

## Response to Editorial Comments (JoVE55313R1)

### Merging Ion Concentration Polarization between Juxtaposed Ion Exchange Membranes for Blocking Propagation of the Polarization Zone

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*1. Please proofread the manuscript for numerous minor grammatical and spelling errors (most occur in the procedures section). Examples include, but are not limited to:*

*-Line 78: “ion depletion near a permselective membrane”*

*-1.1.2: “Both etching the silicon wafer by deep reactive ion etching and piling the microstructures on the wafer with a photoresist are available.” – odd phrasing*

*-1.2.3: “in order to attach on a glass slide”*

*-1.3.2. “Then they are attached”. Sentences rarely need to begin with “then”.*

*- 2. “Experiment of ICP Preconcentration” should just be ICP Preconcentration, or ICP Preconcentration Experiment.*

*-2.1.5: “anode on the left reservoir”*

**Response 1:** We reviewed the manuscript thoroughly, and corrected grammatical and spelling errors.

*2. Detail is needed for step 1.2.1: “place the cup with an uncured PDMS in a vacuum jar” - how much PDMS?*

**Response 2:** 30-40 ml of the uncured PDMS is required to replicate microstructures on a 4-inch silicon wafer. We added this detail in the step 1.2.1.

*3. Discussion: Please discuss further applications of the demonstrated technique, and it's advantages over any other similar methods.*

**Response 3:** ICP preconcentrator has been used in the wide range of biomicrofluidic platforms for preconcentrating various bio-agents, amplifying the signals of various assays, and finally detecting the targets such as therapeutic proteins [Ouyang et al., *Anal. Chem.*, 2016, **88**, 9669-9677], peptides [Cheow et al., *Anal. Chem.*, 2014, **86**, 7455-7462], aptamers [Cheow and Han, *Anal. Chem.*, 2011, **83**, 7086-7093], and enzymes [Chen et al., *J. Am. Chem. Soc.* 2011, **133**, 10368-10371]. As one can notice, these previous works targeted fluorescence-labeled biomolecules. This is because that we cannot specify the exact operating condition (e.g. voltage and flow rate) to maintain the preconcentration site, so we need to find the proper condition to preconcentrator targets first.

Starting from the same motivation of our work, Yossifon et al. [*Phys. Rev. E*, 2010, **81**, 046301] suggested the device that can focus the electric field geometrically with nanoslits. Although this method successfully slowed down the propagation of the depletion zone, it could not suppress the propagation perfectly, especially at high voltage and long-time operation for preconcentration applications. Senapati et al. and Slouka et al. accumulated nucleic acids in the ion enrichment zones, and directly used an ion exchange membrane as a

sensor[*Biosens. Bioelectron.* 2014, **60**, 92-100; *Talanta* 2015, **145**, 35-42]. This can bypass the problem of the transient depletion zones, but we should hold the membrane material and the sensing spot on the membrane. Therefore, this platform cannot enjoy the enormous modulations of conventional ICP preconcentrators in materials, geometry, and integrations.

Departing from the previous trials, the merged ICP phenomenon allows us to fix the preconcentrated plugs always at broad range of operating conditions, while maintaining the ICP devices' high flexibility. This indicates that now we can extend the applications of ICP preconcentrators for label-free detection techniques without visualization instruments and tracers. This unique advantage on the spatiotemporal controllability would provide a strong commercial opportunity to integrate the ICP device into generic benchtop platforms, such as for polymerase chain reactions and mass spectrometers.

We added this content in DISCUSSION (Page 9).

*4. References: Please include DOI for references, where possible.*

*5. JoVE reference format requires that the DOIs are included, when available, for all references listed in the article. This is helpful for readers to locate the included references and obtain more information. Please note that often DOIs are not listed with PubMed abstracts and as such, may not be properly included when citing directly from PubMed. In these cases, please manually include DOIs in reference information.*

**Response 4-5:** We added the DOI for the references.

*6. If your figures and tables are original and not published previously, please ignore this comment. For figures and tables that have been published before, please include phrases such as "Re-print with permission from (reference#)" or "Modified from.." etc. And please send a copy of the re-print permission for JoVE's record keeping purposes.*

**Response 6:** The phrases regarding reprint permission are added in the figure captions. We also attached a copy of the reprint permission in the package of this revision.