NH_3 nucleation rates by 1–3 orders of magnitude and may dominate marine upper-tropospheric new particle formation (https://doi.org/10.1073/pnas.2606521123). These recent studies suggest that the present manuscript may underestimate the contribution of MSA to the initial nucleation process. The authors should cite and discuss these studies and clarify why the present thermodynamic analysis

leads to a different interpretation of the role of MSA.

Author reply:

We thank the reviewer for highlighting these important recent studies. The study by Baalbaki *et al.* (2026) was published after the original submission of our manuscript and was therefore not available for consideration at that time. Nevertheless, we agree that it is directly relevant and have incorporated it, together with the study by Ning *et al.* (2026), into the revised manuscript.

We agree that our original statement that MSA contributes primarily to early growth rather than initial nucleation was too general. Baalbaki *et al.* (2026) demonstrated that MSA can nucleate with NH_3 at and below −10 °C at rates comparable to those of SA–NH_3 and can participate in synergistic multi-acid nucleation. Similarly, Ning *et al.* (2026) predicted that MSA can enhance SA–NH_3 nucleation rates by 1–3 orders of magnitude under cold marine upper-tropospheric conditions.

These studies consider NH_3, multi-MSA compositions, and kinetic nucleation processes, whereas the present work investigates the thermodynamic stability of selected neutral clusters containing AM, MA, or DMA and restricts the mixed-acid series to one MSA molecule. Our calculations therefore cannot provide quantitative nucleation rates or exclude an important contribution of MSA to initial nucleation under cold, NH_3-containing conditions.

An additional important distinction is that the present calculations do not include water. Recent CLOUD experiments by Yu *et al.* (2026) demonstrated that the contribution of MSA to particle growth is strongly dependent on relative humidity. Between +10 °C and −10 °C, MSA drove rapid particle growth at high relative humidity ($> 50\%$), whereas its contribution was negligible under low-humidity conditions ($< 16\%$). Our unhydrated calculations cannot capture this water-mediated enhancement of MSA uptake and cluster stabilization. Consequently, our results are not necessarily inconsistent with the CLOUD observations; rather, the comparison highlights the important role of water in determining the contribution of MSA to atmospheric particle formation and growth.

We have therefore cited and discussed Baalbaki *et al.* (2026) and Ning *et al.* (2026) in the revised Introduction. We have additionally cited Yu *et al.* (2026) and discussed the influence of water and relative humidity in the revised Conclusions.

Added sentence (Lines 83–87):
More recently, Baalbaki *et al.* (2026) reported that MSA can substantially enhance both nucleation and particle growth through synergistic interactions with sulfuric acid under cold marine conditions. Consistently, Ning *et al.* (2026) showed through quantum-chemical calculations, cluster-dynamics simulations, and global modeling that MSA can enhance SA–NH_3 nucleation rates by 1–3 orders of magnitude and may dominate marine upper-tropospheric new particle formation.

We have removed the original statement from conclusion

> "The calculations further indicate that MSA contributes primarily during the early growth regime rather than the initial nucleation step itself."

and replaced it with the following text in the Conclusions (Page 14, Lines 333–341):

> Within the specific neutral amine-containing systems and single-MSA compositions investigated here, the calculations indicate that MSA incorporation becomes thermodynamically more favourable as the cluster size increases. This trend should not, however, be interpreted as evidence that MSA contributes exclusively or predominantly to growth rather than initial nucleation under all atmospheric conditions.

An important limitation of the present calculations is the omission of water. Recent CLOUD experiments demonstrated that, between +10 °C and −10 °C, MSA drives rapid particle growth at high relative humidity (> 50%), whereas its contribution is negligible under low-humidity conditions (< 16%) (Yu *et al.*, 2026). The comparatively weak contribution of MSA predicted by our unhydrated calculations is therefore not necessarily inconsistent with these experimental observations. Rather, the comparison highlights the important role of water in stabilizing MSA-containing clusters and indicates that hydration should be included in future thermodynamic and kinetic investigations.

Minor Comments

Minor Comment 1. Abstract, line 17: "a secondary species that participate." "Participate" should be changed to "participates".

Author reply:

corrected

Minor Comment 2. Page 2, line 41: "Experimental characterization of clusters smaller than 2nm remains extremely challenging". "2nm" should be changed to "2 nm".

Author reply:

corrected

Minor Comment 3. Page 2, lines 47–48: "Moreover, these measurements are typically limited to clusters containing up to roughly ten acid and base molecules Almeida et al. (2013)". Please add the citation of Almeida et al. (2013) in a correct format.

Author reply:

corrected

Minor Comment 4. Page 5, lines 140–150, Equation (1): "Equation (1) above describe" should be changed to "Equation (1) above describes".

Author reply:

corrected

Minor Comment 5. Page 6, lines 169–172: The font used for several numerical values and mathematical symbols, such as "-264," "-183," "approximately 81," and "approximately 55–62 kcal mol^{-1}," is inconsistent with the font of the surrounding text. Please standardize the font and formatting of all numerical values, mathematical symbols, and units throughout the manuscript.

Author reply:

corrected as suggested

Minor Comment 6. Figure 4: The panel headings use "298Lmsa," whereas the caption and main text define the condition as "298Hmsa." Please verify the intended condition and use the label consistently throughout the manuscript.

Author reply:

Corrected as suggested. They have now been corrected to “298Lmsa” to be consistent with the caption and main text.

Minor Comment 7. Figures 1 and 3–7: Many composition labels overlap and are difficult to read.

Author reply:

The figures are now updated accordingly.