

# NANOELECTROKINETIC PURIFICATION DEVICE FOR A CONTINUOUS PERITONEAL DIALYSATE RECYCLER

Wonseok Kim<sup>1+</sup>, Kihong Kim<sup>1+</sup>, Hajeong Lee<sup>2</sup>, Yon Su Kim<sup>2</sup>, Jung Chan Lee<sup>3</sup>,  
Gun Yong Sung<sup>4</sup> and Sung Jae Kim<sup>1,5,6\*</sup>

<sup>1</sup>Department of Electrical and Computer Engineering, Seoul National University,

<sup>2</sup> Department of Internal Medicine, Seoul National University Hospital,

<sup>3</sup>Department of Biomedical Engineering, Seoul National University,

<sup>4</sup>Department of Material Science and Engineering, Hallym University,

<sup>5</sup>Inter-university Semiconductor Research center, Seoul National University,

<sup>6</sup>Big Data Institute, Seoul National University

## ABSTRACT

Ion concentration polarization (ICP) phenomenon has been extensively researched for electro-desalination and purification applications because of its efficient capability of separating any charged species from brines. In this work, the ICP purifier, for the first time, was applied for a novel continuous peritoneal dialysate recycler. Most of charged hazardous substances were sufficiently removed by conventional ICP mechanisms. Moreover, slightly charged toxic molecule (creatinine) was mostly eliminated through nanoporous membrane, and uncharged toxic molecule (urea) was perfectly decomposed by electrochemical reactions. Based on the combined removal mechanisms confirmed in a micro/nanofluidic platform, a macro ICP purifier was finally demonstrated for practical applicability. We would expect significant advances in a quality of life for chronic kidney disease patients by this ICP purifier.

## INTRODUCTION

### Purification for small scale system

Reverse osmosis are representative purification technologies but its utilization are suitable for large scale system due to escalated energy consumption depending the source concentration and additional filtration steps for large molecules. Recently reported ion concentration polarization (ICP) based purification technology [1] is suitable for small scale system since it was initially based on micro/nanofluidic system. Perm-selectivity occurs when the pore size is under Debye length, and is accelerated by an applied electric field across a nanoporous membrane. Only counter-ion can pass through the membrane and remained co-ions started to repel each other so that an ion depletion zone is formed at the anodic side in the case of cation-selective membrane [2]. Ion depletion zone has been utilized as an electrical filter for several engineering applications [3], but practical applications for small scale system were yet reported.

### Continuous peritoneal dialysate purification using ICP

Peritoneal dialysis is a recently introduced invaluable treatment for the kidney disease patients. The process uses peritoneum of patient as a membrane so that dissolved substances such as urea, creatinine (CRN), albumin (ALB), and other toxins in the blood are exchanged with injected pure dialysate (~2 L). After diffusion and osmotic chemical exchange from blood to dialysate, extractions of used dialysate and injections of pure dialysate should be

manually done in every 4 to 6 hours [4]. These inconveniences would be resolved by a portable dialysate regeneration system. It should be capable of automatic withdrawing, purifying the used dialysate and refilling the recycled dialysate into peritoneum. Among a number of components, the efficient purification of biological toxic substances would be the key building block. While few mechanisms such as biochemical adsorption or physical filtering has been suggested, the performance was beyond the criterions.

Here we proposed the nanoelectrokinetic ICP purifier for the continuous dialysate recycling system as shown in Figure 1. Micro wastes in a used dialysate rejected outside ion depletion zone since most of them had an electrical charge and cationic species in a used dialysate was removed by cationic flux through nanojunction. Therefore, we would continuously obtain a purified dialysate by extracting stream from ion depletion zone. Micro/nanofluidic platform was initially investigated to meet the criterions and a 3D printed macro system for practical throughput was also presented.

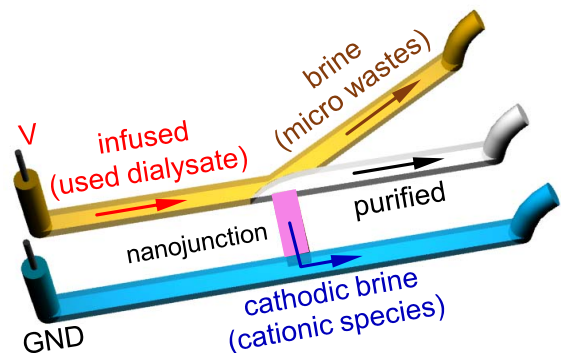


Figure 1: Schematic diagram of nanoelectrokinetic purifier for continuous peritoneal dialysate recycler. Micro wastes in used dialysate rejected outside the ion depletion zone since most of them had an electrical charge, and cationic species were transported (or removed) through the nanojunction. Purified dialysate would be obtained from continuous extraction of stream inside ion depletion zone.

## VERIFICATION OF ICP PURIFICATION

### Fabrication of microscale device

Micro/nanofluidic device, consisted of anodic bifurcated microchannel, nanojunction, and cathodic

single microchannel, was fabricated as shown in Figure 2.

Firstly, to build fluidic channels, both the anodic and the cathodic microchannels were designed to have the dimension under 500  $\mu\text{m}$  width and 15  $\mu\text{m}$  depth. Polydimethyl siloxane (PDMS, Sylgard 184 Silicone elastomer kit, Dow Corning) was used as a material for microchannels. A pre-polymer and curing agent were mixed with 10:1 ratio and bubbles were bled in a vacuum chamber about an hour. Pouring the mixed polymer solution onto the microchannels patterned master and curing it in an oven about 4 hours. Secondly, to build nanojunction, Nafion solution (20 w.t.% resin, Sigma Aldrich) was utilized as a cationic perm-selective nanoporous material and patterned between bifurcated point of the anodic microchannel and the cathodic microchannel using surface patterning method. [5] Finally, the PDMS block having fluidic channels and the slide glass having the solid Nafion nanojunction were accurately aligned at the bifurcated position of the anodic side microchannel and chemically bonded by using a plasma bonder (Cute-MP, Femto Science, Korea).

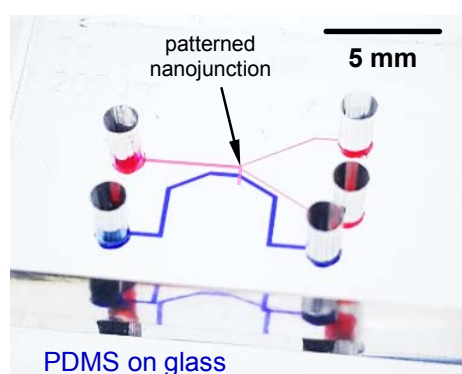


Figure 2: Micro/nanofluidic device of microchannels patterned on PDMS and Nafion nanojunction on glass.

### Demonstration of used dialysate purification

An external voltage (50 V) was applied across the nanojunction using a source measurement unit (SMU 238, Keithley). The analyte and buffer solution (used dialysate, from Seoul National University Hospital) were continuously injected with a constant flow rate (0.1  $\mu\text{L}/\text{min}$ ) into both the anodic and cathodic microchannels using a syringe pump (PHD 2000, Harvard apparatus). An inverted fluorescence microscope (IX-51, Olympus) and a CCD camera (DP73, Olympus) were used to observe the electrokinetic flow and the concentration profiles in the microchannels visibly. Under these experimental conditions, we successfully generated ICP phenomenon and developed bifurcated ion depletion boundary in used dialysate solution as shown in Figure 3(a). Brine, purified streams in the anodic side and cathodic brine stream in the cathodic side were visibly observed due to ICP development.

Each stream was extracted individually and concentration profiles of  $\text{Na}^+$ , CRN, ALB, phosphorus (P),  $\text{Cl}^-$ , and urea were quantitatively measured by Renal Panel (HITACHI 7180) as shown in Figure 3(b). The positively charged species ( $\text{Na}^+$ , CRN and ALB) were removed depending on their electrophoretic mobility. Since  $\text{Na}^+$  ion

has the highest electrophoretic mobility among major components in used dialysate solution, most (~80 %) of  $\text{Na}^+$  ions were transported through the nanojunction by cationic flux and only ~15 % were repelled from ion depletion boundaries. Finally 90 % desalted stream was collected. CRN, sub nanometer molecule and one of the major toxin of body wastes from used dialysate, is electrically neutral at pH 7.4 but a positively charged under pH 7.4. Since dialysate showed slightly acidic property, we confirmed that CRN particles showed cation like transportation mechanism under the ICP operation. ~55 % of CRN passed through the nanojunction and ~30 % of them flew through the brine stream. Finally CRN concentration was decreased around 70 % in the purified stream. ALB is a kind of protein existed in a human body. It showed less removal ratio than  $\text{Na}^+$  and CRN.

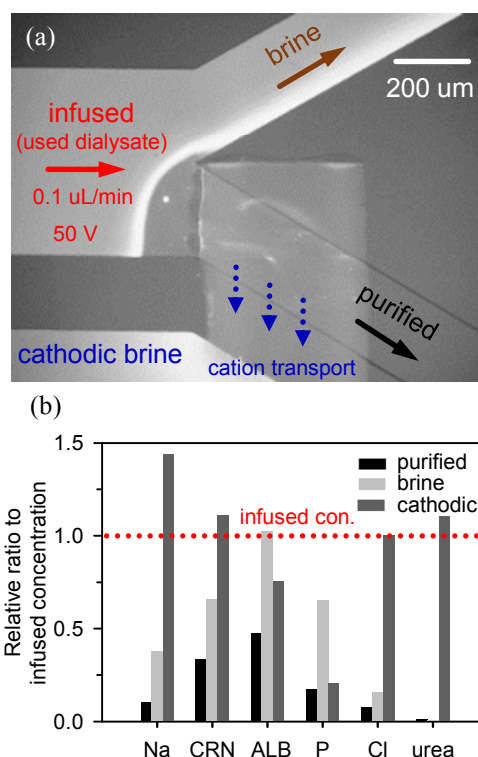


Figure 3: (a) Demonstration of ICP purifier. ICP phenomenon was generated and formed 3 different streams for the toxic substances in used dialysate at 50 V and 0.1  $\mu\text{L}/\text{min}$ . (b) Concentration of extracted each stream. The removal ratio of  $\text{Na}^+$  was the highest among positively charged substances ( $\text{Na}^+$ , CRN, ALB) since electrophoretic mobility of it was the highest. ~80 % of  $\text{Na}^+$  passed through the nanoporous membrane by cationic flux and only ~15 % of it went through the brine stream. CRN was removed likewise cation removal mechanism but the removal ratio was less than  $\text{Na}^+$ . ALB showed less removal ratio than  $\text{Na}^+$  and CRN. Weakly charged P was mostly precipitated inside a channel and negatively charged  $\text{Cl}^-$  was consumed by electrode reaction. Neutrally charged urea was completely decomposed in both the purified and the brine stream.

On the other hand, weakly charged P could not pass through the nanoporous membrane and precipitated on a channel surface. Negatively charged  $\text{Cl}^-$  was consumed by

electrochemical reactions on the anodic electrode so to satisfy electro-neutrality in a solution due to ICP which rearranged concentration profiles near nanojunction. Remarkably, urea (known as uncharged molecule), one of the major toxin of body waste along with CRN, was completely eliminated both at the brine and the purified streams. Following section would explain cause of elimination.

### Performance of nanoelectrokinetic purification

Specific conditions for a dialysate purification was shown in Figure 4. To confirm removal mechanism of urea and other species in used dialysate solution, control experiments were done with various types of junction and electrode. Firstly, non-ICP condition was demonstrated without using nanojunction in a microchip. Electrodes were set inside a single microchannel without any junction and filled in used dialysate solution. Positive voltage and pressure were applied in anodic reservoir, and outward stream was collected from cathodic reservoir. In this case, only urea was completely eliminated and other species were remained without any change. We obtained same results when microjunction was built between anodic bifurcated microchannel and cathodic microchannel instead of building nanojunction.

Secondly, ICP condition was implemented with using nanojunction in a microchip. As we mentioned in the previous section, urea was completely eliminated and other species were removed by electrical transportation due to ICP phenomenon. To separate ICP and electrochemical removal mechanism, we built 3 independent microchannels, one for anodic at the top side, another for sample flowing at the middle side and the other for cathodic at the bottom side. In this case, ICP was still successfully developed at the middle bifurcated channel by electric field across the nanojunction from top anodic channel to bottom cathodic channel. Urea and  $\text{Cl}^-$  was remained without any change, but other components were removed by electrical transportation due to ICP phenomenon.





	Junction Type	Electrode type	Schematic	Relative ratio of purified to infused (%)					
				Na	CRN	ALB	P	Cl	urea
non-ICP	x	direct		100	100	100	100	100	0
	micro	direct		100	100	100	100	100	0
ICP	nano	direct		10	30	45	15	5	0
	nano	indirect		10	30	45	15	100	100

Figure 4: Results of control experiments.  $\text{Na}^+$ , CRN and ALB were removed during ICP operation while urea was decomposed only with directly contacted electrode to the infused stream, regardless of ICP operation. Urea was unaffected by the ion depletion boundary layer, and participated in electrochemical reactions on the electrode surface.

From these results, we found out two key conclusions. First, urea was eliminated not by ICP phenomenon but by electrochemical decomposition. Since urea was electrically

neutral molecule, it did not change its traveling direction with or without ion depletion boundary layer. It was observed that urea was participated in electrochemical reaction on the electrode surface. Second, the successful dialysate purification would be achieved only when ICP was triggered by a directly contacted electrode with infused stream.

## MACRO DEVICE FOR PRACTICAL UTILITY

### Fabrication of macrofluidic device using 3D printer

To extend these findings in micro/nanofluidics toward a practical dialysate recycling application, 3000 times throughput enhanced macro-fluidic device was fabricated with a 3D printer (Figure 5).

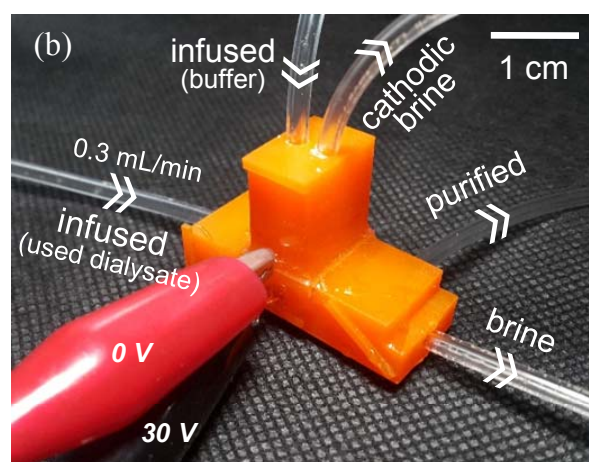
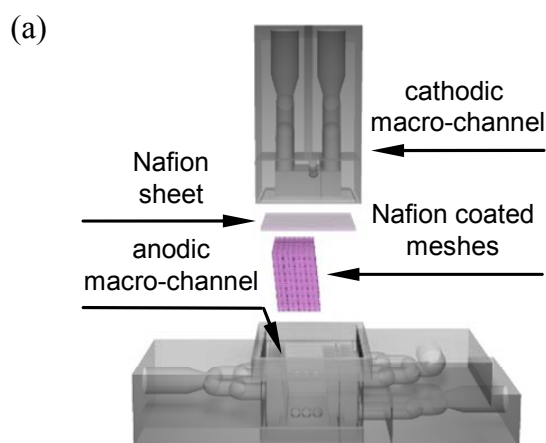


Figure 5: (a) Exploded view of 3D printing blocks for a macro-fluidic device. To assemble a macro-fluidic device, nanoporous Nafion sheet and Nafion coated mesh blocks were inserted between anodic and cathodic macro-blocks. (b) Assembled macro-fluidic device. 0.3 mL/min and 30 V external sources were applied to the device and the purified, the brine and the cathodic brine streams were collected and analyzed.

The expansion of ICP layer is requisite to filter dialysate at macrofluidic system. Thus, we contrive the novel system which has Nafion coated mesh as a key structure. The frame of the mesh is made of 3D-printed photopolymer and coated by Nafion. It performs as the transportation pathway of cations to arise ICP, which carries out the similar role of surface-patterned Nafion at



micro/nanofluidic system. The mesh was designed to maximize contacting area with dialysate flux, for high cation transportation rate. Divided by Nafion sheet, cations migrate from anodic macro-channel to cathodic macro-channel without flow interference. Cations are depleted at the vicinity of Nafion sheet after applying electric field from anodic to cathodic channel. The mesh performs as the medium to expand ion depletion layer, which enable to occur only thin (<100  $\mu\text{m}$ ) depletion layer if there were no mesh structure.

Anodic electrode is located on brine channel and cathodic electrode is located on buffer channel. The products from electrode reaction go to each brine/buffer channel so that do not affect purified dialysate.

#### Performance of purification using macrofluidic device

The performance of the device depends on voltage and flow rate. Purification ratio enhances as higher voltage at the same flow rate, because more cation transported through Nafion coated mesh. In addition, the products from electrode reaction could bring imbalance of pressure distribution, so that we also consider it to decide voltage and flow rate. At the 0.3 mL/min and 30 V condition, CRN was removed ~30 % and urea was removed over 90 %. These removal ratio is enough to running the continuous peritoneal dialysate recycler for several physiological reasons, while the condition for potable water is much restricted. Throughput could be increased by stacking the devices with identical operation principle.

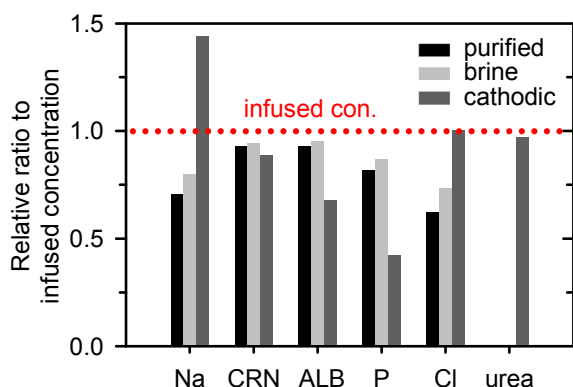


Figure 6: Removal efficiency of the macro ICP purifier. The results satisfied the operation criteria of the continuous dialysate recycler (~30 % removal) with completely removed urea.

#### CONCLUSION

Firstly, continuous dialysate recycler for peritoneal dialysis was successfully demonstrated using nanoelectrokinetic phenomenon including ICP in micro/nanofluidic format. We confirmed that the most of toxic substances were substantially removed. Charged substances such as  $\text{Na}^+$ , creatinine and albumin were electrically transported through nanojunction or repelled from ion depletion boundary depending on their electrophoretic mobility, and electrically neutral substance such as urea was electrochemically decomposed. Moreover, we proposed the novel macrofluidic dialysate recycler using ICP phenomenon which significantly

enhance the throughput. Although nanofluidic device with great performance has been actively developed for a decade, several impassable limitations of throughput still impeded commercial applications. The macrofluidic ICP recycler was demonstrated to have 0.3 mL/min of throughput with used dialysate (50~150 mM) at 30 V, ~30 % removal ratio as a result. Throughput and removal ratio would be regulated by leveraging electric conditions and pressure field. These results would be a key technology for chronic kidney disease patients to improve the quality of their life.

#### ACKNOWLEDGEMENTS

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#### CONTACT

\*S. J. Kim, tel: +82-2-880-1665; gates@snu.ac.kr

+ These authors contributed equally