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.

Specific Comments:

Comment 1: Page 3 lines 82–84: "Specifically, we perform quantum chemical calculations on clusters of the form $(MSA)_n(base)_n$ and $(SA)_{n-1}(MSA)_1(base)_n$, 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.

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.

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.

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.

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.

Minor Comments:

Comment 1: Abstract, line 17: "a secondary species that participate."

"Participate" should be changed to "participates".

Comment 2: Page 2 line 41: "Experimental characterization of clusters smaller than 2nm remains extremely challenging".

"2nm" should be changed to "2 nm".

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.

Comment 4: Page 5 lines 140–150, Equation (1).

“Equation (1) above describe” should be changed to “Equation (1) above describes”.

Comment 5: Page 6, lines 169–172.

The font used for several numerical values and mathematical symbols, such as “-264,” “-183,” “~81,” and “~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.

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.

Comment 7: Figures 1 and 3–7.

Many composition labels overlap and are difficult to read.