jz-2022-01872u.R1

Name: Peer Review Information for "Charge Gradients Around Dendritic Voids Cause Nanoscale Inhomogeneities in Liquid Water"

First Round of Reviewer Comments

Reviewer: 1

Comments to the Author

This manuscript reports experimental femtosecond elastic second harmonic scattering (fs-ESHS) and simulations pertaining to the charge and polarizability fluctuations associated with voids in water and a CCl4 or a Lennard-Jones fluid. The comparisons of the experimental and simulation results are interpreted as indicating that the angle and polarization dependent fs-ESHS from water arises primarily from voids of approximately nanometer size and picosecond lifetime. Although this is an interesting suggestion, it seems that this is a possible rather than definitive interpretation. Nevertheless, this strikes me as a valuable contribution to open questions regarding the dynamic structure and charge fluctuations in liquid water.

1.   The first three sentences of the abstract seem to me to be out of place in this work as they suggest that the primary objective is to critically test the two-state model of liquid water, while the manuscript indicates that "… this study neither confirms nor disproves the two state water hypothesis." Thus, it seems to me that the manuscript might more realistically be framed as addressing the nature of the charge fluctuations associated with voids in liquid water. In other words, I would advise staying away from two-state hypothesis for the structure of water, or if the authors insist in relating their work to such controversial hypotheses then they might present this work as an experimental and theoretical study of "nano-bubbles" in water.

2.   The following three phrases at the end of the abstract are overly vague:

a.   "…do not necessarily relate to the proposed two state model of water…"

b.   "…underscore the elusive nature of liquid water…"

c.   "…undoubtedly have an impact on any type of transition that occurs in liquid water."

3.   The above comment also pertains to the last sentence of the conclusions – I suggest that both sentences be made more specifically informative.

4.   Can the results shown in Fig. 1C be fit to the same model that was used to fit the points in Figure 1B? If so, what do those fits look like and what does that mean? If they can't be fit accurately, then it would still be useful to show what the best fit looks like, and to explain what that means.

5.   What void sizes were probed in generating the histogram in Fig. 2C?

6.   The following text on page 6 is confusing as it looks like it is citing reference number 6: "…of (size)6 for…"

7.   It is not clear if, or how, LS-DFT was used to determine there are no charge density fluctuations in the LJ fluid. Do the LJ fluid calculations pertain to a classical LJ fluid? If so, then a more relevant comparison would be for liquid Argon or better yet liquid CCl4.

Reviewer: 2

Comments to the Author

The authors confirmed the existence of cavities or voids in liquid water by means of fs-ESHS measurements of liquid CCl4 and water in combination with MD simulation. They also analyzed the lifetime of the voids and temperature dependence of void volumes with the help of molecular dynamics simulation, and the consistency with the fs-ESHS measurements was discussed. The manuscript is well written, and the topics and the reported results are interesting.

1.   What is the major advance reported in the paper?

The authors proposed a novel picture of the hydrogen-bonding liquid water by defining "void" in the bulk liquid. This report may be a breakthrough for discussing a new aspect of liquid water, and is worth publishing in J. Phys. Chem. Lett.

2. What is the immediate significance of this advance?

There have been many controversial discussions on the structure of water such as "uniform water picture", "2-state water hypothesis", "polymeric water", and so forth. The author's experiments and theoretical calculations will attract much attention in the physical chemistry community, because their findings are completely original and novel.

2.   Technical suggestions

Major:

1.   Though I think the interpretation of the author's experiments and calculations is correct, I wonder whether "void" is a general structure for other hydrogen bonding liquids such as methanol.

2.   In terms of Fig. 2B, why does IC density show positive near the void? Is this consistent with the charge distribution at an air/water interface?

3.   In terms of Fig. 3D, the authors measured the ratio of the measured coherent to incoherent SH intensity at about 265 K. Does this mean crystal ice also has voids similar to those in liquid water? In addition, I wonder if the authors could elaborate on a sudden increase of PPP/SSS at about 278K in Fig. 3D.

4.   In terms of Fig. 3C, the authors confirmed the temperature dependence of probability distribution of void volumes. I think its pressure dependence can be easily addressed by the MD simulation, which should be discussed in the SM.

Minor:

5.   At Line 59 on Page 4: "This date is provided" should be "This data is provided"

6.   The caption of Fig. S4 states that A), B), C), and D), but I cannot find D) in the figure. The labels are also inconsistent with those in the figure.

7.   In the sentences below Eq.(S5), the authors state "Eq.(S6) gives the contribution of the subsystem …". I think "Eq.(S6)" should be "Eq.(S5)" in this context. Is this my misunderstanding?

8.   In the caption of Fig. S5, "(2)" should be "(b)".

Author's Response to Peer Review Comments:

Answers to the referee reports:

We would like to thank the referees for carefully reading our manuscript and for providing us with valuable comments and suggestions to improve the manuscript. We have revised the manuscript on the basis of the comments and we present our detailed replies below. Our responses to the comments are blue.

Reviewer: 1

Recommendation: This paper is publishable subject to minor revisions noted. Further review is not needed.

Comments:
This manuscript reports experimental femtosecond elastic second harmonic scattering (fs-ESHS) and simulations pertaining to the charge and polarizability fluctuations associated with voids in water and a CCl4 or a Lennard-Jones fluid. The comparisons of the experimental and simulation results are interpreted as indicating that the angle and polarization dependent fs-ESHS from water arises primarily from voids of approximately nanometer size and picosecond lifetime. Although this is an interesting suggestion, it seems that this is a possible rather than definitive interpretation. Nevertheless, this strikes me as a valuable contribution to open questions regarding the dynamic structure and charge fluctuations in liquid water.

1. The first three sentences of the abstract seem to me to be out of place in this work as they suggest that the primary objective is to critically test the two-state model of liquid water, while the manuscript indicates that "… this study neither confirms nor disproves the two state water hypothesis." Thus, it seems to me that the manuscript might more realistically be framed as addressing the nature of the charge fluctuations associated with voids in liquid water. In other words, I would advise staying away from two-state hypothesis for the structure of water, or if the authors insist in relating their work to such controversial hypotheses then they might present this work as an experimental and theoretical study of "nano-bubbles" in water.

We thank the reviewer for these comments and suggestions. We have now revised the abstract in a manner that reports on the findings without making reference to the two-state structure hypothesis. The Abstract now reads as the following:

Water is the matrix of life and serves as a solvent for numerous physical and chemical processes. The origins of the nature of inhomogeneities that exist in liquid water and the timescales over which they occur, remains an open question. Here, we report femtosecond elastic second harmonic scattering (fs-ESHS) of liquid water in comparison to an isotropic liquid (CCl$_4$) and show that water is indeed a non-uniform liquid, The coherent fs-ESHS intensity was interpreted, using molecular dynamics simulations, as arising from charge density fluctuations with enhanced nanoscale polarizabilities around transient voids having

an average lifetime of 300 fs. Although voids were also present in CCl$_4$, they were not characterized by hydrogen bond defects and did not show strong polarizability fluctuations, leading to fs-ESHS of an isotropic liquid. The voids increased in number at higher temperatures above room temperature, in agreement with the fs-ESHS results.

2. The following three phrases at the end of the abstract are overly vague:
a. "…do not necessarily relate to the proposed two state model of water…"
b. "…underscore the elusive nature of liquid water…"
c. "…undoubtedly have an impact on any type of transition that occurs in liquid water."

We agree completely with the reviewer and have edited the three phrases.

3. The above comment also pertains to the last sentence of the conclusions – I suggest that both sentences be made more specifically informative.

We agree with the reviewer. The last sentence is now more informative and reads as the following:

Femtosecond transient nanoscale structural inhomogeneities in water as reported here are likely to influence physical and chemical properties of solutions and interfaces. The non-uniform potential energy landscapes that are connected to their presence will impact diverse properties such as solubility, chemical reaction intermediates, and electrostatic potentials.

4. Can the results shown in Fig. 1C be fit to the same model that was used to fit the points in Figure 1B? If so, what do those fits look like and what does that mean? If they can't be fit accurately, then it would still be useful to show what the best fit looks like, and to explain what that means.

Yes, this will result in the below graph:
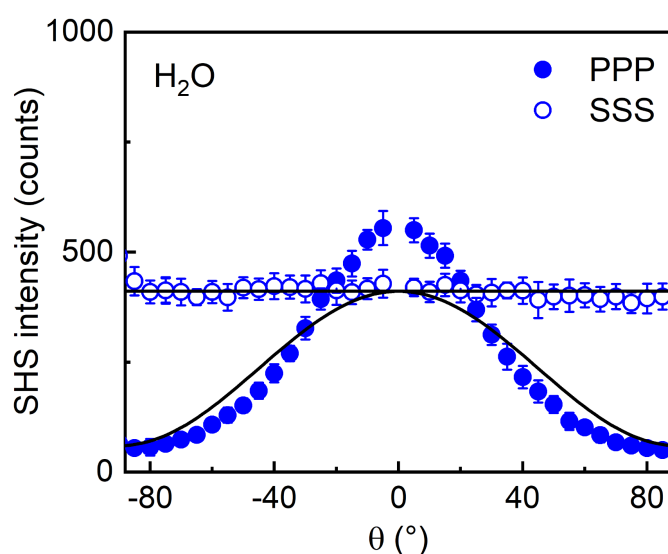
Figure 1: fs- ESHS patterns of neat H_2O (C) collected at room temperature, using beams with all electromagnetic fields oscillating in the horizontal scattering plane (PPP) and the orthogonal vertical plane (SSS). The lines in the panel represent the fs-ESHS emission of isotropic liquid (S2).

It means that the obtained SHS response cannot be described by incoherent light scattering. Since the hallmark of that is the scattered intensity around the forward direction we do not think there is a whole lot of added value in the presented analysis. We therefore haven't included it in the manuscript.

5. What void sizes were probed in generating the histogram in Fig. 2C?

Figure 2C reports on the distribution of the lifetime of the voids. It is constructed using voids of different sizes ranging from volumes ~25 to ~200 $Å^3$ and is the source of the rather broad distribution.

6. The following text on page 6 is confusing as it looks like it is citing reference number 6: "…of (size)6 for…"

We corrected the text to: … *of size to the power of six for* …

7. It is not clear if, or how, LS-DFT was used to determine there are no charge density fluctuations in the LJ fluid. Do the LJ fluid calculations pertain to a classical LJ fluid? If so, then a more relevant comparison would be for liquid Argon or better yet liquid CCl4.

We thank the reviewer for this question. In fact, the LJ liquid that was used was that of liquid argon. However, as one might expect without even doing the LS-DFT calculation, there is no charge transfer between argon atoms and therefore there are no charge oscillations. We agree that CCl_4 would be interesting to examine. However, it was beyond the scope of the current study to conduct both MD and LS-DFT calculations on CCl_4.

Reviewer: 2

Recommendation: This paper is probably publishable, but major revision is needed; I do not need to see future revisions.

Comments:
The authors confirmed the existence of cavities or voids in liquid water by means of fs-ESHS measurements of liquid CCl4 and water in combination with MD simulation. They also analyzed the lifetime of the voids and temperature dependence of void volumes with the help of molecular dynamics simulation, and the consistency with the fs-ESHS measurements was discussed. The manuscript is well written, and the topics and the reported results are interesting.
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2. What is the immediate significance of this advance?
There have been many controversial discussions on the structure of water such as "uniform water picture", "2-state water hypothesis", "polymeric water", and so forth. The author's experiments and theoretical calculations will attract much attention in the physical chemistry community, because their findings are completely original and novel.

2. Technical suggestions

Major:
1. Though I think the interpretation of the author's experiments and calculations is correct, I wonder whether "void" is a general structure for other hydrogen bonding liquids such as methanol.

We thank the reviewer for this question. Indeed the voids are not specific to just liquid water. In previous studies we have demonstrated the presence of voids in many other non-hydrogen bonded liquids. The voids have to do the packing of molecules and how they arrange relative to each other modulated by the chemical details which can affect the roughness of the voids.

In unpublished work, we also examined the voids in methanol and found large dendritic voids. The difference between the liquids is then how the electronic fluctuations along hydrogen bonds or non-polar interactions are coupled with the density fluctuations (voids).

2. In terms of Fig. 2B, why does IC density show positive near the void? Is this consistent with the charge distribution at an air/water interface?

We thank the reviewer for this question. Indeed also at the air-water interface, closer to the surface, there is a layer of positively charged water, albeit to a much lesser degree than what is observed around the voids. Recall that the origins of the fluctuations in charge leading to the presence of positive and negatively charged layers, originates from asymmetries in the

hydrogen bond network. The concentration of these defects are obviously different at the surface of water than compared to water around a void. Figure R1 below shows the different charge contributions of the different types of water topologies for the perusal of the reviewer and editor:
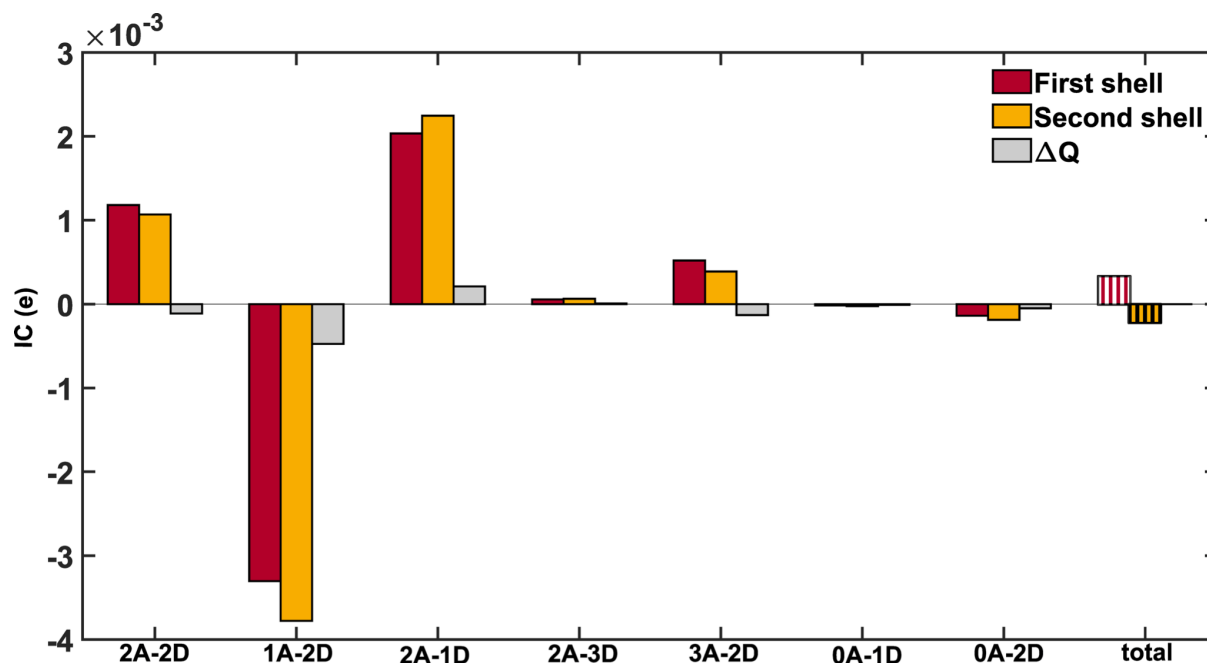

Fig. R1: Integrated charge associated with different types of defects within the probe volume of radius 3 Å (First shell) and 5 Å (Second shell). ΔQ is the difference between the charge of the first and second shell.

3. In terms of Fig. 3D, the authors measured the ratio of the measured coherent to incoherent SH intensity at about 265 K. Does this mean crystal ice also has voids similar to those in liquid water? In addition, I wonder if the authors could elaborate on a sudden increase of PPP/SSS at about 278K in Fig. 3D.

The water was not frozen, but supercooled (266 K). The increase at 277 K is real as it has been reproduced many times. We agree with the referee that this is extremely interesting and are planning to do more measurements in that temperature range. For now our temperature cell is broken, so we cannot check.

4. In terms of Fig. 3C, the authors confirmed the temperature dependence of probability distribution of void volumes. I think its pressure dependence can be easily addressed by the MD simulation, which should be discussed in the SM.

We thank the reviewer for the question. We have already shown in previous work that under pressure, the hydrogen bond network evolves so that the second shell collapses which ultimately leads to the creation of only spherical voids. We reproduce in Figure R2 below the figure from an earlier paper where we reported in the Supporting Information the distribution of the size of the voids for water under pressure:
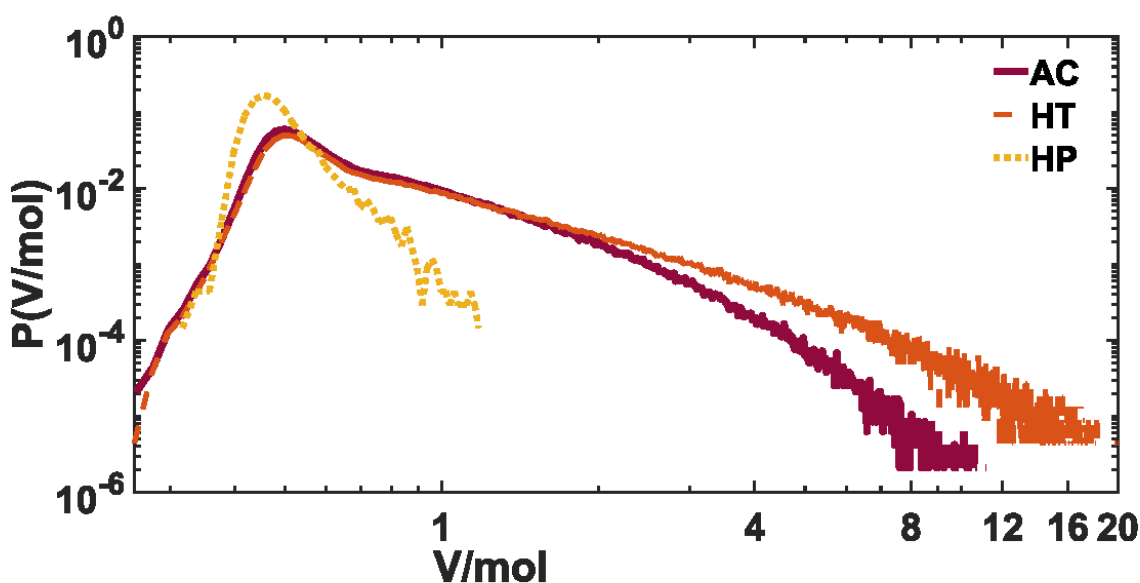
Fig. R2: The distribution of the volume of voids in liquid water at three thermodynamic conditions: 1) ambient condition (AC) where T=300 K and P=1 Pa, 2) high temperatures (HT) where T=350 K and 3) high pressure (HP) where P=1 GPa. The volumes of the voids are normalised to the molecular volume of water at ambient condition (30 Å^3).

Minor:
5. At Line 59 on Page 4: "This date is provided" should be "This data is provided"

We corrected the typo.

6. The caption of Fig. S4 states that A), B), C), and D), but I cannot find D) in the figure. The labels are also inconsistent with those in the figure.

We corrected the text in the caption.

7. In the sentences below Eq.(S5), the authors state "Eq.(S6) gives the contribution of the subsystem …". I think "Eq.(S6)" should be "Eq.(S5)" in this context. Is this my misunderstanding?

We thank the reviewer for spotting this typo. We corrected it.

8. In the caption of Fig. S5, "(2)" should be "(b)".

We corrected the typo.