nature portfolio

Peer Review File

Parameterization and quantification of two key operando physio-chemical descriptors for water assisted electro-catalytic organic oxidation

Corresponding Author: Professor Mengning Ding

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

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
In this study, Tian and co-workers study electro-oxidation of organic molecules including alcohols, aldehydes and amines using NiCo oxides. They perform in-situ characterization to develop mechanistic insights into the process and propose design principles for active electrocatalysts. Overall, the study is rigorous and provides new insights on electro-oxidation of organic molecules and I support publication of this work. I have a few comments that the authors can consider:

1. Under highly alkaline conditions, the relevant species involved in the oxidation are proposed to be the alkoxide and geminal diol species (https://pubs.acs.org/doi/abs/10.1021/acscatal.1c04163). Can the authors comment on the exact identity of substance* in their equations?

2. Have the authors performed ECSA analysis to estimate the roughness of the oxides as a function of Ni/Co concentration? Do all the oxides have similar roughness?

3. Some recent work indicates the impact of non-kinetic effects on OER kinetics and Tafel analysis (https://onlinelibrary.wiley.com/doi/full/10.1002/anie.202216477). Can the authors comment on the possibility of the OER tafel slope analysis being affected by factors mentioned in this study?

4. Can error bars be provided for Figure 2d?

5. Can the authors explain how exactly can these insights be applied in future materials screening studies? Particularly the criteria for "enough sites for substance adsorption"?

Reviewer #2

(Remarks to the Author)
This article discusses an analysis of Co/Ni-oxyhydroxides that are known to be active for various organic oxidation reactions as well as OER. The authors perform Fourier-transform alternating current voltammetry (FTacV) to probe the materials' chemistry. The measurement essentially relies on the fact that there are various processes that do not have a linear response to voltage changes and thus show high order harmonic contributions in an FT of the response. These harmonics are isolated by filtering and reverse-FT'ed to highlight the nonlinear processes as a function of the conditions. Isolating the nonlinear pieces in this manner allows assignment of features to a particular condition such as potential, whereas they might be more subjective from other measures—e.g. redox peaks are shown to be insensitive to scan rate using FTacV, whereas peak positions can depend on scan rate and be misinterpreted (by inexperienced practitioners at least) using conventional CV to see what potential yields a given process.

Overall this is a novel approach to understanding the present chemistry and I was intrigued by the possibilities for wider use of the technique. However, the method itself is already developed and the conclusions applying it here turned out to be very obvious and intuitive. The take-away insights are not anything that standard kinetic analyses and myriad other characterization tools haven't told us already: OH* competes with organic substrates for surface sites and these factors must

be balanced. I am not clear where the “Nature-level” advancement is and would suggest this for a more specialized journal.

More specific points:

1) The article focuses on the oxidation activity without much regard for how the proposed descriptors will impact selectivity/product distributions among the organics. Simply having the highest current does not always make the best catalyst as it could over-oxidize past a desired product, for example. This is particularly problematic where the authors try to generalize their design principles (Figure 5 and surrounding discussion) to apply to numerous classes of molecules.

2) Langmuir-Hinshelwood kinetics is a crude model for a general qualitative behavior, but the next level of depth in understanding what the actual elementary steps are, how particular surface ensembles are involved etc is just not here. The paper feels like it is really overselling the level of insight into mechanism and I am not convinced that for a given arbitrary substrate molecule that there could not be additional processes that are equally important. I further completely disagree with the statement “As electro-organic reactions typically do not involve surface adsorption/micro-reactions (i.e., the organic substance presumably completes the interfacial electron transfer process with a simple collision with the electrodes)…” There could be specific instances of electrode/substrate combinations where this holds but it is absolutely not true in general. Pt-group metals often become poisoned by CO during organic oxidations. Noble metals often accumulate carboxylates. I am less familiar with the exact mechanism on oxyhydroxides but one would have to assume adsorption (possibly needing multi-site ensemble for some molecules) to transfer OH* in a Langmuir Hinshelwood mechanism—so the argument is not even internally consistent within the paper.

3) The correlations between ‘delta-V_harmonics’ and adsorption energy as well as ‘delta-I_harmonics’ and coverage are oversold in terms of their quantitative power. I do not dispute there are positive correlations, but:
a) For delta-V, we cannot cleanly extract the thermodynamic delta G because there are still kinetic contributions to these peaks. The system is not sufficiently well-defined to extract precise thermodynamic values. This effort is further obscured by the fact that we are not dealing with homogeneous (e.g. single-crystal) surfaces, but rather an ensemble of sites with different Ni-Co local coordination ratios, potential-dependent defects populations, etc
b) Delta-I only contains one particular harmonic component so I do not see how it can reliably be transformed into a quantitative estimate for change in coverage.

4) Electron transfer to create a higher oxidation state (one descriptor) is presumably correlated with the OH* coverage (other chosen descriptor). Can the authors better justify what separates them and how strategies to tune one could be implemented without affecting the other?

5) Readers will be much more familiar with the use of EIS, which is somewhat related but sticks to the region of linear response. It would seem one could in principle take a series EIS measurements about different potentials and map fitted charge transfer resistances (as a functional of potential) to acquire similar information. Could the authors speak to that? It would be valuable for a journal targeted at broader readership.

6) In general the paper is crammed with assertions about the meaning of data and not given adequate exposition. It relies extremely heavily on SI to the point it is frustrating to read and evaluate the arguments. In my opinion should simply not be written as a communication.

Reviewer #3

(Remarks to the Author)
In this manuscript, the authors present a systematic study on the electrochemical oxidation of various model organic molecules, including furfural, furfural alcohol, and benzylamine, on a series of cobalt/nickel-based oxyhydroxides (α-CoxNi1-x(OH)2) with varying Ni/Co ratios. They employed in situ ETS for α-Co(OH)2 and confirmed the generation of active oxygenate species (Co3+δ–OH*/O*) on the surface and their consumption during the oxidation of organic molecules. They demonstrated that α-CoxNi1-x(OH)2 with different Co:Ni ratios exhibited different reaction tendencies towards OER or the oxidation of organics. Two key operando physio-chemical descriptors provided by high-order harmonics extracted from Fourier transformed alternating current voltammetry (FTacV) measurements. The two descriptors were used to construct an electro-catalytic activity diagram which enables identification of optimal microscopic surface states of Co/Ni oxyhydroxides during the oxidation of each type of molecules. They proposed that the descriptors can be used to quantitatively determine the generation and consumption of active surface intermediates, which can be used to optimise reaction performance (yield, faraday efficiency, etc) for different organic oxidations for rational design of catalyst and mechanistic model. The techniques used in this work are not widely explored by researchers in this field, which can greatly inspire others for future mechanistic studies. Therefore, I recommend this manuscript to be published in Nature Communications after minor revision. Some specific comments are listed below:

In the introduction, the author did not clarify the reason of using a general Langmuir-Hinshelwood (L-H) mechanism instead of Eley-Rideal Mechanism, and why is the L-H mechanism representative and applicable to their system model which involve different reaction conditions (reactant concentrations, pH), different catalyst compositions and organic molecules (molecular structures) – although later confirmed by S16 that furfural, furfuryl alcohol and benzylamine do follow the L-H mechanism.

In Fig. 1a, they did not specify in the texts the definition of θ sub*, and which organic molecules (C1, C2, C3 or long chain C)

were tested experimentally to be compared with simulation results that followed the L-H mechanism.

For the simulation in Fig 1a, was the fixed pH value the bulk pH or surface pH? Because local pH does change while the alcohol oxidation reaction takes place.

What valance state is the metal site that's adsorbing the organic substrate? And will it change as potential increases or as the oxidation reaction takes place?

The type of HPLC column is not specified in SI Note 3.

Please specify the term 'substrate' used for product yield calculation.

While the authors employed EDX to determine the atomic ratio of Co:Ni before electrochemical testing, it is essential to acknowledge the method's limitations. EDX is known to have an error range of approximately 20%, it is suitable only as a qualitative tool for elemental analysis. For quantitative analysis, confirmation of Co:Ni ratio before and after reactions via techniques such as ICP-MS is advisable.

The manuscript notes the conversion of measured potential vs. E Ag/AgCl to reverse hydrogen electrode potential (RHE) using the Nernst equation without actual calibration with respect to RHE. Calibration against RHE should be conducted to ensure accuracy.

Reviewer #4

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Version 1:

Reviewer comments:

Reviewer #2

(Remarks to the Author)
This revised manuscript adds substantial new data and clarifying remarks to the authors' original discussion of organic oxidation as characterized by FTacV. They have taken review comments seriously and while I still think the paper would be better in a less condensed format, it is okay from my perspective to publish in this journal. I have two comments that the authors should still take into consideration for final revision:

1) It was stated that this is "the first paper to use the classical Langmuir-Hinshelwood (L-H) mechanism to describe electrocatalytic organic oxidation reactions assisted by partial water oxidation" This is obviously not true, and the most salient example would be methanol oxidation, which has easily >50 years worth of papers that fit data to microkinetic models. If the authors refer specifically to larger organic molecules then this might be closer to true, although I might argue the reason is that one can only really fit an empirical L-H scheme that overlooks a lot of elementary step detail since these reactions can be quite cumbersome and not all elementary processes are resolvable. The simple concept of competition between O/OH* and organic* is known, if perhaps no one bothered to write down/publish the equations for this simplistic picture.

2) I am still struggling to accept (on an intuitive level) that 'delta-V_harmonics' will only capture the change in adsorption energy. While I admittedly have not worked through the papers that are referenced, I key on the statement that "the contribution from non-Faradaic charging, diffusion and [chemical] catalytic processes in d.c. CV can be effectively excluded in high-order (>4th) harmonics". This all makes sense as these phenomena should be expected to have linear response. What is not directly addressed is the situation where there would be a potential-dependent kinetic limitation to the OH* adsorption process itself, and I worry that is being neglected. It seems like one has to assume this reaction is equilibrating, but maybe it can be proven otherwise?

Reviewer #3

(Remarks to the Author)
The authors have addressed the comments in great detail and the manuscript quality has largely improved after revision. Therefore, I recommend the manuscript to be published by the journal.

Reviewer #4

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Version 2:

Reviewer comments:

Reviewer #2

(Remarks to the Author)
The authors have adequately addressed all remaining questions and the paper is suitable for publication

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July 18, 2024

Dear Referees,

We are re-submitting a revised manuscript (NCOMMS-24-06463) "*Parameterization and quantification of two key operando physio-chemical descriptors for water assisted electro-catalytic oxidation of organic molecules*" for your consideration of publication in ***Nature Communications***.

We highly appreciate this opportunity for a revision, as well as the thoughtful comments and valuable suggestions, which have motivated significant improvement on the quality of our revised manuscript. Per your comments and suggestions, we have conducted additional experiments (characterization, electrochemical/spectroscopic measurements, and thorough data analysis), with new results (new **Figures 1a**, **2d**, **2g**, **2h**, **3**, **4**, **5b**, **5c**, **5d**, modified **Scheme 1**, new **Figs. S2**, **S9**, **S17**, **S18**, **S19**, **S22**, **S23**, **S27**, **S28**, **S29**, **S33, S41**, **S42**, **S44**, new **Supplementary Note 6**, modified **Table 1**, new **Table S2**, **S3** and new **References 73**, **74**, **86**, **90**, **91**, **91**, **92**, **93**, **94**, **96**, **99**, **100**, **101**, **102**, **103**, **104**, **105**, **106)**, and corresponding discussions included in the revised manuscript and supplementary information. We have carefully revised our manuscript to fully address all the comments and concerns, with all major revisions highlighted. A point-to-point response letter is included here. We look forward to hearing back from you.

Sincerely,

Mengning Ding William A. Goddard III

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

In this study, Tian and co-workers study electro-oxidation of organic molecules including alcohols, aldehydes and amines using NiCo oxides. They perform in-situ characterization to develop mechanistic insights into the process and propose design principles for active electrocatalysts. Overall, the study is rigorous and provides new insights on electro-oxidation of organic molecules and I support publication of this work. I have a few comments that the authors can consider:

Reply: We greatly appreciate the referee's positive comments on our study, and thank for carefully reading our manuscript and the insightful comments that have inspired further improvement on the manuscript. In the revised manuscript and supplementary information, we added more data and detailed discussions accordingly.

1. Under highly alkaline conditions, the relevant species involved in the oxidation are proposed to be the alkoxide and geminal diol species (https://pubs.acs.org/doi/abs/10.1021/acscatal.1c04163). Can the authors comment on the exact identity of substance* in their equations?

Reply: We thank the referee for pointing out this important issue that needs to be clarified.

1) The identification of surface intermediate states during (electro)catalytic processes regarding organic reactants is indeed an important research field in catalysis and surface chemistry. In this work, alcohol, aldehyde and amie were chosen as the model organic reactants. We believe that the intermediates of aldehydes and alcohols in this work are also geminal diol and alkoxide species under highly alkaline solution, as concluded in the reference mentioned by the referee (we added this paper as new **reference 90** in the revised manuscript). The conclusions in this paper, that aldehydes and alcohols dominantly undergo "indirect oxidation" and "potential-dependent oxidation", respectively, are consistent to our conclusions that the higher $\Delta(\Delta G_{OH*})$ observed in alcohol electro-oxidation compared with aldehyde. As a comparison, amine species undergo relatively simpler, direct surface adsorption yet with multiple surface intermediate states in the subsequent series of elementary steps (e.g., *J. Am. Chem. Soc.* **2022**, *144*, 15185, *ACS Nano* **2022**, *16*, 9572 and *ACS Catal.* **2023**, *13*, 2916). However, for other the oxidation of other organic species less studied by systematic electrochemical and *in situ* spectroscopic investigations, identifying the relevant intermediates is more challenging.

2) More importantly, it should be noted that the intermediates of different organic species (alcohols, aldehydes, amines) are inherently different, and the adsorption intermediates may vary even within the same class of compounds depending on the molecular structure and/or reaction pathways. However, for the investigation of electro-catalytic micro-kinetics, once the rate-determining intermediates (those participating in the RDS) follow the same reaction mechanism (e.g., L-H mechanism between OER related OH* and Sub*), all reactions can be described and analyzed using a unified kinetic model. This is the core statement of this work.

On this basis, we aim to explore how to design efficient catalytic materials applicable to all aldehydes, alcohols, amines and potentially other organic substrates by studying the key elementary steps involving the water activation pathways. Therefore, the use of "Sub*" can be a more general term that can potentially be applicable to different types of organic substrates in the corresponding discussions

and summaries. Following the referee's suggestion, we have distinguished R-CHO*, R-CH_2OH*, and R-CH_2NH_2* in the equations and scheme in the main text in revised manuscript, as following:

Page 2, line 19: "The kinetic analysis for electro-oxidation of different organic molecules shown in **Figure 1a** (also see **Supplementary Figure S1**, **S2**) suggest a general Langmuir-Hinshelwood (L-H) mechanism for R-CHO, R-CH_2OH, and R-CH_2NH_2 molecules"

Page 11, line 16: "Therefore, we expand this methodology to different electro-organic oxidation reactions with different catalytic systems, including electrocatalytic oxidation of alcohol (to either aldehyde or carboxylic acids), aldehyde (to carboxylic acids), and amine (to nitriles), to seek more detailed electro-kinetic rules that apply to the general EOORs following the electrochemical EC model, regardless of the kinetically-insignificant details on adsorption states of organic substances[90]."

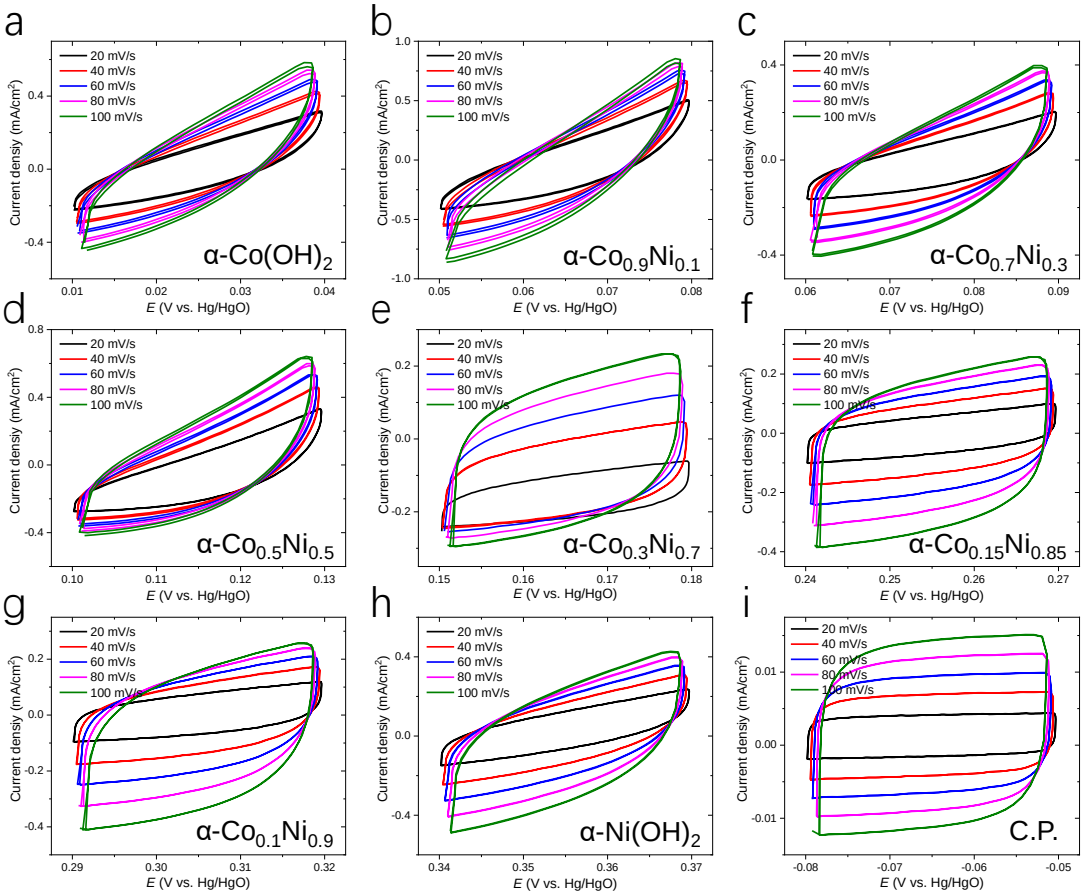
Page 14, line 13: The alcohol oxidation points in the α-$Co_xNi_{1-x}(OH)_2$ activity diagram located in the moderate $\Delta\theta_{OH^*}/\theta_{OH^*}^{OER}$ and $\Delta\Delta G_{OH*}^{EOOR-OER}$ regions, closer to the aldehydes' oxidation region (red points), presumably due to the similar yet slightly more complex oxidation mechanisms (dehydrogenation and subsequent insertion of one O atom, see equation S55), which is consistent with the previous conclusion that aldehydes and alcohols dominantly undergo "indirect oxidation" and "potential-dependent oxidation", respectively.[43, 90]"

2. Have the authors performed ECSA analysis to estimate the roughness of the oxides as a function of Ni/Co concentration? Do all the oxides have similar roughness?

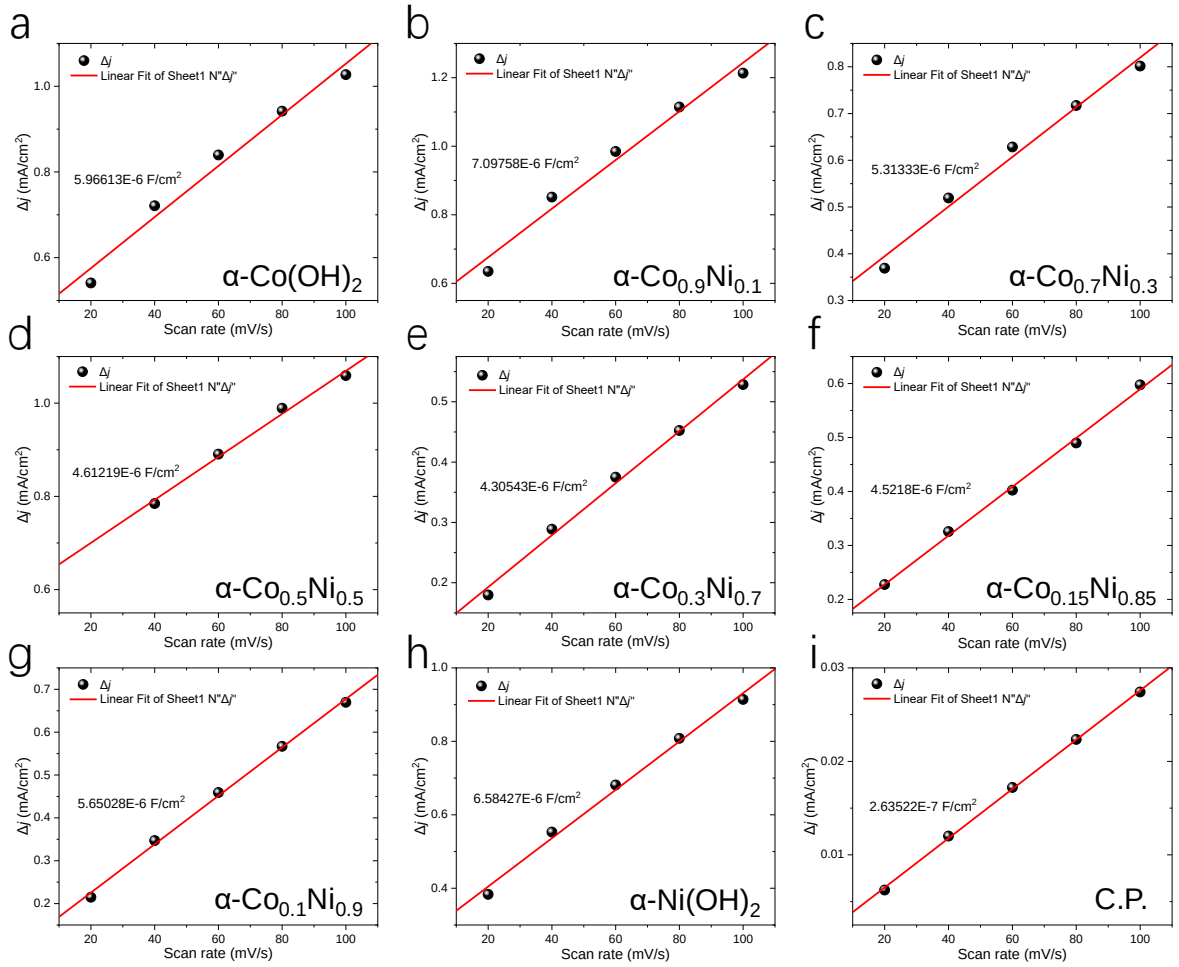
Reply: We thank the referee for this valuable question. To address this issue, electrochemical active surface areas (ECSA) were further measured for all the Ni/Co samples (see new **Supplementary Figure S17-19**), and subsequently all the data in **Figure 2d** were calibrated using the roughness factor (roughness factor = $ECSA_{\_catalyst}$ / $ECSA_{\_blank\ carbon\ paper}$). The new results indicate that the roughness factor of all materials is similar without significant difference (within the same order of magnitude). The new results were added as new **Figure S17-19** in the revised SI, and updated new **Figure 2d** in revised manuscript. The corresponding description has been added, as following:

In Revised Manuscript, Page 6, line 6: "All α-$Co_xNi_{1-x}(OH)_2$) samples showed similar electrochemical active surface areas (ECSAs) determined by CV measurements (**Supplementary Figure S17-19**)."

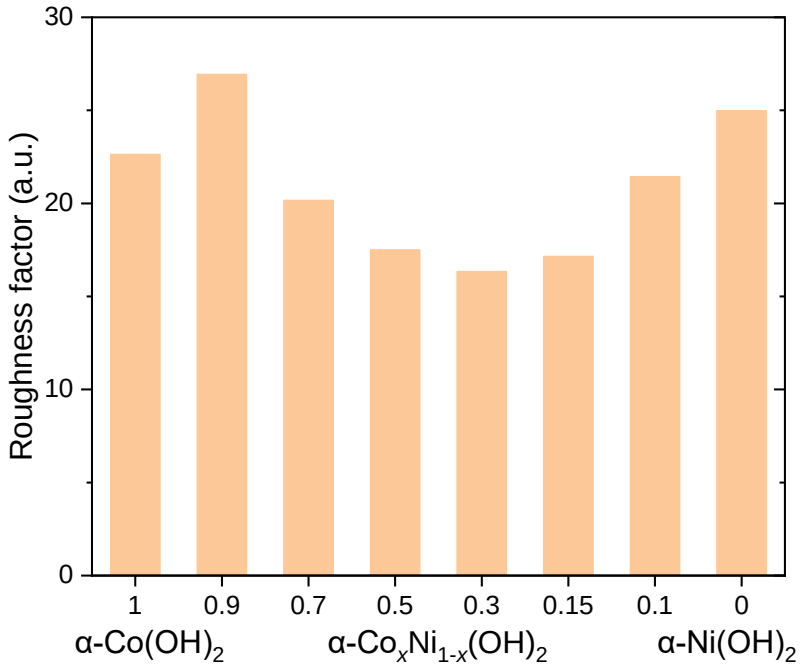
In Revised Manuscript, Page 6, line 14: "As shown in **Fig. 2d**, the OER and EOOR current densities (normalized by roughness factor, defined as $ECSA_{\_catalyst}/ECSA_{\_blank\ carbon\ paper}$)"



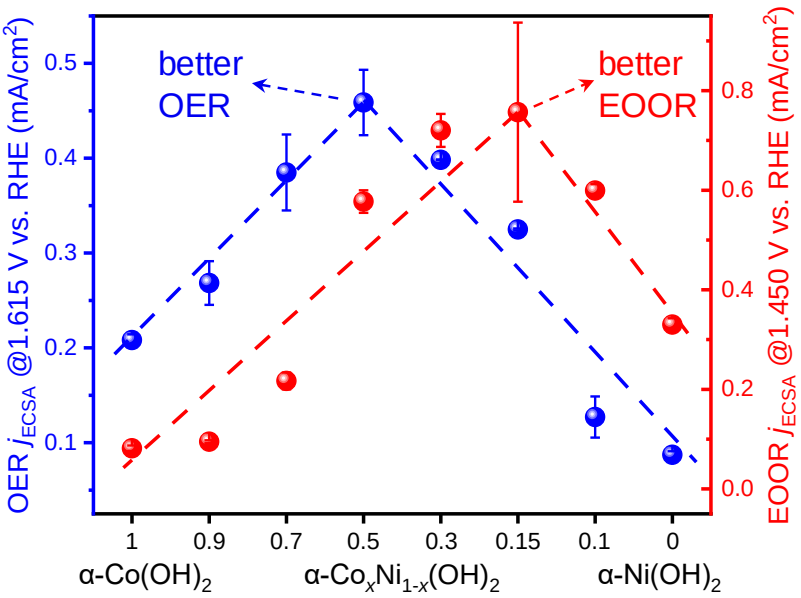
New **Supplementary Figure S17**. The electrochemical active surface area (ECSA) measurements for different α-$Co_xNi_{1-x}(OH)_2$ (x = 0~1) (a-h) and blank carbon paper (i).



New **Supplementary Figure S18**. The linear fitting results and the fitted slopes for ECSA calibration.



New **Supplementary Figure S19**. The roughness factors of different α-$Co_xNi_{1-x}(OH)_2$ (x = 0~1), defined as $ECSA_{\_catalyst}/ECSA_{\_blank\ carbon\ paper}$.

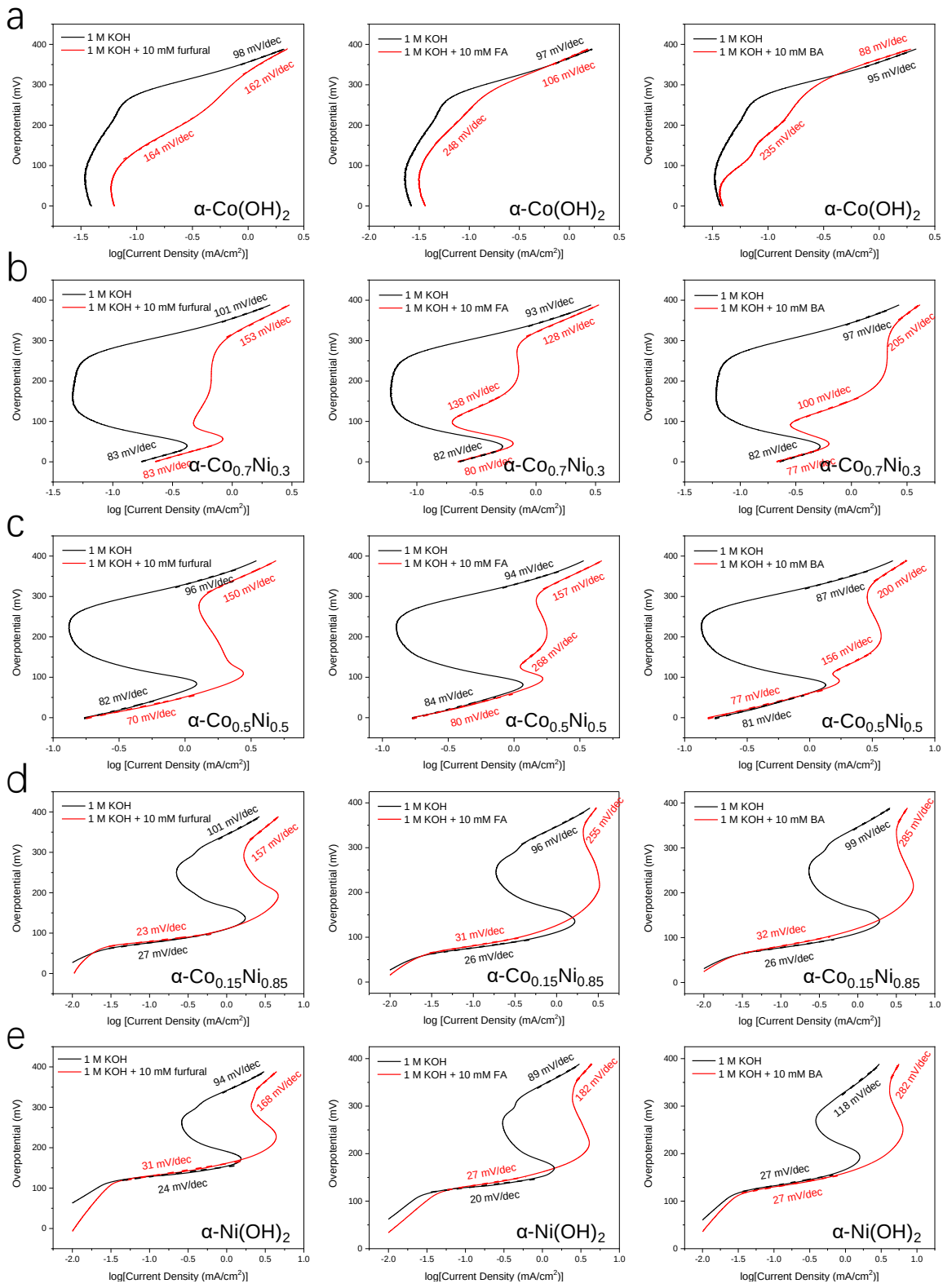


New **Figure 2d**. The OER and EOOR catalytic activities (normalized by roughness factor) of different α-$Co_xNi_{1-x}(OH)_2$ (x = 0~1), where two sets of volcano-like correlations can be observed.

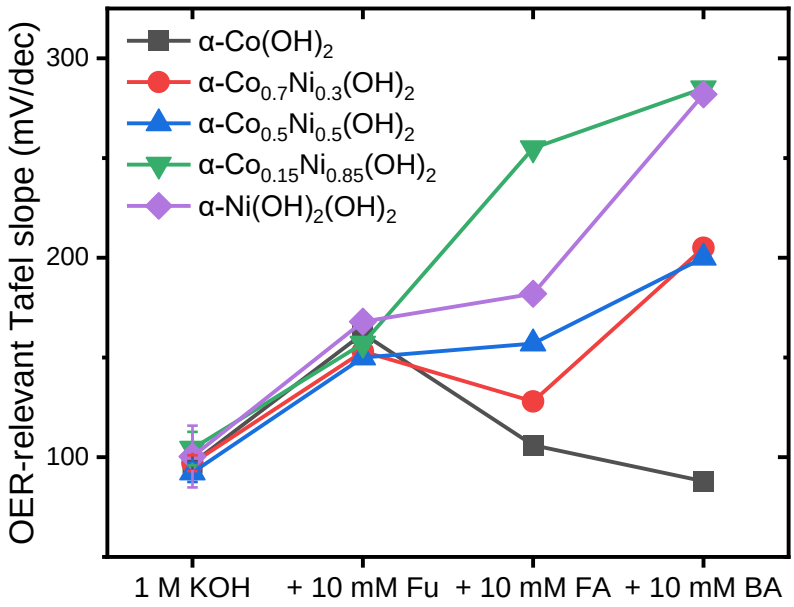
3. Some recent work indicates the impact of non-kinetic effects on OER kinetics and Tafel analysis (https://onlinelibrary.wiley.com/doi/full/10.1002/anie.202216477). Can the authors comment on the possibility of the OER tafel slope analysis being affected by factors mentioned in this study?

Reply: We thank the referee for highlighting this important issue that calls for further clarification. Actually, the Tafel slope range selected in this investigation largely follows to the standards suggested in the above-mentioned paper, namely the kinetic Tafel slope region (log(2 ~ 5 mA/cm^2) = 0 ~ 0.70), rather than the non-Tafel kinetic region (log(> 6 mA/cm^2) = > 0.78). This important work was added as new reference 96 in the section of Tafel slope analysis in revised manuscript. Based on the recommendations in this paper, we further standardized the potential range for all the Tafel slope analysis, and the new results were added as new **Supplementary Figure S22** and **Figure 5b**. The corresponding discussion was updated in the revised manuscript, as following:

In revised manuscript, Page 12, line 23: "As shown in **Fig. 5b**, each of the α-$Co_xNi_{1-x}(OH)_2$ catalysts exhibit an increased OER-relevant Tafel slope (derived from kinetic Tafel region[96] and potential range of 1.5−1.6 V_{RHE}, see **Supplementary Fig. S22**, where the OER electro-dynamics are dominant, i.e., FE_{OER} > 80%), from an identical value of ~97 mV/dec to another identical value of ~155 mV/dec with the addition of 10 mM aldehydes."



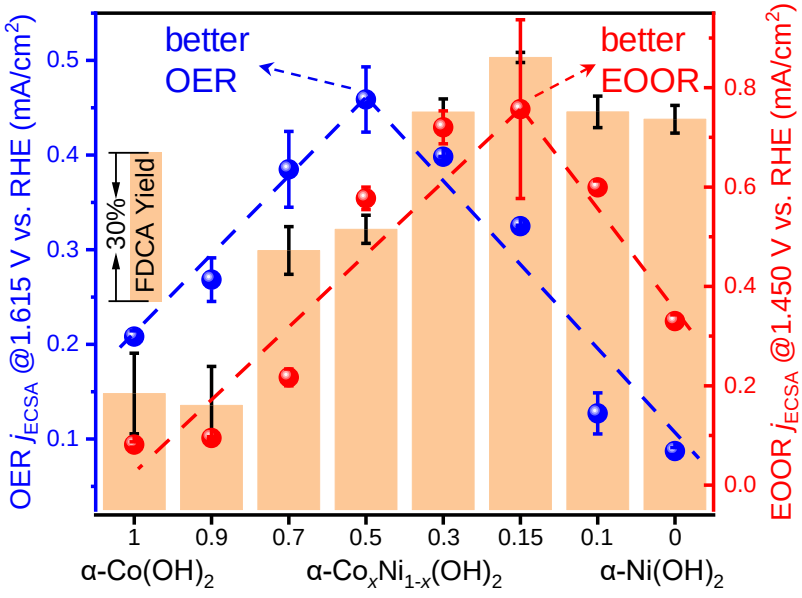
New **Supplementary Figure S22**. The OER-relevant Tafel slope analysis of a series of nickel doped cobalt hydroxides α-$Co_xNi_{1-x}(OH)_2$ (x = 0~1) under the condition of OER and electro-oxidation of different organic substrates. Note that the OER-relevant Tafel slopes are derived from kinetic Tafel region at the potential range of 1.5−1.6 V_{RHE}, where the OER electro-dynamics are dominant, i.e., FE_{OER} > 80%, which is determined by the HPLC and GC analysis of products.



New **Figure 5b**. The OER-relevant Tafel slopes derived in the kinetic Tafel region (at the potential range of 1.5−1.6 V_{RHE}, where the FE_{OER} > 80%).

4. Can error bars be provided for Figure 2d?

Reply: We thank the referee for this valuable suggestion on the reproducibility. We have conducted new electrolysis experiments and added error bars in new **Figure 2d**.



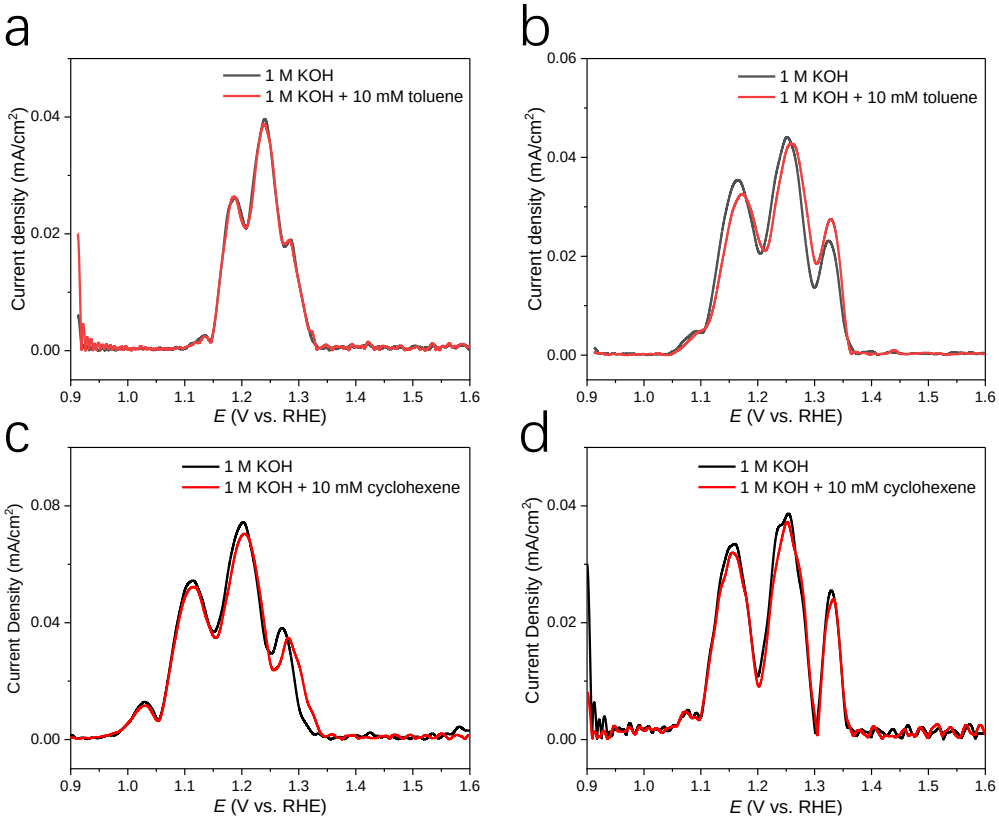
New **Figure 2d**. The catalytic activities (normalized by roughness factor) of OER and EOOR of different α-$Co_xNi_{1-x}(OH)_2$ ($x = 0 \sim 1$), where two sets of volcano-like correlations can be observed. The yield of FDCA (2,5-furandicarboxylic acid) products (orange column) in bulk electrolysis is also presented. Standard error bars were obtained from three independent electro-organic oxidation reactions.

5. Can the authors explain how exactly can these insights be applied in future materials screening studies? Particularly the criteria for "enough sites for substance adsorption"?

Reply: We appreciate the referee for this inspiring question. We believe the key physio-chemical descriptors obtained from our study can be applied to optimize catalytic materials for electro-oxidation of other organic species where water is involved as key and green source of oxygen, specifically:

1) For relatively more active organic molecules which assume monolayer chemisorption and undergo the L-H oxidation mechanism, it is necessary to design appropriate $\theta_{sub*}/\theta_{OH*}$ ratios for different organic substrates. Ensuring "enough sites" can be achieved through methods such as creating vacancies, metal leaching, or amorphization.

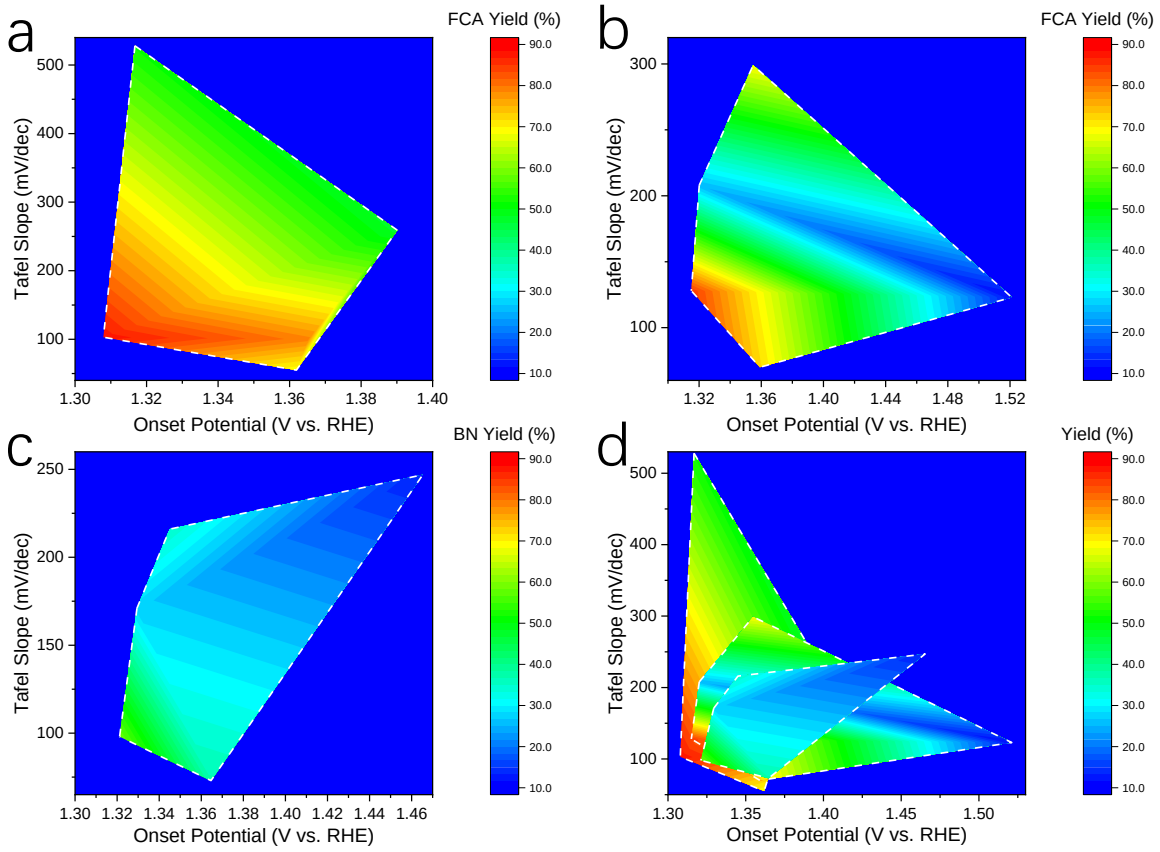
2) For another possible scenario dealing with activation of organic molecules with weak polarity and more inert bonds, we have conducted additional electrolysis and FTacV measurements for toluene (for selective oxidation of benzyl C-H bond) and cyclohexene (for selective epoxidation). The new results showed that the addition of toluene and cyclohexene substrates resulted in minimal changes in FTacV harmonics (new **Supplementary Fig. S42**), confirming their weak adsorption and the weak interference towards OER cycle, which consequently lead to the extreme difficulty to achieve high-efficiency electro-oxidation. Therefore, for the inert organic molecules exhibiting weak surface adsorption, *in situ* generation of extra strong redox mediator (such as HOCl, as reported by Sargent *et al.*) or radicals (such as Cl· or Br·) is expectedly required to achieve efficient activation and high yields for selective oxidation.



New **Supplementary Figure S42**. The high-order (6th) harmonics of α-$Co_{0.15}Ni_{0.85}(OH)_2$ (a, c) and α-$Ni(OH)_2$ (b, d) in pure 1 M KOH and with the addition of 10 mM toluene and cyclohexene, respectively, where the signals show no significant variation.

3) Additionally, for high-throughput prediction or evaluation of the reaction outcome, it should be noted that a machine-learning (ML) model engaging experimental-based descriptors poses equal importance as quantum mechanics (QM)-based *in silico* descriptors, as it provides experiment-relevant information that better represent the characteristics under operando reaction conditions. The use of appropriate experimental-based descriptor features could presumably address the issue of imbalanced representation from just theoretical calculations under ideal assumptions, avoid the possible overfitting with just QM-based descriptors, and bridges the gap between experiments and theory without requesting a high demand of complex physical theorems. In a recent example, the experimental electro-descriptors (e.g., Onset potential and Tafel slope derived from experimental cyclic voltammetry) developed for homogeneous electro/photo-organic reactions (*Angew*. *Chem*. *Int*. *Ed*. **2021**, *60*, 4199, *J*. *Am*. *Chem*. *Soc*. **2024**, *146*, 19019) was used to construct efficient ML models for reaction yield prediction. The same electro-descriptors were later utilized by *Hou et al*. (*Chem* **2024**, *10*, 2283) established a new ML model by embedding these d.c. CV-derived experimental descriptors for the development/optimization of new reaction conditions.

These recent works on ML investigations demonstrated examples that the development of precisely-measured, chemistry-informed, experimental-based descriptors can indeed benefit the future development of AI-for-chemistry methodologies. In this work, we have identified new physio-chemical descriptors, through FTacV measurements, that efficiently describe the *operando* surface processes, allowing for a more accurate and balanced representation (with reduced data dimensionality) of the micro-kinetics of heterogeneous electrocatalysis, where the apparent electro-descriptors (Onset potential and Tafel slope) become less effective (**Supplementary Fig. S45, S46**). Therefore, we are confident that this methodology holds promise for the high-throughput screening of heterogeneous electrocatalytic materials for the conversion of different organic species, and the development of new physio-chemical descriptors for electro-catalysis will also help the future ML investigations in this important field. The correlated data-driven investigation on the heterogeneous electrocatalysis is currently underway, which goes beyond the scope of this manuscript.



Supplementary Figure S45. The activity diagrams drawn by the data extracted from d.c. CV of a series of Ni doped Co hydroxides for (a) yield of FCA (oxidation from furfural), (b) yield of FCA (oxidation from furfuryl alcohol) and (c) BN yield (oxidation from BA), respectively. The summarized results can be seen in (d), it is obvious that the reactive areas of three substrates overlap with each other.

Based on above discussions, the corresponding statements were added in the revised manuscript, as following:

Page 17, line 2: "Aldehyde oxidation typically requires no harsh conditions, the catalysts should provide enough sites through vacancies creation, metal leaching or amorphization for molecular adsorption and $M^{3+\delta}$–OH* generation"

Page 14, line 24: "For molecules that are more challenging to be activated (with less polarity), such as toluene and cyclohexene (model substrates for selective oxidation of benzyl C-H bonds and selective epoxidation of alkenes, respectively), the corresponding FTacV results were shown in **Supplementary Fig. S42**. The minimal variation in signals indicates weak organic adsorptions even under high anodic potentials, which are consistent to their chemical inertness. In such cases, *in situ* generating extra strongly oxidizing radicals (such as Cl· or Br·)[99] or redox mediators (such as HOCl)[100] is presumably required to achieve high yields. Based on the innovation and scalability of measurement and kinetics analysis methods, key information and conclusions that were not easily obtained in previous literatures have been obtained in this work."

Page 16, line 20: “It is also relevant to note that effective performance prediction maps were developed using apparent electrochemical parameters for homogenous electro-organic synthesis[95] and photo generated electrochemical charge for homogenous photo-organic synthesis[103], respectively, offering improved efficiency and robustness for constructing machine learning (ML) models compared with DFT-descriptors.[104]”

Page 16, line 29: “more intrinsic physio-chemical parameters are necessary to achieve precise and efficient representation of the (surface) chemical space for machine learning (ML) investigations in heterogeneous electrocatalysis.”

Reviewer #2 (Remarks to the Author):

This article discusses an analysis of Co/Ni-oxyhydroxides that are known to be active for various organic oxidation reactions as well as OER. The authors perform Fourier-transform alternating current voltammetry (FTacV) to probe the materials' chemistry. The measurement essentially relies on the fact that there are various processes that do not have a linear response to voltage changes and thus show high order harmonic contributions in an FT of the response. These harmonics are isolated by filtering and reverse-FT'ed to highlight the nonlinear processes as a function of the conditions. Isolating the nonlinear pieces in this manner allows assignment of features to a particular condition such as potential, whereas they might be more subjective from other measures—e.g. redox peaks are shown to be insensitive to scan rate using FTacV, whereas peak positions can depend on scan rate and be misinterpreted (by inexperienced practitioners at least) using conventional CV to see what potential yields a given process.

Overall this is a novel approach to understanding the present chemistry and I was intrigued by the possibilities for wider use of the technique. However, the method itself is already developed and the conclusions applying it here turned out to be very obvious and intuitive. The take-away insights are not anything that standard kinetic analyses and myriad other characterization tools haven't told us already: OH* competes with organic substrates for surface sites and these factors must be balanced. I am not clear where the "Nature-level" advancement is and would suggest this for a more specialized journal.

Reply: We greatly thank the referee for carefully reading our manuscript and for the valuable comments that have inspired more clarified discussions. In addition, the referee has been kind enough to break down the major issue into several detailed questions/comments below, and the corresponding response have substantially improved the clarity and quality of the revised manuscript. In addition to the point-to-point response to each question, we would like to first briefly address referee's issue with the novelty and significance of our study, and how it contributes to the field.

First, in line with existing literatures in the field, we would like to emphasize here that this is the first paper to use the classical Langmuir-Hinshelwood (L-H) mechanism to describe electrocatalytic organic oxidation reactions assisted by partial water oxidation. Other previous studies on similar electro-organic reactions (such as *Chem*, **2020**, *6*, 2974) have only used a more general term of "nucleophilic attack" to describe the process without any detailed micro-kinetic information or precise quantification on the correlations between surface adsorbed species, or only calls for balance between OER and EOOR activities on specific type of reaction without raising up a clear micro-kinetic model that can be extended to more general cases (such as *J*. *Am*. *Chem*. *Soc*. **2022**, *144*, 15185). In the field of electrocatalysis that heavily relies on the interfacial/surface processes, using classical models from textbooks is highly beneficial for simplified understanding of key intermediate steps in complex reaction processes. For instance, in a recent electrocatalytic studies (*Science*, **2024**, *383*, 49), through experiments and microkinetic simulations, the authors proposed that the water oxidation-assisted propylene epoxidation reaction follows the Eley-Rideal mechanism.

Second, our work here quantitatively describes the competitive adsorption of aldehydes, alcohols, and amines with OH* species using experimental characterization and electro-micro-kinetic simulations (as a response to one of the referee's questions, benzyl C(sp^3)−H and alkene substrates have also been investigated in revised manuscript). Conventional kinetic tests (Figure 1a) and micro-kinetic fitting

results (Figure 1c) qualitatively confirm that the surface L-H bimolecular reaction mechanism is generally applicable to the water-oxidation-assisted electro-oxidation system. However, the key *operando* surface parameters, including the θ_{sub*}, $\theta_{OH*}/\theta_{sub*}$ ratio, and whether higher ($\Delta G_{O*} - \Delta G_{OH*}$) is (or is not) beneficial to different substances, still require precise experimental quantification approaches. The realization of these objectives will provide rational explanation on the observed correlation between specific Ni/Co ratio and the OER/EOOR performance, and further promote the field of electro-organic synthesis by contributing to the rational design principles of optimal electrocatalytic characteristics for different EOORs.

Most importantly, our precise experimental measurements of the two parameters (which were proved to be quantitatively correlated the proposed *operando* physio-chemical descriptors, $\Delta(\Delta G_{OH*})$ and $\Delta\theta_{OH^*}/\theta_{OH^*}^{OER}$, **reply to question #3**) of the key OER elementary steps, allowed us to quantitatively describe the *in situ* surface states of catalytic materials favorable for the electro-oxidation of different types of molecules, and how to design efficient catalysts for these different reactions, rather than relying on microkinetic simulations that only provide some fitted values (which are, to some extent, only auxiliary). The two descriptors are also proved to be very less correlated with each other by the analysis of Pearson, Spearman and Kendall coefficients, **reply to question #4**. Our experimental results in new **Table 1** lead to the summary of optimal conditions and physio-chemical parameters for achieving the best EOOR yields, which would be the good correction to the kinetic simulation results. Other apparent electro-chemical descriptors such as Tafel slope and Onset potential developed in previous works (*Angew. Chem. Int. Ed.* **2021**, *60*, 4199, *J. Am. Chem. Soc.* **2024**, *146*, 19019) lose their efficiency in distinguishing different EOORs where electrocatalytic surface/interfacial processes are critical. Thus, the physio-chemical parameters identified in this work provides additional fundamental insights that are closely corelated to the complex surface process/kinetics, which is of great significance in heterogeneous electrocatalysis. With the novelty and significance thoroughly discussed in this response letter and revised manuscript, we feel that our submitted work here is expected to attract significant interest from a broad readership.

Per referee's suggestions, we have added additional data along with more detailed and thorough discussions. With improved the quality of this paper, we hope to convince the referee that it reaches a Nature-level standard that can be considered publishable in this journal.

1. The article focuses on the oxidation activity without much regard for how the proposed descriptors will impact selectivity/product distributions among the organics. Simply having the highest current does not always make the best catalyst as it could over-oxidize past a desired product, for example. This is particularly problematic where the authors try to generalize their design principles (Figure 5 and surrounding discussion) to apply to numerous classes of molecules.

Reply: We thank the referee for pointing out the issue of product selectivity when generalizing the design principles for different catalysts.

Firstly, we would like to clarify that, in the original **Figure 5**, we did NOT simply use "highest current" to plot the reactive "hot zones" for the three types of reactions. Instead, quantitative yields from electrolysis were used, which were determined from standard HPLC/GC quantification (Supplementary Note 4).

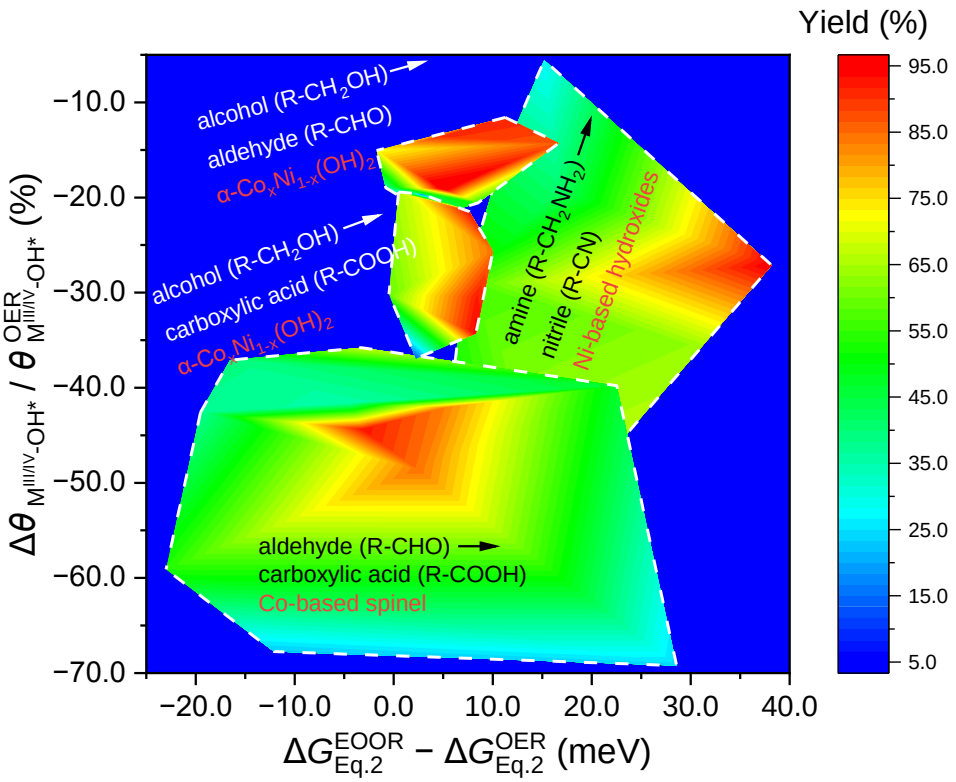
Secondly, we totally agree with the referee that, as we are targeting the general "selective oxidation of organics", the selectivity is indeed a key parameter and this issue should be addressed in this investigation. Among the three types of EOORs demonstrated in this investigation, the electro-oxidation of aldehyde and amine typically have single oxidation product (aldehyde to carboxylic acid and amine to nitrile), which do not pose the issue of selectivity (instead, issue of conversions and FEs levels should be taken into account in these cases). In contrast, the alcohol electro-oxidation on transition metal oxyhydroxides produces two possible types of products, carboxylic acid and aldehyde, in which case the selectivity should be indeed considered rather than just reaction yields. To better address this issue, additional synthesis, the selective electro-oxidation of benzyl alcohol that can produce both benzaldehyde and benzoic acid, were further conducted to demonstrate the catalyst design principles regarding the optimization of selectivity. In addition to the original synthetic conditions, 1 M K_2CO_3 was utilized to reduce the water activity and increase the selectivity of benzaldehyde (adapted from *Angew. Chem. Int. Ed.* **2022**, *61*, e202210123, added as new **Ref.101**). The electrolysis yields and FEs for selective electro-oxidation of benzyl alcohol were added as new **Supplementary Fig. S33**.

The FTacV tests were further conducted to extract the two *operando* physio-chemical descriptors to add the benzyl alcohol selective oxidation region. As shown in new **Figure 5c**, the reactive hot region of alcohol to aldehyde conversion moves up slightly, in comparison to the original reactive region of alcohol to carboxylic acid conversion. These results clearly indicate the design principle of alcohol oxidation catalysts towards the selectivity of different products. The selectivity of aldehyde over acid product can be associated to the reduced surface OH* and alcohol* coverages, presumably via (but not limited to) lowering pH values and/or water activity (with more cations). Overall, to include the selectivity characteristics in the reactivity diagram using yield as the reaction outcome, we only need to separately include the production of two products as two reactions for analysis. The selective oxidation region and preferred physio-chemical parameters for alcohol to aldehyde were added in the new **Figure 5c** and **Table 1**, with corresponding discussion in the revised manuscript, as following:

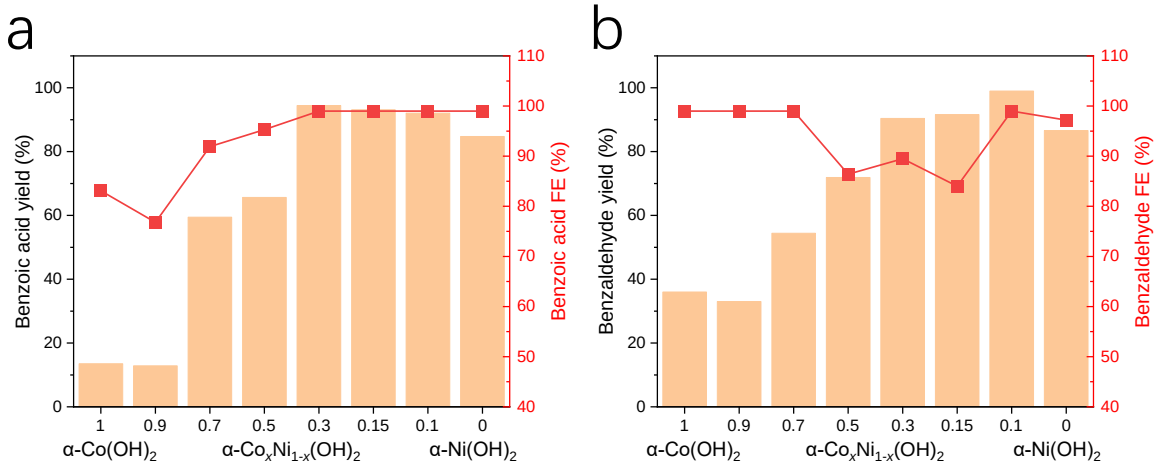
On Page 15, line 5: "To this end, we chose spinel (Co-based) catalyzed Fu oxidation,[50] α-$Co_xNi_{1-x}(OH)_2$ catalyzed benzyl alcohol selective oxidation to benzaldehyde and benzoic acid (Supplementary Fig. S33) and Ni-based hydroxide catalyzed benzylamine oxidation[11] as model systems to represent the four EOORs with more suitable catalyst categories."

On Page 15, line 26: "The selective electro-oxidation of benzyl alcohol to benzaldehyde can be efficiently achieved by reducing pH and water activity (with more cations)[101] to decrease the θ_{OH*} and $\theta_{alcohol*}$."

On Page 17, line 9: "iv) The efficiently selective oxidation of alcohol to aldehyde could be achieved by reducing the surface θ_{sub*} and θ_{OH*} via lowering pH and/or water activity."



New **Figure 5c**. The summarized catalytic activity diagrams for four EOOR systems, using two *operando* physio-chemical descriptors.



New **Supplementary Figure S33**. The electro-oxidation yields and FEs of benzoic acid (a, in 1 M KOH) and the selective oxidation yields and FEs of benzaldehyde (b, in 1 M K_2CO_3) from benzyl alcohol.

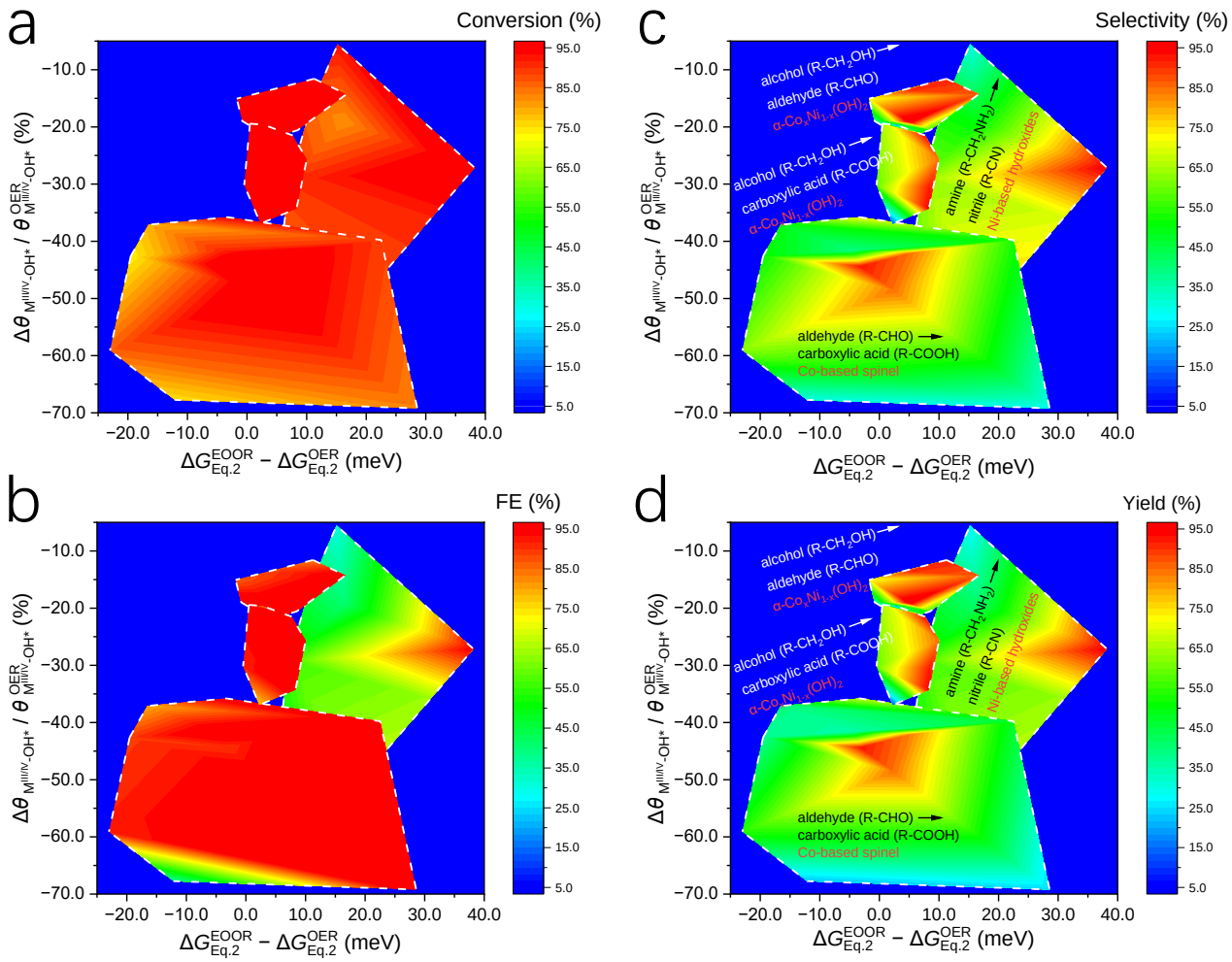
New **Table 1.** Summarized key parameters and design principles for EOOR systems.

Substances	Products	Oxidation Potential	Relative Change of θ_{OH*} [a]	Reaction Kinetic Complexity	Altered $\Delta G_{Eq.2}$	$M^{3+\delta}$–OH* Requirement
aldehyde	carboxylic acid	low	25%~55%	simple	−5~5 meV	relatively low
alcohol	aldehyde	relatively high [b]	13%~20%	simple	0~12 meV [b]	relatively low
	carboxylic acid	moderate	25%~35%	moderate	5~10 meV	balanced $\theta_{OH*}/\theta_{sub*}$
amine	nitrile	high	20%~32%	complex	20~35 meV	high level of θ_{OH*}

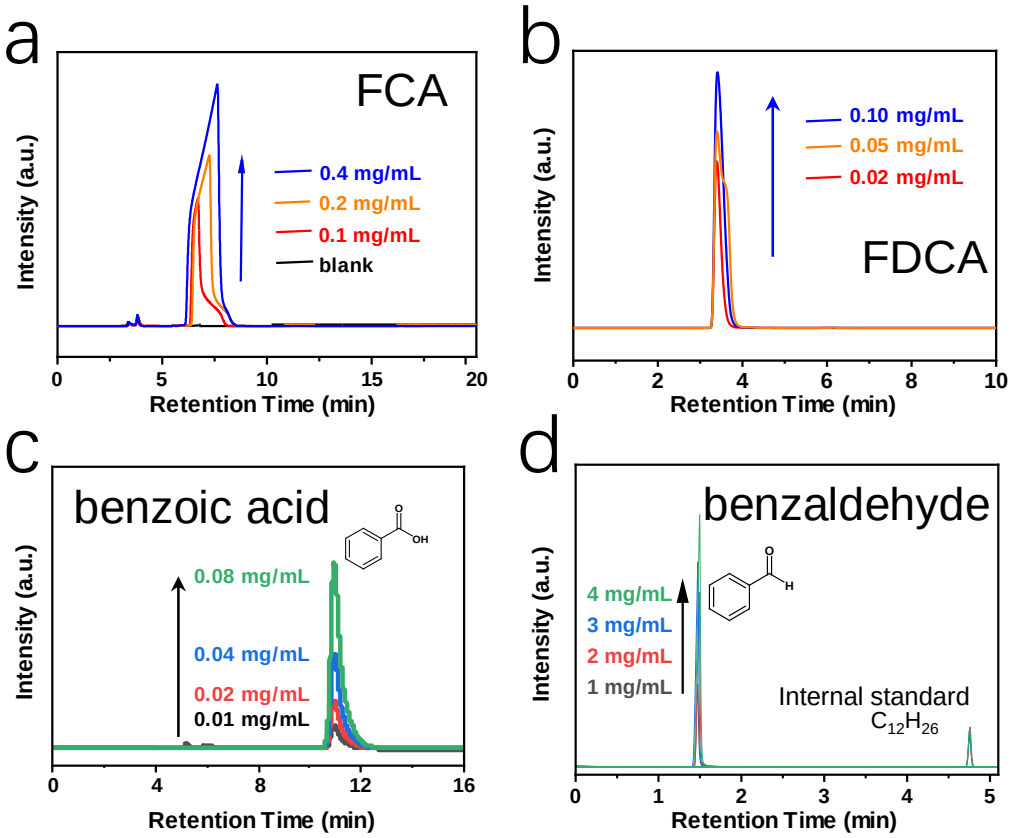
[a] coverage relative to the θ_{OH*} under OER conditions

[b] in weak alkaline solution (1 M K_2CO_3)

In addition to the above clarification, one could be further inspired by referee's question and realize that, in the EOOR system, **four key parameters, conversion, yield, selectivity and FEs, are all important to evaluate the performance of a catalytic system**. Although in some cases (such as aldehyde and amine oxidations in this investigation) part of these four parameters is equivalent to each other, it is not always the case. **To better address this issue, we have constructed the full set of reaction performance diagrams regarding the four performance parameters using the same *operando* descriptors obtained in this work.** As shown in the new **Supplementary Fig. S44**, for model reactions where reactants are relatively easy to activate and have fewer side reactions (confirmed by the HPLC/GC quantification, see Supplementary Fig. S30), the conversion is generally high, and the reaction yield approximately equal to the selectivity. Note that when the selectivity of a reaction (such as alcohol to aldehyde or carboxylic acid conversion) is critical, it can be divided into two separate reactions (alcohol to aldehyde and alcohol to carboxylic acid) for performance consideration. Furthermore, FE reflects the overall energy efficiency for the utilization of electron, and can be influenced by other non-organic side reactions such as OER. It is therefore a relatively independent parameter from yield /selectivity that provides additional information.



New **Supplementary Figure S44**. The catalytic activity diagrams for EOORs, constructed by two operando physio-chemical descriptors and four key parameters, conversion, yield, selectivity and FEs.



Supplementary Figure S30. The calibration curves used to quantitatively determine the products concentration.

The related discussions about the correlations between conversion, yield, selectivity and FE in the EOOR performance evaluation were added in the revised manuscript, as following:

Page 11, line 24: "Analogous to our previously-developed analytical approach,[95] we draw two-dimensional catalytic activity diagrams from the two descriptors to study the relationship between surface coverage alternation of key intermediates ($\Delta\theta_{OH^*}/\theta_{OH^*}^{OER}$) and the change in ΔG_{eq2} ($\Delta\Delta G_{OH*}^{EOOR-OER}$) with the yield of oxidation products, the results are shown in **Fig. 5**. For more systematic performance analysis, the catalytic performance diagrams constructed by the conversion, yield, selectivity and FE can be found in **Supplementary Fig. S44**. Specifically, for model EOORs that have relatively easy-to-activate substrates with few side reactions (confirmed by the HPLC/GC quantification, see **Supplementary Fig. S30**), the conversion is generally high, and the reaction yield is equivalent to the selectivity. In case of multiple possible products (such as alcohol to aldehyde or carboxylic acid conversion) when selectivity is critical, it can be divided into two separate reactions (alcohol to aldehyde and alcohol to carboxylic acid) for performance consideration. Furthermore, FE corelates to the overall energy efficiency in EOORs and reflects other non-organic side reactions such as OER. It is therefore a relatively independent parameter from yield /selectivity offering additional information."

2. Langmuir-Hinshelwood kinetics is a crude model for a general qualitative behavior, but the next level of depth in understanding what the actual elementary steps are, how particular surface ensembles are involved etc is just not here. The paper feels like it is really overselling the level of insight into mechanism and I am not convinced that for a given arbitrary substrate molecule that there could not be additional processes that are equally important. I further completely disagree with the statement "As electro-organic reactions typically do not involve surface adsorption/micro-reactions (i.e., the organic substance presumably completes the interfacial electron transfer process with a simple collision with the electrodes)…" There could be specific instances of electrode/substrate combinations where this holds but it is absolutely not true in general. Pt-group metals often become poisoned by CO during organic oxidations. Noble metals often accumulate carboxylates. I am less familiar with the exact mechanism on oxyhydroxides but one would have to assume adsorption (possibly needing multi-site ensemble for some molecules) to transfer OH* in a Langmuir Hinshelwood mechanism—so the argument is not even internally consistent within the paper.

Reply: We thank the referee for pointing out this important issue that needs to be clarified.

1) As referee mentioned, the Langmuir-Hinshelwood (L-H) mechanism only describes "***general qualitative behavior***" of the co-adsorption of sub* and OH*. However, the major content in this investigation goes beyond a simple identification of the L-H mechanism on the investigated electro-organic oxidation reactions. **Compared to the numerous previous reports on oxidation of alcohols catalyzed by transition metal oxide/hydroxides, we decisively identify the involvement of partial OER (water activation) elementary steps and its critical role in the water-assisted EOOR micro-kinetics. More importantly, we consequently introduce two new descriptors to study the micro-kinetics and evaluate/predict the reaction outcome of different EOOR systems. The novel application of FTacV measurement and the new *operando* parameters, and the microkinetic and thermodynamic insights on these bases, provides more detailed and specific principles for efficient catalyst design.** Furthermore, by "***how particular surface ensembles are involved***", the referee is probably suggesting the details in the transitions states formed by the initial surface adsorbed states in the rate determining elementary steps. This atomic level of mechanistic detail is certainly important to demonstrate the exact surface reaction mechanism (from molecular point of view) and to identify other key micro-kinetic parameters such as activation energy, yet the precise and accurate experimental identification of such chemical reaction process (proceeding in the short time frame of fs level) has been a long-standing challenge for experimental chemists, and the corresponding mechanistic insights heavily relies on the theoretical (DFT, ab initio, *etc*) calculations, which certainly is not expected to be solved by this single work using FTacV and classical *in situ* spectroscopic methods.

2) For the issue of generality of our model to "***arbitrary substrate molecule***", we agree with the referee that there will be additional EOOR reactions that demonstrates equally or even more important elementary steps. According to the theoretical calculations in *J. Am. Chem. Soc.* **2022**, *144*, 15185 and *ACS Catal.* **2023**, *13*, 2916, the RDS of the amine and alcohol electro-oxidations are typically the first dehydrogenation step, while the following elementary steps are usually much faster and kinetically less significant (see equations S54, S55 below). Although intermediates of different organic species (alcohols, aldehydes, amines) are inherently different and the adsorption intermediates may vary even within the same class of compounds depending on the molecular structure and/or reaction pathways,

for the investigation of electro-catalytic micro-kinetics, once the rate-determining intermediates (those participating in the RDS) follow the same pathway (e.g., L-H mechanism between OER related $M^{3+\delta}$–OH* and Sub*), all reactions can be described using a unified kinetic model. This is the core statement of this work. As OER and the EOORs share several initial key elementary steps (can be viewed as partial-OER), we are aiming to focus on the kinetically more significant steps that corelate to the electrochemical processes, which could be effectively detected by FTacV measurements. Through the unified "electrochemical OH* generation (E) → L-H bimolecular reaction between OH* and Sub* (C)" electrochemical model (the specific Pt-catalyzed methanol oxidation reactions between OH* and CO*/CHO* may also comply to this category), the quantitively determined physio-chemical parameters revealed the distinct reactive "hot zones" for different EOORs, providing the efficient guidelines for the catalyst design strategies towards different substances.

$$R-CH_2NH_2 \xrightarrow{\text{possible RDS}} R-CH_2NH \rightarrow R-CHNH \rightarrow R-CHN \rightarrow R-CN$$

New **Equation S54**. The simplified amine oxidation process including four dehydrogenation steps.

$$R-CH_2OH \xrightarrow{\text{possible RDS}} R-CH_2O \rightarrow R-CHO \rightarrow\rightarrow R-COOH$$

New **Equation S55**. The simplified alcohol oxidation process including three dehydrogenation steps and one OH insertion step.

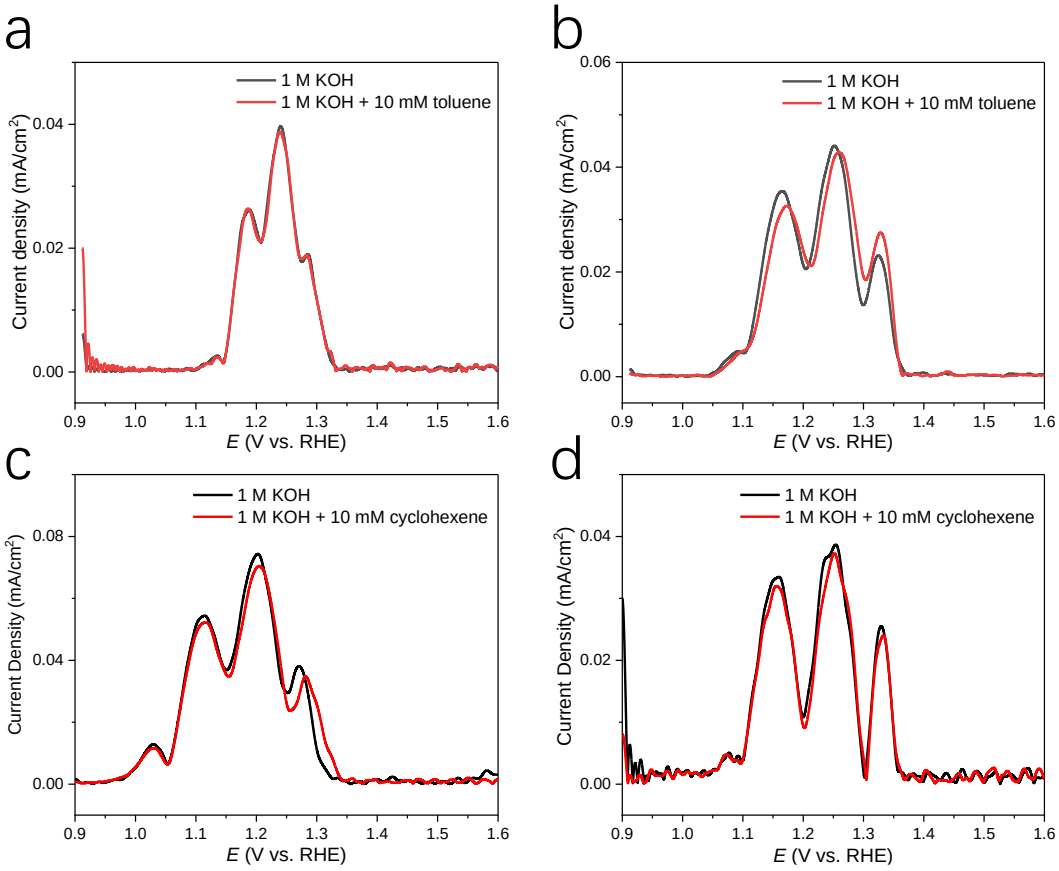
To better clarify how the model EOORs in this investigation share the same kinetic model, we have added the corresponding discussions in the revised manuscript, as following:

On Page 11, line 8: "With the two key *operando* physio-chemical descriptors ($\Delta\theta_{OH^*}/\theta_{OH^*}^{OER}$ and $\Delta\Delta G_{OH*}^{EOOR-OER}$) extracted from high-order FTacV harmonics, we can effectively quantify the partial-OER-assisted electro-organic oxidation processes following a surface EC model (i.e., surface electrochemical OH* generation (E) → L-H bimolecular reaction between OH* and Sub* (C) mechanism), from both electro-micro-kinetic and thermodynamic aspects."

On Page 11, line 16: "Therefore, we expand this methodology to different electro-organic oxidation reactions with different catalytic systems, including electrocatalytic oxidation of alcohol (to either aldehyde or carboxylic acids), aldehyde (to carboxylic acids), and amine (to nitriles), to seek more detailed electro-kinetic rules that apply to the general EOORs following the electrochemical EC model, regardless of the kinetically-insignificant details on adsorption states of organic substances[90]. Other electro-catalytic organic oxidations aiming for their complete conversion to CO_2, such as Pt-catalyzed methanol oxidation for fuel cell applications reactions, may also comply to this category (with key rds to be surface reactions between OH* and CO*/CHO*[91-94]) but are not the major focus in this investigation."

3) More importantly, the referee's question on the possible EOOR reactions with other kinetically-significant elementary steps certainly inspired us to conduct further investigations. For the organic

molecules with weak polarity and more inert bonds, the additional electrolysis and FTacV measurements for toluene (for selective oxidation of benzyl C-H bond) and cyclohexene (for selective epoxidation) were conducted. Our new results showed that these reactions (such as propylene epoxidation reaction in *Science*, **2024**, *383*, 49) do not follow the L-H mechanism, but it does not hinder us from using the FTacV methodology to provide new insights into the key elementary steps. As shown in new **Supplementary Figure S42**, the addition of toluene and cyclohexene resulted in minimal changes in FTacV harmonics, confirming their weak adsorption and the weak interference towards OER cycle, which consequently lead to the extreme difficulty to achieve high-efficiency electro-oxidation. Therefore, for the inert organic molecules exhibiting weak surface adsorption, *in situ* generation of external strong redox mediator (such as HOCl) or radicals (such as Cl· or Br·) is expectedly required to achieve efficient activation and high yields for selective oxidation. Based on such innovative application of FTacV and kinetic analysis methods, key information and conclusions that were not easily obtained in previous literatures have been obtained in this work. Thus, we hope to convince the referee that there is no "overselling the level of insights".



New **Supplementary Figure S42**. The high-order (6th) harmonics of α-$Co_{0.15}Ni_{0.85}(OH)_2$ (a, c) and α-$Ni(OH)_2$ (b, d) in pure 1 M KOH and with the addition of 10 mM toluene and cyclohexene, respectively, where the signals show no significant variation.

The corresponding discussions have been added in the revised manuscript, as following:

On Page 14, line 24: "For molecules that are more challenging to be activated (with less polarity), such as toluene and cyclohexene (model substrates for selective oxidation of benzyl C-H bonds and

selective epoxidation of alkenes, respectively), the corresponding FTacV results were shown in **Supplementary Fig. S42**. The minimal variation in signals indicates weak organic adsorptions even under high anodic potentials, which are consistent to their chemical inertness. In such cases, *in situ* generating extra strongly oxidizing radicals (such as Cl· or Br·)[99] or redox mediators (such as HOCl)[100] is presumably required to achieve high yields. Based on the innovation and scalability of measurement and kinetics analysis methods, key information and conclusions that were not easily obtained in previous literatures have been obtained in this work."

4) On the other hand, we apologize for the inaccurate and confusing description of "As electro-organic reactions typically do not involve surface adsorption/micro-reactions (i.e., the organic substance presumably completes the interfacial electron transfer process with a simple collision with the electrodes)…" in the original discussion. Note that this was in the final paragraph of the manuscript, where **we intended to make a simply comparison between the use of different parameters (apparent redox vs. surface-relevant) between electro-organic reactions that DOES or DOES NOT involve the surface catalytic processes (adsorptions, surface reactions, etc.)**. In the numerous literature reports on the electro-organic synthesis (typically conducted by organic chemists), it is a general understanding that there is no such surface catalytic process when chemically inert electrodes (such as carbon-based electrodes or sacrificial electrodes) were used, and organic reactions occur in the homogenous phase (see classical reviews in *Chem. Rev.* **2017**, *117*, 13230 and *Nat. Rev. Chem.* **2022**, *6*, 275, which have been added as new **references 105**, **106** in the revised manuscript). The EOORs investigated in this work are intrinsically different from the above electrochemical organic synthesis reactions. As long as there are surface adsorptions of both organic molecules (Sub*) and the OH*, followed by consequent reactions between Sub* and OH*, they all comply to the L-H mechanism. In this sense, the specific Pt-catalyzed methanol oxidation reactions as mentioned by the referee, which focus on the bimolecular reaction between OH* and CO*/CHO* (*J. Phys. Chem. C* **2012**, *116*, 11980, *ACS Catal.* **2020**, *10*, 543, *Nat. Catal.* **2022**, *5*, 231 and *Adv. Mater.* **2023**, *35*, 2211099, add as new **references 91-94**), may also fall into this category. To better clarify this issue, we have added the related description in the revised manuscript, as following:

On Page 11, line 16: "Therefore, we expand this methodology to different electro-organic oxidation reactions with different catalytic systems, including electrocatalytic oxidation of alcohol (to either aldehyde or carboxylic acids), aldehyde (to carboxylic acids), and amine (to nitriles), to seek more detailed electro-kinetic rules that apply to the general EOORs following the electrochemical EC model, regardless of the kinetically-insignificant details on adsorption states of organic substances[90]. Other electro-catalytic organic oxidations aiming for their complete conversion to CO_2, such as Pt-catalyzed methanol oxidation for fuel cell applications reactions, may also comply to this category (with key RDS to be surface reactions between OH* and CO*/CHO*[91-94]) but are not the major focus in this investigation."

On Page 16, line 24: "However, construction of the reactivity diagram from d.c. CV-derived parameters is inefficient for the heterogeneous electro-catalytic organic oxidations targeted in this study. As classical electrochemical organic synthesis on inert electrode such as glassy carbon typically does not involve surface adsorption/micro-reactions[105, 106] (i.e., the organic substance presumably undergoes an interfacial electron transfer process with a simple collision on the electrodes and proceeds with homogeneous reactions), more intrinsic physio-chemical parameters are necessary for the efficient

description, evaluation and machine learning (ML) investigations in the chemical conversions based on heterogeneous electrocatalysis."

3. The correlations between 'delta-V_harmonics' and adsorption energy as well as 'delta-I_harmonics' and coverage are oversold in terms of their quantitative power. I do not dispute there are positive correlations, but:

a) For delta-V, we cannot cleanly extract the thermodynamic delta G because there are still kinetic contributions to these peaks. The system is not sufficiently well-defined to extract precise thermodynamic values. This effort is further obscured by the fact that we are not dealing with homogeneous (e.g. single-crystal) surfaces, but rather an ensemble of sites with different Ni-Co local coordination ratios, potential-dependent defects populations, etc

Reply: We thank the referee for pointing this important issue that needs to be clarified. We totally agree with the referee that it is extremely challenging to experimentally measure precise ΔG values for each elementary step, as the observed electrochemical potentials were intrinsically determined by both equilibrium potential of the reaction and the activation energy barriers regarding the transitions state, and the non-single-crystal surfaces of NiCo oxyhydroxides casts further challenges for experimental measurements. It should be noted that, in some recent works (*Joule* **2018**, *2*, 225 and *J. Am. Chem. Soc.* **2022**, *144*, 7622), the d.c. CV redox peak potentials were used to evaluate the free energy difference ($\Delta G_{O*} - \Delta G_{OH*}$) for the rate-determining step M^{3+}–OH* → $M^{3+\delta}$–O* + e^- on Ni oxyhydroxides during OER. Whereas the redox peak values are easily influenced by the factors such as scan rate, non-Faradaic charging current, and chemical catalytic current, the previous mathematical confirmation by A.M. Bond *et al*. (*J. Electroanal. Chem*. 2007, *600*, 23) and our experimental results (**Supplementary Figure S40**) confirmed that the contribution from non-Faradaic charging, diffusion and catalytic processes in d.c. CV can be effectively excluded in high-order (>4^{th}) harmonics. Thus, the high-order harmonic peak could be used to correlate the equilibrium potential of the electron transfer step with higher accuracy (*Proc. Natl. Acad. Sci. U.S.A.* **2015**, *112,* 14506 and *ACS Catal*. **2017**, *7*, 4846).

More importantly, what we actually propose in this work, is that the change of peak potential in high-order harmonic (ΔV) actually reflects the CHANGES in ΔG under OER and different EOOR conditions, i.e., $\Delta\Delta G_{OH*}^{EOOR-OER} = \Delta G_{OH*}^{EOOR} - \Delta G_{OH*}^{OER}$, rather than the absolute value of any ΔG_{OH*}. Given that the OER and EOOR mechanism shown in eq 1-9 in **Scheme 1** share the fast electron transfer step ($M^{\delta+}$–OH* → $M^{\delta+1}$–OH* + e^-), the $\Delta V_{harmonics}$ values measured by FTacV is numerically equivalent to $\Delta\Delta G_{OH*}^{EOOR-OER}$, which can therefore be used to evaluate the probability of different EOOR reactions to shift from the OER pathway. This new parameter is of great significance towards catalysts design as it represents the intrinsic factor that determines whether the electrocatalytic reactions favors the EOOR or OER pathways, which can be rationally modulated by tailoring the electronic structures of metal sites for different organic substances. It is also worth mentioning that a similar concept, the variation in OH* adsorption energy on transition metal oxide surfaces, which can be modulated by changing the number of active sites and can only be estimated by parameter fitting, were proposed to be important for the electro-kinetic modeling in OER (DFT calculation and parameter fitting investigations, *J. Am. Chem. Soc*. **2019**, *141*, 13803 and *ACS Catal*. **2020**, *10*, 8597, "*less than*

25~50 meV"). The $\Delta(\Delta G_{OH*})$ values (of key OH* species) proposed and measured under different EOOR conditions in this work (summarized in new **Table 1**), caused by the competitive adsorption and consumption of active OH* by organic molecules, fall in the similar range. Therefore, we believe that this first experimental measurement of $\Delta(\Delta G_{OH*})$ correlates well to the theoretical values, serving as an effective experimental complement for the micro-kinetic analysis, specifically in EOOR systems that share the same kinetically significant steps that overlap with OER. Furthermore, for the issue of "***homogeneous surface***", since it is the changes in ΔG values that was measured by FTacV, the single crystal surface is NOT necessary for the measurement as long as the intrinsic surface characteristics for a tested catalyst materials remain the same in two reactions (OER and EOOR). In addition, while we certainly agree that the surface of a single crystal is an ideal platform for mechanistic studies, it should be noted that the major point in this work is to introduce a new application of FTacV method and propose two new physio-chemical parameters. Therefore, we believe the same methodology can be applied to the single crystalline surface as well, which is not the major focus of this investigation. The methodology can be efficiently used to measure many catalytic material systems regardless of this crystallinity, such as NiCo oxyhydroxides in this article, only demonstrates its significant practical value.

Overall, we gratefully thank the referee for this valuable question that has led to significant improvement on the clarity of the discussions, which have been updated in the revised manuscript, as following:

New **Table 1.** Summarized key parameters and design principles for EOOR systems.

Substances	Products	Oxidation Potential	Relative Change of θ_{OH*} [a]	Reaction Kinetic Complexity	Altered $\Delta G_{Eq.2}$	$M^{3+\delta}$–OH* Requirement
aldehyde	carboxylic acid	low	25%~55%	simple	−5~5 meV	relatively low
alcohol	aldehyde	relatively high [b]	13%~20%	simple	0~12 meV [b]	relatively low
	carboxylic acid	moderate	25%~35%	moderate	5~10 meV	balanced $\theta_{OH*}/\theta_{sub*}$
amine	nitrile	high	20%~32%	complex	20~35 meV	high level of θ_{OH*}

[a] coverage relative to the θ_{OH*} under OER conditions
[b] in weak alkaline solution (1 M K_2CO_3)

On Page 10, line 20: "As OER and EOOR mechanism (eq 1-9) share the same fast electron transfer step ($M^{\delta+}$–OH* → $M^{\delta+1}$–OH* + e^-), the shifted *Process I* main peak values in harmonics ($\Delta V_{harmonics}$

from OER to EOOR in **Fig. 3c-f**) correlate to the $M^{\delta+1}$–OH* formation free energy (ΔG_{OH*}, as also illustrated by red ladder in **Fig. 4**) under the interference of organics. Note that the observed electrochemical potentials were intrinsically determined by both equilibrium potentials of the reaction and the activation energies regarding the transitions state, quantifying exact value of ΔG_{OH*} is still challenging. To this end, the $\Delta V_{harmonics}$ values (V) measured by FTacV is numerically equivalent to $\Delta\Delta G_{OH*}^{EOOR-OER}$ (defined as $\Delta\Delta G_{OH*}^{EOOR-OER} = \Delta G_{OH*}^{EOOR} - \Delta G_{OH*}^{OER}$), which can therefore be used to evaluate the variations in different EOOR reactions that share the same thermodynamic parameter with OER pathway. This parameter is of great significance towards catalyst design as it represents an intrinsic thermodynamic factor that determines whether the electrocatalytic reactions favors the EOOR or OER pathways, which can be rationally modulated by tailoring the electronic structures of metal sites for different organic substances."

On Page 16, line 3: "It is worth mentioning that the $\Delta(\Delta G_{OH*})$ values we measured under different EOOR conditions (**Table 1**), caused by the competitive adsorption and consumption of active OH* by organic molecules, correlates well to the variation in OH* adsorption energy during OER simulated by changing the number of active sites in the literature (less than 25~50 meV)[53]. This indicates the kinetic role of organic adsorptions through a similar mechanism, the reduction of active sites. It further reveals the power of FTacV measurement as an effective tool to experimentally obtain key physio-chemical parameters that have only been provided by the parameter fitting in theoretical micro-kinetic simulation/analysis."

b) Delta-I only contains one particular harmonic component so I do not see how it can reliably be transformed into a quantitative estimate for change in coverage.

Reply: We thank the referee for this important question that needs to be better clarified. The correlation between FTacV peak current (from high-order harmonics) and the quantity of the electro-active sites have been thoroughly discussed in the literature, especially in the pioneering works from A. M. Bond and co-workers (see references 75-82 in the original manuscript). Based on the general model of a single-surface-confined electroactive species with a surface concentration that follows the Nernst equation with no thermodynamic (single and constant E^0) or kinetic dispersion (single and constant k^0), the quantitative parameters including the surface concentration of active sites and rate constant (of the elementary step corresponding to the fast electron transfer process) can be extracted from the simulation by fitting to experimental data, and there is a well-developed software package MECSim that can be used for such model simulation. One good example is the recent use of FTacV measurement to determine the absolute number of electroactive species in Fe-NC-catalyzed ORR, demonstrated by Elbaz *et al.* (*Nat. Catal.* **2022**, *5*, 163 and *Nat. Catal.* **2024**, *7*, 139).

Briefly, quoting from Bond's work in *Phys. Chem. Chem. Phys.* **2014**, *16*, 19035 (add as new **reference 86**): "*in FTAC voltammetry, the peak current magnitude directly reflects the electrode kinetics with fast processes giving large currents and slow ones giving smaller currents*". The specific fast electron transfer steps can be written as $M^{\delta+}$–OH* → $M^{\delta+1}$–OH* + e^-, where M=Fe (+2 to +3) in Elbaz's work for ORR and M=Co, Ni (+3 to +4) in our work for OER and EOOR. **As a result, the Δ*I* in FTacV exclusively reflects the kinetics of this specific fast electron transfer step, which is proportional to the amount of electrochemically active species ($M^{\delta+}$–OH*).** This correlation can be demonstrated by the following numerical expression:

$$j_{FTacV} \propto r_{fast\ e-process} = \frac{\partial c_{M^{\delta+}-OH^*}}{\partial t} = k_0 \exp\left[\frac{\alpha F(E-E^0)}{RT}\right] c_{M^{\delta+}-OH^*}$$

where $c_{M^{\delta+}-OH^*}$ is the surface concentration of electrochemically active species ($M^{\delta+}$–OH*). With the experimental determination of the initial surface concentration of the active metal sites, $c_{M^{\delta+}-OH^*}$ can be converted to $\theta_{M^{\delta+}-OH^*}$.

Furthermore, the water oxidation-assisted EOOR focused in this work is a typical surface EC reaction. Once the electrochemically active $M^{3+\delta}$–OH* species are generated, the surface reaction between $M^{2++\delta}$–Sub* and $M^{3+\delta}$–OH* proceeds spontaneously. Meanwhile, the adsorption of organic substance to form $M^{2++\delta}$–Sub* will in turn reduce the available sites for the OH* adsorption, practically reduce the surface coverage of $M^{3+\delta}$–OH* (as compared to intrinsic $M^{3+\delta}$–OH* coverage during OER). **Hence, we take a step forward in this work to focus more on the relative change in coverage of active $M^{3+\delta}$–OH* species (designated as $\Delta\theta_{OH^*}/\theta^{OER}_{OH^*} = (\theta^{EOOR}_{OH^*} - \theta^{OER}_{OH^*})/\theta^{OER}_{OH^*}$) by calculating the relative change in harmonic peak currents, rather than extracting the absolute values of $c_{M^{\delta+}-OH^*}$ or $\theta_{M^{\delta+}-OH^*}$.** Specifically:

$$\frac{\Delta I^{EOOR-OER}_{harmonics}}{I^{OER}_{harmonics}} = \frac{I^{EOOR}_{harmonics} - I^{OER}_{harmonics}}{I^{OER}_{harmonics}} = \frac{k'(c^{EOOR}_{surface\ OH^*} - c^{OER}_{surface\ OH^*})}{k' c^{OER}_{surface\ OH^*}}$$

$$= \frac{(c^{EOOR}_{surface\ OH^*} - c^{OER}_{surface\ OH^*})/c_{overall\ sites}}{c^{OER}_{surface\ OH^*}/c_{overall\ sites}} = \frac{\theta^{EOOR}_{OH^*} - \theta^{OER}_{OH^*}}{\theta^{OER}_{OH^*}} = \frac{\Delta\theta^{EOOR-OER}_{OH^*}}{\theta^{OER}_{OH^*}}$$

Note that the change in surface coverage $|\Delta\theta_{OH^*}/\theta^{OER}_{OH^*}|$ further reflects the quantity of $\theta^{EOOR}_{Sub^*}$, assuming the same surface density of overall active metal sites under OER and EOOR conditions, i.e., $\theta^{EOOR}_{Sub^*} + \theta^{EOOR}_{OH^*} = \theta^{OER}_{OH^*}$. This is a specifically useful experimental quantification method that further confirms the general kinetic simulations in **Supplementary Figure S2**. The quantitative *operando* parameter of $\Delta\theta_{OH^*}/\theta^{OER}_{OH^*}$ was effectively determined by FTacV measurements in this work, as demonstrated in **Figure 5a**, **5c** and **Table 1**, providing the optimal *operando* surface conditions for the efficient electro-oxidation of each type of substance, therefore showing the great potential in the study of complex (bi-molecular and beyond) heterogeneous electro-catalysis. For example, the FTacV results indicated the gradually increasing substances' concentration to reach the fastest reaction rate (i.e. $\theta_{Sub^*} = \theta_{OH^*} = 0.5$), suggesting the decreasing trend in the adsorption energy and *operando* surface coverage from aldehydes, alcohols to amines. For comparison, a recently published work (*Nat. Commun.* **2024**, *15*, 3986, add as new **reference 102**) proposed a similar parameter of $\Delta(\theta_{OH^*}/\theta_{CO^*})$ obtained by *operando* Raman spectroscopy, which was proved to be an important descriptor for the products distribution in CO_2RR.

Overall, we gratefully thank the referee for this valuable question that has led to significant improvement on the clarity of the discussions, which have been updated in the revised manuscript, as following:

On Page 9, line 18: "Based on the general "surface confined catalysis" model[78, 79, 83, 85, 86] where the concentration of a surface electroactive species follows the Nernst equation with no thermodynamic (single and constant E^0) or kinetic dispersion (single and constant k^0), the quantitative parameters including the surface concentration of active sites and rate constant (of the elementary step corresponding to the fast electron transfer process) can be extracted from the simulation of FTacV data using the MECSim package[87], ($I_{\text{harmonics}} \propto c_{\text{M}^{\delta+}-\text{OH}^*}$, see more detailed discussions on the mathematical model in **Supplementary Note 6**). As shown in the simulation results in **Supplementary Fig. S39**, the peaks in the *Process I* region and the surface redox conversion in the d.c. CV correlate well with experimental results. Therefore, the partial-OER-initiated EOOR on α-$Co_xNi_{1-x}(OH)_2$ indeed fits into a surface EC mechanism, where the generation of electrochemically active $M^{3+\delta}$–OH* species are followed by the spontaneous reaction between $M^{2++\delta}$–Sub* and $M^{3+\delta}$–OH* (equations 1, 2 & 4). For quantitative analysis in this work, during the water-oxidation-assisted EOOR, the adsorption of organic substance to form $M^{2++\delta}$–Sub* will in turn occupy the available sites for the OH*, practically reduce the surface coverage of $M^{3+\delta}$–OH* (as compared to intrinsic $M^{3+\delta}$–OH* coverage during OER). As confirmed in **Fig. 3 c-f**, with the addition of 10 mM organics, the FTacV harmonic peak current of *Process I* shows an obvious decrease in value. On this basis, we take a step forward to focus more on the change in coverage of active $M^{3+\delta}$–OH* species (designated as $\Delta\theta_{\text{OH}^*}/\theta_{\text{OH}^*}^{\text{OER}} = (\theta_{\text{OH}^*}^{\text{EOOR}} - \theta_{\text{OH}^*}^{\text{OER}})/\theta_{\text{OH}^*}^{\text{OER}}$) by calculating the relative change in harmonic peak currents:

$$\frac{I_{\text{harmonics}}^{\text{EOOR}} - I_{\text{harmonics}}^{\text{OER}}}{I_{\text{harmonics}}^{\text{OER}}} = \frac{k\prime(c_{\text{surface OH}^*}^{\text{EOOR}} - c_{\text{surface OH}^*}^{\text{OER}})/c_{\text{overall sites}}}{k\prime c_{\text{surface OH}^*}^{\text{OER}}/c_{\text{overall sites}}} = \frac{\theta_{\text{OH}^*}^{\text{EOOR}} - \theta_{\text{OH}^*}^{\text{OER}}}{\theta_{\text{OH}^*}^{\text{OER}}} \quad (10)$$"

More detailed discussions about the connection between two experimental parameters and physio-chemical descriptors were also added in the revised Supplementary Information, as new **Supplementary Note 6**:

"**Mathematical correlation between the experimental parameters and two physio-chemical descriptors (Note 6)**

(1) The correlations between FTacV peak current (from high-order harmonics) and the quantity of the electro-active sites can be found in previous discussions.[17, 20-24] Based on the general model of a single-surface-confined electroactive species with a surface concentration that follows the Nernst equation with no thermodynamic (single and constant E^0) or kinetic dispersion (single and constant k^0), the quantitative parameters including the surface concentration of active sites and rate constant (of the elementary step corresponding to the fast electron transfer process) can be extracted from the simulation by fitting to experimental data. In this work, the software package MECSim[19] was used for such model simulation.

Briefly, the specific fast electron transfer steps of OER and EOOR in this investigation can be written as $M^{\delta+}$–OH* → $M^{\delta+1}$–OH* + e^-, where M=Co, Ni (+3 to +4). As a result, the ΔI in FTacV exclusively reflects the kinetics of this specific fast electron transfer step, which is proportional to the amount of electrochemically active species ($M^{\delta+}$–OH*). This correlation can be demonstrated by the following

numerical expression:

$$j_{FTacV} \propto r_{fast\ e-process} = \frac{\partial c_{M^{\delta+}-OH^*}}{\partial t} = k_0 \exp\left[\frac{\alpha F(E-E^0)}{RT}\right] c_{M^{\delta+}-OH^*} \quad (52)$$

where $c_{M^{\delta+}-OH^*}$ is the surface concentration of electrochemically active species ($M^{\delta+}$–OH*). With the experimental determination of the initial surface concentration of the active metal sites, $c_{M^{\delta+}-OH^*}$ can be converted to $\theta_{M^{\delta+}-OH^*}$.

Furthermore, the water-assisted EOOR is a typical surface EC reaction. Once the electrochemically active $M^{3+\delta}$–OH* species are generated, the reaction between $M^{2+\delta}$–Sub* and $M^{3+\delta}$–OH* proceeds spontaneously. Meanwhile, the adsorption of organic substance to form $M^{2+\delta}$–Sub* will in turn reduce the available sites for the OH* adsorption, practically reduce the surface coverage of $M^{3+\delta}$–OH* (as compared to intrinsic $M^{3+\delta}$–OH* coverage during OER). Hence, this work focused more on the change in coverage of active $M^{3+\delta}$–OH* species (designated as $\Delta\theta_{OH^*}/\theta_{OH^*}^{OER} = (\theta_{OH^*}^{EOOR} - \theta_{OH^*}^{OER})/\theta_{OH^*}^{OER}$) by calculating the relative change in harmonic peak currents, rather than extracting the absolute values of $c_{M^{\delta+}-OH^*}$ or $\theta_{M^{\delta+}-OH^*}$. Specifically, at the fixed potential:

$$\frac{\Delta I_{harmonics}^{EOOR-OER}}{I_{harmonics}^{OER}} = \frac{I_{harmonics}^{EOOR} - I_{harmonics}^{OER}}{I_{harmonics}^{OER}} = \frac{k'(c_{surface\ OH^*}^{EOOR} - c_{surface\ OH^*}^{OER})}{k' c_{surface\ OH^*}^{OER}}$$

$$= \frac{(c_{surface\ OH^*}^{EOOR} - c_{surface\ OH^*}^{OER})/c_{overall\ sites}}{c_{surface\ OH^*}^{OER}/c_{overall\ sites}} = \frac{\theta_{OH^*}^{EOOR} - \theta_{OH^*}^{OER}}{\theta_{OH^*}^{OER}} = \frac{\Delta\theta_{OH^*}^{EOOR-OER}}{\theta_{OH^*}^{OER}} \quad (53)$$

(2) It should be noted that, experimentally measure precise ΔG values for each elementary step is extremely challenging, as the observed electrochemical potentials were intrinsically determined by both equilibrium potential of the reaction and the activation energy barriers regarding the transitions state, and the non-single-crystal surfaces of NiCo oxyhydroxides casts further challenges for experimental measurements. However, the $\Delta V_{harmonics}$ in FTacV reflects the changes in ΔG under OER conditions and different EOOR conditions, i.e., $\Delta\Delta G_{OH*}^{EOOR-OER}$ (defined as $\Delta\Delta G_{OH*}^{EOOR-OER} = \Delta G_{OH*}^{EOOR} - \Delta G_{OH*}^{OER}$), which can therefore be used to evaluate the variations in different EOOR reactions that share the same thermodynamic parameter with OER pathway. The measured $\Delta V_{harmonics}$ (V) values using FTacV is numerically equivalent to $\Delta(\Delta G_{OH*})$ (eV) to evaluate the variations in different EOOR systems that share the same thermodynamic parameter. This parameter is of great significance towards catalysts design as it represents an intrinsic thermodynamic factor that determines whether the electrocatalytic reactions favors the EOOR or OER pathways, which can be rationally modulated by tailoring the electronic structures of metal sites for different organic substances."

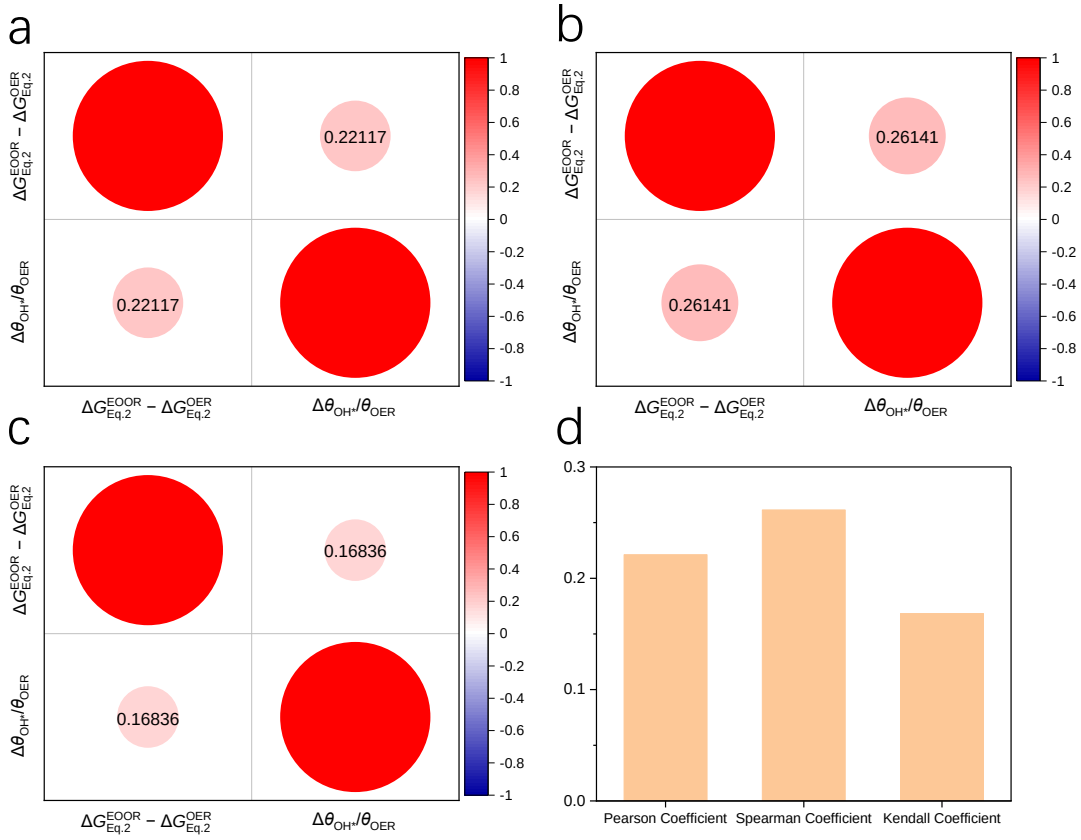
4. Electron transfer to create a higher oxidation state (one descriptor) is presumably correlated with the OH* coverage (other chosen descriptor). Can the authors better justify what separates them and

how strategies to tune one could be implemented without affecting the other?

Reply: We thank the referee for pointing out this important issue that needs to be further clarified.

1) We agree with the referee that "***electron transfer to create a higher oxidation state***" is correlated with the "***the OH* coverage***". However, we would like to point out that "***electron transfer to create a higher oxidation state***" is NOT a descriptor proposed in our work. Instead, we propose a different descriptor, the ***alternation in the Gibbs free energy change*** of the key electron transfer step from OER to EOOR conditions, $\Delta\Delta G_{OH*}^{EOOR-OER} = \Delta G_{OH*}^{EOOR} - \Delta G_{OH*}^{OER}$, to reflect the thermodynamic aspects differentiating OER and water-assisted EOOR. The other descriptor (discussed in detail in the above question) that reflects the alternation in surface coverage of $M^{3+\delta}$–OH* species is correlated with the key electron transfer step from the kinetic perspective, which we believe is intrinsically distinct to each other.

To better address this issue, we further apply the mathematical approach to analyze the correlation between the two physio-chemical descriptors regarding kinetics and thermodynamics. The Pearson, Spearman and Kendall coefficients were shown here (also add as new **Supplementary Fig. S41**). All of the three coefficients are < 0.3, indicating very small correlation between the two descriptors. Therefore, the two descriptors can be effectively used for mechanistic and micro-kinetic investigation in heterogeneous electrocatalysis. The FTacV methodology and surface adsorption related physio-chemical descriptors will also help the future ML investigations in this field.



New **Supplementary Figure S41**. The Pearson, Spearman and Kendall coefficients of two physio-chemical descriptors, $\Delta\Delta G_{OH*}^{EOOR-OER}$ and $\Delta\theta_{OH^*}/\theta_{OH^*}^{OER}$, all of them indicate the relatively small

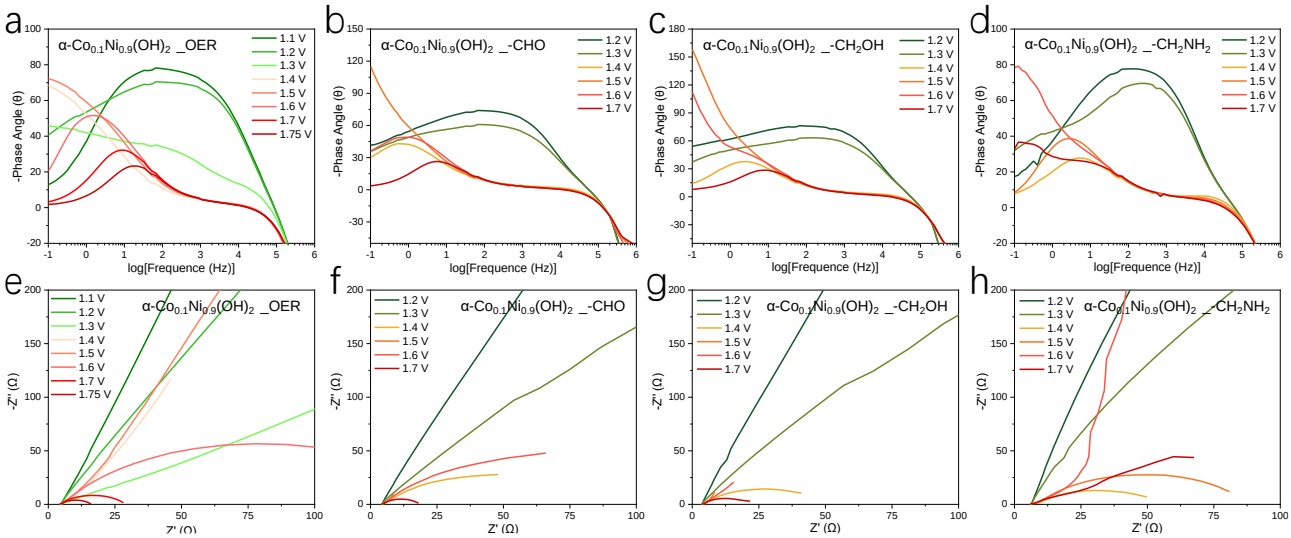
correlation between the two descriptors.

2) On this basis, the complete separation of "***electron transfer to create a higher oxidation state***" and "***the OH* coverage***" is not possible and not a major perspective in this work. However, "***how strategies to tune one could be implemented without affecting the other***" is indeed an inspiring question for the discussion on the catalyst design principles. Based on the clear distinction between the surface adsorptions under OER and EOOR conditions, as reflected by the two descriptors in this work, one can assume that the alternation of chemical environment (including organic additives, different solvent molecules, cation/anion from electrolytes, etc.) could effectively modulate the surface adsorption of key intermediate species without significantly changing the electronic structure of the catalytic sites; whereas typical modulation on the catalytic materials, such as doping with other transition metals (e.g., $Ni_{1-x}M_xOOH$ in *Angew. Chem. Int. Ed.* **2021**, *60*, 16448 and *J. Am. Chem. Soc.* **2022**, *144*, 15185) in the surface lattice will change the electronic structure that modulates the surface adsorption energies of the involving species (the Mn doping would greatly increase the ΔG_{O*} of α-$Ni(OH)_2$ to further hamper the OER pathway and increase $M^{3+\delta}$–OH* coverage). The new results and corresponding discussion were updated in the revised manuscript, as following:

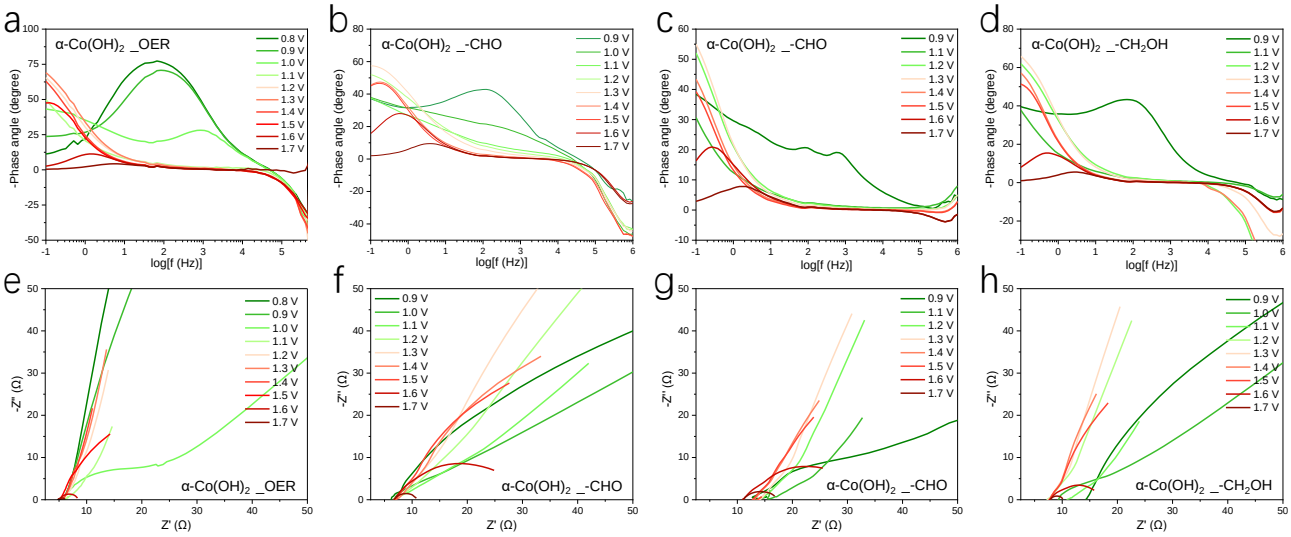
On Page 11, line 12: "Additionally, the small Pearson coefficient (~0.22, see **Supplementary Fig. S41**) indicates insignificant correlation between the two physio-chemical descriptors, suggesting their distinct representations (from thermodynamic and micro-kinetic perspectives) in the mechanistic investigation on the surface electro-catalytic processes."

5. Readers will be much more familiar with the use of EIS, which is somewhat related but sticks to the region of linear response. It would seem one could in principle take a series EIS measurements about different potentials and map fitted charge transfer resistances (as a functional of potential) to acquire similar information. Could the authors speak to that? It would be valuable for a journal targeted at broader readership.

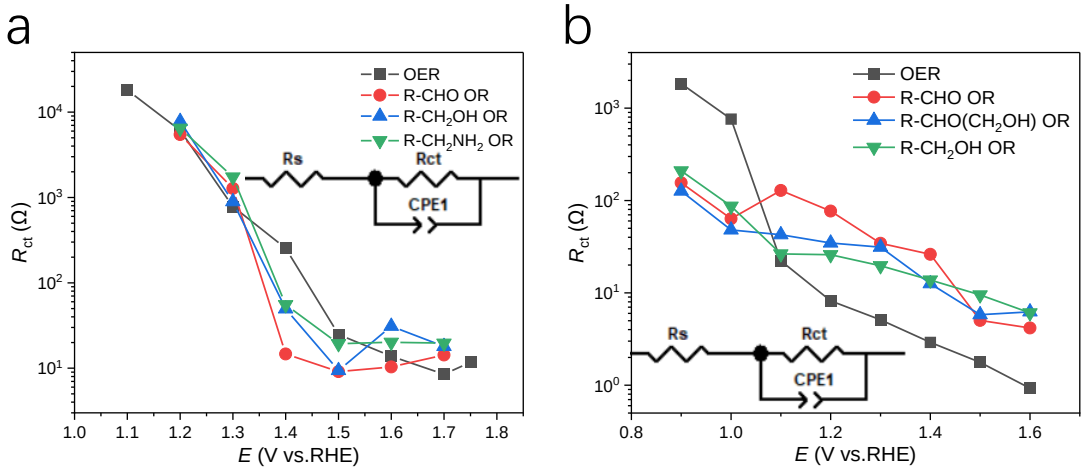
Reply: We thank the referee for raising this valuable suggestion, the *in situ* EIS characterization is indeed an efficient supplementary for the mechanistic investigation, and has been widely employed in the electrocatalytic studies. Per your suggestion, we conducted *in situ* EIS measurements of typical α-$Co_xNi_{1-x}(OH)_2$ in the conditions of OER and EOORs, and the new results were added as new **Supplementary Figure S27-28**. More importantly, the fitted charge transfer resistances (R_{ct}) as a function of potential were plotted in the new **Supplementary Figure S29**.



New **Supplementary Figure S27**. The *in situ* EIS measurements of α-$Co_{0.1}Ni_{0.9}(OH)_2$ (representative of good EOOR catalyst) in the conditions of OER and electro-oxidation reactions. (a-d) The Bode plots. (e-h) The Nyquist plots.



New **Supplementary Figure S28**. The *in situ* EIS measurements of α-$Co(OH)_2$ (representative of poor EOOR catalyst) in the conditions of OER and electro-oxidation reactions. (a-d) The Bode plots. (e-h) The Nyquist plots.



New **Supplementary Figure S29**. Correlation of the charge transfer resistances (R_{ct}) and electrochemical potentials of α-$Co_{0.1}Ni_{0.9}(OH)_2$ (a) and α-$Co(OH)_2$ (b).

It can be observed that for optimal EOOR catalyst α-$Co_{0.1}Ni_{0.9}(OH)_2$, the R_{ct} value under OER conditions is relatively large at electrolysis potentials (1.4 ~ 1.5 V_{RHE}). In contrast, under the EOOR conditions with three different types of molecules, the R_{ct_EOOR} values are all smaller than R_{ct_OER}, with the order of R-CHO OR < R-CH_2OH OR < R-CH_2NH_2 OR. For α-$Co(OH)_2$ that tends to undergo OER pathway over EOOR (with the lowest EOOR yields and FEs) on the other hand, the R_{ct_EOOR} value at electrolysis potentials (1.4~1.5 V_{RHE}) is larger than R_{ct_OER}.

Overall, *in situ* EIS conveniently quantifies the charge transfer resistance, which accurately links to the electro-kinetics of the reactions. Combined with the Bode plots, it can be further used to analyze the evolution of the surface states (phases) of the catalytic material under varying electrochemical potentials (see *Nat. Commun.* **2022**, *13*, 2916 and *Nat. Commun.* **2022**, *13*, 4602, reference 41 and new **reference 73**).

Although EIS and FTacV (or other a.c. voltammetry) fall into the same category of "Techniques based on concepts of impedance" by both superimposing a sinusoidal disturbance on the d.c. electrochemical potential (as well-summarized in the chapter 10 in the textbook of "Electrochemical Methods: Fundamentals and Applications" by A. J. Bard), they still vary in terms of detailed signaling principles.

The small sinusoidal disturbance (5~10 mV) in typical EIS test would not induce the significant non-linear response, which could be further used to fitting with the equivalent circuit. The R_{ct} information extracted from equivalent circuit can be correlated with the phase transition in Co/Ni hydroxides typically from top to inner lattice during electrochemical processes, serving as the fundamental basis for the use of R_{ct} or $|Z|$ to confirm the formation of a stable interface (circuit), as shown in above additional results and also in literatures. However, "*such equivalent circuits are not unique and one cannot easily guess the form or structure of the equivalent circuit from the processes involved in the reaction scheme*" (page 388, section 10.4.3 in "Electrochemical Methods: Fundamentals and Applications" by A. J. Bard), and it does NOT provide *operando* quantification on Sub* and OH* nor the $\Delta\Delta G_{OH*}$ parameter/descriptors proposed in this work.

On the other hand, the high amplitude of voltage (100~200 mV) applied in FTacV substantially induces the higher non-sinusoidal waveforms of currents that composed with harmonics (*f*, 2*f*, 3*f* …n*f* terms in

the Taylor expansion of current). It has been established that the high-order (>4th) harmonics contain only the fast electron transfer process could be effectively used to study the partial-OER related $M^{3+\delta}$–OH* species. In this work, we take a step forward to focus on the change in coverage of active $M^{3+\delta}$–OH* species ($\Delta\theta_{OH^*}/\theta_{OH^*}^{OER}$) and the alternation in the Gibbs free energy change of the key electron transfer step from OER to EOOR ($\Delta\Delta G_{OH^*}$), and the constructed activity diagrams provide the general catalyst design principles for water-oxidation-assisted organics electro-oxidation.

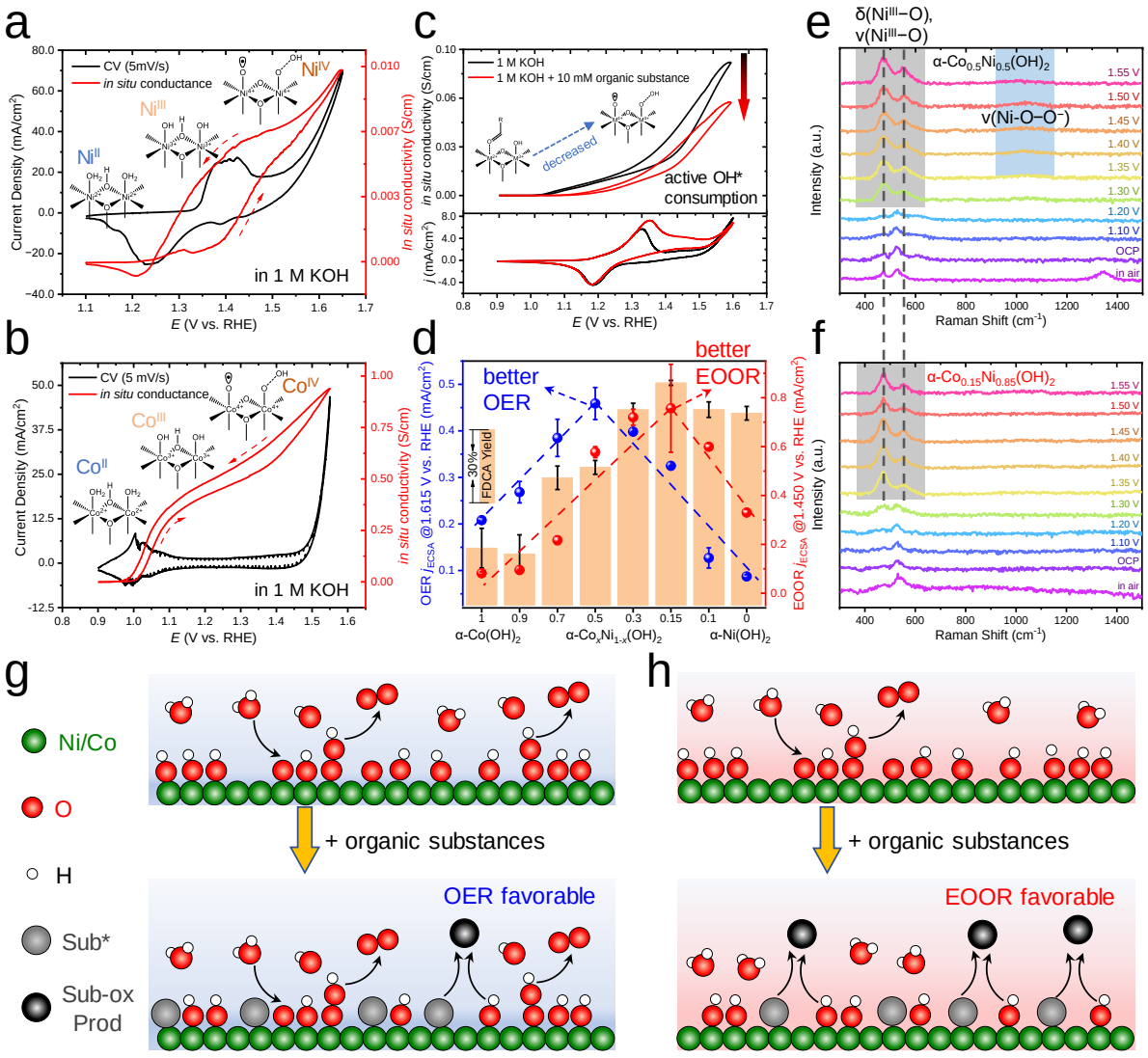
Therefore, we consider *in situ* EIS a useful supplementary characterization technique that provides *in situ* information (but) from different signaling perspective. We thank the referee's question that inspired more comprehensive characterization and mechanistic insights into the system, and the new *in situ* EIS results were added as new **Supplementary Figure S27-S29** (see above), with corresponding discussions added in the revised manuscript, as following:

Page 7, line 9: "The *in situ* EIS measurements[41, 73, 74] (**Supplementary Figure S27-S29**) provide charge transfer resistance (R_{ct}) under different conditions. For catalysts with higher EOOR activity, a reduced R_{ct} value from OER to EOOR conditions ($R_{ct}^{EOOR} < R_{ct}^{OER}$) can be observed, consistent to the faster electro-kinetics probably from the reactions between OH* and Sub*. Opposite trend ($R_{ct}^{EOOR} > R_{ct}^{OER}$) was observed for catalysts with poor EOOR activity, suggesting the preference of O*/OOH* formation pathway."

6. In general the paper is crammed with assertions about the meaning of data and not given adequate exposition. It relies extremely heavily on SI to the point it is frustrating to read and evaluate the arguments. In my opinion should simply not be written as a communication.

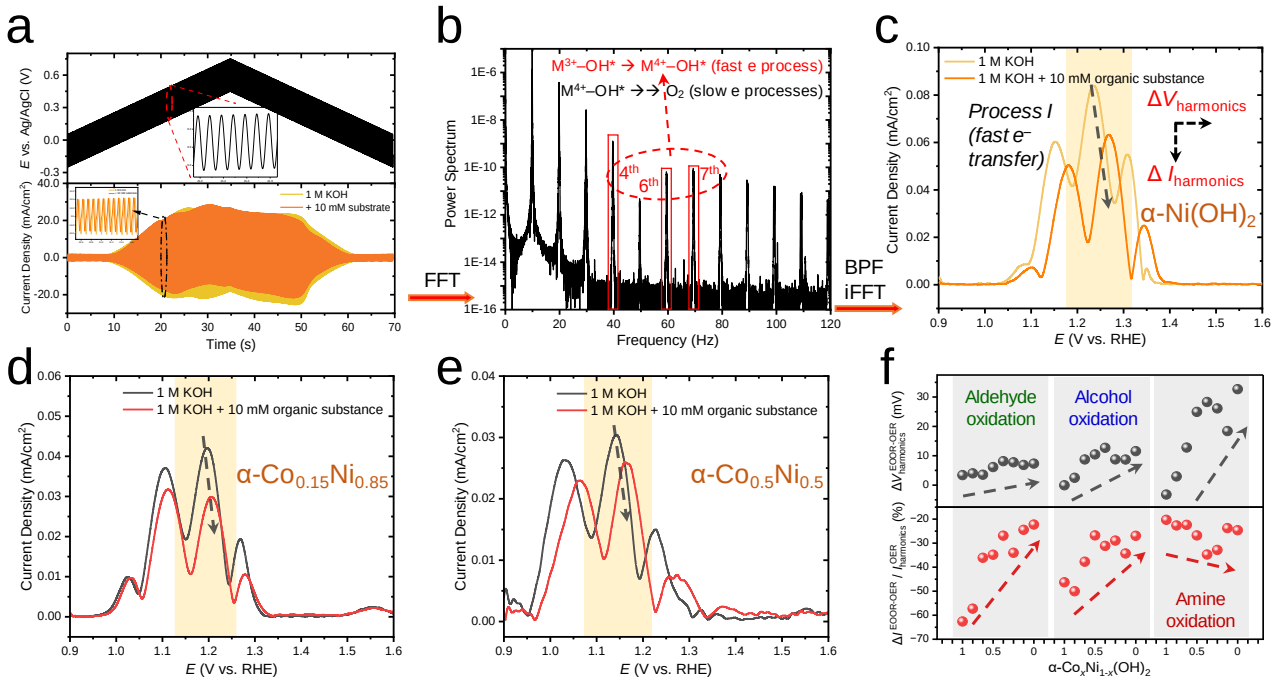
Reply: We thank the referee's valuable comment on the issue of clarity, which indeed requires substantial improvement for a general readership. Thanks to several detailed points raised by the referee in the above comments #1-5, additional results, more clarified definitions (on the two physio-chemical descriptors) and data analysis, with much more detailed discussions on the fundamental principles of FTacV signaling and their intrinsic correlations to the two physio-chemical descriptors, have been provided correspondingly in the revised documents. With these additional improvements, we hope we can convince the referee that adequate exposition has been provided for the understanding of the results and conclusions in this work. In addition to the revisions corresponding to above questions #1-5, we have made the following modifications in the main text to help readers better understanding the data presented in this manuscript:

Firstly, in new **Fig. 2**, we have added the schematic illustration of the *operando* surface processes (**g, h**) in the OER and EOOR pathways, respectively.



New **Figure 2.** (g, h) Schematic illustration of surface processes on the catalysts that favor OER and EOOR pathway, respectively.

Secondly, in new **Fig. 3d-f**, the FTacV harmonic responses for α-$Co_{0.5}Ni_{0.5}(OH)_2$ and α-$Co_{0.15}Ni_{0.85}(OH)_2$ (**Fig. 3d and 3e**) were separately plotted for easier understanding of the measurement, whereas the original grouped FTacV raw data (original Fig. 3e and 3f) were changed to the summery of two subtracted descriptor values in the new **Fig. 3f**. The updated configuration of the new **Figure 3** aims to provide more clarified demonstration of the FTacV data that is easier for the readers to interpretate.



New **Figure 3. The principle and results of the FTacV measurements on OER and EOOR.** (a) The applied electrochemical potential (d.c. + a.c.) and collected overall currents. (b) The power spectrum of overall current processed after FFT and the target harmonics filtered by a band pass filter (BPF) followed with iFFT algorithms. (c) The $\Delta I_{\text{harmonics}}$ and $\Delta V_{\text{harmonics}}$ parameters extracted from the harmonics of α-Ni(OH)$_2$. (d and e) The FTacV harmonic responses for α-$Co_{0.5}Ni_{0.5}(OH)_2$ (d) and α-$Co_{0.15}Ni_{0.85}(OH)_2$ (e) in 1.0 M KOH and the addition of 10 mM organic substances (benzylamine). Here both the absolute values of peak currents and the peak potentials (*Process I*) change, indicating the varied $\theta_{M(3+\delta)-OH^*}$ and ΔG_{OH^*}. (f) Summarized values of the two physio-chemical descriptors ($\Delta I_{\text{harmonics}}^{\text{EOOR-OER}} / I_{\text{harmonics}}^{\text{OER}}$ and $\Delta V_{\text{harmonics}}^{\text{EOOR-OER}}$) in the electro-oxidation of aldehyde (furfural), alcohol (furfuryl alcohol), and amie (benzylamine).

Thirdly, the sub-section for the descriptions, explanations and data processing of FTacV methodology have also been thoroughly revised to make it easier for readers to understand. For this part, please see our **reply to question #3** (Revised manuscript, page 9 and new **Supplementary Note 6**).

Reviewer #3 (Remarks to the Author):

In this manuscript, the authors present a systematic study on the electrochemical oxidation of various model organic molecules, including furfural, furfural alcohol, and benzylamine, on a series of cobalt/nickel-based oxyhydroxides (α-CoxNi1-x(OH)2) with varying Ni/Co ratios. They employed in situ ETS for α-Co(OH)2 and confirmed the generation of active oxygenate species (Co3+δ−OH*/O*) on the surface and their consumption during the oxidation of organic molecules. They demonstrated that α-CoxNi1-x(OH)2 with different Co:Ni ratios exhibited different reaction tendencies towards OER or the oxidation of organics. Two key operando physio-chemical descriptors provided by high-order harmonics extracted from Fourier transformed alternating current voltammetry (FTacV) measurements. The two descriptors were used to construct an electro-catalytic activity diagram which enables identification of optimal microscopic surface states of Co/Ni oxyhydroxides during the oxidation of each type of molecules. They proposed that the descriptors can be used to quantitatively determine the generation and consumption of active surface intermediates, which can be used to optimize reaction performance (yield, faraday efficiency, etc) for different organic oxidations for rational design of catalyst and mechanistic model. The techniques used in this work are not widely explored by researchers in this field, which can greatly inspire others for future mechanistic studies. Therefore, I recommend this manuscript to be published in Nature Communications after minor revision. Some specific comments are listed below:

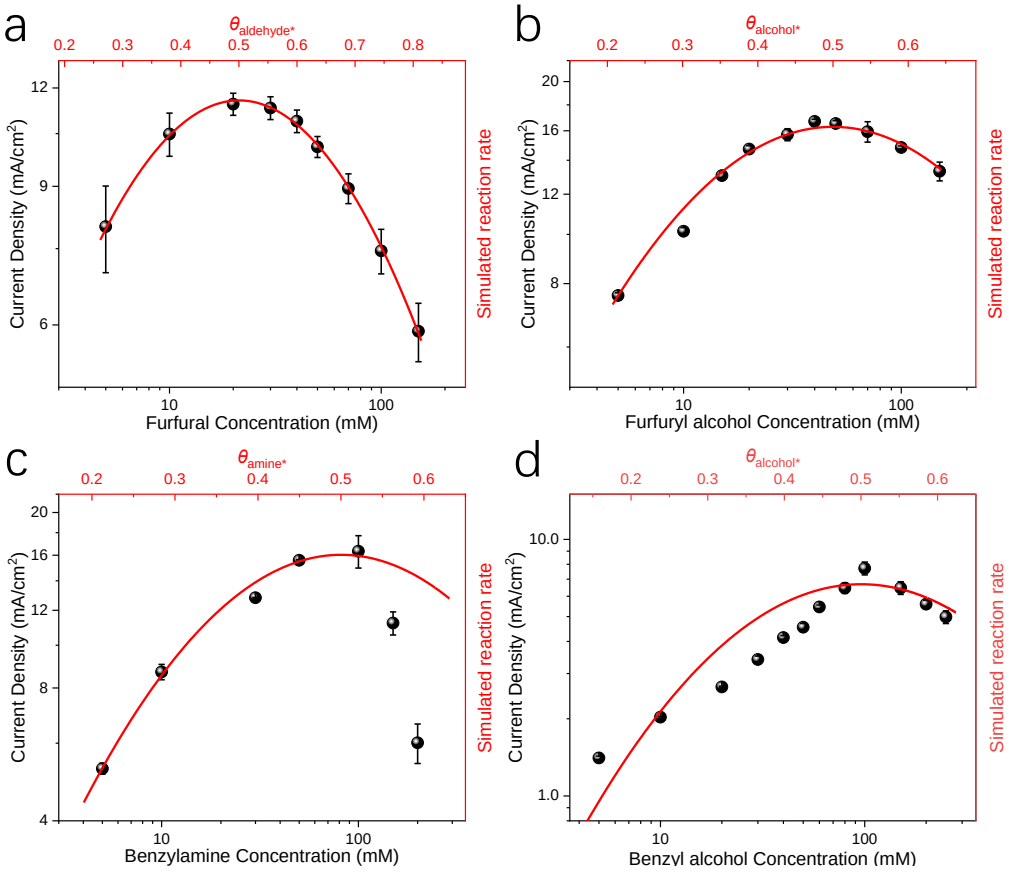
Reply: We greatly appreciate the referee's positive comments on our study, and thank for the valuable comments. Per referee's suggestions, we have added additional data along with more detailed and thorough discussions, which we believe have further improved the quality of this paper.

1. In the introduction, the author did not clarify the reason of using a general Langmuir-Hinshelwood (L-H) mechanism instead of Eley-Rideal Mechanism, and why is the L-H mechanism representative and applicable to their system model which involve different reaction conditions (reactant concentrations, pH), different catalyst compositions and organic molecules (molecular structures) – although later confirmed by S16 that furfural, furfuryl alcohol and benzylamine do follow the L-H mechanism.

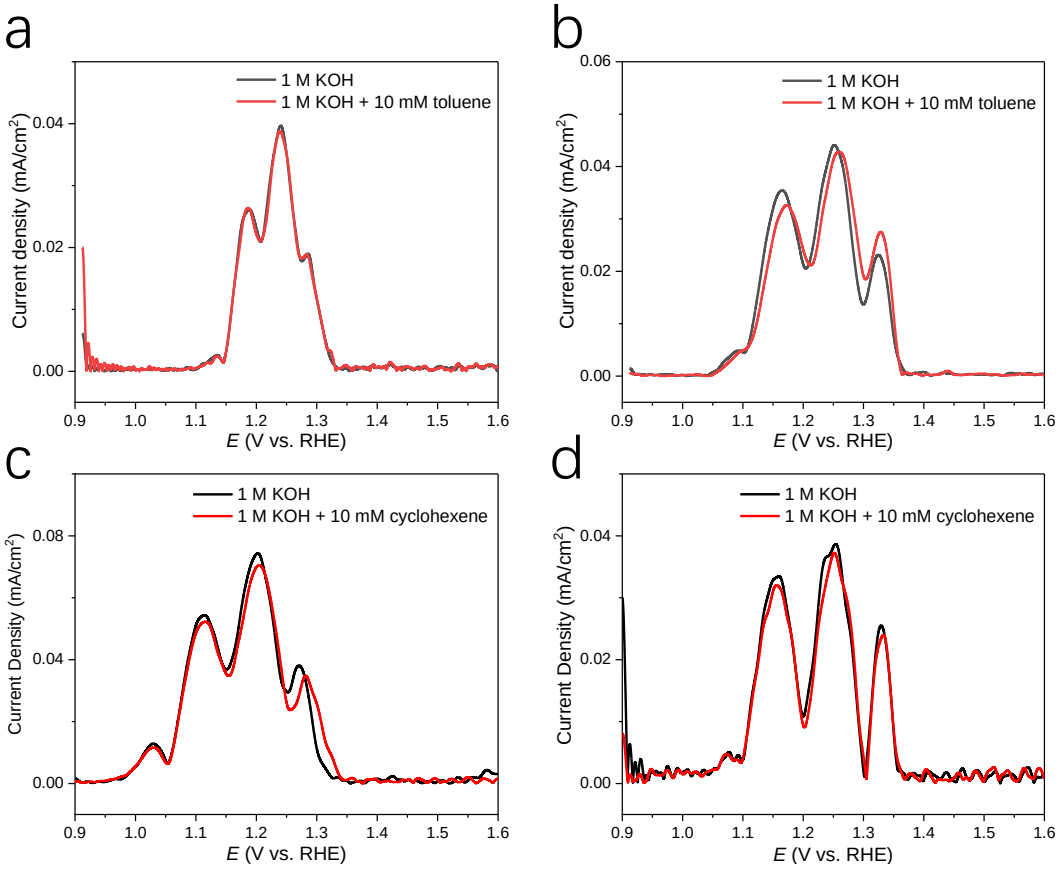
Reply: We thank the referee for pointing out this issue that calls for further clarification. The aldehydes, alcohols, and amines presented in the original investigation are all high polarity molecules that have considerable adsorption energies and are relatively easy to activate. During EOOR processes, these organic molecules are presumably adsorbed on the surface of catalytic materials and take over the surface OH* species generated on transition metal oxyhydroxides. Combining the kinetic experiments in new **Supplementary Figure S2**, it can be clearly observed that these reactions indeed follow the Langmuir-Hinshelwood (L-H) mechanism (with the presence of a reaction rate vertexes) rather than the Eley-Rideal (E-R) mechanism (reaching a saturated reaction rate at high concentrations). Note that we have further conducted similar investigations on other non-polar, difficult-to-activate molecules such as toluene and cyclohexene (results shown in new **Supplementary Fig. S42**). The oxidation of these molecules does not follow the L-H mechanism, and the corresponding discussion on the comparison of these two different categories of organic molecules make a more systematic argument. To address this issue, more clarified discussions have been added in the revised manuscript, as following:

On Page 2, line 19: "The kinetic analysis for electro-oxidation of different organic molecules shown in **Figure 1a** (also see **Supplementary Figure S1**, **S2**) suggest a general Langmuir-Hinshelwood (L-H) mechanism for the R-CHO, R-CH_2OH and R-CH_2NH_2 molecules."

On Page 14, line 24: "For molecules that are more challenging to be activated (with less polarity), such as toluene and cyclohexene (model substrates for selective oxidation of benzyl C-H bonds and selective epoxidation of alkenes, respectively), the corresponding FTacV results were shown in **Supplementary Fig. S42**. The minimal variation in signals indicates weak organic adsorptions even under high anodic potentials, which are consistent to their chemical inertness. In such cases, *in situ* generating extra strongly oxidizing radicals (such as Cl· or Br·)[99] or redox mediators (such as HOCl)[100] is presumably required to achieve high yields. Based on the innovation and scalability of measurement and kinetics analysis methods, key information and conclusions that were not easily obtained in previous literatures have been obtained in this work."



New **Supplementary Figure S2**. The experimental kinetic and simulation results for electro-catalytic organic oxidation reactions (EOOR) assuming a surface bimolecular adsorption/reaction (Langmuir-Hinshelwood) mechanism. Dependence of electro-oxidation partial current densities on the varying organic substrate concentrations for (a) furfural (in 1.0 M KOH), (b) furfuryl alcohol (in 1.0 M KOH), (c) benzylamine (in 1.0 M KOH) and (d) benzyl alcohol (in 1.0 M K_2CO_3, weak alkaline) in which reaction rate vertexes @θ_{sub*} = 0.5 were observed.



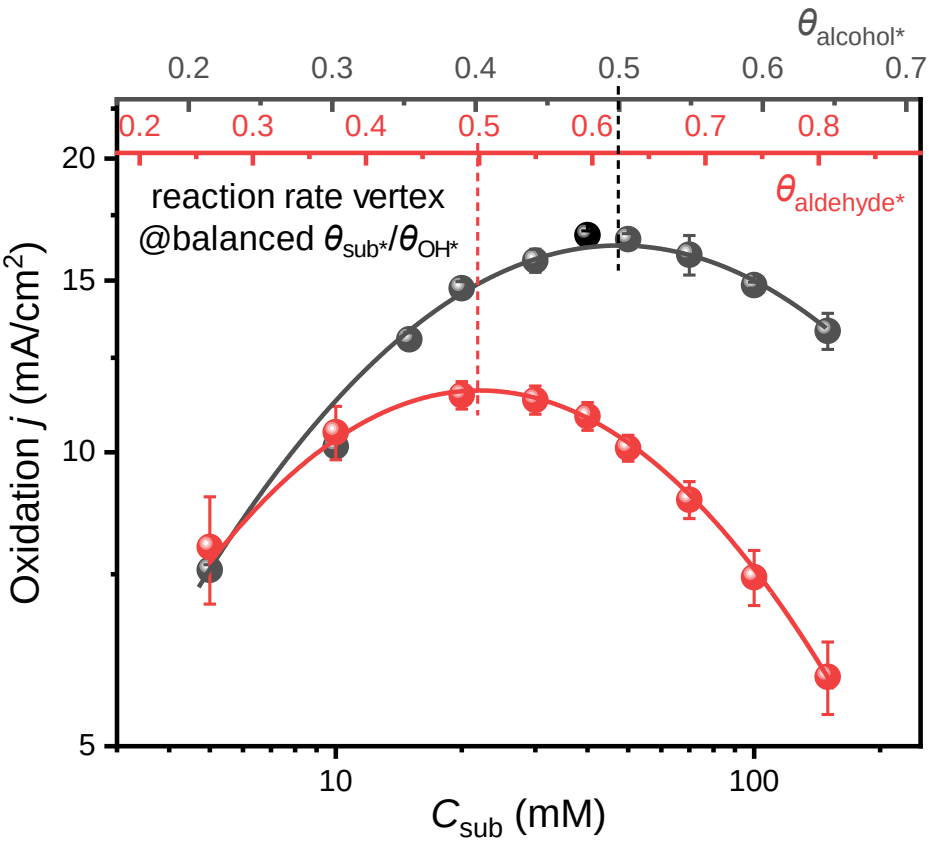
New **Supplementary Figure S42**. The high-order (6th) harmonics of α-$Co_{0.15}Ni_{0.85}(OH)_2$ (a, c) and α-$Ni(OH)_2$ (b, d) in pure 1 M KOH and with the addition of 10 mM toluene and cyclohexene, respectively, where the signals show no significant variation.

2. In Fig. 1a, they did not specify in the texts the definition of θ sub*, and which organic molecules (C1, C2, C3 or long chain C) were tested experimentally to be compared with simulation results that followed the L-H mechanism.

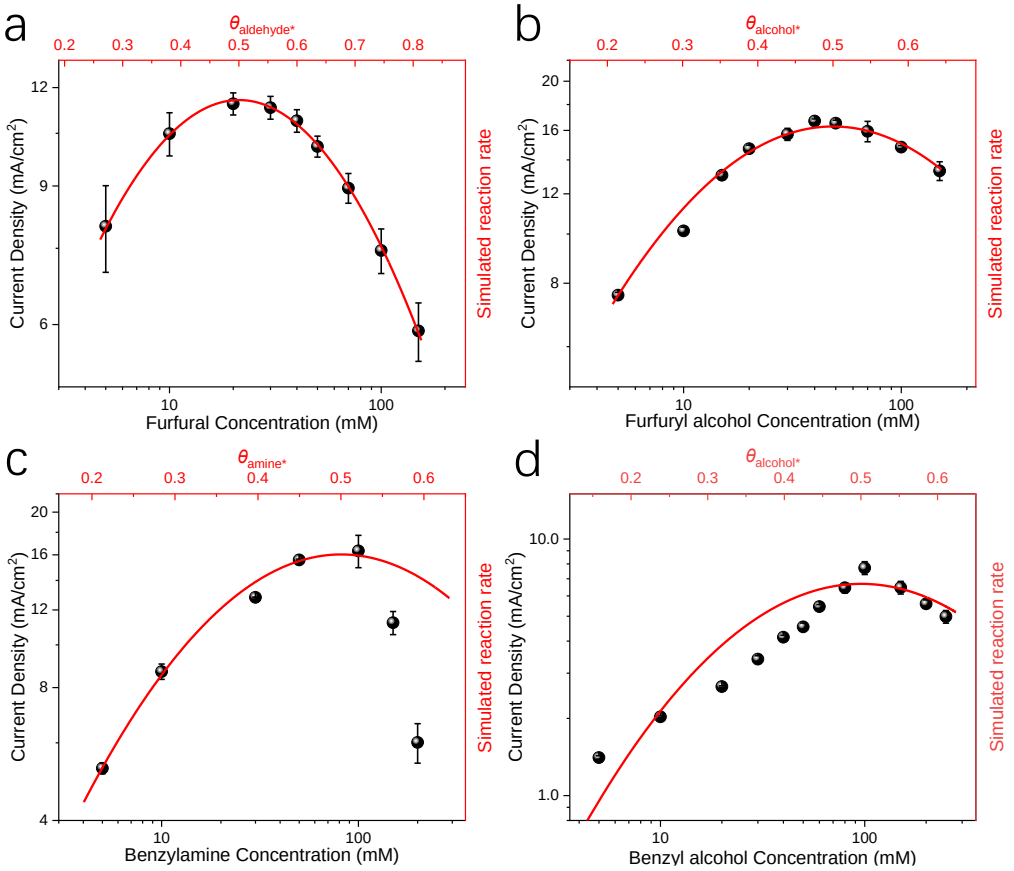
Reply: We thank the referee for pointing out this issue that needs clear description. In the former **Figure 1a**, the θ_{sub*} represents the model furfuryl alcohol molecule. Indeed, the data points and simulated results are different for different molecules. In the new **Supplementary Figure S2**, we tested other molecules (including furfural, furfuryl alcohol, benzylamine and benzyl alcohol) and found that they all follow the Langmuir-Hinshelwood (L-H) mechanism. We also observed that the concentration at which aldehydes, alcohols, and amines achieve the maximum reaction rate (i.e., θ_{sub*} = 0.5) gradually increases, indicating a gradual decrease in their adsorption energy. This is consistent with our quantitative FTacV measurement results. In addition to new **Supplementary Figure S2**, the representative experimental and simulation curves of alcohols and aldehydes were plotted together in new **Figure 1a**, for a clear yet less confusing demonstration of the general kinetic model (L-H mechanism). More clarified discussions have also been added in the revised manuscript, as following:

Page 2, line 23: "These kinetic data further reveal electro-oxidation rate vertexes in regards to the concentrations (surface coverages) of the furfural and furfuryl alcohol molecules (solid curves in **Fig.**

1a, the kinetic data of other molecules can be found in **Supplementary Fig. S2**), which clearly indicates the importance of balancing these surface parameters for their optimal reaction efficiency."



New **Figure 1a**. Experimental and simulated reaction rates of organic electro-oxidation following the Langmuir-Hinshelwood (L-H) mechanism, using furfuryl alcohol (black) and furfural (red) as the example. Round points depict the experimental partial current densities (for organic oxidation) over the organic substrate concentrations (C_{sub}). Solid curves illustrate the simulated reaction rates as a function of θ_{sub*}, with a fixed bulk pH value (i.e., C_{OH^-} = 1.0 M, which does not change significantly during the reaction).



New **Supplementary Figure S2**. The experimental kinetic and simulation results for electro-catalytic organic oxidation reactions (EOOR) assuming a surface bimolecular adsorption/reaction (Langmuir-Hinshelwood) mechanism. Dependence of electro-oxidation partial current densities on the varying organic substrate concentrations for (a) furfural (in 1.0 M KOH), (b) furfuryl alcohol (in 1.0 M KOH), (c) benzylamine (in 1.0 M KOH) and (d) benzyl alcohol (in 1.0 M K_2CO_3, weak alkaline) in which reaction rate vertexes @θ_{sub*} = 0.5 were observed.

3. For the simulation in Fig 1a, was the fixed pH value the bulk pH or surface pH? Because local pH does change while the alcohol oxidation reaction takes place.

Reply: We agree with the referee's point that the local pH may change during the reaction. This simulation uses a simple quadratic function to fit the bimolecular reaction rate at the fixed bulk pH, comparing it with the experimentally measured electrochemical current (which is positively related to the reaction rate). We assume that $\theta_{sub*} + \theta_{OH*} = 1$, and by fitting to obtain θ_{sub*}, we can determine the value of θ_{OH*} (since at the actual reaction potential of ~1.42 V_{RHE}, most active oxygen species are OH*). In addition, the 1.0 M KOH would not change significantly during the whole oxidation of 10 mM substances. Moreover, note that in the typical identification of Langmuir-type electro-adsorption isotherm ($E = E^0 + \frac{RT}{nF}\ln\frac{\theta}{(1-\theta)*a_{OH^-}}$) in the research field of OER, the activity of OH^- used in fitting is also the bulk concentration (*J. Am. Chem. Soc.* **2024**, *146*, 8928−8938 and *J. Am. Chem. Soc.* **2024**, *146*, 8915−8927). Therefore, we consider that the using of fixed bulk pH in a simple kinetic fitting is reasonable. We further agree with the referee that the variation of local pH certainly may make an

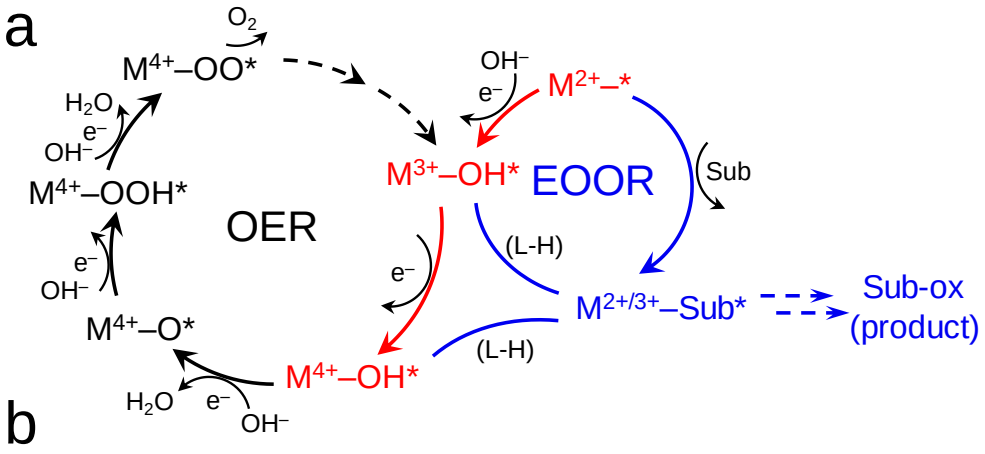
impact especially on the kinetic model simulation and parameter fitting, given that the real pH value at the catalytic sites cannot be precisely obtained experimentally. This issue is actually another indication that questions the accuracy of parameters extracted from kinetic simulation with numerical fittings, and calls for the development of effective tools that can experimentally measure the kinetically significant key physio-chemical parameters, which is the key point of this work.

We have updated the new caption of **Figure 1** for more clarified description in the revised manuscript, as following:

On Page 3, line 6: "solid curves illustrate the simulated reaction rates as a function of θ_{sub*}, with a fixed bulk pH value (i.e., C_{OH-} = 1 M, which would not change significantly during the whole reaction)."

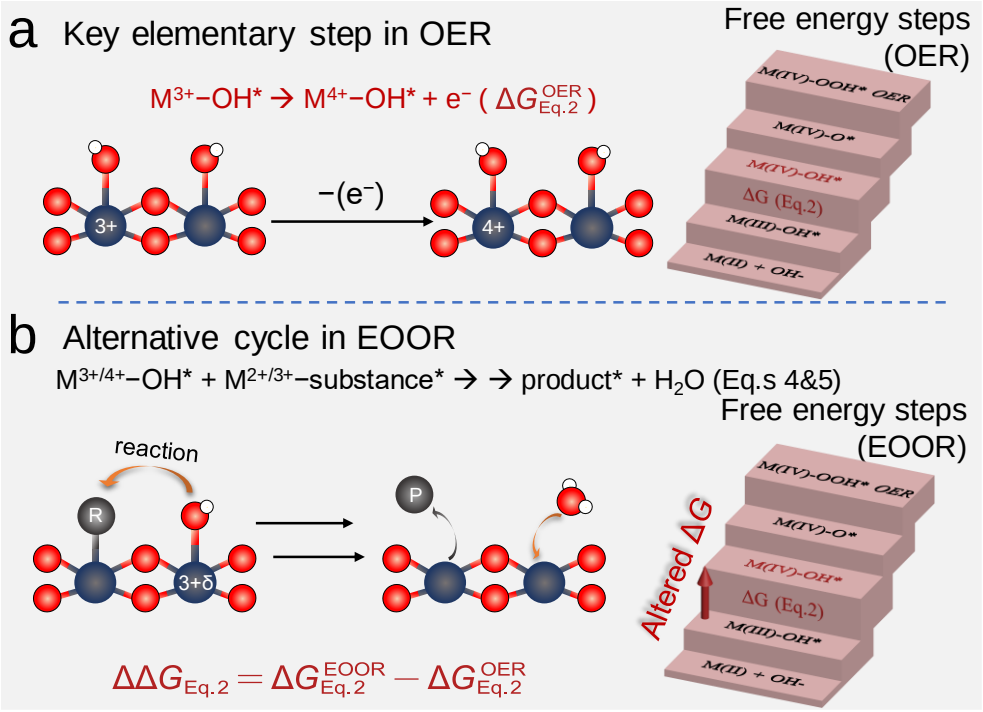
4. What valance state is the metal site that's adsorbing the organic substrate? And will it change as potential increases or as the oxidation reaction takes place?

Reply: We thank the referee for pointing out this important issue that needs to be clarified. We believe that at low potentials (0.9 ~ 1.2 V_{RHE}), the metal sites adsorbing organic substrates are in the oxidation state of +2. However, when the Ni/Co hydroxide materials were pre-activated electrochemically with repeated CV scans (this is the case for both FTacV measurement and actual electrolysis), some of the metal sites will be irreversibly transitioned to +3 state (i.e., to oxyhydroxides) under the oxidation potentials. In such cases, based on the previous high-quality theoretical calculations from Goddard *et al.* (Figure 1 in *Angew. Chem. Int. Ed.* **2021**, *60*, 16448; Figure 4 in *J. Am. Chem. Soc.* **2022**, *144*, 15185 @1.40 V_{RHE}), we infer that at the actual electrolysis potential (~1.42 V_{RHE}), the organic substrates can also be adsorbed on the metal sites with the oxidation state of +3. To summarize, the organic substrate molecules can assume the metal sites with both +2 and +3 states to form $M^{2+/3+}$–sub*. It should be further emphasized that once with organic adsorption, neither M^{2+}–sub* nor M^{3+}–sub* will continue to lose electrons to higher oxidation states, which requires the participation of adsorbed OH*. We have revised former "M^{2+}–sub*" to $M^{2+/3+}$–sub* in the new **Scheme 1** and **Figure 4**:



$M^{2+}{}^{*} + OH^{-} \rightleftharpoons M^{3+} - OH^{*} + e^{-}$	*partial – OER (1st)*	(1)	initial shared steps
$M^{3+} - OH^{*} \rightleftharpoons M^{4+} - OH^{*} + e^{-}$	*OER step (1.5th)*	(2)	
$M^{2+/3+} + substance \rightarrow M^{2+/3+} - substance^{*}$	*organics adsorption*	(3)	EOOR steps
$M^{3+/4+} - OH^{*} + substance^{*} \Rightarrow \Rightarrow product^{*}$	*catalytic organics oxidation*	(4)	
$product^{*} \rightarrow {}^{*} + product$	*organics desorption*	(5)	
$M^{4+} - OH^{*} + OH^{-} \rightleftharpoons M^{4+} - O^{*} + H_2O + e^{-}$	*RDS of OER (2nd)*	(6)	OER steps
$M^{4+} - O^{*} + OH^{-} \rightleftharpoons M^{4+} - OOH^{*} + e^{-}$	*OER (3rd)*	(7)	
$M^{4+} - OOH^{*} + OH^{-} \rightleftharpoons M^{4+} - OO^{*} + H_2O + e^{-}$	*OER (4th)*	(8)	
$M^{4+} - OO^{*} \rightarrow {}^{*} + O_2$	*O2 desorption*	(9)	

New **Scheme 1**. The proposed OER and EOOR pathways with shared initial steps (a) and list of reactions (b).



New **Figure 4**. Schematic illustration of the electrochemical generation of $Co^{3+\delta}/Ni^{3+\delta}$–OH* species during OER and EOOR, and the Gibbs free energy steps under the two conditions.

5. The type of HPLC column is not specified in SI Note 3.

Reply: We thank the referee for reminding us this important experimental detail in supplementary information. The specific HPLC column was the Agilent Eclipse XDB-C18 (5μm, 4.6 × 250 mm).

We have added the column information for HPLC in the revised SI (in new **Note 4**): "The HPLC column is Agilent Eclipse XDB-C18 (5μm, 4.6 × 250 mm)."

6. Please specify the term 'substrate' used for product yield calculation.

Reply: We thank the referee for pointing this important issue regarding the product quantification. We added specific substrates in the corresponding product quantification section in the revised Supplementary Information. FCA and FDCA were quantified by HPLC, while BN was quantified by GC.

We have added the information on substrates and products in the revised SI (in new **Note 4**): "Furoic acid (FCA), 2,5-furandicarboxylic acid (FDCA) and benzoic acid were quantified by HPLC, benzonitrile (BN) and benzaldehyde were quantified by GC."

7. While the authors employed EDX to determine the atomic ratio of Co:Ni before electrochemical testing, it is essential to acknowledge the method's limitations. EDX is known to have an error range of approximately 20%, it is suitable only as a qualitative tool for elemental analysis. For quantitative analysis, confirmation of Co:Ni ratio before and after reactions via techniques such as ICP-MS is advisable.

Reply: We thank the referee for pointing out this important issue in the elemental analysis of the electrode materials.

To address this issue, we further performed quantitative analysis of the Co/Ni ratio before and after the reactions using inductively coupled plasma optical emission spectrometer (ICP-OES). The results show that the Co/Ni ratios of catalysts are very close to the synthesis ratio, and no significant differences were observed after the electrolysis experiments. The new experimental results were added in the revised Supplementary Information: "The ICP-OES test results of the series of Co/Ni hydroxides were listed in **Supplementary Table S2** and **S3**."

New **Table S2**. The ICP-OES test results of the series of Co/Ni hydroxides (as prepared).

Catalysts	Mass (mg)	Co (mg/L)	Ni (mg/L)	Total (mg/L)	Co ratios (%)	Ni ratios (%)
α-$Co_{0.9}Ni_{0.1}(OH)_2$	5.14	46.6	5.68	52.28	**89.14**	**10.86**
α-$Co_{0.7}Ni_{0.3}(OH)_2$	5.06	33.7	16.1	49.80	**67.67**	**32.33**
α-$Co_{0.5}Ni_{0.5}(OH)_2$	5.20	24.0	26.6	50.60	**47.43**	**52.57**
α-$Co_{0.3}Ni_{0.7}(OH)_2$	5.21	13.8	37.3	51.10	**27.01**	**72.99**
α-$Co_{0.15}Ni_{0.85}(OH)_2$	4.99	6.32	41.1	47.42	**13.33**	**86.67**
α-$Co_{0.1}Ni_{0.9}(OH)_2$	5.12	4.81	50.50	55.31	**8.70**	**91.30**

The Co/Ni ratios match very well (less than 3% error) with the preset ratios during the metal salt solutions preparation.

New **Table S3**. The ICP-OES test results of the series of Co/Ni hydroxides (post electrolysis).

Catalysts	Co (mg/L)	Ni (mg/L)	Total (mg/L)	Co ratios (%)	Ni ratios (%)
α-$Co_{0.9}Ni_{0.1}(OH)_2$	10.1	1.16	11.26	**89.70**	**10.30**
α-$Co_{0.7}Ni_{0.3}(OH)_2$	6.46	2.92	9.38	**68.87**	**31.13**
α-$Co_{0.5}Ni_{0.5}(OH)_2$	4.48	4.68	9.16	**48.91**	**51.09**
α-$Co_{0.3}Ni_{0.7}(OH)_2$	1.74	4.38	6.12	**28.43**	**71.57**
α-$Co_{0.15}Ni_{0.85}(OH)_2$	2.74	17.0	19.74	**13.88**	**86.12**
α-$Co_{0.1}Ni_{0.9}(OH)_2$	2.48	23.5	25.98	**9.55**	**90.45**

The carbon papers after electrolysis were dissolved in dilute HCl for later ICP-OES tests. The Co/Ni ratios in the catalysts after long-term electrolysis stayed close to the as-prepared catalysts, indicating the excellent stability of Co/Ni hydroxides.

The corresponding descriptions have been added in the revised manuscript, as following:

On Page 6, line 8: "The atomic ratios of Co/Ni in different hydroxide samples were determined by inductively coupled plasma optical emission spectrometer (ICP-OES) characterizations (**Supplementary Table S2-S3**), indicating the successful synthesis of target Co/Ni ratios."

On Page 18, line 3: "Inductively coupled plasma optical emission spectrometer (ICP-OES) (Perkin Elmer Avio500) was used to test the Co/Ni ratios of the series of as prepared and post-electrolysis catalysts."

8. The manuscript notes the conversion of measured potential vs. E Ag/AgCl to reverse hydrogen electrode potential (RHE) using the Nernst equation without actual calibration with respect to RHE. Calibration against RHE should be conducted to ensure accuracy.

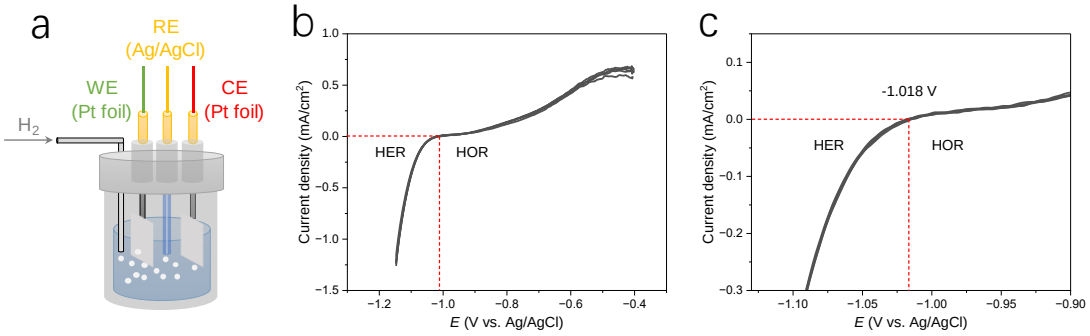
Reply: We thank the referee for pointing this important issue, the experimental detail of reference electrochemical potential calibration should certainly be clarified in the paper.

It should be noted that all long-term electrolysis experiments a Hg/HgO was used as reference electrode, which is stable in alkaline solutions. We have added details about this, previously placed in the supplementary information, to the methods section of the revised manuscript:

On Page 18, line 24: "All electrolysis measurements were performed in a typical three-electrode system using a CS3004 electrochemical workstation in 1.0 M KOH. Hg/HgO (1.0 M KOH) and Pt electrode were used as reference electrode and counter electrode, respectively. The potentials were

quoted with respect to the RHE through $E_{RHE} = E_{Hg/HgO} + 0.059 \times pH + 0.098$ V."

For the Ag/AgCl reference electrode, we performed calibration tests in 1.0 M KOH (99.999%) following the method as described in the literature (*Nat. Catal.* **2023**, *6*, 402–414). The new experimental results have been added to the new **Supplementary Figure S9**. We found that the potential of the Ag/AgCl electrode (1.018 V) is very close to the value calculated using the Nernst equation (0.059 × 13.8 + 0.2046 = 1.0188 V). Therefore, for relatively short-term *in situ* tests (100 ~ 200 s) such as ETS, FTacV, Raman and EIS characterization, the potential values calculated using the Nernst equation for the Ag/AgCl electrode were assumed to be reliable. The new results were added as new Figure S9 in the revised SI, with corresponding description added in the revised manuscript, as following:



New **Supplementary Figure S9**. Potential calibration of the Ag/AgCl reference electrode. (a) Schematic illustration for RE calibration. Pt foils were used as both the working electrode and counter electrode. (b) Cyclic voltammetry curves for Ag/AgCl electrode calibration in 1.0 M KOH (99.999%) solution. (c) Zoom-in of the (b). The CV tests were carried out after pumping high-purity hydrogen for 30 mins to saturate the electrolyte. HER, hydrogen evolution reaction, HOR, hydrogen oxidation reaction.

On Page 18, line 12: "The measured potential vs. $E_{Ag/AgCl}$ was converted to reverse hydrogen electrode potential (RHE) based on the Nernst equation, $E_{RHE} = E_{vs.\ Ag/AgCl} + 0.059 \times pH + 0.2046$ V, which was further calibrated by CV curves in 1.0 M KOH (99.999%) (**Supplementary Fig. S9**). The CV tests were carried out after pumping high-purity hydrogen for 30 min to saturate the electrolyte."

Reviewer #4 (Remarks to the Author):

I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Reply: We gratefully thank the referee for carefully reading our manuscript and for the constructive comments. Per referees' comments and suggestions, we have added additional results along with more detailed and thorough discussions, which we believe have further improved the quality of this paper for the publication in Nature Communications.

Reviewers' comments:

Reviewer #2 (Remarks to the Author):

This revised manuscript adds substantial new data and clarifying remarks to the authors' original discussion of organic oxidation as characterized by FTacV. They have taken review comments seriously and while I still think the paper would be better in a less condensed format, it is okay from my perspective to publish in this journal. I have two comments that the authors should still take into consideration for final revision:

Reply: We greatly appreciate the referee's positive comments on our study, and thank the referee for carefully reading our revised manuscript and for the insightful comments, which have inspired further improvement on the manuscript. In the revised manuscript and supplementary information, we added more detailed discussions accordingly.

1. It was stated that this is "the first paper to use the classical Langmuir-Hinshelwood (L-H) mechanism to describe electrocatalytic organic oxidation reactions assisted by partial water oxidation" This is obviously not true, and the most salient example would be methanol oxidation, which has easily >50 years worth of papers that fit data to microkinetic models. If the authors refer specifically to larger organic molecules then this might be closer to true, although I might argue the reason is that one can only really fit an empirical L-H scheme that overlooks a lot of elementary step detail since these reactions can be quite cumbersome and not all elementary processes are resolvable. The simple concept of competition between O/OH* and organic* is known, if perhaps no one bothered to write down/publish the equations for this simplistic picture.

Reply: We thank the referee for pointing out this issue, and we agree that we should not make any overstatement.

We agree with the referee that the kinetic data of methanol oxidation has definitely been fitted to the L-H mechanism for describing the reaction between OH* and CO*/CHO*. Therefore, we apologize for the description of "***the first paper to use the classical Langmuir-Hinshelwood (L-H) mechanism to describe electrocatalytic organic oxidation reactions assisted by partial water oxidation***" in the previous response letter. We only intended to show the different focus on reactions studied in this work and Pt-catalyzed methanol fuel cell reactions.

On the other hand, it should be emphasized that for the specific field of **selective electro-oxidation conversion of larger organic molecules**, the L-H mechanism was first introduced in this work to describe the specific bimolecular reactions between OH* and Sub*. As comparison, the traditional alcohol oxidation mechanism proposed by Fleishmann ($R\text{-}CH_2OH_{ads}$ + NiOOH →→ $R\text{-}COOH_{sol}$ + $Ni(OH)_2$) and the recent "hydride transfer" mechanism ($R\text{-}CH_2O^-_{ads}$ + NiO_2 →→ $R\text{-}CHO_{sol}$ + $Ni(OH)O^-$) obviously ignore the involvement of partial-OER initiated surface OH* species from water molecules. Similarly, the "nucleophile electrooxidation" model ignore the adsorption process of polar organic substances.

Therefore, the introduction of the L-H mechanism in this study allows for an accurate and general micro-kinetic description/analysis of water-oxidation-assisted selective electro-organic oxidative conversions. This further helps to motivate the development of novel physio-chemical

parameters/descriptors corelated to OER/EOOR, enabling systematic evaluation and investigations on different electro-organic reactions via surface biomolecular reaction pathway. We further agree with the referee that "***these reactions can be quite cumbersome and not all elementary processes are resolvable***". In fact, we only focused on the **key elementary steps** where electrochemical generated OH* species initiated the biomolecular reactions, and the extracted physio-chemical parameters corresponds to these key steps in different electro-oxidation systems provide efficient-enough evaluation of *operando* surface difference and OER-related catalysts promotion strategies.

Overall, to fully address this issue of potential over-statement, we have deleted all statement of "first use of L-H to describe electrocatalytic organic oxidation reactions", and modified the related description to be more specified in revised manuscript, as following:

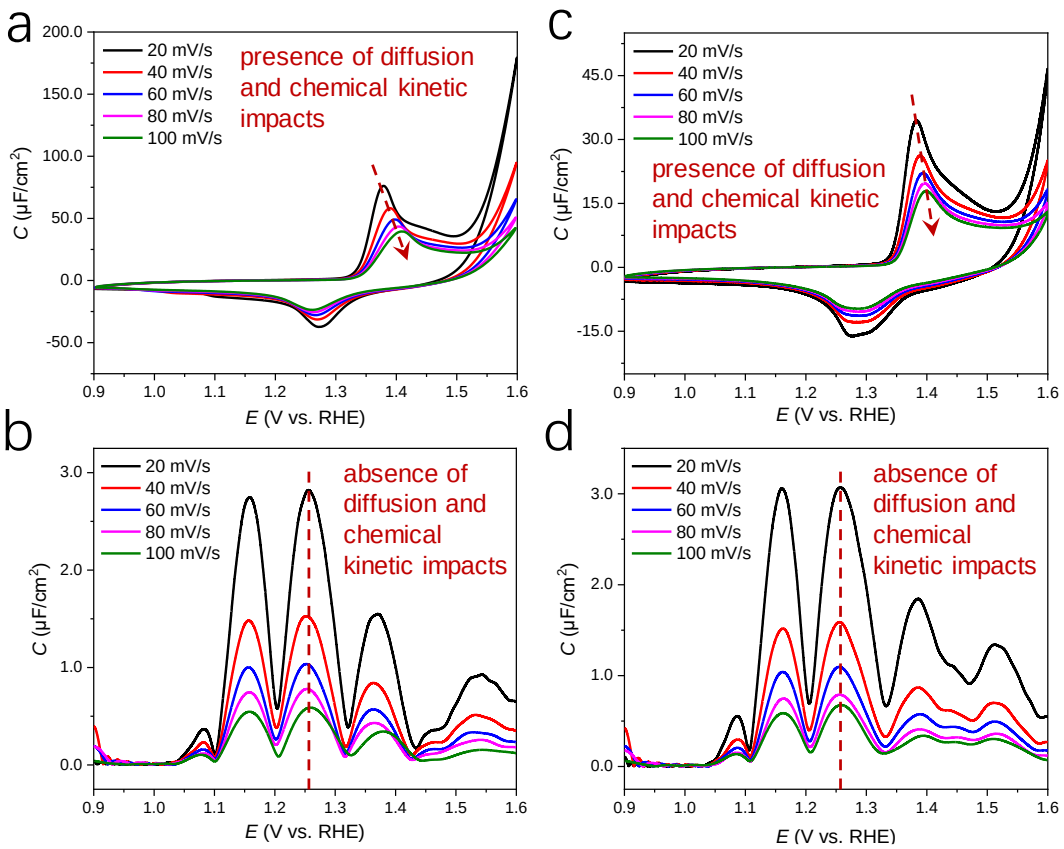
Page 2, line 19: "The kinetic analysis for selective electro-oxidative conversion of different organic molecules is shown in **Figure 1a** (also see **Supplementary Figure S1**, **S2**), which suggest a general surface biomolecule reaction (Langmuir-Hinshelwood) mechanism for the R-CHO, R-CH_2OH and R-CH_2NH_2 molecules."

Page 3, line 2: "**Reaction pathway and kinetics in the water-oxidation-assisted selective electro-oxidation reaction following a surface biomolecular reaction (Langmuir-Hinshelwood) mechanism.**"

2. I am still struggling to accept (on an intuitive level) that 'delta-V_harmonics' will only capture the change in adsorption energy. While I admittedly have not worked through the papers that are referenced, I key on the statement that "the contribution from non-Faradaic charging, diffusion and [chemical] catalytic processes in d.c. CV can be effectively excluded in high-order (>4th) harmonics". This all makes sense as these phenomena should be expected to have linear response. What is not directly addressed is the situation where there would be a potential-dependent kinetic limitation to the OH* adsorption process itself, and I worry that is being neglected. It seems like one has to assume this reaction is equilibrating, but maybe it can be proven otherwise?

Reply: We thank the referee for pointing this important issue that needs to be further clarified for the convenience of general readership of this paper.

1) First of all, whether or not a potential-dependent kinetic limitations exist in a voltammetry method can be experimentally confirmed through voltammograms obtained at different potential scan rates. To this aim, the comparison of d.c. CV and FTacV results at different scan rates were obtained, as shown in revised **Supplementary Figure S41**. It can be clearly observed that, the peak potential in d.c. CV is indeed influenced by diffusion and chemical kinetic limitations, resulting in obviously shift to the varying scan rates. In contrast, the peak potential measured by FTacV high-order harmonics remain unchanged, clearly indicating the absence of diffusion and chemical kinetic limitations, which are known to be slower than the fast electron transfer process. As a result, the $\Delta V_{harmonics}$ in FTacV measurements can experimentally exclude the kinetic contribution and mainly capture the thermodynamic aspects.



Revised Supplementary Figure S41. The comparison of d.c. CV and FTacV in the condition of different scan rate, the capacitance have been converted by C = current density / scan rate. It can be seen that the redox peak potential in a and c varies with the scan rate, while the *Process I* peaks in (b) and (d) stay unchanged. Therefore, the extracted peak potential well represents the ΔG of M^{III}–OH* → M^{IV}–OH* + e^-, excluding the diffusion and chemical kinetic (electro-adsorption) impacts.

2) We further provide theoretical rationalization of the absence of chemical kinetic limitations in $\Delta V_{harmonics}$ (enabling it to capture the thermodynamic aspects), as the following:

In classical d.c. CV, with the linear increasing of electrochemical potential, the diffusion of H_2O/OH^- and electro-adsorption of OH* proceed gradually when the scan rate was not so high. Then the peak potential of M^{II}–H_2O* + OH^- → $M^{III/IV}$–OH* + H_2O + e^- in the potential range of 1.3~1.4 V is influenced by both diffusion of H_2O/OH^- and electro-adsorption of OH* ($\ln[\theta_{OH*}/(1-\theta_{OH*})]$).

In the FTacV measurement, the potential varies at a large amplitude of sinusoidal wave ($E = E^0 + vt + A\sin(2\pi ft)$) so fast that the reactive species in the solution phase (such as H_2O/OH^-) do not have enough time to diffuse appreciably to the electrode surface. In such condition, only the electron transfer steps involving pre-adsorbed OH*/H_2O* (with fast enough kinetics) would generate the current response at the measured potential (in this work, M^{III}–OH* → M^{IV}–OH* + e^- or M^{II}–H_2O* → M^{III}–OH* + e^- + H*-μ_2O (bridge O, according to the theoretical models in *Angew. Chem. Int. Ed.* **2021**, *60*, 16448 and *J. Am. Chem. Soc.* **2022**, *144*, 15185)). The redox transition between these pre-adsorbed states do not involve solution phase reactants and structural rearrangement, exhibiting much faster kinetics compared to other elementary steps ($k_{fast} / k_{slow} > 10^2$), and thus solely contribute to the high-order FTacV harmonic signals. The specific potential-dependent electro-adsorption process of OH* with

slower kinetics leads to negligible FTacV signal response, and would not be reflected in the overall FTacV results (see Chapter 3, *Zouraris Dimitrios*, Electrochemical study of redox enzymes and their utilization on modified electrodes, Doctoral Thesis). For better clarifying this issue, the Equation 1 was updated to include more surface details in revised manuscript as: $M^{II}–H_2O^* \rightarrow M^{III}–OH^* + e^- + H^*\text{-}\mu_2O$ (bridge O). Moreover, the rate constant k of the fast electron transfer step, as a function of pre-exponential factor and activation energy (T), would not demonstrate apparent change without the structural variation of the $M^{III}–OH^*$ and $M^{II}–H_2O^*$ sites, even in the condition of EOOR.

Based on the above analysis, the principal peak potential of high-order FTacV harmonics directly reflects the standard (or formal) electrode potential of the fast electron transfer steps (electron transfer steps involving pre-adsorbed OH^*/H_2O^*), reflecting no impact of diffusion or potential-dependent chemical kinetic limitations. Therefore, the experimentally extracted value of $\Delta V_{harmonics}$ in high-order FTacV harmonic signal mostly represent the change in ΔG of eq 1 and/or eq 2 in the manuscript, with negligible kinetic contribution of other elementary steps.

To better clarify this part, the description and discussion for $\Delta V_{harmonics}$ in FTacV signals have been updated in the revised manuscript, as following:

Page 7, line 22: "E stands for the electron transfer step from surface $M^{2+}–H_2O^*$ to $M^{3+\delta}–OH^*$ species (Eqs. 1 and 2 in **Scheme 1**), which are not accompanied with any atomic rearrangement and thus kinetically much faster compared to the following steps."

Page 7, line 21: "These high-order harmonics (> 4*f*) in the time domain are highly sensitive to the fast surface electron transfer step, with negligible contribution from subsequent, comprehensive, yet slow electron transfer and chemical processes.[85] As a result, FTacV analysis appears to be ideal for quantitative characterization of surface intermediates ($Co^{3+\delta}/Ni^{3+\delta}–OH^*$) formed through fast electron transfer step (Eqs. 1 and 2), and for micro-electro-kinetics investigations on α-$Co_xNi_{1-x}(OH)_2$, while excluding interference from subsequent chemical steps in the surface EC model and diffusion-controlled factors in d.c. CV signals."

Page 9, line 17: "Nevertheless, in the Ni case, as the intrinsic kinetic for Eq. 2 is presumably faster than the Eq. 1 judging by the comparison of complexity from both steps (see rate constants fitting results in **Supplementary Table S2** according to our recent work[86]), the main peak is expected to originate from the $Ni^{III\rightarrow IV}$ transition with higher rate constant (Eq. 2)."

Page 10, line 26: "To this aim, high-order FTacV harmonic signals only reflect these fast-kinetic transitions (excluding solution phase reactants and structural rearrangement as in other elementary steps), thereby offering unique advantages for the potential-dependent thermodynamic evaluation of the key fast electron transfer step.[91]"

Page 10, line 39: "Meanwhile, it can be confirmed that negligible potential-dependent diffusion and kinetic contributions from OH* formation itself and subsequent steps was observed in the FTacV peak values (and therefore $\Delta V_{harmonics}$), see experimental results and theoretical discussions in **Supplementary Fig. S41** and **Supplementary Note 8**."

The discussions about the thermodynamic and kinetic contribution of $\Delta V_{harmonics}$ were also added in

the revised Supplementary Information:

Page 57 in revise SI: "**Theoretical considerations on the thermodynamic and kinetic contributions in $\Delta V_{harmonics}$ signals (Note 8)**

In classical d.c. CV, with the linear increasing of electrochemical potential, the diffusion of H_2O/OH^- and electro-adsorption of OH* proceed gradually when the scan rate was not so high. Then the peak potential of $M^{II}–H_2O^* + OH^- \rightarrow M^{III/IV}–OH^* + H_2O + e^-$ in the potential range of 1.3~1.4 V is influenced by both diffusion of H_2O/OH^- and electro-adsorption of OH* ($\ln[\theta_{OH^*}/(1-\theta_{OH^*})]$).

In the FTacV measurement, the potential varies at a large amplitude of sinusoidal wave ($E = E^0 + vt + A\sin(2\pi ft)$) so fast that the reactive species in the solution phase (such as H_2O/OH^-) do not have enough time to diffuse appreciably to the electrode surface. In such condition, only the electron transfer steps involving pre-adsorbed OH*/H_2O* (with fast enough kinetics) would generate the current response at the measured potential (in this work, $M^{III}–OH^* \rightarrow M^{IV}–OH^* + e^-$ or $M^{II}–H_2O^* \rightarrow M^{III}–OH^* + e^- + H^*\text{-}\mu_2O$ (bridge O)[6, 21]. The redox transition between these pre-adsorbed states do not involve solution phase reactants and structural rearrangement, exhibiting much faster kinetics compared to other elementary steps ($k_{fast} / k_{slow} > 10^2$), and thus solely contribute to the high-order FTacV harmonic signals. The specific potential-dependent electro-adsorption process of OH* with slower kinetics leads to negligible FTacV signal response, and would not be reflected in the overall FTacV results (see Chapter 3, *Zouraris Dimitrios*, Electrochemical study of redox enzymes and their utilization on modified electrodes, Doctoral Thesis). For better clarifying this issue, the Equation 1 was updated to include more surface details in revised manuscript as: $M^{II}–H_2O^* \rightarrow M^{III}–OH^* + e^- + H^*\text{-}\mu_2O$ (bridge O). Moreover, the rate constant k of the fast electron transfer step, as a function of pre-exponential factor and activation energy (T), would not demonstrate apparent change without the structural variation of the $M^{III}–OH^*$ and $M^{II}–H_2O^*$ sites, even in the condition of EOOR.

Based on the above analysis, the principal peak potential of high-order FTacV harmonics directly reflects the standard (or formal) electrode potential of the fast electron transfer steps (electron transfer steps involving pre-adsorbed OH*/H_2O*), reflecting no impact of diffusion or potential-dependent chemical kinetic limitations.[28] Therefore, the experimentally extracted value of $\Delta V_{harmonics}$ in high-order FTacV harmonic signal mostly represent the change in ΔG of eq 1 and/or eq 2 in the main text, with negligible kinetic contribution of other elementary steps."

Reviewer #3 (Remarks to the Author):

The authors have addressed the comments in great detail and the manuscript quality has largely improved after revision. Therefore, I recommend the manuscript to be published by the journal.

Reply: We greatly thank the referee for carefully reading our revised manuscript and for the valuable comments that have inspired us for substantially improving the quality of this manuscript.

Reviewer #4 (Remarks to the Author):

I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Reply: We gratefully thank the referees for carefully reading our revised manuscript and for the positive comments on our study, which help improve the quality of this manuscript.