

Intrinsic Physicochemical Activity at Microplastic-Water Interfaces

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This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Attachments originally included by the reviewers as part of their assessment can be found at the end of this file.

Version 0:

Reviewer comments:

Referee #1

(Remarks to the Author)

Review of manuscript 2025-11-29713

Qian et al. present a timely and provocative study that challenges the long-standing assumption that microplastics (MPs) are chemically inert in aqueous environments. The authors begin with reporting that polystyrene microplastics (PS-MPs), when simply dispersed in water, spontaneously generate hydroxyl radicals, supported by several independent experimental measurements. The finding that addition of surfactants such as Triton X-100 fully suppresses this reactive oxygen species (ROS) signal strongly suggests that the MP-water interface is essential to the observed reactivity. The authors further link this ROS formation to charge accumulation on the MPs.

Next, the authors demonstrate that this phenomenon extends across multiple MP chemistries, implying a more general interfacial mechanism rather than a polymer-specific artifact. Complementary molecular dynamics simulations and ab initio calculations are employed to rationalize the origin of the OH radicals, proposing that interfacial dangling hydroxide species donate electrons to the polymer surface, producing negatively charged MPs and releasing radicals. The overall narrative is coherent, and the mechanistic hypothesis is plausible, logically smooth, though certain aspects require clearer exposition in the current form. The manuscript also extends the discussion to potential biological implications, including interactions with biomolecules and cells.

The reported ROS generation associated with MP uptake in cells has been widely observed but usually interpreted as a cellular stress response (few more citations and discussion shall be added). Qian et al.'s results raise the possibility that MPs themselves may be the ROS source, which in my opinion, has not been previously recognized. This work therefore opens an important line of inquiry into an interface that has been largely overlooked. The potential impact spans environmental chemistry, toxicology, materials science, and water research.

In my view, the study presents interesting findings via substantial experiments, that could be suitable for publication in Nature. However, several key discussions are currently unclear, fragmented, incorrect, and unvalidated. In its current form, it is not suitable for publication.

Below I outline major concerns:

1. Insufficient comparison for the theoretical findings.

The authors report vertical ionization energy (VIE) distributions of interfacial OH⁻ near PE and PMMA surfaces, where PE exhibits a small but distinct low-VIE tail. This shift is interpreted as evidence that “dangling” interfacial hydroxide species are more energetically favored to electron transfer, thereby rationalizing the observed ROS release and charge accumulation on MPs. Conceptually, this is a reasonable mechanistic link.

However, the current analysis relies only on two materials representing opposite extremes: PE (positive) and PMMA (negative, showing no VIE shift). Using two data points is insufficient to establish a robust correlation between VIE behavior and the experimentally observed chemical activity.

At minimum, a third MP system (such as PVC or PS) should be included to strengthen the argument. It appears that the simulations for additional polymers already exist (e.g., Fig. 4e) and incorporating VIEs from at least one of these into Fig. 4a&b would substantially enhance the credibility and generality of the proposed mechanism.

2. Discussion of accumulation and electrostatics of OH⁻.

The manuscript proposes that negatively charged MPs facilitate electron transfer from interfacial OH⁻. Later authors report the observation that removal of Na⁺ (to mimic a stronger local electric field) yields an even lower VIE for OH⁻ near the PE surface.

The current discussion is too brief and not very convincing. First, simply removing Na⁺ will not capture the fact that charges come from the MP and the resulting electric field's direction. Also, if progressively more negative MPs monotonically lower the VIE of nearby OH⁻, one might expect an unrealistic runaway accumulation of charge. To make the mechanistic picture quantitatively credible, the authors should clarify this balance.

A better way of representing a charged MP (but not the entire system) should replace the current over-simplification to show more realistic behavior.

3. Benchmarking of combined forcefield.

In the Supporting Information, the authors employ a mixed force-field scheme: ReaxFF/CGem for water and ions, and OPLS-AA for the polymer matrices. While each component of this hybrid setup is individually well established, the key phenomena reported in this study: interfacial OH⁻ behavior, charge redistribution, and electron-transfer relevant configurations, occur precisely at the interface where the two FFs interact. This raises a concern about the reliability of cross-interface energetics and structural features, especially considering that the ReaxFF and OPLS use completely different formulas. It is unclear under such coupling whether OH⁻ truly "sees" the polymer surface with appropriate energetics or effectively interacts with something closer to a vacuum environment decorated with point charges.

It is unclear to me whether the specific ReaxFF/CGem + OPLS-AA combination has been benchmarked in previous studies involving polymer–water interfaces or ion–polymer interactions. The authors should either cite appropriate prior work validating such cross-FF coupling or provide benchmarking of their own. Examples could include energies comparison with DFTs, interfacial RDF profiles, hydration structure around polymer surfaces, or comparison of ion adsorption propensities with established results. Even limited tests would help establish that the hybrid representation does not introduce systematic bias.

At the very least, the authors should explicitly discuss which aspects of interfacial physics may be over/underestimated by the combined FF. Given the centrality of the simulations to the mechanistic interpretation, transparent acknowledgment of potential limitations is necessary to support the robustness of the computational conclusions.

Also, more detailed narration of how the two FFs interact (and how their cross-terms are handled) are needed.

4. Inclusion of interfacial surroundings in the VIE calculations

The Supporting Information describes a reasonable and established protocol for computing VIE. However, the authors note that "each calculation includes explicit solvent within 6 Å of the hydroxide ion." It is unclear whether this truncation removes the MP surface itself from the quantum region.

I think this point is critical. In Fig. 4e, the authors show that MPs can directly form hydrogen bonds or other specific interactions with OH⁻ at the interface. PMMA may also build those HBs. If these polymer–OH⁻ contacts are excluded from the VIE environment, an essential component of the interfacial electronic structure may be missing.

Authors should clarify whether the polymer surface is explicitly included in the VIE calculations, and if not, provide justification for why its exclusion would not materially affect the computed ionization energies.

5. Surface of MPs in simulation

In the current version, the manuscript lacks discussion of what the MP surfaces actually look like in the simulations. A key aspect of MPs is their structural flexibility, so their surface can be amorphous. Also, several of the polymers used in the simulations (e.g., PVC, PET) have functional groups, meaning that if the polymer surface can reorganize, it may selectively expose different functional groups to the aqueous phase. Such surface reconstruction may strongly influence local hydration structure, hydrogen-bonding patterns, and ion accessibility, etc.

Authors shall report some basic characteristics such as polymer density, the distribution of exposed functional groups, and whether surface segments remained stable or underwent significant rearrangement during the simulations. A brief characterization of the polymer models would considerably improve interpretability.

In addition, while the study shows properties of MP, in simulation authors apply a slab of plastic, which essentially means an infinitely large plastic surface. Surely, this is a certain trade-off as experimentally micro-size MPs are used. Yet, some theoretical discussion would strengthen the study. For example, the authors may also consider reproducing the PE results using a more crystalline or otherwise rigid surface as a comparison, to illustrate the sensitivity of interfacial behavior to polymer structural rigidity.

6. Discussion of biomolecule and cells.

The final section of the manuscript extends the narrative to interactions between MPs, biomolecules, and cells. While this topic is inherently interesting, the current presentation feels disconnected from the central mechanistic findings. The manuscript does not clearly articulate how the proposed interfacial radical release from MPs translates into the biological effects described, nor how the biological observations feed back into the mechanistic framework. Also, things like MP-protein corona have been widely reported.

The causal chain needs to be explicitly established. For example, authors reported cell damage caused by MPs, but is it from the OH radical attack? Alternatively, if the biological section is meant to be speculative or contextual rather than mechanistically grounded, this should be stated clearly. As of current, this part only reports a r-score. As it stands, the section reads as an isolated discussion without sufficient integration into the main narrative.

Some of my minor concerns are listed as well:

1. The title is confusing. The “intrinsic physicochemical activity” appears to be too broad.
2. PS-MP can be de-color the MO, presumably through OH radical. If the radical trapper (HDMP=O) is also added with PS-MP, can MO maintain its color?
3. The role of surfactants is central to experimental observations. However, the theoretical treatment of this component is extremely limited. In the main text, the simulations involving Triton are addressed only in a single sentence, and the Supporting Information provides only one figure (Fig. S10) without further mechanistic discussion. Since these simulations are done, authors shall elaborate more.
4. A few more discussions about the MP-water interfaces, compared to that of air-water/oil-water interfaces, may strengthen the influence and broaden the readership.
5. Fig. 1f appears only at the end of the figure sequence (after Fig. 1k), which disrupts the flow. Reordering the panels so that Fig. 1f appears in its natural position would improve readability.
6. In my view, the fluorescence measurement in Fig. 2g conveys more critical information than the individual pictures shown in Fig. 2d–f. However, Fig. 2g is presented to be much smaller. Enlarging Fig. 2g would improve clarity.
7. Fig. 4d illustrates the simulation configuration, which is essential for readers to understand the computational framework. The panel is currently small and difficult to see. Enlarging it or improving its visual clarity would be very helpful.
8. Authors add NaOH in simulation to manually add OH⁻. It seems to have only 4 NaOH (so 4 OH⁻), then how could dangling OH ratio to be around ~15%? Maybe it is time-resolved, then methods and equations for these analysis and sampling are entirely missing here.

Referee #2

(Remarks to the Author)

I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

Referee #3

(Remarks to the Author)

This manuscript presents a carefully executed study that investigates physicochemical activity at microplastic-water interfaces. While the experimental work is thorough and the combination with computational simulations is commendable, I have significant reservations regarding the novelty and conceptual advance of the core findings in the context of the recently published literature, specifically in relation to Nature 640, 87–93 (2025), titled “Water structure and electric fields at the interface of oil droplets.” The central mechanistic claim—that hydrophobic aqueous interfaces can generate strong electric fields which lower the energetic barrier for hydroxide ion oxidation, leading to spontaneous hydroxyl radical generation—appears to be a direct extension of principles already established in the realm of water microdroplet and liquid-liquid interface chemistry. The cited Nature 2025 paper (Ref. 34 in the manuscript) provides a detailed experimental and theoretical framework for this phenomenon at oil-water interfaces. The present study effectively applies this established framework to a new substrate (solid microplastics) rather than discovering a fundamentally new mechanism. The observation that this activity correlates with hydrophobicity and can cause biomolecular damage is logical and expected based on the prior work, thus diminishing the sense of a paradigm-shifting breakthrough.

The societal relevance of microplastics is undeniable, and the demonstration that this interfacial chemistry operates on a pervasive environmental contaminant is an important application. However, for publication in Nature, where the threshold for fundamental new conceptual insight is extremely high, the work in its current form may be perceived as an incremental, albeit well-performed, advance within an already emerging field, rather than the initiation of a new one.

Major Comments:

1. The authors' previous study published in Nature (2025, 640, 87–93) focused on electric field formation and radical generation at hydrophobic–water interfaces. It would be helpful for the authors to further clarify whether the microplastic–

water interfaces discussed in the present manuscript share mechanistic similarities with those systems, and to more explicitly articulate the conceptual novelty of this work in relation to their prior findings.

2. The detection of radicals at plastic–water interfaces is not inherently contradictory to the chemical inertness of commercial plastics. Chemical inertness should primarily be understood as the long environmental persistence of polymeric materials, i.e., their resistance to bulk degradation or transformation, rather than the inability of their surfaces to participate in interfacial radical processes. Indeed, previous studies have shown that aged microplastics (e.g., after light exposure or chemical oxidation) can generate persistent radicals and exhibit appreciable degradation activity toward aqueous pollutants, while the polymer matrix itself remains largely intact over extended reaction periods. This distinction could be more clearly articulated in the manuscript.

3. From a biosafety perspective, the presence of radical-active interfaces would be expected to induce oxidative stress responses in biological systems, particularly for charged biomolecules. This outcome appears to be largely foreseeable.

4. In Figure 1c, appreciable methyl orange (MO) degradation is observed only in PS-dispersed aqueous systems, which is relatively intuitive, as alcohols are frequently employed as hydroxyl radical scavengers in radical identification experiments. In this context, the statement “In contrast, PS–ethanol interface, which does not exhibit evident ROS generation or MO degradation (Fig. 1c, d), shows near-neutral surface zeta potentials and minimal Rh800 surface partitioning (Fig. 2c, f, g). This again highlights the crucial role of water in activating microplastic surfaces with negative charges” may require further justification, as the interpretation could be influenced by radical quenching effects rather than solely by interfacial electrification.

5. While the manuscript emphasizes the role of hydroxyl radicals at the interface, it would be valuable to consider the contribution of surface-adsorbed hydroxyl radicals. For instance, comparative experiments using NaF could help distinguish between free and adsorbed $\bullet\text{OH}$ species by examining changes in detectable radical concentrations. In addition, the possible involvement of other reactive species in the reaction system should be evaluated, and more comprehensive experimental evidence is recommended.

6. The correlation between interfacial activity (APF signal, zeta potential) and biological outcomes (hemolysis, protein aggregation) is compelling but remains correlative. To establish that interface-generated $\bullet\text{OH}$ is a direct driver of toxicity, control experiments with specific radical scavengers (e.g., mannitol, DMSO) should be performed. Demonstrating that $\bullet\text{OH}$ quenching significantly attenuates hemolysis and protein aggregation would provide critical causal support and elevate the mechanistic claim.

7. The experiments are conducted under controlled, idealized conditions (PBS, pure water). Given the study's environmental implications, it is essential to discuss—or ideally, test—whether this interfacial activity persists in more complex, real-world matrices (e.g., seawater, freshwater with natural organic matter, or simulated biological fluids). The Supplementary Fig. S2 suggests surface oxidation reduces activity; this should be explicitly discussed in the main text as it relates to environmental aging and the “lifecycle” of microplastic reactivity.

8. While the APF assay is excellent for detection, readers need a quantitative sense of the $\bullet\text{OH}$ production rate. Can the authors estimate the steady-state concentration or flux of $\bullet\text{OH}$ at the interface (e.g., using HPLC data from SI)? Comparing this value to known physiological or environmentally relevant $\bullet\text{OH}$ levels would help assess whether the observed activity is sufficient to drive the reported bio-effects.

9. The current discussion is strong but could be further enriched by: a) Explicitly linking the findings to the emerging field of microdroplet chemistry, highlighting how solid microplastics represent a new, widely distributed platform for such interfacial phenomena. b) Proposing concrete materials-design principles (e.g., how surface hydrophilization or permanent charging could suppress this intrinsic activity to engineer safer plastics). c) Speculating on how this activity might influence the environmental fate of co-pollutants (e.g., degradation of adsorbed organic pollutants).

Minor Comments:

1. Fig. 1: Please indicate the statistical significance of the differences in panels b, i, and k. Error bars are present but no statistical test is mentioned.

2. Fig. 2g: The x-axis appears to be partially obscured and should be corrected for clarity. A careful check of all figures and labels throughout the manuscript is also recommended to avoid similar presentation issues.

3. Page 3, last paragraph: The transition to microdroplet chemistry feels slightly abrupt. Consider a smoother bridging sentence.

4. Supplementary Methods: The description of ReaxFF/CGeM simulations is excellent. Please also briefly state why this method was chosen over alternative reactive force fields.

Referee #4

(Remarks to the Author)

I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

Referee #5

(Remarks to the Author)

This manuscript presents an ambitious and potentially impactful study combining experiments and simulations to argue for intrinsic physicochemical activity at microplastic–water interfaces. While my expertise lies primarily in computational modeling and simulations rather than experimental techniques, I find the overall conceptual framework compelling and the computational component central to the mechanistic interpretation of the experimental observations.

The simulation and ab initio calculations provide valuable insight into the proposed structure–activity relationship, particularly the role of interfacial water structure, partial solvation of hydroxide ions, and electrostatic effects in lowering the

vertical ionization energy at hydrophobic plastic–water interfaces. These results are generally consistent with recent advances in interfacial water chemistry and help rationalize the experimentally observed trends. However, several important methodological details related to the simulations are missing or insufficiently described, which currently limits reproducibility and a full assessment of the robustness of the conclusions:

1. The manuscript does not clearly justify the choice of modeling a single long polymer chain rather than multiple polymer chains of moderate length. Because the polymer necessarily interacts with its periodic images under periodic boundary conditions, it is important to clarify whether the resulting chain conformations are physically representative. In particular, the authors should demonstrate that key conformational metrics, such as the radius of gyration and end-to-end distance distributions, are consistent with the expected behavior for this polymer under the simulated conditions.
2. While the Willard–Chandler interface is referenced, further details on how the interface was identified in practice and how long the systems were equilibrated before and after introducing water (and ions) should be clearly stated.
3. Figure 4e correlates dangling OH populations with water contact angles. It is unclear whether the contact angles shown are directly computed from the current simulations or taken from literature databases. If they are not derived from the present simulations, this should be stated explicitly; if they are, the computational protocol used to obtain them should be described.
4. The number of independent configurations used for the vertical ionization energy calculations is briefly mentioned, but additional clarification on sampling, convergence, and uncertainty estimates would strengthen confidence in the reported low-energy tails.
5. Furthermore, how sensitive are the VIE distributions to the assumed surface charge density? To what extent does the chosen charge density represent an upper bound versus a typical experimental condition? Can the authors comment on whether similar trends are observed without explicit charge manipulation, relying solely on structural undercoordination?
6. It would be helpful if the authors explicitly discuss potential sources of deviation between simulations and experiments, such as surface roughness and heterogeneity in real microplastics and the role of trace oxidation or additives in real-world samples (even though pristine samples are emphasized).
7. The authors are also advised to discuss prior studies on polymer surface charging arising from contact electrification, which are directly relevant to the present work. In particular, the recent study published in *Nature Communications* 15, 2616 (2024) provides important insights into interfacial charge generation on polymeric surfaces, and the references therein would offer valuable context for interpreting the observed interfacial electrostatics.

Version 1:

Reviewer comments:

Referee #1

(Remarks to the Author)

Qian et al. have done really substantial work in revising the manuscript and have addressed the majority of my concerns, especially regarding the application of the combined force field. The revised figures are much better as well. Overall, the manuscript has been greatly improved.

However, the current mechanistic interpretation remains insufficiently quantitative for a high-impact claim. While I appreciate the great revision and authors' efforts, I still have a few remaining questions and suggestions that should be addressed before I can recommend the manuscript for publication, as listed below.

1. The revision addresses my previous concern regarding the limited comparison across polymers by adding PVC, the VIE calculation is now rather convincing. But, the mechanistic interpretation of VIE remains insufficiently clarified.

I would still like to ask how this VIE should be used linking with experiments. Even in the cases where the authors refer to the “lower tail” of the VIE distribution, the value is still around 100 kcal/mol, which corresponds to a process that appears impossible to occur thermally at room temperature. The authors may correct me if my understanding is inaccurate, but I understand VIE here as corresponding to the process

$\text{OH}^- (\text{surface}) \rightarrow \text{OH}^\cdot (\text{surface}) + e^-$

The fate of the electron is missing. There should then be a second half-process, in which the released electron is either solvated (similar to that in 10.1021/acs.jpcclett.2c01721) or accepted by another species, for example by the plastic phase: $\text{PLASTIC}x^- + e^- \rightarrow \text{PLASTIC}(x+1)^-$

This second step is related to the electron-accepting ability of the surrounding species or interfacial environment. It may be sufficiently favorable to compensate for part of the VIE penalty.

I would therefore like to see a comparison between different possible electron destinations, for example a solvated electron near the surface versus electron acceptance by the plastic phase. Calculating the electron-accepting energy of the plastic surfaces, or of relevant interfacial trap states, would provide supporting evidence. Assuming the process has no additional barrier, the overall energy change could provide an upper-bound estimate for the kinetics, or at least help judge whether the process is thermodynamically plausible under the given conditions, which helps to explain how the proposed VIE lowering corresponds to a real kinetic pathway that can occur over experimentally relevant timescales, such as days.

Overall, I expect to see a clearer mechanistic explanation and description of the full process. Currently author only state a powerful first-half process, which is great but seems not completed.

2. The authors now clearly explain that the charge of the plastics arises from the combination of the plastic itself and the surrounding OH^- (and perhaps also electrons), which is reasonable.

However, I remain being confused by the claim that “(in a negatively charged surface), VIE distribution toward energies well

below 100 kcal/mol (even approaching zero) to more readily create OH[·]. I believe this is due to the lack of discussion, as I noted in Suggestion 1.

The authors appear to have missed my point regarding the possible “runaway” behavior of charge. As currently presented, the manuscript seems to suggest that when the system is negatively charged, the VIE becomes lower, and OH[·] radical production becomes easier.

My understanding is that, in a negatively charged system, even if the VIE of OH⁻ is lowered, the species receiving the electron is already negatively charged. Therefore, the second half-process of electron acceptance, (or equivalently the solvation of an additional electron near the interface) should become less favorable. Whether the overall OH[·] production is accelerated should depend on the competition between these two effects.

I therefore expect more discussion and, if possible, more quantitative analysis from the authors regarding this point.

3. I would encourage the authors to open-source a minimum reproducible example for their combined force-field implementation. For instance, although the authors cite the original work on the Reax/CGem (10.1021/acs.jpcclett.0c02516) force field, that work does not appear to provide force-field parameters for Na⁺ or Cl⁻.

Providing a minimal working example would greatly enhance the reproducibility and transparency of this work. This would be particularly valuable for a Nature-level manuscript, as the method has the potential not only to support the present conclusions, but also to guide and even teach the broader community in applying similar combined force-field approaches to related interfacial systems.

4. I would also like to see a discussion of why OH radicals produced at the plastic–water interface do not react directly with the plastic surface, but can instead be released back into bulk water. Does OH[·] have a weaker interfacial preference than OH⁻? What is the probability, or expected timescale, for such release into the bulk phase? This point is important for connecting interfacial OH[·] formation with experimentally observed ROS release in the aqueous phase.

Referee #2

(Remarks to the Author)

I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

Referee #3

(Remarks to the Author)

In this reviewer's assessment, despite the substantial revisions made by the authors, the novelty of the work does not reach the threshold required for publication in Nature. The conceptual depth, mechanistic completeness, and evidentiary standard remain below what is expected for this journal.

Specifically:

1. Regarding the issue of novelty, although the authors have responded by providing textual explanations and a comparative table to clarify the differences between this study and their previous work, we still consider that the core content of the present manuscript is more likely an extension of the previous study to a specific application scenario, rather than a substantial breakthrough in terms of scientific questions or mechanistic understanding. In addition, this manuscript focuses on radical behavior at the microplastic interface, but the current descriptions may lead readers to mistakenly assume that plastics can undergo spontaneous degradation relatively easily in natural environments. In fact, microplastic degradation in natural environments is usually constrained by multiple factors, including light intensity, oxidant availability, reaction interfaces, environmental matrices, and time scales, and therefore cannot be simply equated with the enhanced degradation process observed in the experimental system. We suggest that the authors further clarify the differences between the experimental conditions and real environmental processes in the manuscript, so as to avoid overgeneralization or misleading interpretations regarding the natural degradability of microplastics.

2. Regarding Comment 4 raised in the first round of review, the authors' current response does not sufficiently exclude the possibility that the alcohols used in this study may directly act as radical scavengers. It is therefore recommended that the authors supplement their response with appropriate control experiments involving the addition of the alcohols alone, in order to provide more direct experimental evidence and further strengthen the mechanistic interpretation.

3. Direct experimental evidence of interfacial electric fields. The central mechanistic hypothesis relies on strong interfacial electric fields lowering the ionization energy of hydroxide at the microplastic surface. However, current support for this claim appears largely indirect, based on zeta potential measurements and molecular simulations. While these approaches are informative, they do not directly measure interfacial electric field strength. Given the conceptual importance of this mechanism, more direct interfacial-sensitive experimental evidence (for example, nonlinear optical spectroscopy or related techniques) would substantially strengthen the causal argument. At present, the electric field is inferred rather than directly demonstrated.

4. Causal relationship between electric field strength and radical formation. Beyond establishing the presence of interfacial electric fields, the manuscript does not yet demonstrate a quantitative relationship between field strength and radical generation kinetics. To meet the mechanistic rigor expected for publication in Nature, it would be important to show whether modulation of interfacial electrostatics—such as by systematically varying ionic strength or surface charge—produces predictable changes in radical yield. Demonstrating field-dependent scaling behavior would significantly reinforce the proposed causality between interfacial electrostatics and hydroxyl radical formation.

5. Exhaustive exclusion of alternative radical sources. Given the extraordinary nature of the claim that pristine microplastics intrinsically generate hydroxyl radicals without external stimuli, comprehensive exclusion of alternative pathways remains critical. Although additional controls have been included in this revision, further clarification is needed regarding the potential roles of dissolved oxygen, trace oxidative defects, residual polymerization initiators, photochemical effects, or mechanical perturbations. Importantly, real-world plastics are chemically complex materials that often contain a variety of

additives, stabilizers, plasticizers, and residual monomers. Moreover, environmental aging processes (e.g., UV exposure, oxidation, hydrolysis) can introduce surface functional groups such as carbonyls, peroxides, and hydroxylated species, which themselves may participate in redox chemistry. Even trace amounts of such chemical heterogeneities could potentially contribute to reactive oxygen species formation and confound attribution to a purely intrinsic interfacial electric-field mechanism. A more systematic characterization of polymer chemical purity and surface functionality, as well as explicit differentiation between pristine laboratory-grade polymers and environmentally aged materials, would therefore substantially strengthen confidence in the proposed intrinsic interfacial origin.

6. Universality across diverse polymer systems. Importantly, as also raised by Reviewer 1 regarding the issue of generality, the manuscript proposes a potentially generalizable interfacial physicochemical phenomenon rooted in hydrophobic surface effects. However, the range of polymers examined remains relatively limited. To substantiate claims of generality, it would be valuable to extend the analysis to additional commodity polymers with distinct dielectric properties and surface chemistries, as well as environmentally aged microplastics. Demonstrating consistent behavior across chemically diverse systems would elevate the conceptual robustness and broader relevance of the work.

7. Physical representativeness and boundary definition of the polymer–water model. While the simulations provide important mechanistic insight, the physical representativeness of the polymer–water interfacial model warrants further clarification. The use of a single long polymer chain under periodic boundary conditions raises concerns regarding artificial self-interaction and constrained conformational sampling, which may influence interfacial water structuring and local electrostatics. In realistic microplastic systems, surfaces arise from densely packed polymer chains with finite curvature, surface roughness, and heterogeneous chain orientations, rather than an effectively periodic single-chain construct. Given that the proposed mechanism critically depends on interfacial water structure and electrostatic effects, it is important to demonstrate that key conformational metrics (e.g., radius of gyration, end-to-end distributions, surface density) and interfacial properties are not artifacts of boundary choices. A clearer justification of model design and its physical relevance to experimentally studied microplastic surfaces would substantially strengthen confidence in the mechanistic interpretation.

8. Robustness and sensitivity of the VIE distributions to modeling assumptions. The reduction in vertical ionization energy (VIE) at the interface is central to the mechanistic argument; however, the robustness of the reported low-energy tail requires further substantiation. In particular, it remains unclear how sensitive the VIE distributions are to key modeling parameters, such as imposed surface charge density, system size, sampling depth, and configuration selection. Since the proposed mechanism relies on rare low-energy configurations, rigorous convergence analysis and uncertainty quantification are essential to establish statistical reliability. Moreover, it would be important to clarify whether similar energetic trends emerge without explicit surface charge manipulation, relying solely on structural undercoordination at the hydrophobic interface. Demonstrating that the energetic lowering is stable across reasonable variations in modeling assumptions would significantly strengthen the credibility of the computational conclusions.

Referee #4

(Remarks to the Author)

我与一位提供上述报告的审稿人共同评审了这份手稿。

Referee #5

(Remarks to the Author)

The authors have carefully addressed all my comments.

Version 2:

Reviewer comments:

Referee #1

(Remarks to the Author)

the authors addressed our concerns

Referee #2

(Remarks to the Author)

I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

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Response to Reviewer reports

Referee #1 (Remarks to the Author):

Qian et al. present a timely and provocative study that challenges the long-standing assumption that microplastics (MPs) are chemically inert in aqueous environments. The authors begin with reporting that polystyrene microplastics (PS-MPs), when simply dispersed in water, spontaneously generate hydroxyl radicals, supported by several independent experimental measurements. The finding that addition of surfactants such as Triton X-100 fully suppresses this reactive oxygen species (ROS) signal strongly suggests that the MP-water interface is essential to the observed reactivity. The authors further link this ROS formation to charge accumulation on the MPs.

Next, the authors demonstrate that this phenomenon extends across multiple MP chemistries, implying a more general interfacial mechanism rather than a polymer-specific artifact. Complementary molecular dynamics simulations and ab initio calculations are employed to rationalize the origin of the OH radicals, proposing that interfacial dangling hydroxide species donate electrons to the polymer surface, producing negatively charged MPs and releasing radicals. The overall narrative is coherent, and the mechanistic hypothesis is plausible, logically smooth, though certain aspects require clearer exposition in the current form. The manuscript also extends the discussion to potential biological implications, including interactions with biomolecules and cells.

The reported ROS generation associated with MP uptake in cells has been widely observed but usually interpreted as a cellular stress response (few more citations and discussion shall be added). Qian et al.'s results raise the possibility that MPs themselves may be the ROS source, which in my opinion, has not been previously recognized. This work therefore opens an important line of inquiry into an interface that has been largely overlooked. The potential impact spans environmental chemistry, toxicology, materials science, and water research.

In my view, the study presents interesting findings via substantial experiments, that could be suitable for publication in Nature. However, several key discussions are currently unclear, fragmented, incorrect, and unvalidated. In its current form, it is not suitable for publication.

We thank the reviewer for the clear summary of our paper and for viewing our work as potentially important in regarding the role of ROS induced by MPs for many fields. We have addressed reviewer concerns in detail below.

Below I outline major concerns:

1. Insufficient comparison for the theoretical findings.

The authors report vertical ionization energy (VIE) distributions of interfacial OH⁻ near PE and PMMA surfaces, where PE exhibits a small but distinct low-VIE tail. This shift is interpreted as evidence that “dangling” interfacial hydroxide species are more energetically favored to electron transfer, thereby rationalizing the observed ROS release and charge accumulation on MPs. Conceptually, this is a reasonable mechanistic link.

We respectfully suggest the reviewer might have a misunderstanding on this point. To be clear, it is the hydroxide ions that are near the interfacial dangling OH bonds that tend to exhibit low vertical ionization energies (VIEs). Hence, waters with dangling OHs are not the source of electrons, but the hydroxide ions that tend to be near them that are the source of electrons. Hence, dangling OH serve as structural indicator of the interfacial water hydrogen-bond network where hydroxide anions tend to lose an electron.

However, the current analysis relies only on two materials representing opposite extremes: PE (positive) and PMMA (negative, showing no VIE shift). Using two data points is insufficient to establish a robust correlation between VIE behavior and the experimentally observed chemical activity. At minimum, a third MP system (such as PVC or PS) should be included to strengthen the argument. It appears that the simulations for additional polymers already exist (e.g., Fig. 4e) and incorporating VIEs from at least one of these into Fig. 4a&b would substantially enhance the credibility and generality of the proposed mechanism.

Although we picked PE and PMMA because they are extremes, we agree that establishing a robust correlation between VIE and interfacial chemistry would greatly strengthen our work to go beyond the two initial MPs presented in the original manuscript. Following the reviewer's recommendation, we have incorporated an additional MP system, PVC, which provides an intermediate and chemically distinct case compared to PE and PMMA. After performing extended simulations, we observe that interfacial hydroxides near PVC also exhibits a discernible low-VIE tail, as shown in the revised Fig. 4a, but at a reduced level compared to PE. In turn, Fig. 4b shows that the hydrogen-bond network is more undercoordinated in the order PE > PVC > PMMA and supports the generality of the proposed mechanism. Taken together, the trend across all three systems strengthens the correlation between interfacial water structure and VIE distributions, and provides more robust support for the proposed mechanistic link between interfacial hydroxide environments and reactivity. We have revised the figure and main text as follows:

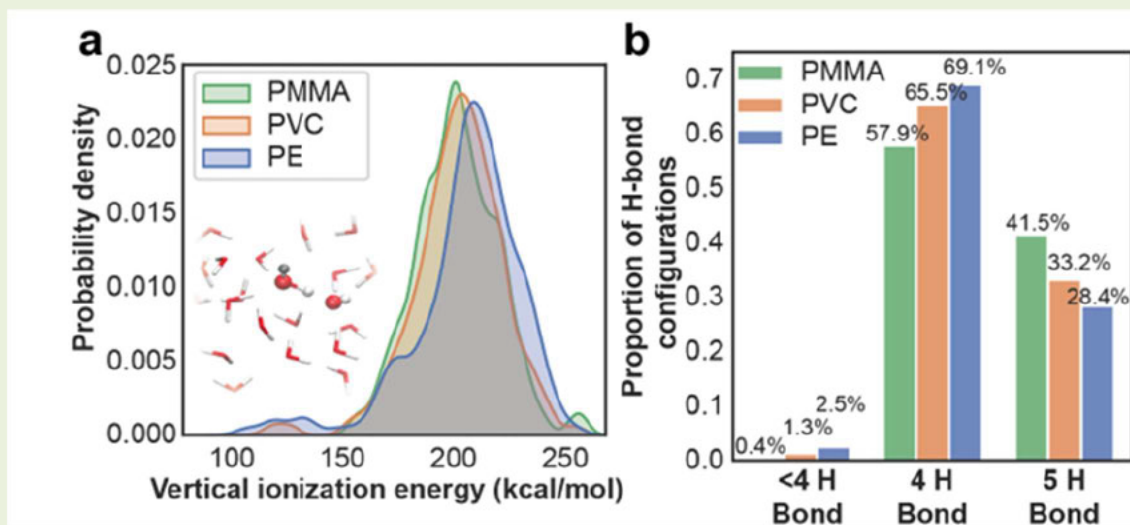


Fig. 4.| Molecular structure-activity relationship at plastic-water interfaces. (a) Vertical ionization energy (VIE) distributions for OH⁻ obtained from ~200 configurations, each including explicit solvent molecules within 6 Å of the ion. The PE and PVC system exhibits a distinct low-VIE tail (<130 kcal/mol), which predominantly arises from undercoordinated OH⁻ configurations at the interface; inset showing a

representative snapshot sampled from the lower VIE tail region for water-PE, involving a direct H-bond to a water with a surface dangling O-H bond (gray). **(b)** Probability distribution of OH⁻ hydrogen-bond coordination within ~5 Å of the WCI. Compared with PMMA, OH⁻ at the PE-water interface shows a much higher fraction of undercoordinated states (≤ 4 hydrogen bonds), while PVC exhibits intermediate behavior between the two systems.

The VIE results for the PE-, PVC- and PMMA-water interfaces are summarized in **Fig. 4a**. All three systems exhibit a primary VIE peak at ~210 kcal/mol, in excellent agreement with the experimental value (207 kcal/mol) for OH⁻ in bulk water¹. However, both the PE-water and PVC-water systems have OH⁻ groups that exhibit VIE values below 130 kcal/mol, with the more hydrophobic PE-water system showing a higher fraction of OH⁻ groups that can more easily liberate an electron. The emergence of this sub-population with substantially lower VIE is in line with the energy lowering observed at the air-water interface to favor hydroxyl radical formation². It is well known that the hydroxide ion has a water coordination numbers between of ~5.5-6.0^{3,4}, and we find that the low-VIE tail for PE- and PVC-water arises exclusively from undercoordinated OH⁻ configurations (i.e., partial solvation⁵) located within ~5 Å of the Willard-Chandler Interface⁶ (WCI, the instantaneous interface defined as the isodensity surface of the water oxygen density field at half of the bulk liquid density) as seen in **Fig. 4b**. These low VIE configurations are characterized by an OH⁻ that has a direct hydrogen bond to a water with a surface dangling OH (inset to **Fig. 4a**), or the water with a dangling OH is in the second solvation shell of the OH⁻.

2. Discussion of accumulation and electrostatics of OH⁻.

The manuscript proposes that negatively charged MPs facilitate electron transfer from interfacial OH⁻. Later authors report the observation that removal of Na⁺ (to mimic a stronger local electric field) yields an even lower VIE for OH⁻ near the PE surface. The current discussion is too brief and not very convincing. First, simply removing Na⁺ will not capture the fact that charges come from the MP and the resulting electric field's direction. Also, if progressively more negative MPs monotonically lower the VIE of nearby OH⁻, one might expect an unrealistic runaway accumulation of charge. To make the mechanistic picture quantitatively credible, the authors should clarify this balance. A better way of representing a charged MP (but not the entire system) should replace the current oversimplification to show more realistic behavior.

We appreciate the reviewer's concern regarding the description of a "charged MP." We would like to clarify that the effective interfacial charge does not originate from the microplastic itself, but it arises from the accumulation of hydroxide ions near the interface, i.e. from electrical double layer formation due to ion redistribution near the interface, consistent with long-standing discussions on the origin of the negative zeta-potential of oil droplets⁷.

Regarding the concern that progressively more negative interfaces might lead to an unrealistic runaway accumulation of charge, we note that the interfacial charge density considered here is physically constrained. Based on experimentally reported zeta potentials for MP in aqueous environments, the estimated surface charge density corresponds to approximately one hydroxide ion per ~3 nm²⁷⁻⁹. This level of interfacial charge is well within experimentally relevant bounds and does not imply unphysical charge accumulation.

Since the experimentally measured zeta potential reflects the potential at the slip plane, this implies a net charge imbalance within the interfacial region, i.e. the droplet effectively carries excess negative charge. In this sense, removing Na^+ serves as a practical way to reproduce this charge imbalance in a finite simulation setup. Explicitly resolving the electrical double layer would require substantially larger system sizes and longer time scales than are currently feasible. Removing Na^+ therefore provides a simple but direct way to impose an experimentally motivated interfacial charge density consistent with experimentally measured zeta potentials.

We have revised the text as follows:

Hydrophobic water interfaces are often characterized by the accumulation of negative charges and the associated interfacial electric fields.^{10–13} For example, the oil-water interface in nanoemulsion has recently been shown to exhibit a large electric field of $\sim 50\text{--}90$ MV/cm.³⁴ The same electrostatic trend is observed for plastics, in which PS and PE exhibit a large negative zeta potential (**Fig. 2** and **Fig. S10**), whereas PMMA is weakly hydrophobic with a much smaller zeta potential¹⁵. Hence, to model the enhanced surface electrostatics on PE, we remove Na^+ counterions to create a net negative charge for the PE-water system. Since the experimentally measured zeta potential reflects the potential at the slip plane, this implies a net charge imbalance within the interfacial region (i.e., the droplet effectively carries excess negative charge). In this sense, removing Na^+ serves as a practical way to reproduce this charge imbalance and impose an interfacial charge density consistent with experimentally measured zeta potentials. The resulting surface charge density, about 1 negative OH^- charge per 3 nm^2 , matches well with the experimentally determined values for oil nanodroplets and also for solid nanoparticles suspended in water^{10,16}.

3. Benchmarking of combined forcefield.

In the Supporting Information, the authors employ a mixed force-field scheme: ReaxFF/CGem for water and ions, and OPLS-AA for the polymer matrices. While each component of this hybrid setup is individually well established, the key phenomena reported in this study: interfacial OH^- behavior, charge redistribution, and electron-transfer relevant configurations, occur precisely at the interface where the two FFs interact. This raises a concern about the reliability of cross-interface energetics and structural features, especially considering that the ReaxFF and OPLS use completely different formulas. It is unclear under such coupling whether OH^- truly “sees” the polymer surface with appropriate energetics or effectively interacts with something closer to a vacuum environment decorated with point charges. It is unclear to me whether the specific ReaxFF/CGem + OPLS-AA combination has been benchmarked in previous studies involving polymer–water interfaces or ion–polymer interactions. The authors should either cite appropriate prior work validating such cross-FF coupling or provide benchmarking of their own.

We agree with the reviewer that more detail is needed in regard the use of mixed force fields across the polymer–water interface. While we did not provide sufficient context in the original manuscript, this modeling strategy has been used and validated in previous studies, including systems involving both neutral and charged reverse micelles in which ReaxFF/C-Gem was used for water and embedded in OPLS/AA.^{17,18} In those studies, the FF combination was benchmarked against a range of experimental observables from dielectric relaxation and THz spectroscopy related to interfacial proton-transfer-related phenomena, and was found to reliably capture key interfacial physics. We have now added a more detailed justification and relevant references to

clarify the reliability of this approach for the present MP systems. We have made the following changes:

Figure 4 caption:

See Supplementary Information for details of the simulated polymer and water models and VIE calculations.

Supplementary Information has been updated for more completeness:

Non-reactive and Reactive Force Fields: For many of the structural analyses used in this study we used the force field combination of OPLS-AA for the polymer and the SPC/E water model. But for the vertical ionization energy (VIE) calculations, we used a more sophisticated ReaxFF/C-GeM model to describe water, OH⁻ and Na⁺. Previous studies have shown that classical fixed-charge OH⁻ force fields often predict overcoordinated hydration environments, frequently yielding coordination numbers exceeding six. In contrast, ab initio simulations and experimental evidence indicate that hydroxide is best described as a hypercoordinated species with approximately three to five hydrogen bonds. In this context, reactive force-field approaches such as ReaxFF/C-GeM provide a more physical description by explicitly accounting for charge redistribution and proton-transfer dynamics. ReaxFF/C-GeM has been shown to accurately capture the energetics and dynamics of hydronium and hydroxide ion species.¹⁹ In particular, proton-transfer events that interconvert different hydration states of hydroxide (e.g., transitions between four- and three-hydrogen-bond configurations) have been identified as rate-controlling steps for hydroxide diffusion. ReaxFF/C-GeM have been shown to reproduce both the solvated structure of hydroxide and its diffusion coefficient in water with reasonable accuracy (e.g., $\sim 0.40 \text{ \AA}^2 \text{ ps}^{-1}$ from ReaxFF/C-GeM compared to $\sim 0.56 \text{ \AA}^2 \text{ ps}^{-1}$ experimentally). Such capabilities are especially relevant for resolving interfacial hydration structure and ion mobility at polymer–water interfaces, which are central to the present study.

Also, more detailed narration of how the two FFs interact (and how their cross-terms are handled) are needed.

Supplementary Information has been updated:

Electrostatic embedding model for ReaxFF/C-GeM. In this study we performed MD simulations of an interfacial system of an aqueous NaOH solution with three microplastic systems in a slab geometry using an electrostatic embedding scheme by modeling the water and NaOH with the reactive force field ReaxFF/C-GeM^{19,20}, and used the non-reactive OPLS-AA^{21,22} for PE, PVC, and PMMA. The system is partitioned into three components:

- (i) ReaxFF/C-GeM atoms, which include all water and NaOH and are treated using the reactive force field;
- (ii) All polymer atoms and are described entirely by a non-reactive (OPLS-AA) force field;
- (iii) non-bonded interactions between the ReaxFF/C-GeM and OPLS-AA regions, including van der Waals and electrostatic interactions, which provide the coupling between the two force-field descriptions. For the van der Waals interactions, we adopt parameters consistent with the OPLS-AA/SPC/E force field, following the same protocol established in our previous work on

reverse micelle systems¹⁷. Water-polymer electrostatics are treated with fixed charges for the polymer and Gaussian charges density for the water and NaOH. Both use the standard mixing rules of the OPLS force field. Please see reference^{17,18} for further details.

Importantly, this electrostatic embedding modeling strategy has been used and validated in previous studies, including systems involving both neutral and charged reverse micelles^{17,18}. In those studies, the force field combination was benchmarked against a range of experimental observables from dielectric relaxation and THz spectroscopy related to interfacial proton-transfer-related phenomena.^{17,18}

Examples could include energies comparison with DFTs, interfacial RDF profiles, hydration structure around polymer surfaces, or comparison of ion adsorption propensities with established results. Even limited tests would help establish that the hybrid representation does not introduce systematic bias.

We agree and have provided additional benchmarking of the suggested structural and energetic properties suggested by the reviewer.

Further Benchmarking of FF combinations. We have also evaluated interaction energies and hydrogen-bond-related intermolecular distances for representative polymer–water model systems (Table S2), constructed from small-molecule analogues and optimized consistently at each level of theory. As shown in Table S2, both OPLS-AA/SPC/E and OPLS-AA/C-GeM reproduce the correct qualitative trends in interaction strength across the different systems. Notably, the OPLS-AA/C-GeM model shows improved agreement with DFT in both binding energies and intermolecular distances, particularly for PMMA, where stronger hydrogen-bonding interactions are more accurately captured. These results support that the hybrid OPLS-AA/C-GeM approach provides a physically reasonable and reliable description of polymer–water interactions at the interface.

Table S2. Comparison of interaction energies and hydrogen-bond-related intermolecular distances (Å) between water and PE, PVC, and PMMA. Shown are computed quantities using OPLS-AA/SPC/E, OPLS-AA/C-GeM, and DFT (ω B97X-V/def2-TZVPD). Model systems are constructed from small-molecule analogues: $C_{12}H_{26}$ for PE, $CH_2CH_2CHClCH_2$ for PVC, and methyl heptanoate for PMMA. All geometries are optimized at each level of theory prior to analysis.

Binding energy (kcal/mol)	OPLS-AA/SPC/E	OPLS-AA/C-GeM	DFT (wb97x-V/def2tzvpd)
PE	-3.43	-3.52	-4.01
PVC	-3.17	-3.18	-4.01
PMMA	-5.81	-6.72	-6.80
H-Bond distance (Å)			
PE(C...O)	3.43	3.52	3.55
PVC(Cl...O)	3.20	3.34	3.24
PMMA(O...O)	2.73	2.72	2.86

In addition, radial distribution functions (RDFs) between water and representative polymer surface atoms further confirm that both force-field descriptions yield consistent interfacial hydration structures, with only minor quantitative differences as seen in Figure S13. The two force-field descriptions (OPLS-AA/SPC/E and OPLS-AA/C-GeM) yield overall consistent RDF profiles

across the three systems. For the PMMA system, the OPLS-AA/C-GeM model exhibits a more pronounced first peak, indicating stronger water–polymer interactions. This is consistent with interaction energy analysis, which shows that hydrogen-bonding interactions are stronger in the OPLS-AA/C-GeM description compared to OPLS-AA/SPC/E. Notably, this stronger interaction is in closer agreement with DFT-level calculations, suggesting that the C-GeM-based description provides a more accurate representation of interfacial hydrogen bonding in this system.

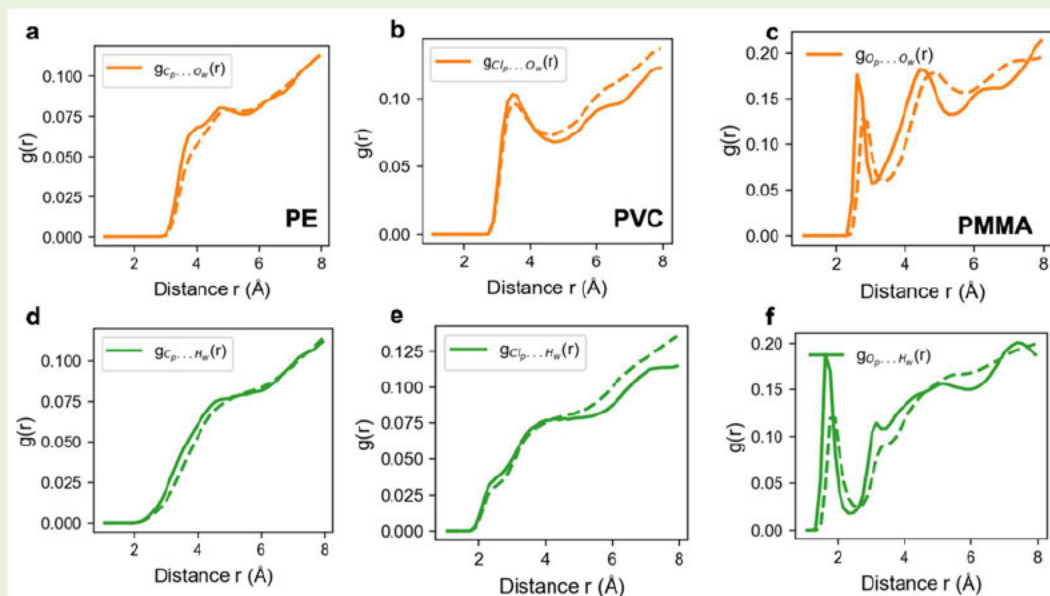


Figure S13| Radial distribution functions between polymer surface atoms and water molecules for PE, PVC, and PMMA systems. Top panels show $g_{\text{polymer-O}_w}(r)$, and bottom panels show $g_{\text{polymer-H}_w}(r)$. For PE, carbon atoms are used as representative surface sites; for PVC, chlorine atoms; and for PMMA, the carbonyl (COOR) oxygen atoms. Solid and dashed lines correspond to different force-field descriptions (OPLS-AA/C-GeM and OPLS-AA/SPC/E, respectively).

At the very least, the authors should explicitly discuss which aspects of interfacial physics may be over/underestimated by the combined FF. Given the centrality of the simulations to the mechanistic interpretation, transparent acknowledgment of potential limitations is necessary to support the robustness of the computational conclusions.

To this end, we have compared the interfacial dangling OH ratios obtained using the OPLS-AA/SPC/E and OPLS-AA/CGeM across the three polymer systems. We find that the OPLS-AA/CGeM hybrid force field systematically yields somewhat higher dangling OH ratios compared to OPLS-AA/SPC/E, **as shown in revised Figure 4e,f**, however, this effect is consistent across all systems and does not alter the relative trends observed between different polymers. Hence, the comparative conclusions and the resulting mechanistic interpretation remain robust.

We have also added the following text to the conclusions:

Despite possible deviation considering the surface heterogeneity of real-life plastics due to roughness and trace oxidation or additives, our model provides a molecular-level mechanism for interfacial reactivity.

4. Inclusion of interfacial surroundings in the VIE calculations

The Supporting Information describes a reasonable and established protocol for computing VIE. However, the authors note that “each calculation includes explicit solvent within 6 Å of the hydroxide ion.” It is unclear whether this truncation removes the MP surface itself from the quantum region. I think this point is critical. In Fig. 4e, the authors show that MPs can directly form hydrogen bonds or other specific interactions with OH⁻ at the interface. PMMA may also build those HBs. If these polymer–OH⁻ contacts are excluded from the VIE environment, an essential component of the interfacial electronic structure may be missing. Authors should clarify whether the polymer surface is explicitly included in the VIE calculations, and if not, provide justification for why its exclusion would not materially affect the computed ionization energies.

We thank the reviewer for raising this important point. In our VIE calculations, configurations are constructed by including explicit solvent molecules within 6 Å of the hydroxide ion, which may exclude direct polymer–OH⁻ contacts in some interfacial configurations. To assess the impact of this approximation, we directly compared VIE values computed with and without configurations involving polymer–OH⁻ proximity. This is now provided in the Supplementary Information.

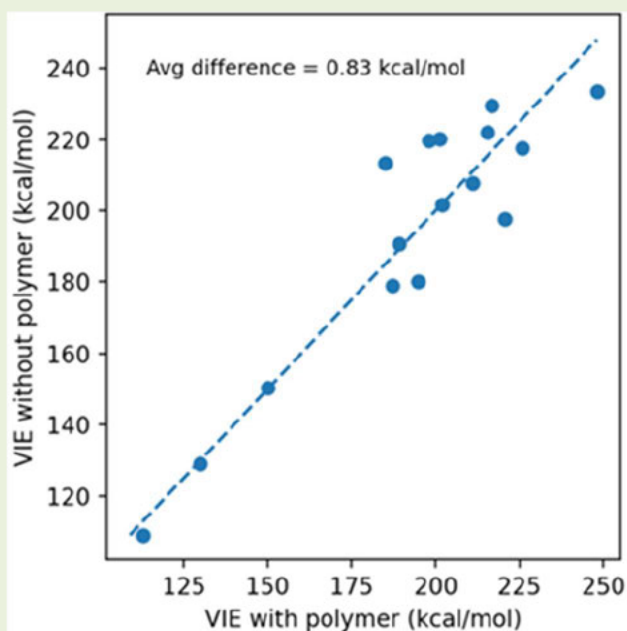


Figure S14| Comparison of VIE values computed with and without inclusion of the PE polymer configurations. Each point corresponds to an individual configuration. The close agreement between the two sets of results indicates that polymer inclusion has a negligible effect on the computed VIE.

In our VIE calculations, configurations are constructed by including explicit solvent molecules within 6 Å of the hydroxide ion, which may exclude direct polymer–OH⁻ contacts in some interfacial configurations. To assess the impact of this approximation, we directly compared VIE values computed with and without configurations involving the OH⁻ proximity to the PE polymer. As shown in **Figure S14**, the two sets of results are in close agreement on a per-configuration basis, with data points distributed near the parity line. The average VIE values are 192.99 and 193.82 kcal/mol, differing by only 0.83 kcal/mol (<0.5%). These results indicate that excluding polymer atoms from the VIE region does not materially affect the computed ionization energies, and that the VIE is primarily governed by the local solvation environment of hydroxide.

5. Surface of MPs in simulation

In the current version, the manuscript lacks discussion of what the MP surfaces actually look like in the simulations. A key aspect of MPs is their structural flexibility, so their surface can be amorphous. Also, several of the polymers used in the simulations (e.g., PVC, PET) have functional groups, meaning that if the polymer surface can reorganize, it may selectively expose different functional groups to the aqueous phase. Such surface reconstruction may strongly influence local hydration structure, hydrogen-bonding patterns, and ion accessibility, etc. Authors shall report some basic characteristics such as polymer density, the distribution of exposed functional groups, and whether surface segments remained stable or underwent significant rearrangement during the simulations. A brief characterization of the polymer models would considerably improve interpretability.

We thank the reviewer for this important suggestion. We have added the following text to the SI:

To better characterize the polymer surfaces in our simulations, we analyzed both the polymer density profiles and the distribution of exposed functional groups at the interface. Specifically, we computed the polymer density profile, $\rho_{\text{poly}}(z)$, to identify the interfacial region. Within this region, surface-exposed functional groups were defined as those located within 4 Å of the WCI. We then evaluated the surface density of functional groups for each polymer system. As PE does not contain functional groups, it is not included in this analysis. For the other systems, we selected representative groups: Cl atoms for PVC, the two oxygen atoms in the COOR group for PET and PMMA, and the aromatic ring centroid for PS.

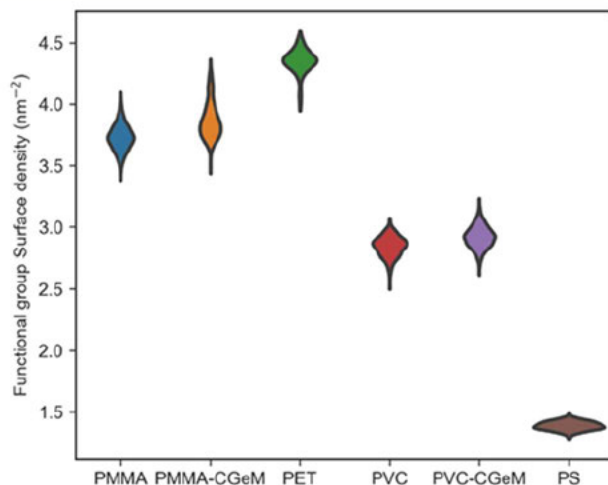


Figure S12| Surface density distributions of exposed functional groups for different polymer systems. Functional groups are defined as atoms or motifs located within 4 Å of the WCI. Representative groups include Cl atoms for PVC, carbonyl oxygen atoms (COOR) for PET and PMMA, and aromatic ring centroids for PS. Results obtained using OPLS-AA/SPC/E for PMMA, PET, PVC, and PS, and OPLS-AA/C-GeM for PMMA and PVC are shown for comparison. The narrow distributions indicate minimal fluctuation in surface composition, consistent with a structurally stable interface.

As shown in **Figure S12**, the surface functional group densities exhibit narrow distributions, with relative fluctuations below ~5%, indicating that the exposed surface composition remains stable over the course of the simulation, without significant interfacial reconstruction. Furthermore, comparisons between OPLS-AA/SPC/E and OPLS-AA/C-GeM show only minor differences in the distributions, suggesting that the interfacial functional group exposure is robust with respect to

the choice of water model. These results indicate that, although the polymer matrices are amorphous, the interfacial surface structure remains statistically stable on the simulation timescale, supporting the reliability of the observed hydration and reactivity trends

In addition, while the study shows properties of MP, in simulation authors apply a slab of plastic, which essentially means an infinitely large plastic surface. Surely, this is a certain trade-off as experimentally micro-size MPs are used. Yet, some theoretical discussion would strengthen the study. For example, the authors may also consider reproducing the PE results using a more crystalline or otherwise rigid surface as a comparison, to illustrate the sensitivity of interfacial behavior to polymer structural rigidity.

We acknowledge that representing the polymer as a slab corresponds to an effectively infinite surface, which differs from the finite size of experimental microplastics. However, this choice is a deliberate modeling approximation that allows us to isolate and characterize the local interfacial environment without introducing additional complexity from curvature or finite-size effects. At the nanometer length scale of our simulations, the curvature of microplastic surfaces is effectively negligible, such that the interface can be well approximated as locally planar. Besides, our focus is on the local interfacial environment governing hydroxide behavior, rather than polymer morphology. Analysis of surface functional group densities shows only minor fluctuations (<5%), indicating that the interfacial surface remains structurally stable over the simulation timescale, without significant rearrangement or reconstruction (**Figure S12**). Therefore, while different polymer morphologies (e.g., crystalline vs. amorphous) may introduce quantitative differences, the primary conclusions of this work—linking interfacial structure to hydroxide VIE and reactivity—are governed by local interfacial chemistry and are expected to remain robust.

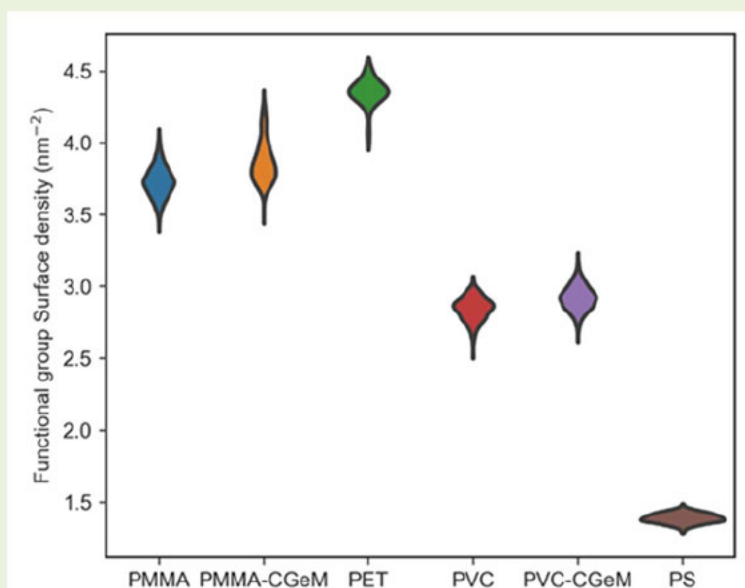


Figure S12| Surface density distributions of exposed functional groups for different polymer systems. Functional groups are defined as atoms or motifs located within 4 Å of the WCI. Representative groups include Cl atoms for PVC, carbonyl oxygen atoms (COOR) for PET and PMMA, and aromatic ring centroids for PS. Results obtained using OPLS-AA/SPC/E for PMMA, PET, PVC, and PS, and OPLS-AA/C-GeM for PMMA and PVC are shown for comparison. The narrow distributions indicate minimal fluctuation in surface composition, consistent with a structurally stable interface.

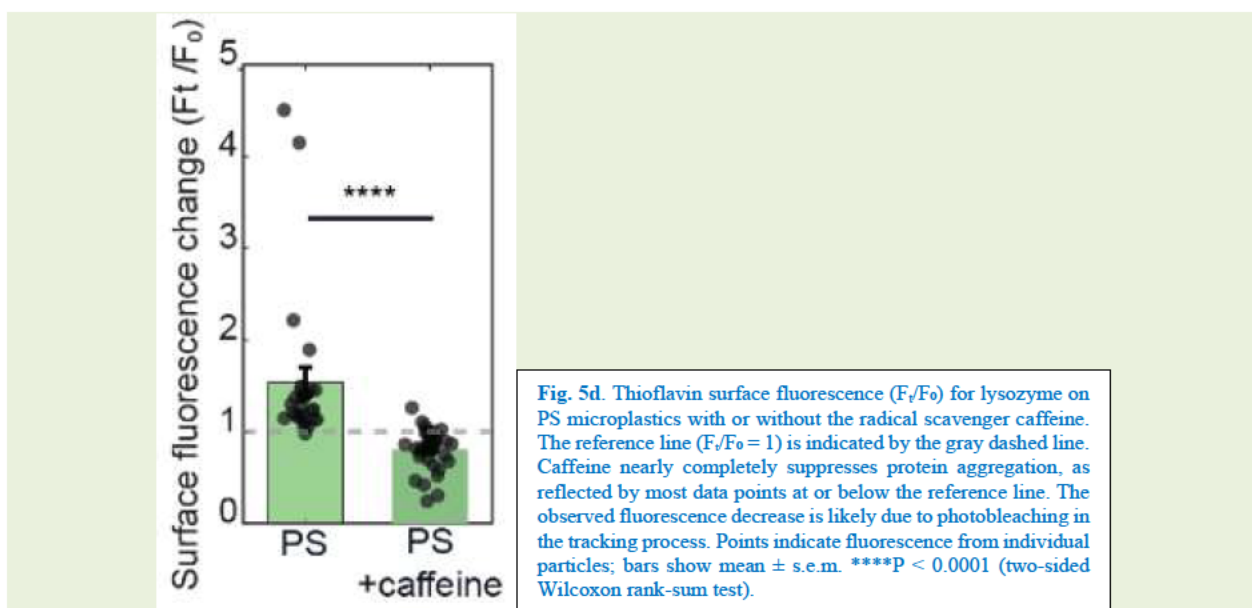
6. Discussion of biomolecule and cells.

The final section of the manuscript extends the narrative to interactions between MPs, biomolecules, and cells. While this topic is inherently interesting, the current presentation feels disconnected from the central mechanistic findings. The manuscript does not clearly articulate how the proposed interfacial radical release from MPs translates into the biological effects described, nor how the biological observations feed back into the mechanistic framework. Also, things like MP-protein corona have been widely reported.

The causal chain needs to be explicitly established. For example, authors reported cell damage caused by MPs, but is it from the OH radical attack? Alternatively, if the biological section is meant to be speculative or contextual rather than mechanistically grounded, this should be stated clearly. As of current, this part only reports a r-score. As it stands, the section reads as an isolated discussion without sufficient integration into the main narrative.

We thank the Reviewer for appreciating the general interest of this topic. The final section highlights, through multiple pairwise comparisons under controlled experimental conditions (e.g., with/without nonionic surfactant, and responses induced by different plastic polymers), that the intrinsic physicochemical activity at the plastic–water interface plays a regulatory role in downstream biological interactions. These effects have broad implications, including both physical adsorption and chemical damage, spanning from biomolecules to cellular systems.

At the same time, we acknowledge that biological interactions can involve mechanisms far more complex than those within the scope of the current manuscript. Nevertheless, we thank the Reviewer for raising the important question of whether a causal relationship can be established between radical generations and the detected damage to the biological system. This concern is also aligned with key suggestions from Reviewers #2 and #3, who recommended testing whether radical scavengers could suppress MP-induced biological damage as a control experiment to establish this causal link. We have now performed these experiments as suggested.



Our results show that radical scavengers can indeed suppress MP-induced biological damage. To further strengthen this point, we updated the manuscript to include caffeine, a radical scavenger, as a control to help establish this causal relationship. The following modifications have been made:

To test whether the observed protein aggregation arises from interfacial radical generation, we employ caffeine, a well-established radical scavenger²³. Protein aggregation at the same plastic-water interface is completely suppressed in the presence of caffeine, indicating that surface radical generation is likely the major driver of this structural damage (**Fig. 5d**).

Some of my minor concerns are listed as well:

1. The title is confusing. The “intrinsic physicochemical activity” appears to be too broad.

We thank the Reviewer for this comment, although we respectfully disagree that the phrase “intrinsic physicochemical activity” appears too broad. We believe it accurately reflects the scope of the manuscript, which encompasses both interfacial electrostatics and chemical reactivity at the microplastic–water interface. These two features are closely related and arise in the same hydrophobic interfacial environment, rather than representing unrelated observations.

We note that the physical and chemical aspects highlighted in the title are deeply connected, both in their mechanistic origin and in their biological implications within the scope of this work. Mechanistically, surface accumulation of hydroxide ions at the water–hydrophobic interface underlies both the observed surface electrostatics and the interfacial chemical reactivity, pointing to a fundamental relationship between charge and chemistry at such interfaces even beyond the context of microplastics^{7,14}. In turn, these two aspects act cohesively in downstream biological interactions including both physical absorption and chemical damage. For this reason, we feel that the term “intrinsic physicochemical activity” accurately captures the phenomenon we aim to highlight.

2. PS-MP can be de-color the MO, presumably through OH radical. If the radical trapper (HDMP=O) is also added with PS-MP, can MO maintain its color?

We thank the Reviewer for their curiosity. Methyl orange degradation by hydroxyl radical is a well-established mechanism²⁴. The inclusion of a radical trapper can certainly further provide mechanistic evidence that MO degradation by PS microplastics is mediated by hydroxyl radicals. The suggested radical trapper, HDMP=O, however, is not commonly used as a hydroxyl radical scavenger in mechanistic studies. Instead, HDMP=O is typically employed as a spin trap that converts highly reactive and transient radicals (such as hydroxyl radicals) into relatively stable radical intermediates for downstream ESR spectroscopic detection. For this reason, we instead employed two alternative scavengers: mannitol, as suggested by Reviewer #2 and 3, and caffeine, a widely used hydroxyl radical scavenger in the literature^{23,25}.

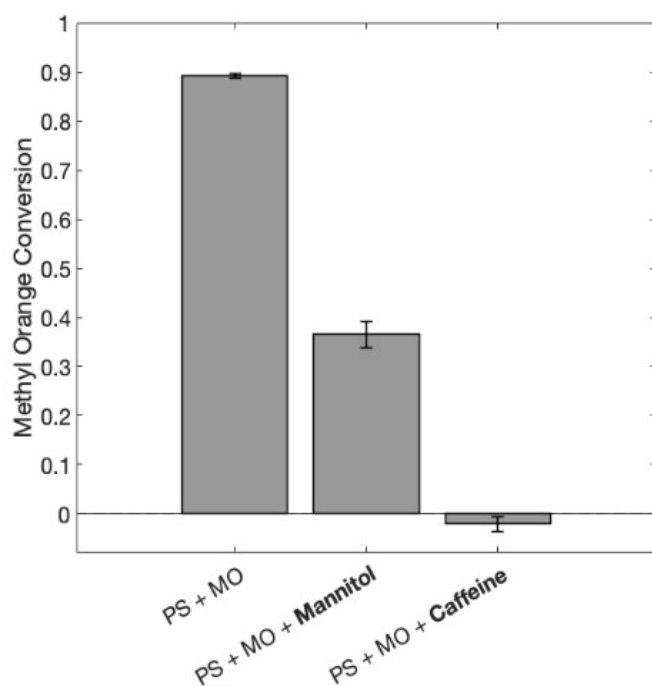


Fig R1| Conversion of methyl orange (MO) degradation induced by PS microplastics in the absence and presence of radical scavengers. A 20 μ M MO solution was mixed with polystyrene powder (10 mg/mL) and incubated under stirring, and degradation was quantified spectroscopically as described in the methods section. Addition of 100 mM mannitol partially suppresses MO degradation, whereas 100 mM caffeine nearly completely inhibits conversion, consistent with hydroxyl radical-mediated oxidation at the PS–water interface. Bars represent mean $\pm$ s.d..

We repeated the same MO degradation experiments in the presence of mannitol and caffeine. Compared with the pure MO/PS-MP mixture, which reaches $\sim 90\%$ conversion after 10 days, MO shows substantially less conversion ($\sim 40\%$) in the presence of mannitol, and no conversion in the presence of caffeine (**Figure R1**). The results provide additional evidence on hydroxyl radicals generated by PS microplastics in water driving the observed degradation of MO.

3. The role of surfactants is central to experimental observations. However, the theoretical treatment of this component is extremely limited. In the main text, the simulations involving Triton are addressed only in a single sentence, and the Supporting Information provides only one figure (Fig. S10) without further mechanistic discussion. Since these simulations are done, authors shall elaborate more.

We thank the Reviewer for this important comment. We agree that the role of Triton X-100 deserves clearer mechanistic discussion. In the revised manuscript, we will elaborate this point in both the main text and the Supporting Information.

Our theoretical results indicate that the low-VIE hydroxide population, which is most favorable for hydroxyl radical generation, arises from undercoordinated hydroxide ions at more hydrophobic plastic–water interfaces. These configurations are associated with interfacial water structures enriched in dangling OH groups, which reflect disrupted hydrogen-bonding networks at hydrophobic surfaces. Within this framework, Triton X-100 can be understood as suppressing the native interfacial water structure: by accumulating at the plastic–water interface, it reduces the dangling OH population and thereby decreases the likelihood of forming undercoordinated hydroxide configurations with lowered VIE. This same perturbation also weakens interfacial charge accumulation and electric field formation, thereby limiting the further shift of the VIE distribution toward lower energies. This provides a mechanistic explanation for why Triton suppresses both the observed surface electrostatics and radical generation.

We have revised the text as follows:

Specifically, Triton X-100 accumulates at the interface and suppresses the hydrophobic interfacial water structure, reducing dangling OH groups and the associated undercoordinated OH⁻ population. The same perturbation also weakens interfacial charge accumulation and electric field formation.

4. A few more discussions about the MP-water interfaces, compared to that of air-water/oil-water interfaces, may strengthen the influence and broaden the readership.

We thank the Reviewer for this helpful suggestion. We agree that comparison with air–water and oil–water interfaces can help broaden the readership and place the present work in a wider interfacial context. As discussed in the manuscript, we view the microplastic–water interface as part of the broader class of water–hydrophobe interfaces, which share fundamental physicochemical features arising from interfacial water, including surface electrostatics and unusual chemical reactivity.

In this sense, the comparison to air–water and oil–water interfaces is important not because these systems are identical in all respects, but because they point to a common underlying principle to understand and regulate such interfacial physicochemical activity. At the same time, while such interfacial chemistry has often been discussed in the context of reaction acceleration and green chemistry, the microplastic–water interface brings this framework into a setting with direct environmental and biological relevance.

The following modifications were made to strengthen this point:

Our work also contributes to a fundamental understanding of interfacial water. Hydrophobic water interfaces exhibit unique structural and physicochemical properties^{13,14,26,27}, underpinning the emerging field of microdroplet chemistry^{28,29,5,30–35}. Recent estimates of a strong interfacial electric field of 50–90 MV cm⁻¹^{8,36} can thus alter the reactivity landscapes at the interface and promote radical generation, including the conversion of OH⁻ ion to •OH^{2,14,25,30–33,37–41}. Our present study not only supports this broader phenomenon of interfacial water reactivity but also provides a facile platform to modulate and study the still-elusive connection between structure and reactivity, offering insights into the factors governing reactivity at other water–hydrophobe interfaces. At the same time, it places this fundamental interfacial chemistry in a context of environmental and public health relevance, particularly given widespread exposure and concerns over chronic biological responses. Lastly, our simulation and calculation not only provide a quantitative measure of the energetic cost of •OH generation but also reveal a synergistic role between interfacial water structure and surface electrostatics in determining the chemical reactivity, laying a framework for further theoretical explorations.

5. Fig. 1f appears only at the end of the figure sequence (after Fig. 1k), which disrupts the flow. Reordering the panels so that Fig. 1f appears in its natural position would improve readability.

We thank the Reviewer for this helpful suggestion. The figure panels have been rearranged as follows to improve the flow of the figure and enhance overall readability.

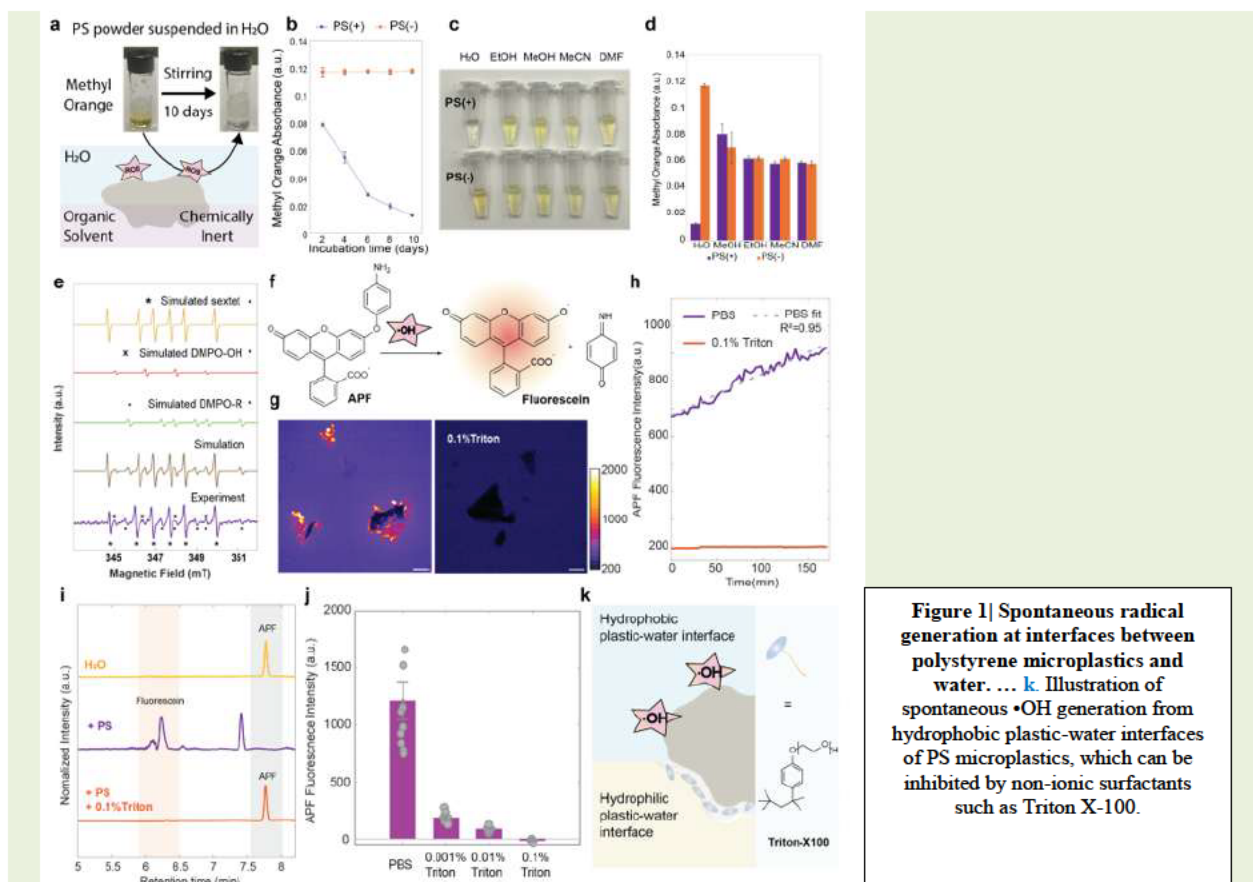


Figure 1| Spontaneous radical generation at interfaces between polystyrene microplastics and water. ... k. Illustration of spontaneous $\cdot\text{OH}$ generation from hydrophobic plastic-water interfaces of PS microplastics, which can be inhibited by non-ionic surfactants such as Triton X-100.

6. In my view, the fluorescence measurement in Fig. 2g conveys more critical information than the individual pictures shown in Fig. 2d–f. However, Fig. 2g is presented to be much smaller. Enlarging Fig. 2g would improve clarity.

We thank the Reviewer for this helpful feedback, which is also consistent with a comment raised by Reviewer #3. We have adjusted the figure accordingly to improve clarity and presentation.

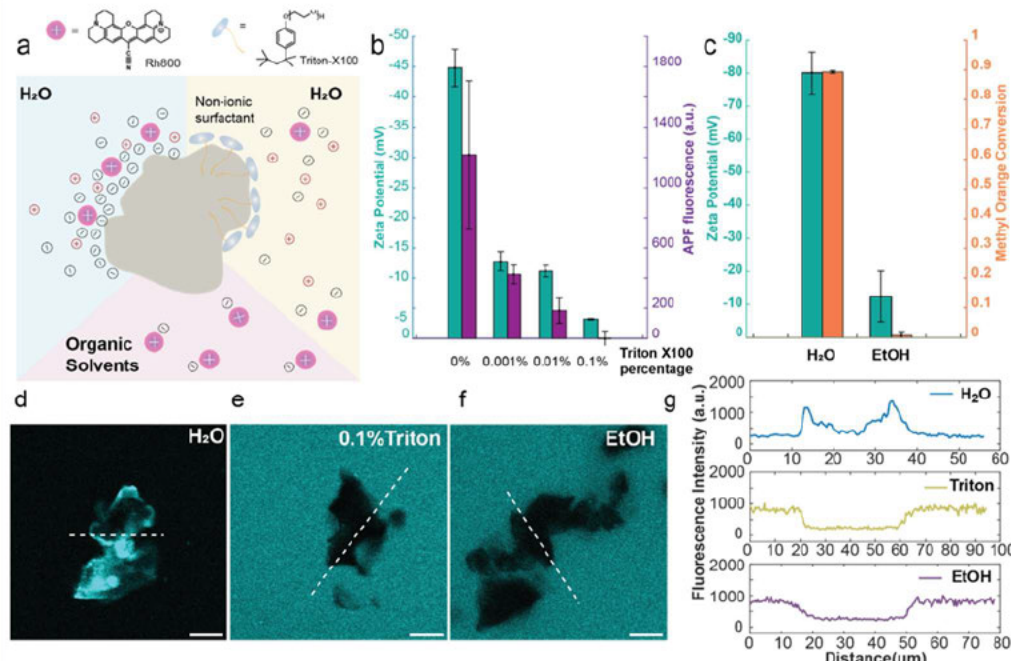


Figure 2| Surface electrostatics at microplastics-water interfaces. a. Illustration of surface electrostatics of PS microplastics in different solvent environments. b. Zeta potential of PS microplastics suspended in 1 mM NaCl solution supplemented with different concentrations of Triton X-100 (left axis) correlates with radical generation measured by APF fluorescence intensity at particle surfaces in PBS with the same surfactant condition (right axis). c. Zeta potential of PS microplastics suspended in water or ethanol (left axis) correlates with radical generation reactivity measured by methyl orange degradation in the same solvent environment (right axis). Visualization of the surface electrostatics using positively charged Rhodamine 800 (1 μ M) in d) water, e) water with 0.1% Triton X-100, and f) ethanol, with g) depicting the corresponding intensity profile with a white dash line marked on each panel. Scale bar: 20 μ m.

7. Fig. 4d illustrates the simulation configuration, which is essential for readers to understand the computational framework. The panel is currently small and difficult to see. Enlarging it or improving its visual clarity would be very helpful.

We thank the reviewer for this suggestion. We have increased the size of Fig. 4d and improved its visual clarity in the revised manuscript

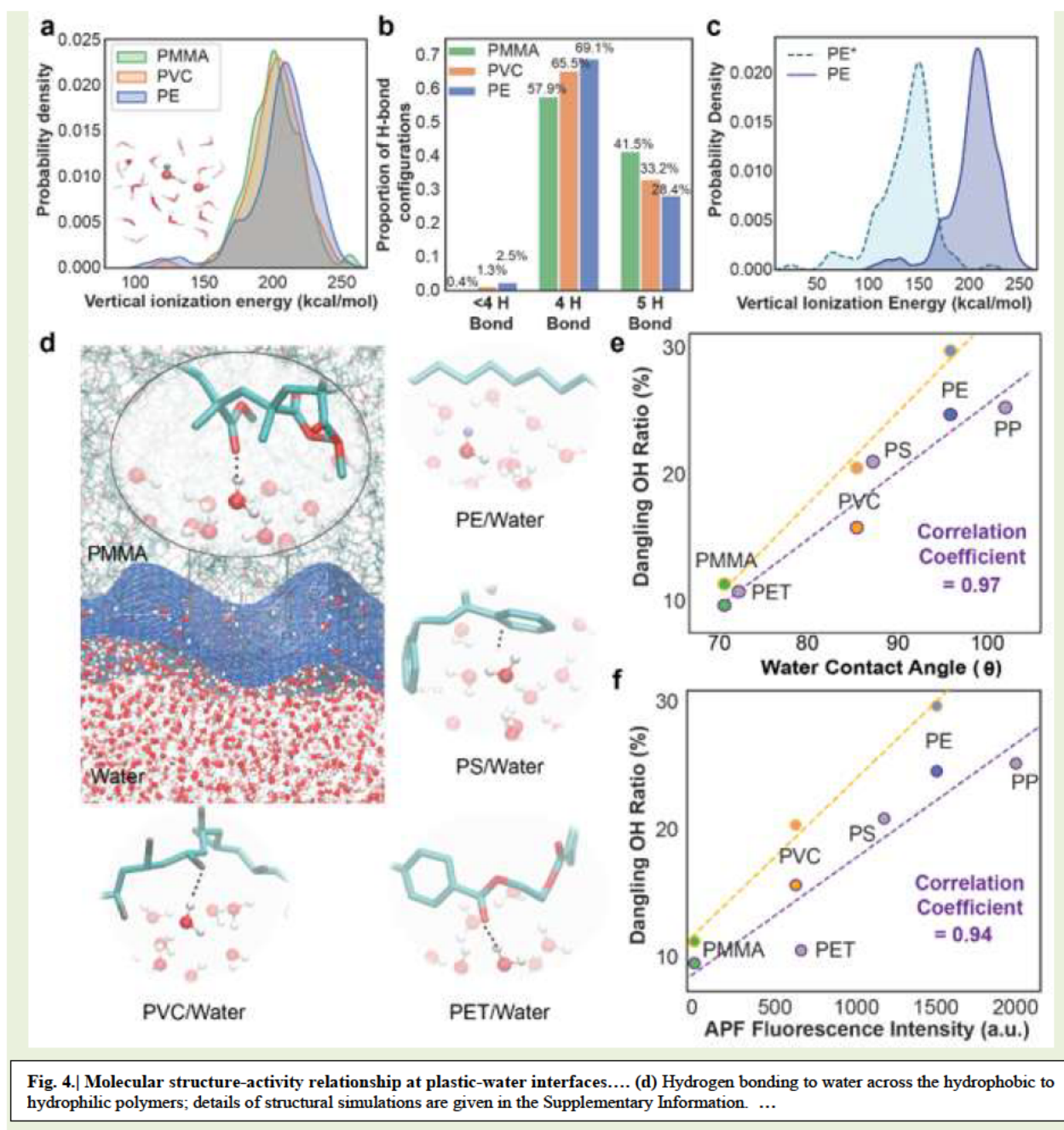


Fig. 4. Molecular structure-activity relationship at plastic-water interfaces.... (d) Hydrogen bonding to water across the hydrophobic to hydrophilic polymers; details of structural simulations are given in the Supplementary Information. ...

8. Authors add NaOH in simulation to manually add OH⁻. It seems to have only 4 NaOH (so 4 OH⁻), then how could dangling OH ratio to be around ~15%? Maybe it is time-resolved, then methods and equations for these analysis and sampling are entirely missing here.

We thank the reviewer for raising this point and would like to clarify a possible misunderstanding. In our work, dangling OH does not mean hydroxide ions (OH⁻). Instead, dangling OH refers to O-H groups of water molecules. An O-H group is called “dangling” if its hydrogen atom is not hydrogen-bonded to any nearby hydrogen-bond acceptor. Therefore, the dangling OH ratio measures how many water O-H bonds at the interface are temporarily not hydrogen-bonded, and it is not determined by how many OH⁻ ions are added. Even when only a few OH⁻ ions are present,

many interfacial water molecules can still have dangling O–H bonds. We have included the simulation detail in the Supplementary Information.

Simulation details for OPLS-AA/ReaxFF/C-GeM used for structural analysis. We simulated molecular dynamics with the electrostatic embedded model using an modified version of LAMMPS for PE, PVC, and PMMA²⁰. Each system consisted of a single long polymer chain in a slab geometry of ~8,000 polymer atoms and ~2,000 water molecules for ReaxFF/C-GeM. Non-bonded interactions were truncated at 10 Å. The simulations used a 0.25 fs, and temperature was maintained at 300 K using a Nosé–Hoover thermostat (damping constant: 100 fs)⁴², and constant pressure in the z-direction (Pzz= 1 atm) was enforced

Vertical ionization energies (VIEs) calculations and sampling details. For VIE calculations, four NaOH molecules were added to the water phase (box size $\approx 3.6 \times 3.6 \times 7$ nm³) based on the surface charge density reported by Beattie et al.⁹

Referee #2 (Remarks to the Author):

I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

This manuscript presents a carefully executed study that investigates physicochemical activity at microplastic-water interfaces. While the experimental work is thorough and the combination with computational simulations is commendable, I have significant reservations regarding the novelty and conceptual advance of the core findings in the context of the recently published literature, specifically in relation to *Nature* 640, 87–93 (2025), titled “Water structure and electric fields at the interface of oil droplets.” The central mechanistic claim—that hydrophobic aqueous interfaces can generate strong electric fields which lower the energetic barrier for hydroxide ion oxidation, leading to spontaneous hydroxyl radical generation—appears to be a direct extension of principles already established in the realm of water microdroplet and liquid-liquid interface chemistry. The cited *Nature* 2025 paper (Ref. 34 in the manuscript) provides a detailed experimental and theoretical framework for this phenomenon at oil-water interfaces. The present study effectively applies this established framework to a new substrate (solid microplastics) rather than discovering a fundamentally new mechanism. The observation that this activity correlates with hydrophobicity and can cause biomolecular damage is logical and expected based on the prior work, thus diminishing the sense of a paradigm-shifting breakthrough

The societal relevance of microplastics is undeniable, and the demonstration that this interfacial chemistry operates on a pervasive environmental contaminant is an important application. However, for publication in *Nature*, where the threshold for fundamental new conceptual insight is extremely high, the work in its current form may be perceived as an incremental, albeit well-performed, advance within an already emerging field, rather than the initiation of a new one.

We thank Reviewer #3 for the thoughtful evaluation and for recognizing both the societal relevance of microplastics and the quality of the experimental and computational work. We also appreciate the opportunity to clarify the conceptual novelty of the present study relative to the recent paper in *Nature* 640, 87–93 (2025).

We respectfully disagree with the assessment that the current work represents a direct extension of the oil–water microdroplet framework. The two studies address fundamentally different scientific questions and operate at different conceptual levels.

The *Nature* 2025 paper is primarily a physical chemistry measurement study that characterizes interfacial water structure and electric fields at oil–water interfaces using Raman spectroscopy. Its central contribution is the identification and quantification of strong interfacial electric fields ($\sim 50\text{--}90\text{ MV cm}^{-1}$), supported by spectroscopy and theoretical modeling. Importantly, that work does not investigate interfacial chemical reactivity, radical generation, or biological consequences. It focuses on fundamental water structure and interfacial electrostatics. Moreover, the system studied—idealized oil droplets—serves as a model platform for fundamental physical chemistry investigations and does not address environmentally relevant materials, structure–activity relationships, or implications for microplastic exposure.

In contrast, the present manuscript addresses a distinct and long-standing conceptual gap in a different context: how chemically inert plastics acquire apparent chemical activity and generate reactive oxygen species (ROS) upon fragmentation into microplastics. Although numerous studies report ROS generation and biological effects associated with microplastics, the underlying physicochemical origin has remained unclear. Resolving this question is essential for understanding the risks associated with microplastic exposure.

Here, we identify a previously unrecognized intrinsic physicochemical activity at microplastic–water interfaces. Specifically, we demonstrate charge accumulation and spontaneous radical generation under ambient conditions, arising from fundamental water–hydrophobe interfacial structure. This mechanism further enables the establishment of a structure–activity relationship across different polymer types, providing a new framework for understanding why different plastics may exhibit different levels of chemical activity and biological impact.

Importantly, the conceptual novelty of this work lies in bridging two previously disconnected areas: fundamental interfacial water structure and the environmental and biological impacts of microplastics. Understanding this societally important microplastics problem requires insight into how water behaves at hydrophobic solid interfaces—an aspect that has largely been overlooked in the microplastics field. By introducing this connection, the present study provides a conceptual framework that links interfacial physics to microplastic reactivity and biological consequences.

We believe this perspective will foster interaction between fundamental physical chemists studying interfacial water and environmental scientists investigating micro- and nanoplastics, thereby opening new directions for mechanistic understanding and mitigation strategies for microplastic pollution.

To help Reviewer better understand the difference between the two work we prepared the following table (**Table R1**)

	Nature 640, 87–93 (2025)	This work
System	Single Model hydrophobic oil–water droplets	Solid microplastics (six/multiple environmentally relevant materials with different hydrophobicity)
Conceptual focus	Interfacial water structure and electric fields	Intrinsic physicochemical activity of microplastic–water interfaces
Scientific question	Water structure and electrostatic environment at water–oil interface	How do chemically inert microplastics generate ROS in water?
Experiments	Raman spectroscopy with multivariate curve resolution to characterize interfacial water structure and electric fields	Detection and modulation of interfacial ROS generation at plastic–water interfaces; characterization of downstream biological effects
Simulation	Monomer-field theoretical model to interpret Raman spectra and interfacial electrostatics	<i>Ab initio</i> calculations of OH [•] vertical ionization energies (VIEs) at plastic–water interfaces to elucidate the molecular mechanism of chemical reactivity
Field / audience	Fundamental interfacial physical chemistry	Microplastics, environmental chemistry, and interfacial science
Conceptual impact	Understanding hydrophobic interface electrostatics	Mechanistic framework for microplastic physicochemical activity

Table R1. Comparison between Nature 640, 87–93 (2025) and current work

Major Comments:

1. The authors' previous study published in Nature (2025, 640, 87–93) focused on electric field formation and radical generation at hydrophobic–water interfaces. It would be helpful for the authors to further clarify whether the microplastic–water interfaces discussed in the present manuscript share mechanistic similarities with those systems, and to more explicitly articulate the conceptual novelty of this work in relation to their prior findings.

We thank the Reviewer for this important comment. In addition to the overall difference between the two works, we are happy to clarify both the similarities and the conceptual advances regarding the mechanistic understanding in this present work relative to our previous 2025 *Nature* study.

Mechanistically, the two systems indeed share a common foundation: water at hydrophobic interfaces. However, the previous study focused on characterizing physical interfacial activity, namely the hydrogen-bonding structure of water and the presence of surface electric fields, at a model oil–water interface via Raman spectroscopy. No chemical reactivity, radical generation, or downstream consequences were examined, which constitute the key experimental advances of the present manuscript.

Moreover, the present work advances the field in several conceptually new directions:

- **Connection between physical interfacial activity and chemical reactivity:** By harnessing this underexplored platform of water–hydrophobe interactions, we demonstrate that charge accumulation at microplastic–water interfaces is accompanied by spontaneous radical generation under ambient conditions. Rather than providing purely physical characterization of interfacial electrostatics, this work establishes an experimental correlation between charge and reactivity, introducing the concept of intrinsic physicochemical activity arising from water–hydrophobe interactions in the context of microplastics.

- **Ab initio VIE calculations of OH[−] at different hydrophobic surfaces:** The previous *Nature* study did not include VIE calculations nor address chemical reactivity in the water–oil system. To our knowledge, no prior *ab initio* studies have systematically rationalized why hydrophobic surface can give rise to chemical reactivity. Our work represents the first to introduce a detailed calculation of the vertical ionization energy (corresponding to the ease of liberating electron to produce free radicals) to explain why radical generation might be possible at water–hydrophobe interface.

- **Structure–activity relationship:** While the previous study examined a single model oil system, here we investigate multiple polymer types and show that different plastics interact with interfacial water in distinct ways. The degree of hydrophobicity, quantified through interfacial dangling OH signatures, correlates systematically with both interfacial charging and radical generation. This establishes the connection between polymer surface and physicochemical activity intrinsic to water interface. Such a structure–activity relationship is conceptually novel and provides a predictive framework for understanding why different microplastics may exhibit different chemical and biological impacts.

Finally, as discussed in the previous section, the experimental systems investigated in the two studies are fundamentally different. The present work focuses on solid microplastic surfaces with direct environmental and biological relevance, rather than a model liquid water–oil interface. The link we establish between fundamental interfacial activity and biomolecular interactions carries important implications for evaluating microplastic hazards and for guiding the design of future materials.

2. The detection of radicals at plastic–water interfaces is not inherently contradictory to the chemical inertness of commercial plastics. Chemical inertness should primarily be understood as the long environmental persistence of polymeric materials, i.e., their resistance to bulk degradation or transformation, rather than the inability of their surfaces to participate in interfacial radical processes. Indeed, previous studies have shown that aged microplastics (e.g., after light exposure or chemical oxidation) can generate persistent radicals and exhibit appreciable degradation activity toward aqueous pollutants, while the polymer matrix itself remains largely intact over extended reaction periods. This distinction could be more clearly articulated in the manuscript.

We thank the reviewer for this insightful comment and for the opportunity to clarify the conceptual framing of “chemical inertness” and how the present work advances beyond previous understanding.

We agree that chemical inertness of commercial plastics is often interpreted as their resistance to bulk degradation and long environmental persistence. However, in common chemical practice, inertness also refers to the absence of some particular functional groups that would be responsible for the or reactivity that cause chemical transformations. This understanding underlies the widespread use of plastics as food containers, laboratory vessels, and chemical storage materials, where their simple hydrocarbon-based structures are generally assumed not to chemically alter surrounding species.

Previous studies reporting radical generation from microplastics have primarily involved light irradiation, or absorption of other reactive chemical species^{43,44}. The radical generation is always attributed to photo-activation of the chemical bond, which is distinct from the mechanism discussed in this current work under ambient environment conditions.

To better clarify this distinction, we have revised the Discussion to explicitly differentiate (i) radical formation arising from aged or chemically oxidized plastics and (ii) the interfacial radical generation observed here for pristine polymers, and to emphasize that these processes occur without bulk polymer degradation.

In *this* context, we identify an important property that has long been overlooked: interfacial water (but not other solvents) interacting with microplastic surfaces can actually create electrified environments that turn microplastics into a factory of spontaneous radical ($\bullet\text{OH}$) generation. Notably, this behavior is mechanistically distinct from the previously studied radical generation

processes such as photo-irradiation or chemical oxidation^{43,44}. Instead, the activity observed here arises intrinsically from water–hydrophobe interactions.

3. From a biosafety perspective, the presence of radical-active interfaces would be expected to induce oxidative stress responses in biological systems, particularly for charged biomolecules. This outcome appears to be largely foreseeable.

We thank the reviewer for this thoughtful comment. We agree that radical-active interfaces capable of generating reactive oxygen species (ROS) would be expected to induce oxidative stress responses in biological systems, and that such biological consequences are, in principle, foreseeable. This expectation further underscores the importance of identifying and characterizing the chemical reactivity of microplastic–water interfaces, as it provides a mechanistic basis for understanding potential biological responses following microplastic exposure.

However, we respectfully note that the foreseeability of downstream biological effects does not diminish the novelty of the present work. The key advance of this study lies in identifying a previously overlooked mechanism of radical generation at plastic–water interfaces under ambient conditions, which differs fundamentally from prior systems that require photoactivation or strong oxidative aging to produce radicals. In many earlier studies, radical formation is induced by UV irradiation or chemical oxidation, conditions that may not be universally present in physiological environments⁴³.

Moreover, even foreseeability still requires experimental validation, as the effect might be too minute to lead to observable biomolecular responses. Experimentally establishing the connection between intrinsic physicochemical activity at microplastic–water interfaces and observable downstream biological interactions therefore constitute an indispensable component of this work, highlighting the profound implications of our findings.

4. In Figure 1c, appreciable methyl orange (MO) degradation is observed only in PS-dispersed aqueous systems, which is relatively intuitive, as alcohols are frequently employed as hydroxyl radical scavengers in radical identification experiments. In this context, the statement “In contrast, PS–ethanol interface, which does not exhibit evident ROS generation or MO degradation (Fig. 1c, d), shows near-neutral surface zeta potentials and minimal Rh800 surface partitioning (Fig. 2c, f, g). This again highlights the crucial role of water in activating microplastic surfaces with negative charges” may require further justification, as the interpretation could be influenced by radical quenching effects rather than solely by interfacial electrification.

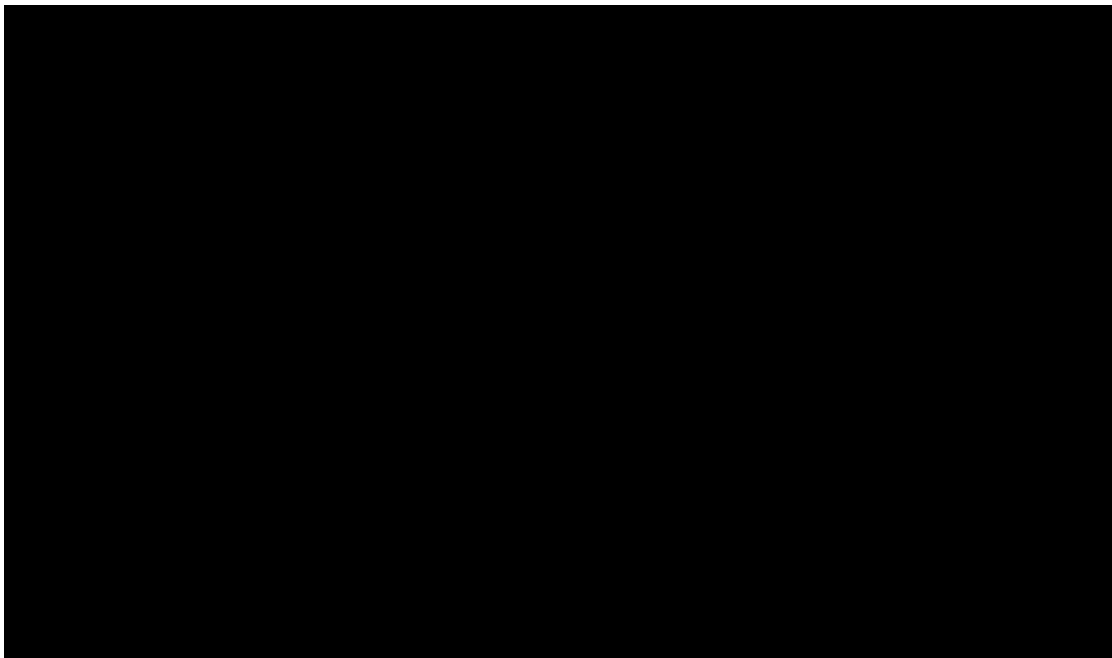
We thank the Reviewer for appreciating the intuitiveness of the MO degradation assay, but we respectfully disagree with this interpretation. We believe that the absence of MO degradation in alcohols is not simply due to radical quenching by the solvent, but instead reflects fundamentally different interfacial physicochemical activity of microplastics in water versus organic solvents.

First, the two non-alcoholic solvents used in Fig. 1c (i.e., DMF and MeCN), which are not typically considered radical quenchers, also show no reactivity toward MO degradation when mixed with PS. This broader observation cannot be explained by the so-called quenching effect of alcohols.

Moreover, alcoholic solvents possess limited scavenging capacity to fully suppress MO degradation. While they can act as hydroxyl radical scavengers, they are not necessarily radical terminators. Instead, hydroxyl radicals can convert alcohols into alkoxy radicals, which may still participate in downstream reactions leading to MO degradation. In fact, MO degradation has been

reported in methanol before, where methoxy radicals were proposed to cleave the azo bond in MO (Fig. R3)⁴⁵. This example is not intended to imply identical behavior of alcoholic solvents in our system, but rather to illustrate that interactions between alcohols and hydroxyl radicals cannot account for the suppressed MO degradation observed in our experiments.

Therefore, the absence of MO degradation in MeOH and EtOH, as well as in other organic solvents, cannot be solely attributed to their radical scavenging properties, but instead reflects the essential role of water–hydrophobe interfaces with intrinsic physicochemical activity.



5. While the manuscript emphasizes the role of hydroxyl radicals at the interface, it would be valuable to consider the contribution of surface-adsorbed hydroxyl radicals. For instance, comparative experiments using NaF could help distinguish between free and adsorbed •OH species by examining changes in detectable radical concentrations. In addition, the possible involvement of other reactive species in the reaction system should be evaluated, and more comprehensive experimental evidence is recommended.

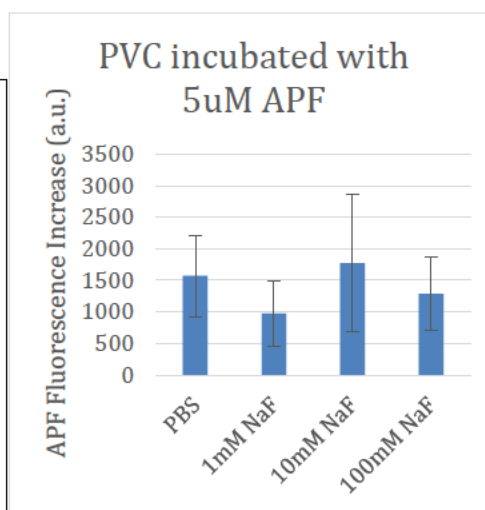
We thank the reviewer's suggestion on examining the NaF dependency surface radical generation. To the best of our knowledge, fluoride influences hydroxyl radical generation primarily through interaction with metal ions or metal-containing surfaces. The mechanisms generally fall into three metal-centered categories:

1. Modification of Fenton / Fenton-like reactions via formation of metal–fluoride complexes that alter redox cycling⁴⁶
2. Interaction with metal surface-bound OH species and facilitate their release^{47,48}

These mechanisms all rely on metal coordination chemistry, which is not mechanistically relevant to the physico-chemical activity of the water-hydrophobe interface we are focusing on here. In particular, surface-adsorbed hydroxyl radicals are less clearly defined in this context, where they are better viewed as interfacial or surface-active species.

Yet as suggested, we have performed the corresponding NaF dependency experiment on plastic-water interface using different concentrations of NaF supplement (**Fig R4**, details described in the caption). From the experiment, there is no consistent change in APF fluorescence increase, which indicates hydroxyl radical generation and release to the solution, with increasing NaF concentration in the solution, nor are there significant statistical differences for each group against the control (without NaF, all p value against control >0.05). These results further support our understanding that the radical generation reactivity is intrinsic to the water-hydrophobe interface under ambient conditions, with no necessary involvement of metal-related catalysis.

Fig.R4| NaF dependence of hydroxyl radical detection at the PVC–water interface measured using APF fluorescence. PVC particles (100 mg) were incubated in 5 μ M APF in PBS supplemented with NaF (0–100 mM) and stirred at 900 rpm. After 1 h, 0.1% Triton X-100 was added to release surface-bound fluorescein products, and 200 μ L supernatant was collected for fluorescence measurement. APF fluorescence increase was calculated from the difference between 1 h and initial levels. No systematic change in APF fluorescence is observed with increasing NaF concentration, and no statistically significant differences were found relative to the control (PBS, $p > 0.05$), supporting that radical generation is intrinsic to the water–hydrophobe interface rather than arising from metal-mediated catalysis. Bars represent mean $\pm$ s.d.



6. The correlation between interfacial activity (APF signal, zeta potential) and biological outcomes (hemolysis, protein aggregation) is compelling but remains correlative. To establish that interface-generated $\bullet$ OH is a direct driver of toxicity, control experiments with specific radical scavengers (e.g., mannitol, DMSO) should be performed. Demonstrating that $\bullet$ OH quenching significantly attenuates hemolysis and protein aggregation would provide critical causal support and elevate the mechanistic claim.

We thank the Reviewer for highlighting the importance of establishing a causal relationship between interfacial hydroxyl radical generation and the observed biological effects. To address this point, we examined whether two radical scavengers—mannitol, as suggested by the Reviewer, and caffeine, a commonly used hydroxyl radical scavenger—could reduce protein aggregate formation (**Fig R5**).

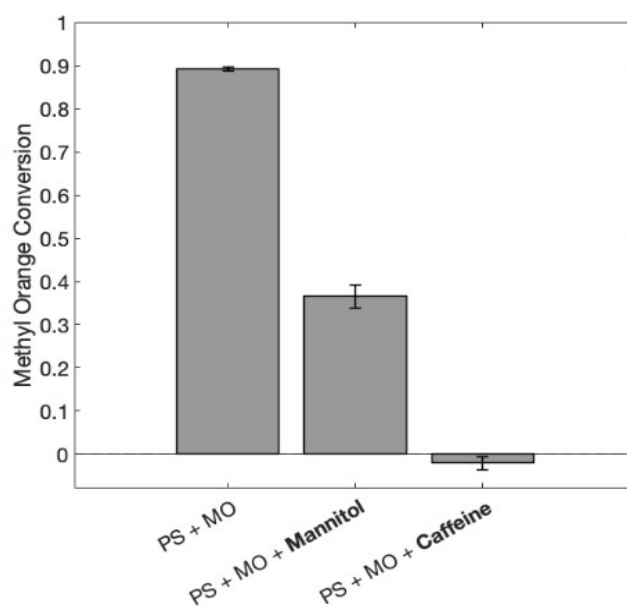
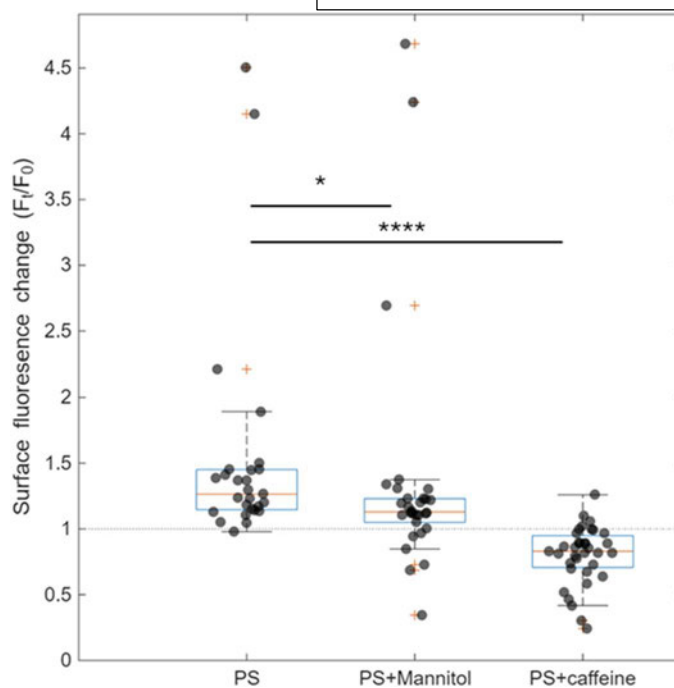


Fig.R5 | Thioflavin surface fluorescence (F_t/F_0) for lysozyme on PS microplastics with or without the radical scavenger mannitol and caffeine. Points indicate individual particles; bars show mean $\pm$ s.e.m. **** $P < 0.0001$ (two-sided Wilcoxon rank-sum test).

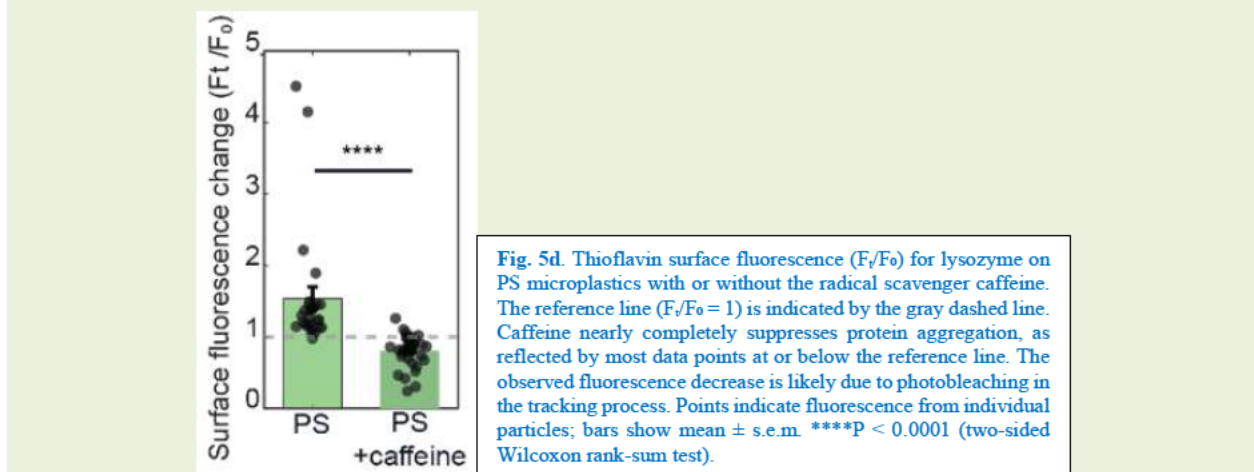


As wisely anticipated by the reviewer, our results show that both radical scavengers suppress protein aggregation at the plastic–water interface, supporting a causal link between interfacial chemical reactivity and downstream biomolecular damage. However, their effectiveness can be different. Mannitol only moderately suppresses lysozyme aggregation induced by PS microplastics

($p = 0.011$), whereas caffeine nearly completely prevents aggregate formation ($p < 0.0001$). Notably, this difference is consistent with the trend observed in our MO degradation experiments (**Fig. R1, also shown here on the top**, as suggested by Reviewer 1), where mannitol only partially suppresses MO degradation, while caffeine fully inhibits it. The disparity can be rationalized by their differing reactivity in hydroxyl radical scavenging. As we have explained in previous section, hydroxyl radical scavengers are not necessarily radical terminators. Upon reaction with hydroxyl radicals, caffeine, with conjugated heteroaromatic core, should form much less reactive radical intermediates compared to mannitol, which contains only alcohol functional groups. The fundamental difference in their chemical structure and reaction mechanism may account for why mannitol is less effective than caffeine in suppressing both MO degradation and lysozyme aggregation.

These results provide mechanistic support that the observed protein aggregation is not merely correlative but is causally linked to the intrinsic interfacial activity of the microplastic–water interface. To strengthen this point and avoid complications, we updated the manuscript by including radical scavenger caffeine as control and help establish this causal relationship. Following modifications are made:

To test whether the observed protein aggregation arises from interfacial radical generation, we employ caffeine, a well-established radical scavenger²³. Protein aggregation at the same plastic–water interface is completely suppressed in the presence of caffeine, indicating that surface radical generation is likely the major driver of this structural damage (**Fig. 5d**).



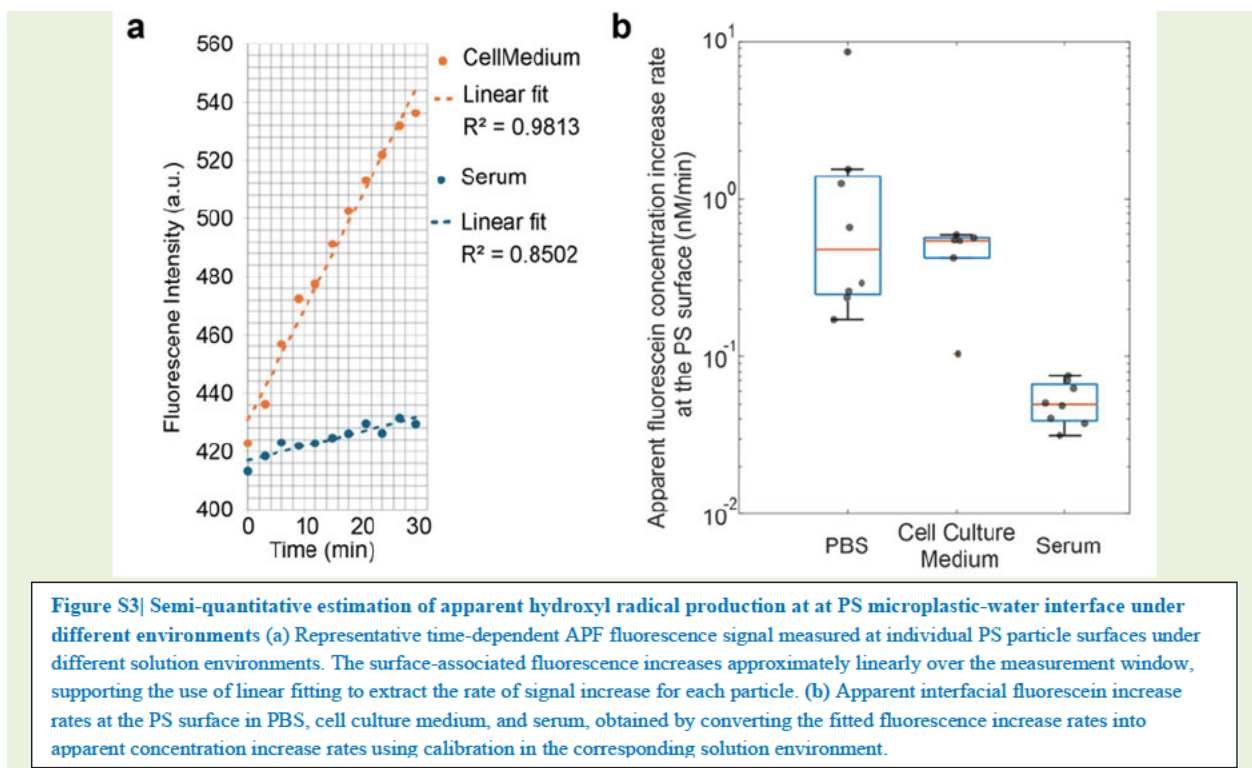
7. The experiments are conducted under controlled, idealized conditions (PBS, pure water). Given the study’s environmental implications, it is essential to discuss—or ideally, test—whether this interfacial activity persists in more complex, real-world matrices (e.g., seawater, freshwater with natural organic matter, or simulated biological fluids). The Supplementary Fig. S2 suggests surface oxidation reduces activity; this should be explicitly discussed in the main text as it relates to environmental aging and the “lifecycle” of microplastic reactivity.

We appreciate the reviewer’s recognition on how surface functionalization can alter the surface hydrophobicity and thus influence reactivity and curiosity to see if this phenomenon can be consistently observed in more complex, real-world matrices. With special interest regarding how surface physicochemical activity of microplastics regulate their biological interactions, we choose two relevant real-world matrices for proof-of-demonstration: cell culture media and serum. In both

cases, we can see surface radical generation indicated by APF fluorescence sensors. Particularly, in the cell culture medium environment the radical production indicated by the APF is comparable to that in the PBS environment. This suggests that physicochemical activity reported in this manuscript can be widely reproduced in complex matrices with real-life relevance.

Predicted plastic-water interface of different hydrophobicities – influenced by the different environment- would have different physico-chemical activities. The surface radical generation indicated by APF is indeed at a much lower level for PS in serum compared to that of the cell culture medium and PBS. We believe such differences can be well-rationalized given the composition difference between cell culture medium and serum. Notably, serum contains up to 6-8% proteins which can readily form protein corona at the plastic surface and make the surface more hydrophilic. Moreover, albumin, which is the major component of protein composition, is known to have antioxidant properties⁴⁹. Therefore, the proteins in the serum can not only physically alter the surface hydrophobicity but also chemically scavenge the surface generated ROS, which explains the observed much lowered APF increase at PS microplastic surface in the serum environment. This also reveals another under-appreciated aspect of the remarkable self-defense mechanism in our body from evolution to protect the body from environmental hazards.

To strength this discussion, we have included the panel in the SI as Figure S3



8. While the APF assay is excellent for detection, readers need a quantitative sense of the •OH production rate. Can the authors estimate the steady-state concentration or flux of •OH at the interface (e.g., using HPLC data from SI)? Comparing this value to known physiological or environmentally relevant •OH levels would help assess whether the observed activity is sufficient to drive the reported bio-effects.

We thank the reviewer for this important suggestion. Estimating the magnitude of •OH production at the plastic–water interface would indeed help place the observed activity in a broader physiological and environmental context.

Quantitative estimation of a true steady-state •OH concentration at the interface is challenging because the radical generation occurs locally on heterogeneous particle surfaces whose effective surface area is difficult to determine precisely. Yet, the reaction occurs within a confined interfacial region rather than in bulk solution, making conventional assessment in homogeneous solution hard to be applied and less relevant for comparison. To obtain a semi-quantitative estimate, we analyzed the time-dependent increase in surface fluorescence observed on individual particles in the APF assay. The fluorescence intensity localized at the particle surface indicated by confocal imaging was first converted to an apparent surface fluorescein concentration using the calibration obtained from the corresponding solution environment. The temporal increase of this signal was then fitted linearly to estimate the apparent rate of fluorescein formation at the particle interface. Because the APF probe generates fluorescein with an approximately 1:1 stoichiometry upon reaction with hydroxyl radicals, in principle, the cumulative fluorescein production provides an estimate of the cumulative •OH generation captured by the probe. In principle, this allows conversion of the fluorescence increase into a lower-bound estimate of interfacial radical production.

We note, however, that several factors may cause this approach to underestimate the true radical generation rate. These include diffusion of fluorescein away from the interface, photobleaching/ side reactions of fluorescein molecules in the surface environment, and incomplete capture of •OH radicals by the probe due to competing reactions or limited probe accessibility at the interface. As a result, the calculated value is likely a conservative lower-limit estimate. Despite these limitations, we perform the quantitative assessment as requested by the reviewer to estimate the lower bound of radical generation rate at the plastic–water interface based on time-resolved fluorescence tracking of individual particles under different conditions (**Figure S3**). The estimated activity is on the order of 0.1-1 nM/min in the PBS solution, which is on the same order hydroxyl radical production rate in natural water under sunlight (**Table R2**)⁴³.

Sample	Condition	Formation rate (nM·min ⁻¹)	References
Lake water, Jiaozuo, Henan province	Sunlight	0.45 ± 0.049	50
Sea water, Qingdao, Shandong province	Sunlight	0.56 ± 0.028	50
Wetland water, Baiyangdian, Hebei province	Sunlight	1.01 ± 0.072	50
Open-ocean surface water – Subtropical coastal water	Sunlight	0.17 ± 0.12	51
DOM-rich freshwater	Sunlight	2.07 ± 0.26	51
Lake water, Piedmont (NW Italy)	xenon lamp	0.41 – 3.54	52
Surface water, Everglades National Park, Florida, USA (Shark River Slough, SRS)	xenon lamp	0.084 ± 0.006	53

Surface water, Everglades National Park, Florida, USA (Taylor Slough, TS)	xenon lamp	2.69 ± 0.13	53
Arctic surface water	UV bulbs	$0.16 - 54$	54
River, Chinese Yangtze Plain	xenon lamp	$3.06 - 7.01$	55
Lake, Chinese Yangtze Plain	xenon lamp	$6.6 - 10.9$	55
Canal Fumemorte (fresh water), Southern France	Hg lamp	0.91 ± 0.006	56
Vaccares (estuarine water), Southern France	Hg lamp	0.116 ± 0.006	56

Table R2. Formation rate of $\cdot\text{OH}$ in different natural waters measured under photoirradiation⁴³

In the cellular system, the normal physiological rate of hydroxyl radical generation is way below this level to be detected. Our estimated surface radical generation rate from microplastic surface is comparable to what estimates for a 20 μM redox mediator drug diaziquone to induce ROS and kill cancer cells⁵⁷. This comparison suggests that the interfacial radical generation observed here is potentially sufficient to contribute to the reported biological effects.

In response to the reviewer's suggestion, we have included the following information in the main text and SI note:

By linearly fitting the time-dependent increase in APF fluorescence, we can estimate the lower bound of $\cdot\text{OH}$ production rate within the interfacial region of microplastics to be on the order of 0.1-1 nM min^{-1} . (**Fig. S3**).

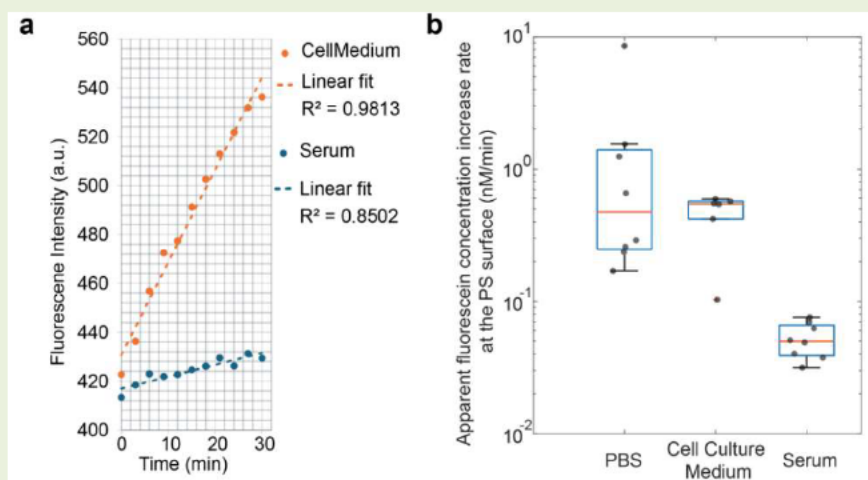


Figure S3| Semi-quantitative estimation of apparent hydroxyl radical production at PS microplastic-water interface under different environments (a) Representative time-dependent APF fluorescence signal measured at individual PS particle surfaces under different solution environments. The surface-associated fluorescence increases approximately linearly over the measurement window, supporting the use of linear fitting to extract the rate of signal increase for each particle. (b) Apparent interfacial fluorescein increase rates at the PS surface in PBS, cell culture medium, and serum, obtained by converting the fitted fluorescence increase rates into apparent concentration increase rates using calibration in the corresponding solution environment.

Supplementary Note 1. Semi-quantitative estimation of apparent hydroxyl radical production rate at the plastic–water interface

To place the observed interfacial physicochemical activity in a broader physiological and environmental context, we sought to obtain a semi-quantitative estimate of hydroxyl radical ($\cdot\text{OH}$) generation at the plastic-water interface. Because the reaction occurs locally within a confined and heterogeneous interfacial region rather than in bulk solution, direct determination of a true steady-state $\cdot\text{OH}$ concentration is not straightforward. In particular, the effective reactive interfacial volume and the true surface area contributing to radical generation are difficult to define precisely for individual particles. Therefore, our analysis was designed to provide a conservative, lower-bound estimate of the apparent interfacial $\cdot\text{OH}$ production rate rather than an absolute interfacial radical concentration.

1. Extraction of time-dependent surface APF fluorescence

Hydroxyl radical generation was monitored using aminophenyl fluorescein (APF), which becomes fluorescent upon oxidation to fluorescein. For each particle, the APF-derived fluorescence signal localized at the particle surface was tracked over time by confocal imaging. The microplastic surface-associated fluorescence region for each particle was segmented to measure the corresponding fluorescence intensity at each time point.

The surface fluorescence signal increased approximately linearly with time for most particles. Therefore, for each particle, the fluorescence trajectory was fit using a linear model:

$$I(t) = k_I t + b$$

where $I(t)$ is averaged surface fluorescence intensity for each particle at time t , k_I is the fitted rate of fluorescence increase, and b is the intercept.

2. Conversion to apparent fluorescein formation rate

As indicated in **Figure 1f**, APF detects the hydroxyl radical generation by reacting with it to form a fluorescein molecule that produces the measured fluorescence signal. To relate the measured fluorescence increase to product formation, fluorescence calibration curves were acquired in the corresponding solution environment (i.e., PBS, serum, and cell culture medium **Figure S17**).

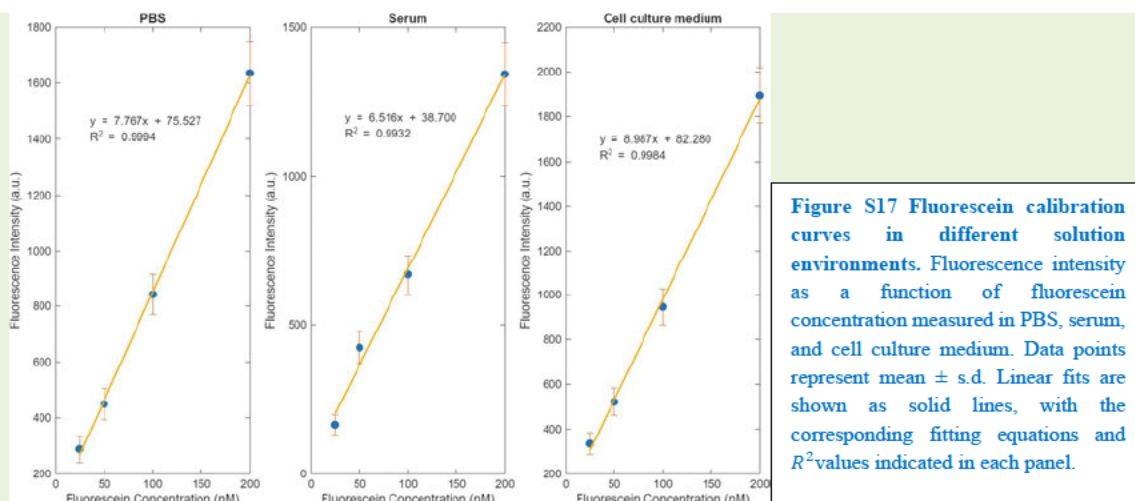


Figure S17 Fluorescein calibration curves in different solution environments. Fluorescence intensity as a function of fluorescein concentration measured in PBS, serum, and cell culture medium. Data points represent mean $\pm$ s.d. Linear fits are shown as solid lines, with the corresponding fitting equations and R^2 values indicated in each panel.

These calibration curves were used to convert fluorescence intensity into an apparent fluorescein concentration at the interfacial region of microplastics. Thus, the fitted slope k_f for each particle was converted to an apparent fluorescein formation rate:

$$C_{\text{Fl}}^{\text{app}}(t) = k_{\text{Fl}}^{\text{app}} t + b'$$

where $C_{\text{Fl}}^{\text{app}}(t)$ is the apparent fluorescein concentration associated with the surface signal, and $k_{\text{Fl}}^{\text{app}}$ has units of concentration per unit time (for example, nM/min).

3. Lower-bound estimate of the $\cdot\text{OH}$ production rate at the plastic–water interface

Assuming approximate 1:1 conversion of APF to fluorescein upon reaction with $\cdot\text{OH}$,

$$R_{\cdot\text{OH}}^{\text{LB}} \approx k_{\text{Fl}}^{\text{app}}$$

the apparent fluorescein formation rate $k_{\text{Fl}}^{\text{app}}$ at the particle surface derived above was used as an operational readout to estimate a lower bound of $\cdot\text{OH}$ production rate $R_{\cdot\text{OH}}^{\text{LB}}$ at the plastic–water interface. This estimate is intended to provide a semi-quantitative measure of the interfacial oxidative activity captured by the APF assay under our experimental conditions, rather than the true total radical generation rate within the full interfacial region.

Several factors make this estimate inherently conservative. First, fluorescein generated near the particle surface may diffuse away from the segmented interfacial region during the measurement, leading to underestimation of local signal accumulation. Second, fluorescein can undergo photobleaching or other side reactions during imaging, further reducing the measured fluorescence increase. Third, radicals generated at the interface may not be fully captured by the APF sensor but rather consumed by competing reactions with surrounding solutes, biomolecules, or the particle surface before being reported through APF-derived fluorescence. In addition, the interfacial region has inevitable heterogeneity on probe accessibility. Together, these factors mean that the measured fluorescence increase reflects only the fraction of interfacial oxidative activity that is retained and captured within the assay readout. Accordingly, the converted apparent

fluorescein increase rate is interpreted here as a lower-bound estimate of the $\cdot\text{OH}$ production rate at the plastic-water interface region, rather than an absolute rate of total radical generation.

9. The current discussion is strong but could be further enriched by: a) Explicitly linking the findings to the emerging field of microdroplet chemistry, highlighting how solid microplastics represent a new, widely distributed platform for such interfacial phenomena. b) Proposing concrete materials-design principles (e.g., how surface hydrophilization or permanent charging could suppress this intrinsic activity to engineer safer plastics). c) Speculating on how this activity might influence the environmental fate of co-pollutants (e.g., degradation of adsorbed organic pollutants).

We sincerely thank the reviewer for these insightful suggestions. We agree that these perspectives substantially broaden the implications of our findings and enhance the overall impact of the manuscript.

For point (a), we have now explicitly connected this finding to the emerging field of microdroplet chemistry. We further elaborate on how solid microplastics, as investigated in our manuscript, may constitute a distinct and environmentally widespread platform for analogous interfacial phenomena.

Our work also contributes to a fundamental understanding of interfacial water. Hydrophobic water interfaces exhibit unique structural and physicochemical properties^{13,14,26,27}, underpinning the emerging field of microdroplet chemistry^{28,29,5,30–35}. Recent estimates of a strong interfacial electric field of $50\text{--}90\text{ MV cm}^{-1}$ ^{8,36} can thus alter the reactivity landscapes at the interface and promote radical generation, including the conversion of OH^- ion to $\cdot\text{OH}$ ^{2,14,25,30–33,37–41}. Our present study not only supports this broader phenomenon of interfacial water reactivity but also provides a facile platform to modulate and study the still-elusive connection between structure and reactivity, offering insights into the factors governing reactivity at other water–hydrophobe interfaces. At the same time, it places this fundamental interfacial chemistry in a context of environmental and public health relevance, particularly given widespread exposure and concerns over chronic biological responses. Lastly, our simulation and calculation not only provide a quantitative measure of the energetic cost of $\cdot\text{OH}$ generation but also reveal a synergistic role between interfacial water structure and surface electrostatics in determining the chemical reactivity, laying a framework for further theoretical explorations.

For point (b), we thank the Reviewer for this valuable suggestion. We agree that our findings not only reveal a previously underappreciated mechanism underlying microplastic interfacial activity, but also suggest possible safer-by-design principles for future materials development. In response, we have revised the Discussion to note that increasing surface hydrophilicity can help suppress the intrinsic physicochemical activity arising from water–hydrophobe interactions, thereby guiding the design of safer plastics.

Moreover, the structure-activity relationship can provide a new engineering perspective beyond empirical strategies to meet the growing demand of sustainability and safety of commodity plastics in modern industry. The empirical strategies to build biocompatible plastics, such as adding hydrophilic plasticizer to reduce hemolytic activity, may lack efficacy, efficiency and cause problems from unexpected behavior such as leaching⁵⁸. Although there can be other factors

involved, such as surface morphology, functionalization, and environmental conditions (e.g., pH, temperature, ionic strength, and chemical contaminants), we identify surface water interaction as one previously unappreciated factor. This insight points to a potential safer-by-design principle via tuning surface hydrophilicity. Looking ahead, the discovery of intrinsic physicochemical activity from water-microplastic interfaces has ample implications spanning environmental science, human health, materials design, and the fundamental science of water.

For point (c), we thank the Reviewer for this valuable suggestion. We agree that the intrinsic surface reactivity revealed in this work could have important implications for the environmental behavior of microplastics, particularly with respect to plastic aging and the fate of co-pollutants associated with their surfaces. Accordingly, we have revised the Discussion to highlight that this interfacial activity may influence processes such as the degradation of adsorbed organic pollutants, thus providing a new perspective for understanding microplastics in environmental settings.

In *this* context, we identify an important property that has long been overlooked: interfacial water (but not other solvents) interacting with microplastic surfaces can actually create electrified environments that turn microplastics into a factory of spontaneous radical ($\bullet\text{OH}$) generation. Notably, this behavior is mechanistically distinct from the previously studied radical generation processes such as photo-irradiation or chemical oxidation^{43,44}. Instead, the activity observed here arises intrinsically from water–hydrophobe interactions. Such reactivity can directly influence plastic aging and environmental fate of co-pollutants^{59–61}. Importantly, its rate can be physiologically relevant to induce damages on biomolecules and cells under ambient environment⁵⁷.

Minor Comments:

1. Fig. 1: Please indicate the statistical significance of the differences in panels b, i, and k. Error bars are present but no statistical test is mentioned.

We thank the reviewer for the suggestion. Statistical significance for panels b was evaluated using two-way repeated-measures ANOVA. Panel i (now Panel h after rearrangement) shows a representative time trace from a single-particle measurement. Because the data points are temporally correlated and do not represent independent replicates, conventional statistical tests are not appropriate. To clarify this, we have revised the figure caption to indicate that the curves represent representative single-particle measurements. and panel k (now Panel j after rearrangement) using one-way ANOVA. The results have been added to the revised figure and caption.

b. Time trace of the absorbance changes in methyl orange water solutions incubated with/without PS microplastics. Statistical significance between curves was evaluated using two-way repeated-measures ANOVA., $p < 0.0001$

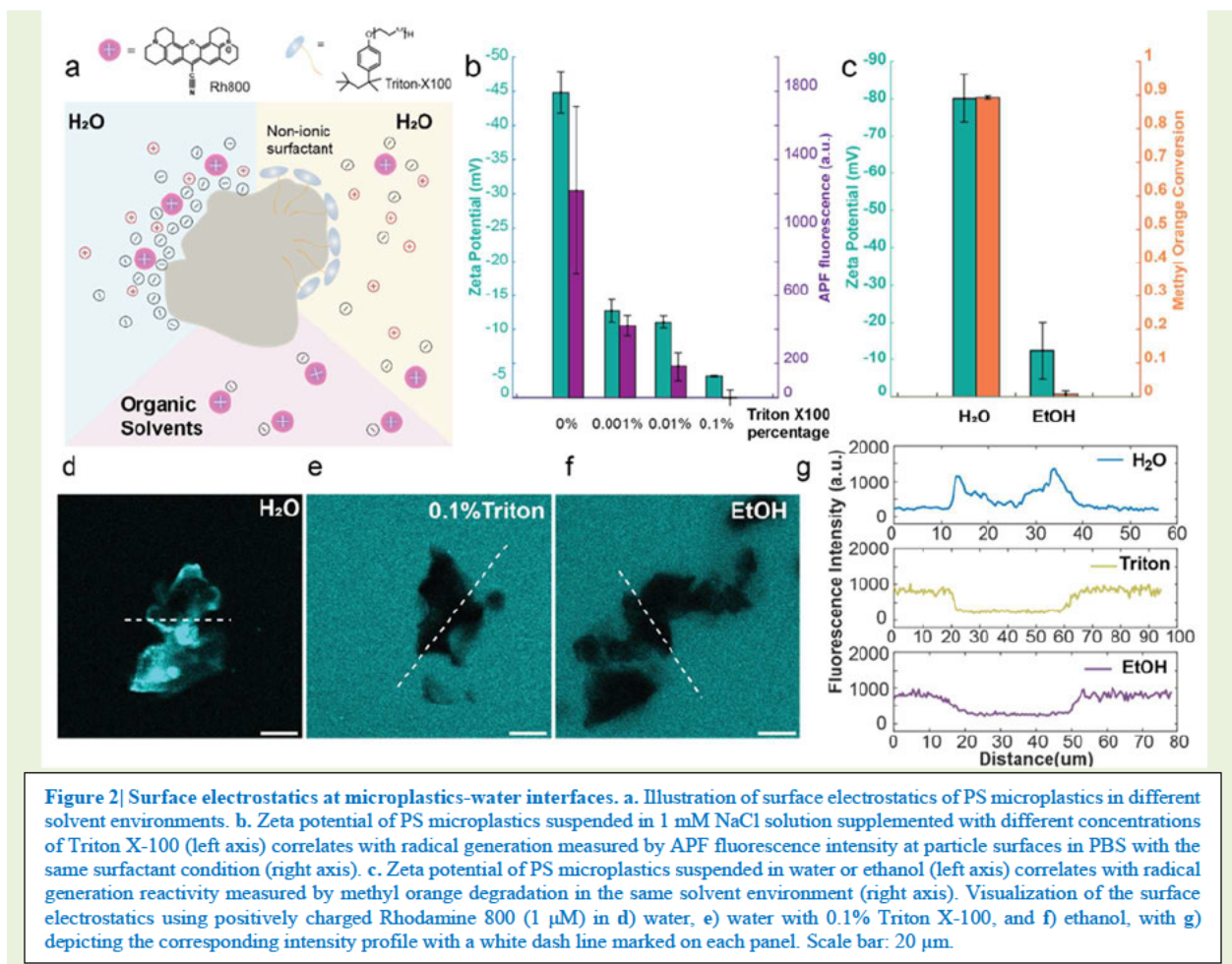
h. Time trace of the APF fluorescence intensity measured at a representative PS microparticle surface in PBS solution with/without Triton X-100. A linear fit to the PBS trace (dashed line, $R^2 = 0.95$) highlights the monotonic increase over time.

j. Quantification of APF fluorescence intensity measured at the surface PS microparticles in PBS solution supplemented with different concentrations of Triton X-100. Background is subtracted from fluorescence intensity of the same APF solution with no PS microplastics. One-way ANOVA with Tukey post hoc test.

APF fluorescence intensity measured at the surface of PS microparticles in PBS solution differs significantly from all Triton conditions ($p < 0.0001$).

2. Fig. 2g: The x-axis appears to be partially obscured and should be corrected for clarity. A careful check of all figures and labels throughout the manuscript is also recommended to avoid similar presentation issues.

We thank the reviewer for pointing this out. The x-axis in Fig. 2g has been corrected in the revised figure for improved clarity. In addition, we have carefully reviewed all figures and labels throughout the manuscript and corrected minor formatting and presentation issues where necessary.



3. Page 3, last paragraph: The transition to microdroplet chemistry feels slightly abrupt. Consider a smoother bridging sentence.

We thank the reviewer for this helpful suggestion. We agree that the transition to microdroplet chemistry in the last paragraph of Page 3 was somewhat abrupt. To improve the logical flow, we have revised this section by adding a bridging sentence that connects the observed plastic-water interfacial reactivity to previously reported interfacial phenomena in microdroplet systems. This modification should provide smoother narrative continuity and better contextualizes our findings within the broader framework of interfacial chemistry.

Importantly, this intrinsic activity arises from water-hydrophobe interfacial physics, including interfacial water structure, electrostatics, and partial solvation. These features closely resemble those implicated in the emerging field of microdroplet chemistry, where air-water interfaces have been shown to accelerate a wide range of reactions and promote redox processes that are otherwise unfavorable in bulk water^{28,29,5,30–35,8,36,14,7,62,37,38,25,39,40,2}. By analogy, the widespread and persistent hydrophobic surfaces of microplastics may serve as an alternative, solid-supported platform for similar interfacial chemical activity.

4. Supplementary Methods: The description of ReaxFF/CGeM simulations is excellent. Please also briefly state why this method was chosen over alternative reactive force fields.

We have revised the Supplementary Information as requested by Reviewer 3, and also included much more theoretical detail as requested by other reviewers.

Non-reactive and Reactive Force Fields: For many of the structural analyses used in this study we used the force field combination of OPLS-AA for the polymer and the SPC/E water model. But for the vertical ionization energy (VIE) calculations, we used a more sophisticated ReaxFF/C-GeM model to describe water, OH⁻ and Na⁺. Previous studies have shown that classical fixed-charge OH⁻ force fields often predict overcoordinated hydration environments, frequently yielding coordination numbers exceeding six. In contrast, ab initio simulations and experimental evidence indicate that hydroxide is best described as a hypercoordinated species with approximately three to five hydrogen bonds. In this context, reactive force-field approaches such as ReaxFF/C-GeM provide a more physical description by explicitly accounting for charge redistribution and proton-transfer dynamics. ReaxFF/C-GeM has been shown to accurately capture the energetics and dynamics of hydronium and hydroxide ion species.¹⁹ In particular, proton-transfer events that interconvert different hydration states of hydroxide (e.g., transitions between four- and three-hydrogen-bond configurations) have been identified as rate-controlling steps for hydroxide diffusion. ReaxFF/C-GeM have been shown to reproduce both the solvated structure of hydroxide and its diffusion coefficient in water with reasonable accuracy (e.g., $\sim 0.40 \text{ \AA}^2 \text{ ps}^{-1}$ from ReaxFF/C-GeM compared to $\sim 0.56 \text{ \AA}^2 \text{ ps}^{-1}$ experimentally). Such capabilities are especially relevant for resolving interfacial hydration structure and ion mobility at polymer–water interfaces, which are central to the present study.

Referee #5 (Remarks to the Author):

This manuscript presents an ambitious and potentially impactful study combining experiments and simulations to argue for intrinsic physicochemical activity at microplastic–water interfaces. While my expertise lies primarily in computational modeling and simulations rather than experimental techniques, I find the overall conceptual framework compelling and the computational component central to the mechanistic interpretation of the experimental observations.

The simulation and ab initio calculations provide valuable insight into the proposed structure–activity relationship, particularly the role of interfacial water structure, partial solvation of hydroxide ions, and electrostatic effects in lowering the vertical ionization energy at hydrophobic plastic–water interfaces. These results are generally consistent with recent advances in interfacial water chemistry and help rationalize the experimentally observed trends.

We thank the reviewer for the clear summary of our paper and see our work as compelling.

However, several important methodological details related to the simulations are missing or insufficiently described, which currently limits reproducibility and a full assessment of the robustness of the conclusions:

We agree that we could be clearer in the narrative as the reviewer points out below. We have addressed the concerns in detail below.

1. The manuscript does not clearly justify the choice of modeling a single long polymer chain rather than multiple polymer chains of moderate length. Because the polymer necessarily interacts with its periodic images under periodic boundary conditions, it is important to clarify whether the resulting chain conformations are physically representative. In particular, the authors should demonstrate that key conformational metrics, such as the radius of gyration and end-to-end distance distributions, are consistent with the expected behavior for this polymer under the simulated conditions.

We thank the reviewer for this important point. The present work focuses on interfacial structural and hydrophobic properties of polymers and their interactions with interfacial water, rather than macroscopic rheological behavior or entanglement dynamics. For this purpose, modeling the polymer as a single sufficiently long chain facilitates the formation of a stable interfacial morphology within accessible simulation times and reduces statistical fluctuations associated with systems containing many shorter chains. In addition, this approach effectively minimizes chain-end artifacts, as the experiments were conducted on polymeric plastics rather than oligomers, in which side-chain functional groups are far more numerous than chain-end groups. These advantages make this approach common in simulation studies.

To verify that the resulting conformations are physically reasonable, we report that the equilibrated systems reproduce physically reasonable bulk densities (Table S3) using a standard 21-step protocol⁶³. Together, these results support that the single-chain representation is appropriate for the present interfacial study.

Table S3: Densities of simulated plastics compared to experiment. Simulated densities of polymer systems using OPLS-AA compared with experimental values for MPs⁶⁴ described in Figure 4. Each system is modeled as a single long chain with a degree of polymerization (DOP, number of repeat units) sufficient to ensure bulk-like behavior; structures are equilibrated using a standard 21-step protocol⁶³.

Plastic	DOP	Simulation Density	Exp. Density
PE	13198	0.821	0.855-0.990
PMMA	2700	1.100	1.170-1.200
PVC	6600	1.339	1.332-1.352
PS	2500	1.008	1.040
PP	4400	0.853	0.855-0.864
PET	1800	1.231	1.300-1.400

2. While the Willard–Chandler interface is referenced, further details on how the interface was identified in practice and how long the systems were equilibrated before and after introducing water (and ions) should be clearly stated.

We thank the reviewer for this point and have clarified the definition of the interface and equilibration procedure in the revised manuscript.

It is well known that the hydroxide ion has a water coordination numbers between of ~ 5.5 - 6.0 ^{3,4}, and we find that the low-VIE tail for PE- and PVC-water arises exclusively from undercoordinated OH⁻ configurations (i.e., partial solvation⁵) located within ~ 5 Å of the Willard-Chandler Interface⁶ (WCI, the instantaneous interface defined as the isodensity surface of the water oxygen density field at half of the bulk liquid density) as seen in Fig. 4b.

3. Figure 4e correlates dangling OH populations with water contact angles. It is unclear whether the contact angles shown are directly computed from the current simulations or taken from literature databases. If they are not derived from the present simulations, this should be stated explicitly; if they are, the computational protocol used to obtain them should be described.

We obtained the contact angles from previously reported database as described in the caption of Fig. 3c and updated in the Fig. 4e.

(e-f) Simulated ratio of surface dangling OH groups (defined as water without any acceptor (X) within an intermolecular O $\cdots$ X distance less than 3.5 Å and with an H–O $\cdots$ X angle (β) smaller than 50°) versus (e) water contact angle (θ) reported from Accu Dyne Test™ Surface Energy Database⁶⁵

4. The number of independent configurations used for the vertical ionization energy calculations is briefly mentioned, but additional clarification on sampling, convergence, and uncertainty estimates would strengthen confidence in the reported low-energy tails.

We thank the reviewer for this comment. To ensure consistency and convergence across systems, we have extended the simulations to timescale of 2 ns for each polymer-water system. The time-resolved VIE distributions demonstrate that the statistics are well converged over the simulation

timescale, while the spatial distributions of undercoordinated hydroxide ions relative to the interface are consistent with the observed trends in VIE behavior across different polymer systems.

We have added the following text and figures to the Supplementary Information.

To ensure consistency and convergence across systems, all MD simulations using ReaxFF/C-GeM are over a timescale of 2 ns for each polymer-water system. The time-resolved VIE distributions demonstrate that the statistics are well converged over the simulation timescale, while the spatial distributions of undercoordinated hydroxide ions relative to the interface are consistent with the observed trends in VIE behavior across different polymer systems. The results shown in the main text (**Figure. 4a and 4c**) were obtained from one representative 500 ps trajectory window, from which configurations were sampled every 2.5 ps. By contrast, **Figure S16** is included primarily to demonstrate convergence across the full 2 ns simulation. For this analysis, the trajectory was divided into four consecutive 500 ps windows, and configurations were sampled every 5 ps within each window, yielding approximately 100 configurations per segment. Due to occasional SCF convergence failures in the electronic structure calculations, the number of successfully evaluated configurations is slightly reduced but remains sufficient to construct statistically meaningful VIE distributions. To improve the sampling of rare interfacial configurations, we additionally employed a targeted sampling scheme based on structural criteria (distance to the WCI < 5 Å and hydrogen-bond coordination number < 4), with configurations selected at 1 ps intervals. As shown in **Figure S16**, the time-resolved VIE distributions reveal distinct behaviors across the three polymer systems. In the PE system, a low-VIE tail is observed in both the early and late trajectory segments, indicating that such configurations are sampled repeatedly over the course of the simulation. In the PVC system, a low-VIE tail emerges in the later trajectory segment (1.5–2.0 ns), consistent with the behavior observed in PE, but with lower frequency, reflecting the presence of rare interfacial configurations. In contrast, as shown in **Figure S15**, the PMMA system exhibits a significantly lower population of undercoordinated hydroxide ions in the interfacial region, and no configurations corresponding to the low-VIE tail are observed over the full 2 ns simulation. These observations further support the connection between interfacial hydroxide structure and VIE behavior across different polymer systems.

5. Furthermore, how sensitive are the VIE distributions to the assumed surface charge density? To what extent does the chosen charge density represent an upper bound versus a typical experimental condition? Can the authors comment on whether similar trends are observed without explicit charge manipulation, relying solely on structural undercoordination?

We thank the reviewer for this important question. The sensitivity of VIE to interfacial charge density has been discussed in previous work (e.g., Fig. 2c in Nat. Commun. 15, 47879 (2024))³⁷, where the VIE shift was shown to vary continuously with the local electric field or effective surface charge density. This behavior is consistent with an electrostatic picture and can be described by a Coulombic model for the interaction between charged species, in which the VIE responds monotonically to changes in the local electrostatic environment, and effectively becoming ~ 0 well below the Rayleigh limit for simple oil droplets (hexadecane).

In the present study, the interfacial charge density is controlled by introducing four NaOH molecules into the water phase (box size $\approx 3.6 \times 3.6 \times 7$ nm³), corresponding to a surface charge density comparable to experimentally reported values (e.g., Beattie et al.⁹). As clarified in the

Supporting Information, this choice represents a physically reasonable estimate of interfacial charge density rather than an extreme upper bound:

Vertical ionization energies (VIEs) calculations and sampling details. For VIE calculations, four NaOH molecules were added to the water phase (box size $\approx 3.6 \times 3.6 \times 7$ nm³) based on the surface charge density reported by Beattie et al.⁹ ...

Since the experimentally measured zeta potential reflects the potential at the slip plane, this implies a net charge imbalance within the interfacial region, i.e. the droplet effectively carries excess negative charge. To model this, we removed a single Na⁺ ion as a practical way to reproduce this charge imbalance in a finite simulation setup. Explicitly resolving the electric double layer would require substantially larger system sizes and longer time scales than are currently feasible. Removing Na⁺ therefore provides a simple but direct way to impose an experimentally motivated interfacial charge density consistent with experimentally measured zeta potentials. All results are shown in **Figure 4c**.

Importantly, our results show that the emergence of low-VIE configurations is not dependent on explicit charge manipulation. Interfacial undercoordination alone leads to a small but discernible low-VIE tail in hydrophobic systems (as reflected in Fig. 4a). The presence of interfacial charge imbalance further lowers the VIE of these configurations (as reflected in Fig. 4c). but does not fundamentally alter the underlying mechanism.

6. it would be helpful if the authors explicitly discuss potential sources of deviation between simulations and experiments, such as surface roughness and heterogeneity in real microplastics and the role of trace oxidation or additives in real-world samples (even though pristine samples are emphasized).

We thank the Reviewer for raising this insightful point. We agree that deviations between simulations and experiments can arise from structural and chemical complexities of real microplastic surfaces that are not explicitly included in the current simulations. In particular, real microplastics can exhibit surface roughness, spatial heterogeneity, and trace surface oxidation or additives, all of which may influence the local interfacial environment and contribute to experimental variability. Indeed, our imaging results reveal clear heterogeneity in the physicochemical activity at plastic–water interfaces, and the Figure S2 in the supplementary information further shows that even for the same type of plastic, differences in surface oxidation are associated with different levels of interfacial activity.

These factors are not explicitly captured in our simulations, which were designed to focus on the intrinsic activity arising from water–hydrophobe interactions at the molecular level from plastic–water interface. As such, the simulations are not intended to reproduce all of the complexity present in real samples, particularly features such as surface roughness or sparsely distributed trace oxidation sites, which are also not practical to model under current computation power. Nevertheless, by focusing on the intrinsic interfacial contribution, the simulations provide a molecular-level picture that qualitatively explains the observed trends across different plastics and under different interfacial conditions.

We appreciate reviewer’s insight and have now added text in the revised manuscript to clarify these possible sources of deviation and the scope of the simulations.

Despite possible deviation considering the surface heterogeneity of real-life plastics due to roughness and trace oxidation or additives, our model provides a molecular-level mechanism for interfacial reactivity.

7. The authors are also advised to discuss prior studies on polymer surface charging arising from contact electrification, which are directly relevant to the present work. In particular, the recent study published in Nature Communications 15, 2616 (2024) provides important insights into interfacial charge generation on polymeric surfaces, and the references therein would offer valuable context for interpreting the observed interfacial electrostatics.

We thank the reviewer for pointing out the relevance of prior studies on polymer surface charging and contact electrification, particularly the recent work published in Nature Communications 15, 2616 (2024). That study demonstrated that contact charging between insulating polymers can be understood as a thermodynamically driven ion-transfer process, in which the preferred charging direction is governed by the free energy of water ions ($\text{H}_3\text{O}^+/\text{OH}^-$) at polymer–water interfaces.

In particular, their simulations showed that hydrogen-bonding polymers stabilize H_3O^+ more strongly, leading to systematic charging trends across polymer contact pairs. This work provides an important thermodynamic framework for understanding the origin of polymer surface charging.

Rather than focusing on contact–separation events or charging trends between polymer pairs, we investigate interfacial reactivity and electrostatics at polymer–water interfaces. Consistent with the thermodynamic picture proposed in the above study, our results support the view that negative polymer zeta potentials and contact electrification phenomena originate from interfacial charge generation mediated by water ions. By explicitly resolving interfacial water structure and VIE of hydroxide at the molecular scale, our study provides mechanistic insight into how such reactivity at water-polymer interface happened.

We have added the following text:

Recent work has shown that polymer surface charging and contact electrification can be understood as a thermodynamically driven ion-transfer process involving water ions at the polymer-water interface⁶⁶. Our calculations instead focus on interfacial reactivity arising from undercoordinated OH^- at the most hydrophobic interface which gives rise to low-VIE states.

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Response to Reviewer 1

Qian et al. have done really substantial work in revising the manuscript and have addressed the majority of my concerns, especially regarding the application of the combined force field. The revised figures are much better as well. Overall, the manuscript has been greatly improved. However, the current mechanistic interpretation remains insufficiently quantitative for a high-impact claim. While I appreciate the great revision and authors' efforts, I still have a few remaining questions and suggestions that should be addressed before I can recommend the manuscript for publication, as listed below.

1. The revision addresses my previous concern regarding the limited comparison across polymers by adding PVC, the VIE calculation is now rather convincing. But, the mechanistic interpretation of VIE remains insufficiently clarified. I would still like to ask how this VIE should be used linking with experiments. Even in the cases where the authors refer to the "lower tail" of the VIE distribution, the value is still around 100 kcal/mol, which corresponds to a process that appears impossible to occur thermally at room temperature. The authors may correct me if my understanding is inaccurate, but I understand VIE here as corresponding to the process



The fate of the electron is missing. There should then be a second half-process, in which the released electron is either solvated (similar to that in 10.1021/acs.jpcclett.2c01721) or accepted by another species, for example by the plastic phase: $\text{PLASTICx}^- + e^- \rightarrow \text{PLASTIC}(x+1)$. This second step is related to the electron-accepting ability of the surrounding species or interfacial environment. It may be sufficiently favorable to compensate for part of the VIE penalty. I would therefore like to see a comparison between different possible electron destinations, for example a solvated electron near the surface versus electron acceptance by the plastic phase. Calculating the electron-accepting energy of the plastic surfaces, or of relevant interfacial trap states, would provide supporting evidence. Assuming the process has no additional barrier, the overall energy change could provide an upper-bound estimate for the kinetics, or at least help judge whether the process is thermodynamically plausible under the given conditions, which helps to explain how the proposed VIE lowering corresponds to a real kinetic pathway that can occur over experimentally relevant timescales, such as days. Overall, I expect to see a clearer mechanistic explanation and description of the full process. Currently author only state a powerful first-half process, which is great but seems not completed.

2. The authors now clearly explain that the charge of the plastics arises from the combination of the plastic itself and the surrounding OH^- (and perhaps also electrons), which is reasonable. However, I remain being confused by the claim that "(in a negatively charged surface), VIE distribution toward energies well below 100 kcal/mol (even approaching zero) to more readily create $\text{OH}^\bullet$ ". I believe this is due to the lack of discussion, as I noted in Suggestion 1. The authors appear to have missed my point regarding the possible "runaway" behavior of charge. As currently presented, the manuscript seems to suggest that when the system is negatively charged, the VIE

becomes lower, and $\text{OH}^\cdot$ radical production becomes easier. My understanding is that, in a negatively charged system, even if the VIE of OH^- is lowered, the species receiving the electron is already negatively charged. Therefore, the second half-process of electron acceptance, (or equivalently the solvation of an additional electron near the interface) should become less favorable. Whether the overall $\text{OH}^\cdot$ production is accelerated should depend on the competition between these two effects. I therefore expect more discussion and, if possible, more quantitative analysis from the authors regarding this point.

Response: We sincerely thank the reviewer for these insightful and helpful comments. We believe comments 1 and 2 are usefully combined to address the deficiency that the VIE alone does not provide a complete thermodynamic description of $\text{OH}^\cdot$ formation that connects to experiments. We also now understand that the reviewer's concern also extends to whether a negatively charged interface would intrinsically disfavor generation or stabilization of an additional electron during $\text{OH}^\cdot$ formation. Therefore our revision addresses more clearly what are the interfacial acceptors and possible fate for the electron.

The hydrophobic MPs are themselves not charged, but the overall negative charge of the more hydrophobic MPs are similar to that of an oil-water emulsion which forms a double layer at the interface in which the zeta potential is measured at the slip plane. To explain the large negative zeta potential of PE, for example, within the slip plane are the hydroxide ions and hydronium counterions, balanced such that there is a net negative charge that electrostatically stabilizes the emulsion or MP from coalescing (Fig.

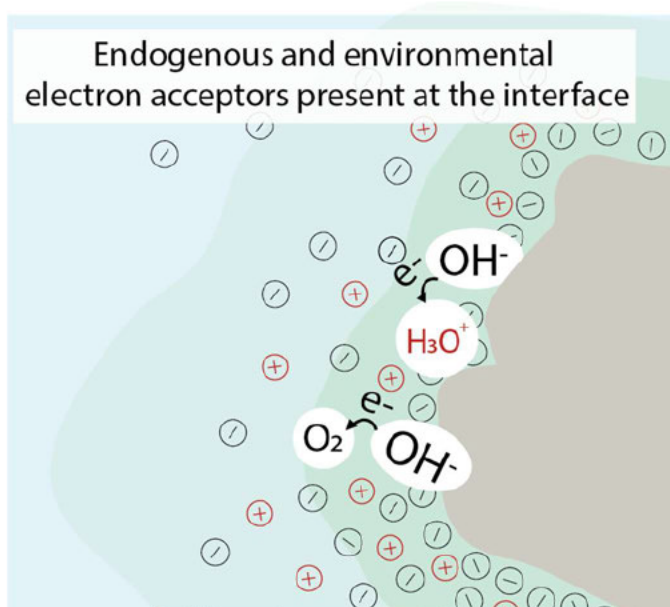


Fig. R1. Double layer structure and presence of possible electron acceptors/sinks on plastic hydrophobic water interfaces

R1). Hence the presence of hydronium is a positive ion that readily accepts an electron. We have calculated the vertical electron attachment to this positive species in previous work¹ and found a favorable energy of $\sim 50\text{-}100$ kcal/mol to form hydrogen radicals. Moreover, environmental sink can be present ubiquitously such as dissolved oxygen in water, which can also act as an electron acceptor to form $\text{O}_2^{\cdot-}$ in a thermodynamically favorable way². Finally, the favorable solvation energy of the hydrated electron is ~ 87 kcal/mol³. Thus, although a VIE value near 100 kcal/mol might appear far too large to be interpreted as a room-temperature thermal event by itself, the synergetic role of multiple potential electron acceptors in the system can compensate for a substantial fraction of this energetic cost.

We have added the following paragraph to the revised Results as follows:

The hydrophobic MPs are themselves not charged, but the overall negative charge of the more hydrophobic MPs are similar to that of an oil-water emulsion which forms a double layer at the interface in which the zeta potential is measured at the slip plane (**Fig. 4f**). Our calculations focus on interfacial reactivity arising from undercoordinated OH^- at the most hydrophobic interface which gives rise to low-VIE states as a molecular-level mechanism for interfacial reactivity. The lowered VIE for electron removal are populations of hydroxide ions at the interface that are undercoordinated, but ~ 100 kcal/mole is still too large to explain how a hydroxide radical can form under ambient conditions. Hence the fate of the electron is critical. Positive hydronium ions or dissolved oxygen could readily serve as electron acceptors with favorable vertical attachment energies of the electrons that create molecular hydrogen or superoxide anion with release of energy of ~ 50 - 100 kcal/mole^{1,2}. Another electron sink could be hydrated electron after it diffuses into the bulk³. Thus, although a VIE value near 100 kcal/mol is far too large to be interpreted as a room-temperature thermal event by itself, stabilization by other electron acceptors/sinks can compensate for a substantial fraction of this thermodynamic cost.

We have revised Figure 4 and caption as follows:

(f) Double layer structure and presence of possible electron acceptors/sinks on plastic hydrophobic water interfaces.

We have revised the Discussion as follows:

Recent estimates of a strong interfacial electric field of 50 – 90 MV cm^{-1} ^{4,5} can thus alter the reactivity landscapes at the interface and promote radical generation, including the conversion of OH^- ion to $\bullet\text{OH}$ with thermodynamics that overcome the reduced but still large VIEs^{1,6–16}.

The question of how the MP systems avoid run-away charge is also understood from the double layer picture. We agree with the reviewer that the negative interfacial potential, while lowering the VIE cost since it destabilizes the OH^- ion, would also not favor indefinite accumulation of the detached electron at the interface. Instead, the detached electron is expected to be consumed by electron acceptors or is stabilized as a hydrated electron, and then screened by the surrounding electrolyte environment. This is supported by time-resolved electronic SFG measurements of hydrated electrons at aqueous hydrophobic interfaces which found that the interfacial hydrated-electron signal decays with a lifetime of approximately 12 ps¹⁷, with simulations showing that the electron diffuses into the bulk and the corresponding neutral radical remains at the interface after electron separation. Therefore, the proposed process should be viewed as interfacial charge separation followed by scavenging by electron sinks (**Fig. R1**), rather than as direct accumulation of additional negative charge on the plastic surface.

3. I would encourage the authors to open-source a minimum reproducible example for their combined force-field implementation. For instance, although the authors cite the original work on the Reax/CGem (10.1021/acs.jpcclett.0c02516) force field, that work does not appear to provide force-field parameters for Na⁺ or Cl⁻. Providing a minimal working example would greatly enhance the reproducibility and transparency of this work. This would be particularly valuable for a Nature-level manuscript, as the method has the potential not only to support the present conclusions, but also to guide and even teach the broader community in applying similar combined force-field approaches to related interfacial systems.

We thank the reviewer for this helpful suggestion. In response, we have provided the relevant source code and example files through the link:

https://github.com/Ruo7Zhao/microplastic_water_interface/tree/main/reaxff-cgem-oplsaa-hybrid-MD/demo-for-PE

To improve reproducibility and make the hybrid force-field setup easier to follow, we added a minimal working example for a PE–water interface using the ReaxFF-CGeM/OPLS-AA hybrid force-field approach. This example includes the LAMMPS input script, the initial data file, the ReaxFF-CGeM force-field parameter file, the hybrid van der Waals parameter file, and a README file describing how to run the example. We hope this addition will make the computational workflow more transparent and useful for researchers who wish to apply similar combined force-field approaches to related interfacial systems.

4. I would also like to see a discussion of why OH radicals produced at the plastic–water interface do not react directly with the plastic surface, but can instead be released back into bulk water. Does OH[•] have a weaker interfacial preference than OH⁻? What is the probability, or expected timescale, for such release into the bulk phase? This point is important for connecting interfacial OH[•] formation with experimentally observed ROS release in the aqueous phase.

We thank the reviewer for raising this important point. We first give two relevant answers as to why the OH radical has a stronger interfacial preference than the OH⁻ ion. One is that when an OH⁻ ion becomes a radical, the solvation energy of the radical is reduced compared to the ion which drives the radical to the lowered dielectric at the interface. In addition, time-resolved electronic SFG measurements of hydrated electrons at aqueous hydrophobic interfaces also showed that the corresponding neutral radical remains at the interface after electron separation and the electron migrates to the bulk liquid to gain the highly favorable solvation energy¹⁷.

Regarding the question of why •OH does not react with the microplastic surface, we would like to offer the following explanation. Despite •OH accumulation on the interface, microplastic surface, which are composed of strong chemical bonds, is relatively inert (but not their interfaces!) compared to our probe molecules (methyl orange, APF sensor, DMPO spin trapper, proteins, etc.). These molecules are designed to contain susceptible functional groups to reactive radicals.

Meanwhile, many of these molecules are charged, including APF sensor, methyl orange, etc., so they will be attracted to the double layer on the interface due to Coulombic force. Given their high concentration and reactivity, it is expected that $\bullet\text{OH}$ will react with these molecules instead of the microplastic surface. In real life when these probe molecules are absent, biomolecules with active functional groups can also act as radical sinks in the similar way. Moreover, microplastics also do not possess easily accessible vacant orbitals to accept the electron. For instance, the band gap for crystalline PE is ~ 200 kcal/mol¹⁸. However, we also would like to acknowledge that the reaction of $\bullet\text{OH}$ with the microplastic surface, despite unlikely, is not completely impossible at a long time scale with constant exposure. $\bullet\text{OH}$ can (1) abstract hydrogen atoms and (2) recombine with carbon radicals and form an alcohol group. However, such rare events on the surface are likely difficult to be observed and beyond the scope of our current study. Having said that, this is a good follow-up question and an important line of future work

We have revised the Discussion in the manuscript as follows.

Notably, this behavior is mechanistically distinct from the previously studied radical generation processes, [commonly in the context of microplastic degradation in natural environments](#), such as photo-irradiation or chemical oxidation^{19,20}.

[Despite possible dependency on surface roughness, trace oxidation, and environmental matrices](#), this reactivity can be ubiquitous beyond tested buffer conditions and pristine microplastics in this study (**Fig. S2-3**), with general implications and real-life relevance.

Response to Reviewer 2 &3

Referee #2 (Remarks to the Author): I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

Referee #3 (Remarks to the Author): In this reviewer's assessment, despite the substantial revisions made by the authors, the novelty of the work does not reach the threshold required for publication in *Nature*. The conceptual depth, mechanistic completeness, and evidentiary standard remain below what is expected for this journal.

Specifically:

1. Regarding the issue of novelty, although the authors have responded by providing textual explanations and a comparative table to clarify the differences between this study and their previous work, we still consider that the core content of the present manuscript is more likely an extension of the previous study to a specific application scenario, rather than a substantial breakthrough in terms of scientific questions or mechanistic understanding.

From the Editor: we are not expecting you to address experimentally some of reviewer 3's comments (the environmentally weathered MPs contained in point 5, for example), and have overruled their issues with novelty (point 1)

In light of the editor's note above, we thank the reviewer for raising this concern again and we would like to take this opportunity to reemphasize on the key conceptual novelty of the present study relative to the previous paper in *Nature* 640, 87–93 (2025).

- Discovery of intrinsic chemical reactivity: By harnessing this underexplored water–hydrophobe interactions, we demonstrate spontaneous radical generation under ambient conditions. Rather than physical characterization of interfacial electrostatics, this work establishes an experimental correlation between charge and reactivity, introducing the concept of intrinsic physicochemical activity arising from water–hydrophobe interactions in the context of microplastics.

- Ab initio VIE calculations of OH⁻ at different hydrophobic surfaces: The previous *Nature* study did not include VIE calculations nor address chemical reactivity in the water–oil system⁴. To our knowledge, no prior *ab initio* studies have rationalized why hydrophobic surfaces can give rise to chemical reactivity. Our work is the first to introduce a detailed calculation of the VIE (the ease of liberating electron to produce free radicals) to explain why radical generation might be possible at water-hydrophobe interface.

- Structure–activity relationship: While the previous study examined a single model oil system⁴, here we investigate multiple polymers and show that different plastics interact with interfacial water in distinct ways. The degree of hydrophobicity, quantified through interfacial dangling OH signatures, correlates systematically with both interfacial charging and radical generation. This establishes the connection between polymer surface and physicochemical activity intrinsic to the

water interface. Such a structure–activity relationship is conceptually novel and provides a predictive framework for understanding why different microplastics may exhibit different chemical and biological impacts.

We believe this perspective will foster interaction between fundamental physical chemists studying interfacial water and environmental scientists investigating micro/nano-plastics, thereby opening new directions for mechanistic studies and mitigation strategies for microplastic pollution.

In addition, this manuscript focuses on radical behavior at the microplastic interface, but the current descriptions may lead readers to mistakenly assume that plastics can undergo spontaneous degradation relatively easily in natural environments. In fact, microplastic degradation in natural environments is usually constrained by multiple factors, including light intensity, oxidant availability, reaction interfaces, environmental matrices, and time scales, and therefore cannot be simply equated with the enhanced degradation process observed in the experimental system. We suggest that the authors further clarify the differences between the experimental conditions and real environmental processes in the manuscript, so as to avoid overgeneralization or misleading interpretations regarding the natural degradability of microplastics.

We understand the reviewers' point but we would like to respectfully point out that our manuscript does not suggest or insinuate that microplastics themselves will easily undergo degradation. In fact, we totally agree that microplastic degradation in natural environments is usually controlled by numerous factors. Having said, water-microplastic interfaces are NOT inert (the central and novel claim of this work) and we showed that with an array of experiments. Our experiments also demonstrated how these reactive interfaces may contribute to downstream biological consequences, which have significant implications for health and environmental perspectives.

We have revised the manuscript as follows.

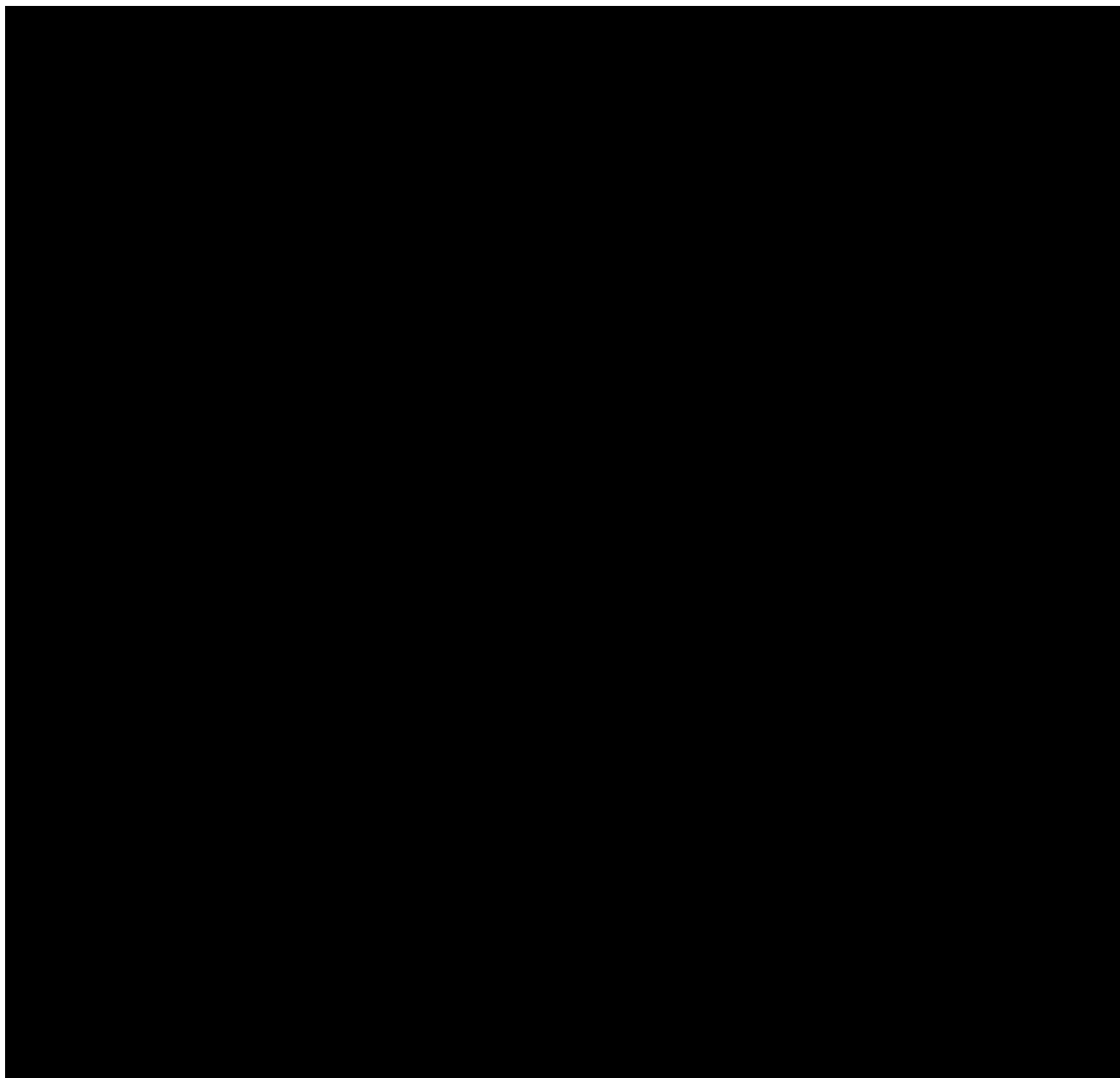
Such reactivity could directly influence plastic aging and environmental fate of co-pollutants^{21–23}. Importantly, its rate can be physiologically relevant to induce damages on biomolecules and cells under ambient environment²⁴. [Despite possible dependency on surface roughness, trace oxidation, and environmental matrices](#), this reactivity can be ubiquitous beyond tested buffer conditions and pristine microplastics in this study (**Fig. S2-3**), with general implications and real-life relevance.

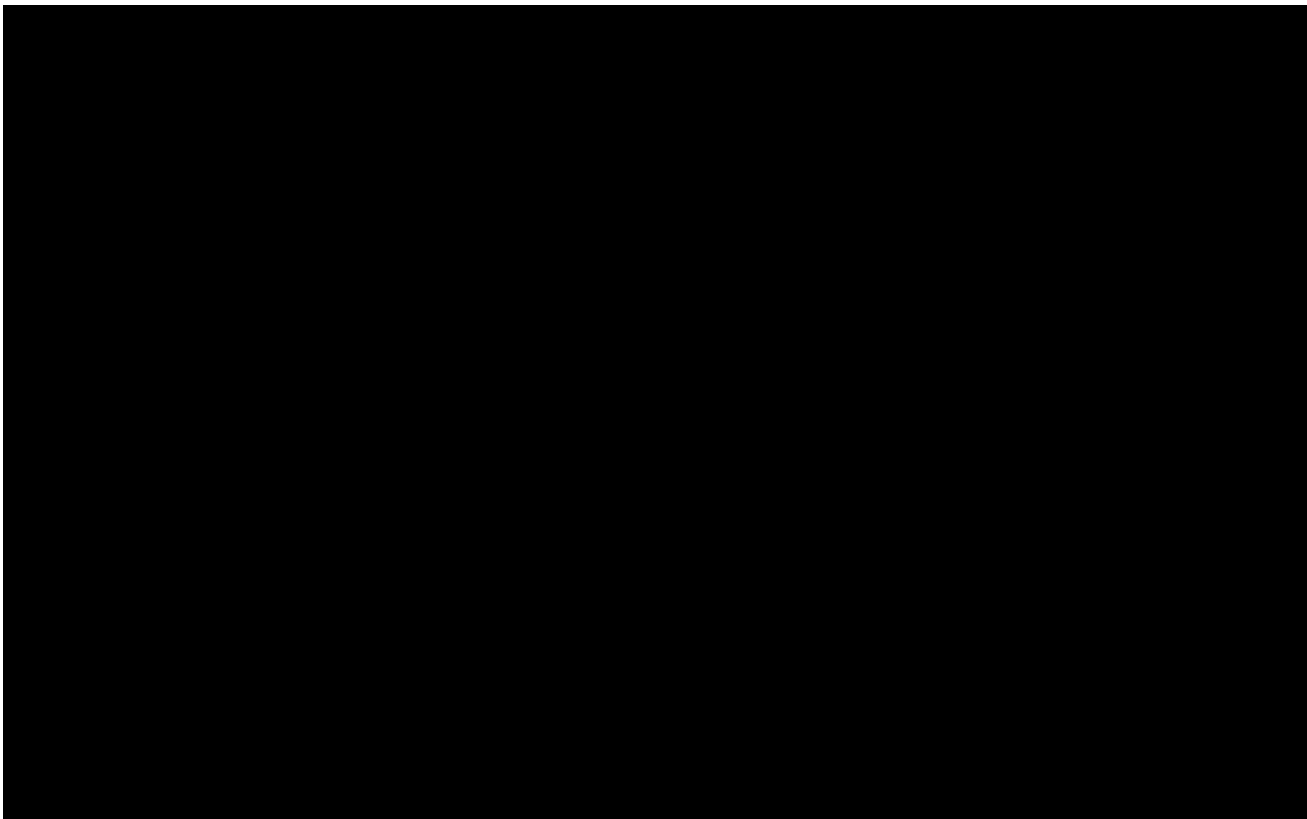
2. Regarding Comment 4 raised in the first round of review, the authors' current response does not sufficiently exclude the possibility that the alcohols used in this study may directly act as radical scavengers. It is therefore recommended that the authors supplement their response with appropriate control experiments involving the addition of the alcohols alone, in order to provide more direct experimental evidence and further strengthen the mechanistic interpretation.

We thank the reviewer for the follow-up question on the role of alcohol (Fig. 1D of the main text) but we would like to respectfully disagree that methyl orange was not degraded in our case simply because the alcohol is a radical scavenger. As demonstrated by Chen et al. in 2000¹⁸, methyl orange can be degraded in methanolic solution by Fenton reaction. Herein, we would like to directly quote two figures from this paper to showcase how methyl orange can be degraded in the presence of methoxy radicals. (1) As shown in their UV-vis spectroscopy, more than half of the methyl orange (with a starting concentration of 0.02 mM) was degraded in the presence of Fe³⁺ (0.02 mM) and H₂O₂ (0.1 mM) with **methanol** as the solvent after 40 mins (**Fig. R2a**). (2) Using DMPO as the spin trapper, radical signals can still be detected using EPR spectroscopy in the presence of MeOH (**Fig. R2b**). These results confirm that alcohol molecules cannot be viewed as universal radical scavengers but rather a chemical species that can react with hydroxyl radicals to form alkoxy radicals, which are also reactive radical species that can degrade methyl orange. Therefore, if radicals did exist in the PS-methanol mixture, as supported by the reported experiment, methyl orange degradation would have been observed regardless of the methanol solvent environment. Yet, as negligible methyl orange degradation was observed in our experiments (**Figure 1d**), consistent with other organic solvents (**Figure 1d**), but in contrast to the behavior in water (**Figure 1d**), alcohols cannot be viewed as a simple radical scavenger here.

3. Direct experimental evidence of interfacial electric fields. The central mechanistic hypothesis relies on strong interfacial electric fields lowering the ionization energy of hydroxide at the microplastic surface. However, current support for this claim appears largely indirect, based on zeta potential measurements and molecular simulations. While

these approaches are informative, they do not directly measure interfacial electric field strength. Given the conceptual importance of this mechanism, more direct interfacial-sensitive experimental evidence (for example, nonlinear optical spectroscopy or related techniques) would substantially strengthen the causal argument. At present, the electric field is inferred rather than directly demonstrated.





4. Causal relationship between electric field strength and radical formation. Beyond establishing the presence of interfacial electric fields, the manuscript does not yet demonstrate a quantitative relationship between field strength and radical generation kinetics. To meet the mechanistic rigor expected for publication in Nature, it would be important to show whether modulation of interfacial electrostatics—such as by systematically varying ionic strength or surface charge—produces predictable changes in radical yield. Demonstrating field-dependent scaling behavior would significantly reinforce the proposed causality between interfacial electrostatics and hydroxyl radical formation.

We thank the reviewer for raising this point. As mentioned in the previous response, our zeta potential measurement is a reasonable indicator of the interfacial electric field. With this in mind, we would like to respectfully point out that we have explicitly demonstrated a quantitative relationship between zeta potential and radical generation activity in Fig. 2b of the main text.

In our experiments, different percentages (0.1%, 0.01%, and 0.001%) of Triton X-100 (a nonionic surfactant) were titrated into the water-PS mixture. The purpose of adding Triton X-100 was to modulate the interfacial electrostatics to understand how the interfacial radical generation activity will be affected. When an increasing amount of Triton X-100 was added to the water-PS mixture, the zeta potential became less negative and eventually zero (**Figure 2b** of the main text), suggesting the loss of surface charges and diminishing interfacial electric fields on PS-water interfaces. Predictably, the APF fluorescence on PS surfaces, which indicates the propensity of radical generation, was also reduced upon an increasing amount of Triton X-100. Therefore, we

have varied the surface charge of water-microplastic interfaces through the introduction of Triton X-100 and the result is consistent with our prediction. Mechanistically, our simulations also showed that Triton X-100 can accumulate on PS-water interfaces and suppress the formation of the hydrophobic interfacial water structure (**Figure S12** of the SI), thereby attenuating the radical generation activity on the interface.

Moreover, another causal evidence comes from the *ab initio* VIE calculation under different surface electrostatics. The removal of positive counterions on PE-water interfaces (to model the accumulation of negative charges on the interface) further reduced the vertical ionization energy of OH⁻ on interfaces to far below 100 kcal/mol (**Figure 4c** of the main text). Together, through experiments and simulations, we have (1) measured surface charges on water-microplastic interfaces, (2) quantified their associated electric field strength, (3) modulated the interfacial electrostatics and observed how radical generation activity changes, and (4) demonstrated how do excess charges reduce the thermodynamic barrier for OH⁻ ionization.

5. Exhaustive exclusion of alternative radical sources. Given the extraordinary nature of the claim that pristine microplastics intrinsically generate hydroxyl radicals without external stimuli, comprehensive exclusion of alternative pathways remains critical. Although additional controls have been included in this revision, further clarification is needed regarding the potential roles of dissolved oxygen, trace oxidative defects, residual polymerization initiators, photochemical effects, or mechanical perturbations. Importantly, real-world plastics are chemically complex materials that often contain a variety of additives, stabilizers, plasticizers, and residual monomers. Moreover, environmental aging processes (e.g., UV exposure, oxidation, hydrolysis) can introduce surface functional groups such as carbonyls, peroxides, and hydroxylated species, which themselves may participate in redox chemistry. Even trace amounts of such chemical heterogeneities could potentially contribute to reactive oxygen species formation and confound attribution to a purely intrinsic interfacial electric-field mechanism. A more systematic characterization of polymer chemical purity and surface functionality, as well as explicit differentiation between pristine laboratory-grade polymers and environmentally aged materials, would therefore substantially strengthen confidence in the proposed intrinsic interfacial origin.

We understand the reviewer's concerns that alternative radical generation pathways may be involved, and our current experiments may not completely rule out these factors. Nevertheless, we would like to take this opportunity to clarify, given the complexity of polymer systems, we fully acknowledge that there are indeed possible confounding factors that may contribute to the generation of radicals. However, exhaustive exclusions of all these factors in a complex system are neither a realistic nor a rational approach. Rather, we evaluated our hypothesis through carefully designed control experiments that isolate our variable of interest.

In the manuscript, our central hypothesis is "interfacial water (but not other solvents) interacting with microplastic surfaces can create electrified environments that turn microplastics into a factory of spontaneous radical ($\bullet$ OH) generation". If interfacial water on microplastic were the key variable

that controls such reactivity, perturbing the interfacial water structure on microplastics, while keeping all other factors constant, would diminish such reactivity in a predictable manner. In our case, we added a nonionic surfactant Triton X-100 at different concentrations to our PS-water mixture to create such perturbations. The same PS microplastic particles were used throughout our experiments and the only difference was the amount of Triton X-100 in the solution. Consistent with our prediction, the radical generation activity on PS-water interfaces decreases progressively in a dose dependent manner (**Figure 1j** of the main text). Importantly, Triton X-100 itself does not quench radical generation (**Figure S4 of SI**). Hence, we conclude that interfacial water structure on microplastics is the pivotal variable governing radical generation in the water-microplastic system. If other confounding factors were to play an appreciable role in the radical generation, observed reactivity would not follow such a systematic and predictable trend simply by adding Triton X-100. Therefore, our conclusion is not drawn from the exhaustive exclusion of all potential confounding factors, but rather from a panel of hypothesis-driven perturbation experiments designed to test our proposed mechanism.

We have also included the following sentences in our discussion section:

Despite possible dependency on surface roughness, trace oxidation, and environmental matrices, this reactivity can be ubiquitous beyond tested buffer conditions and pristine microplastics in this study (**Fig. S2-3**), with general implications and real-life relevance.

6. Universality across diverse polymer systems. Importantly, as also raised by Reviewer 1 regarding the issue of generality, the manuscript proposes a potentially generalizable interfacial physicochemical phenomenon rooted in hydrophobic surface effects. However, the range of polymers examined remains relatively limited. To substantiate claims of generality, it would be valuable to extend the analysis to additional commodity polymers with distinct dielectric properties and surface chemistries, as well as environmentally aged microplastics. Demonstrating consistent behavior across chemically diverse systems would elevate the conceptual robustness and broader relevance of the work.

We thank the reviewer for raising this generality issue. At present, we have already demonstrated this effect among 6 polymer systems. Moreover, in Fig. S2, we also showed how different surface oxidation levels (determined by X-ray photoelectron spectroscopy) on PS from different vendors can affect the interfacial radical generation activity (**Fig. R4, Figure S2**). In our view, the presence of AFP sensor signal in all these samples already provides support for the generality of the effect.

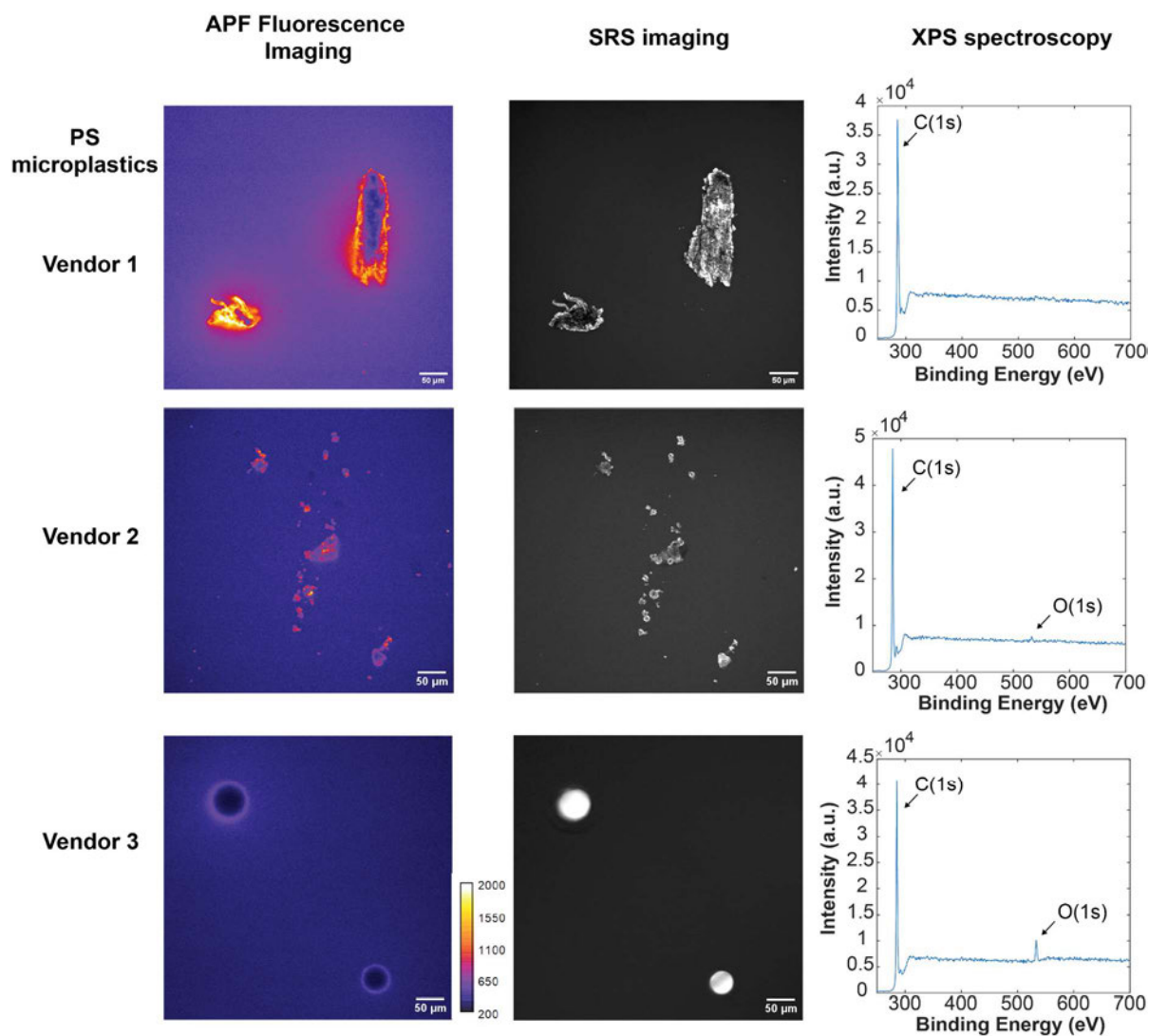


Fig. R4. Universal surface reactivity at PS-water interface in hydroxyl radical generation.

From the Editor: I should note that we do not need you to use environmentally weathered samples (as in reviewer 3's report), but it would likely be helpful to note in the text what complications/confounding factors could arise if you did, or indeed why results on model systems should still hold for such samples.

7. Physical representativeness and boundary definition of the polymer–water model. While the simulations provide important mechanistic insight, the physical representativeness of the polymer–water interfacial model warrants further clarification. The use of a single long polymer chain under periodic boundary conditions raises concerns regarding artificial self-interaction and constrained conformational sampling, which may influence interfacial water structuring and local electrostatics. In realistic microplastic systems, surfaces arise from densely packed polymer chains with finite curvature, surface roughness, and heterogeneous chain orientations, rather than an effectively periodic single-chain construct. Given that the proposed mechanism critically depends on interfacial water structure and electrostatic effects, it is important to demonstrate that key conformational metrics (e.g., radius of gyration, end-to-end distributions, surface density) and interfacial properties are not artifacts of boundary choices. A clearer justification of model design and its physical relevance to experimentally studied microplastic surfaces would substantially strengthen confidence in the mechanistic interpretation.

This question has been addressed in our previous response to Reviewers 1 and 5, both of whom fully acknowledged our answer. We restate it here in case Reviewer 3 may have missed it in the previous round:

The present work focuses on interfacial structural and hydrophobic properties of polymers and their interactions with interfacial water, rather than macroscopic rheological behavior or entanglement dynamics. For this purpose, modeling the polymer as a single sufficiently long chain facilitates the formation of a stable interfacial morphology within accessible simulation times and reduces statistical fluctuations associated with systems containing many shorter chains. In addition, this approach effectively minimizes chain-end artifacts, as the experiments were conducted on polymeric plastics rather than oligomers, in which side-chain functional groups are far more numerous than chain-end groups. These advantages make this approach common in simulation studies. To verify that the resulting conformations are physically reasonable, we report that the equilibrated systems reproduce physically reasonable bulk densities (Table S3) using a standard 21-step protocol⁶³

Analysis of surface functional group densities shows only minor fluctuations (<5%), indicating that the interfacial surface remains structurally stable over the simulation timescale, without significant rearrangement or reconstruction (Figure S12). Therefore, while different polymer morphologies (e.g., crystalline vs. amorphous) may introduce quantitative differences, the primary conclusions of this work—linking interfacial structure to hydroxide VIE and reactivity—are governed by local interfacial chemistry and are expected to remain robust.

8. Robustness and sensitivity of the VIE distributions to modeling assumptions. The reduction in vertical ionization energy (VIE) at the interface is central to the mechanistic argument; however, the robustness of the reported low-energy tail requires further substantiation. In particular, it remains unclear how sensitive the VIE distributions are to key modeling parameters, such as imposed surface charge density, system size, sampling depth, and configuration selection. Since the proposed mechanism relies on rare low-energy configurations, rigorous convergence analysis and uncertainty quantification are essential to establish statistical reliability. Moreover, it would be important to clarify whether similar energetic trends emerge without explicit surface charge manipulation, relying solely on structural undercoordination at the hydrophobic interface. Demonstrating that the energetic lowering is stable across reasonable variations in modeling assumptions would significantly strengthen the credibility of the computational conclusions.

We thank the reviewer for this question, which we addressed in the previous revision in response to Reviewer 5. The sensitivity of VIE to interfacial charge density has been discussed in previous work (e.g., Fig. 2c in ref¹), where the VIE shift was shown to vary continuously with the local electric field or effective surface charge density. This behavior is consistent with an electrostatic picture in which the VIE responds monotonically to changes in increasing charge, and effectively becoming ~0 at higher charge densities well below the Rayleigh limit for simple oil droplets (hexadecane). As Reviewer 5 has fully acknowledged our answer, we restate it here in case Reviewer 3 may have missed it in the previous round:

Since the experimentally measured zeta potential reflects the potential at the slip plane, this implies a net charge imbalance within the interfacial region, i.e. the droplet effectively carries excess negative charge. To model this, we removed a single Na^+ ion as a practical way to reproduce this charge imbalance in a finite simulation setup. Explicitly resolving the electric double layer would require substantially larger system sizes and longer time scales than are currently feasible. Removing Na^+ therefore provides a simple but direct way to impose an experimentally motivated interfacial charge density consistent with experimentally measured zeta potentials. All results are shown in Fig. 4c. Importantly, our results show that the emergence of low-VIE configurations is not dependent on explicit charge manipulation. Interfacial undercoordination alone leads to a small but discernible low-VIE tail in hydrophobic systems (as reflected in Fig. 4a). The presence of interfacial charge imbalance further lowers the VIE of these configurations (as reflected in Fig. 4c) but does not fundamentally alter the underlying mechanism

Response to Reviewer 4 & 5

Referee #4 (Remarks to the Author): I co-reviewed this manuscript with one of the reviewers who provided the listed reports.

Referee #5 (Remarks to the Author): The authors have carefully addressed all my comments.

We thank again the reviewers for help in making our work stronger through their insightful comments.

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This manuscript presents a carefully executed study that investigates physicochemical activity at microplastic-water interfaces. While the experimental work is thorough and the combination with computational simulations is commendable, I have significant reservations regarding the **novelty and conceptual advance** of the core findings in the context of the recently published literature, specifically in relation to *Nature* **640, 87–93 (2025)**, titled “Water structure and electric fields at the interface of oil droplets.” The central mechanistic claim—that hydrophobic aqueous interfaces can generate strong electric fields which lower the energetic barrier for hydroxide ion oxidation, leading to spontaneous hydroxyl radical generation—appears to be a **direct extension of principles already established in the realm of water microdroplet and liquid-liquid interface chemistry**. The cited *Nature* 2025 paper (Ref. 34 in the manuscript) provides a detailed experimental and theoretical framework for this phenomenon at oil-water interfaces. The present study effectively applies this established framework to a new **substrate (solid microplastics)** rather than discovering a fundamentally new mechanism. The observation that this activity correlates with hydrophobicity and can cause biomolecular damage is logical and expected based on the prior work, thus **diminishing the sense of a paradigm-shifting breakthrough**. The societal relevance of microplastics is undeniable, and the demonstration that this interfacial chemistry operates on a pervasive environmental contaminant is an **important application**. However, for publication in *Nature*, where the threshold for **fundamental new conceptual insight** is extremely high, the work in its current form may be perceived as an incremental, albeit well-performed, advance within an already emerging field, rather than the initiation of a new one.

Major Comments:

1. The authors’ previous study published in *Nature* (2025, 640, 87–93) focused on electric field formation and radical generation at hydrophobic–water interfaces. It would be helpful for the authors to further clarify whether the microplastic–water interfaces discussed in the present manuscript share mechanistic similarities with those systems, and to more explicitly articulate the conceptual novelty of this work in relation to their prior findings.
2. The detection of radicals at plastic–water interfaces is not inherently contradictory to the chemical inertness of commercial plastics. Chemical inertness should primarily be understood as the long environmental persistence of polymeric materials, i.e., their resistance to bulk degradation or transformation, rather than the inability of their surfaces to participate in interfacial radical processes. Indeed, previous studies have shown that aged microplastics (e.g., after light exposure or chemical oxidation) can generate persistent radicals and exhibit appreciable degradation activity toward aqueous pollutants, while the polymer matrix itself remains largely intact over extended reaction periods. This distinction could be more clearly articulated in the manuscript.
3. From a biosafety perspective, the presence of radical-active interfaces would be expected to induce oxidative stress responses in biological systems, particularly for

charged biomolecules. This outcome appears to be largely foreseeable.

4. In Figure 1c, appreciable methyl orange (MO) degradation is observed only in PS-dispersed aqueous systems, which is relatively intuitive, as alcohols are frequently employed as hydroxyl radical scavengers in radical identification experiments. In this context, the statement “In contrast, PS–ethanol interface, which does not exhibit evident ROS generation or MO degradation (Fig. 1c, d), shows near-neutral surface zeta potentials and minimal Rh800 surface partitioning (Fig. 2c, f, g). This again highlights the crucial role of water in activating microplastic surfaces with negative charges” may require further justification, as the interpretation could be influenced by radical quenching effects rather than solely by interfacial electrification.
5. While the manuscript emphasizes the role of hydroxyl radicals at the interface, it would be valuable to consider the contribution of surface-adsorbed hydroxyl radicals. For instance, comparative experiments using NaF could help distinguish between free and adsorbed $\bullet\text{OH}$ species by examining changes in detectable radical concentrations. In addition, the possible involvement of other reactive species in the reaction system should be evaluated, and more comprehensive experimental evidence is recommended.
6. The correlation between interfacial activity (APF signal, zeta potential) and biological outcomes (hemolysis, protein aggregation) is compelling but remains correlative. To establish that interface-generated $\bullet\text{OH}$ is a direct driver of toxicity, control experiments with specific radical scavengers (e.g., mannitol, DMSO) should be performed. Demonstrating that $\bullet\text{OH}$ quenching significantly attenuates hemolysis and protein aggregation would provide critical causal support and elevate the mechanistic claim.
7. The experiments are conducted under controlled, idealized conditions (PBS, pure water). Given the study’s environmental implications, it is essential to discuss—or ideally, test—whether this interfacial activity persists in more complex, real-world matrices (e.g., seawater, freshwater with natural organic matter, or simulated biological fluids). The Supplementary Fig. S2 suggests surface oxidation reduces activity; this should be explicitly discussed in the main text as it relates to environmental aging and the “lifecycle” of microplastic reactivity.
8. While the APF assay is excellent for detection, readers need a quantitative sense of the $\bullet\text{OH}$ production rate. Can the authors estimate the steady-state concentration or flux of $\bullet\text{OH}$ at the interface (e.g., using HPLC data from SI)? Comparing this value to known physiological or environmentally relevant $\bullet\text{OH}$ levels would help assess whether the observed activity is sufficient to drive the reported bio-effects.
9. The current discussion is strong but could be further enriched by: a) Explicitly linking the findings to the emerging field of microdroplet chemistry, highlighting how solid microplastics represent a new, widely distributed platform for such interfacial phenomena. b) Proposing concrete materials-design principles (e.g., how surface hydrophilization or permanent charging could suppress this intrinsic activity to engineer safer plastics). c) Speculating on how this activity might influence the environmental fate of co-pollutants (e.g., degradation of adsorbed organic pollutants).

Minor Comments:

1. Fig. 1: Please indicate the statistical significance of the differences in panels b, i, and k. Error bars are present but no statistical test is mentioned.
2. Fig. 2g: The x-axis appears to be partially obscured and should be corrected for clarity. A careful check of all figures and labels throughout the manuscript is also recommended to avoid similar presentation issues.
3. Page 3, last paragraph: The transition to microdroplet chemistry feels slightly abrupt. Consider a smoother bridging sentence.
4. Supplementary Methods: The description of ReaxFF/CGeM simulations is excellent. Please also briefly state why this method was chosen over alternative reactive force fields.

In this reviewer's assessment, despite the substantial revisions made by the authors, the novelty of the work does not reach the threshold required for publication in Nature. The conceptual depth, mechanistic completeness, and evidentiary standard remain below what is expected for this journal.

Specifically:

1. Regarding the issue of novelty, although the authors have responded by providing textual explanations and a comparative table to clarify the differences between this study and their previous work, we still consider that the core content of the present manuscript is more likely an extension of the previous study to a specific application scenario, rather than a substantial breakthrough in terms of scientific questions or mechanistic understanding. In addition, this manuscript focuses on radical behavior at the microplastic interface, but the current descriptions may lead readers to mistakenly assume that plastics can undergo spontaneous degradation relatively easily in natural environments. In fact, microplastic degradation in natural environments is usually constrained by multiple factors, including light intensity, oxidant availability, reaction interfaces, environmental matrices, and time scales, and therefore cannot be simply equated with the enhanced degradation process

observed in the experimental system. We suggest that the authors further clarify the differences between the experimental conditions and real environmental processes in the manuscript, so as to avoid overgeneralization or misleading interpretations regarding the natural degradability of microplastics.

2. Regarding Comment 4 raised in the first round of review, the authors' current response does not sufficiently exclude the possibility that the alcohols used in this study may directly act as radical scavengers. It is therefore recommended that the authors supplement their response with appropriate control experiments involving the addition of the alcohols alone, in order to provide more direct experimental evidence and further strengthen the mechanistic interpretation.

3. **Direct experimental evidence of interfacial electric fields.**

The central mechanistic hypothesis relies on strong interfacial electric fields lowering the ionization energy of hydroxide at the microplastic surface. However, current support for this claim appears largely indirect, based on zeta potential measurements and molecular simulations. While these approaches are informative, they do not directly measure interfacial electric field strength. Given the conceptual importance of this mechanism, more direct interfacial-sensitive experimental evidence (for

example, nonlinear optical spectroscopy or related techniques) would substantially strengthen the causal argument. At present, the electric field is inferred rather than directly demonstrated.

4. **Causal relationship between electric field strength and radical formation.** Beyond establishing the presence of interfacial electric fields, the manuscript does not yet demonstrate a quantitative relationship between field strength and radical generation kinetics. To meet the mechanistic rigor expected for publication in *Nature*, it would be important to show whether modulation of interfacial electrostatics—such as by systematically varying ionic strength or surface charge—produces predictable changes in radical yield. Demonstrating field-dependent scaling behavior would significantly reinforce the proposed causality between interfacial electrostatics and hydroxyl radical formation.
5. **Exhaustive exclusion of alternative radical sources.** Given the extraordinary nature of the claim that pristine microplastics intrinsically generate hydroxyl radicals without external stimuli, comprehensive exclusion of alternative pathways remains critical. Although additional controls have been included in this revision, further clarification is needed regarding the potential roles of dissolved oxygen, trace oxidative defects, residual

polymerization initiators, photochemical effects, or mechanical perturbations. Importantly, real-world plastics are chemically complex materials that often contain a variety of additives, stabilizers, plasticizers, and residual monomers. Moreover, environmental aging processes (e.g., UV exposure, oxidation, hydrolysis) can introduce surface functional groups such as carbonyls, peroxides, and hydroxylated species, which themselves may participate in redox chemistry. Even trace amounts of such chemical heterogeneities could potentially contribute to reactive oxygen species formation and confound attribution to a purely intrinsic interfacial electric-field mechanism. A more systematic characterization of polymer chemical purity and surface functionality, as well as explicit differentiation between pristine laboratory-grade polymers and environmentally aged materials, would therefore substantially strengthen confidence in the proposed intrinsic interfacial origin.

6. **Universality across diverse polymer systems.** Importantly, as also raised by Reviewer 1 regarding the issue of generality, the manuscript proposes a potentially generalizable interfacial physicochemical phenomenon rooted in hydrophobic surface effects. However, the range of polymers examined remains relatively limited. To substantiate claims of generality, it would be

valuable to extend the analysis to additional commodity polymers with distinct dielectric properties and surface chemistries, as well as environmentally aged microplastics. Demonstrating consistent behavior across chemically diverse systems would elevate the conceptual robustness and broader relevance of the work.

7. **Physical representativeness and boundary definition of the polymer–water model.** While the simulations provide important mechanistic insight, the physical representativeness of the polymer–water interfacial model warrants further clarification. The use of a single long polymer chain under periodic boundary conditions raises concerns regarding artificial self-interaction and constrained conformational sampling, which may influence interfacial water structuring and local electrostatics. In realistic microplastic systems, surfaces arise from densely packed polymer chains with finite curvature, surface roughness, and heterogeneous chain orientations, rather than an effectively periodic single-chain construct. Given that the proposed mechanism critically depends on interfacial water structure and electrostatic effects, it is important to demonstrate that key conformational metrics (e.g., radius of gyration, end-to-end distributions, surface density) and interfacial properties are not

artifacts of boundary choices. A clearer justification of model design and its physical relevance to experimentally studied microplastic surfaces would substantially strengthen confidence in the mechanistic interpretation.

8. **Robustness and sensitivity of the VIE distributions to modeling assumptions.** The reduction in vertical ionization energy (VIE) at the interface is central to the mechanistic argument; however, the robustness of the reported low-energy tail requires further substantiation. In particular, it remains unclear how sensitive the VIE distributions are to key modeling parameters, such as imposed surface charge density, system size, sampling depth, and configuration selection. Since the proposed mechanism relies on rare low-energy configurations, rigorous convergence analysis and uncertainty quantification are essential to establish statistical reliability. Moreover, it would be important to clarify whether similar energetic trends emerge without explicit surface charge manipulation, relying solely on structural undercoordination at the hydrophobic interface. Demonstrating that the energetic lowering is stable across reasonable variations in modeling assumptions would significantly strengthen the credibility of the computational conclusions.

