Microvalve-Based Tunability of Electrically Driven Ion Transport through a Microfluidic System with an Ion-Exchange Membrane

Barak Sabbagh, Sinwook Park, and Gilad Yossifon*

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ABSTRACT: Microfluidic channels with an embedded ion permselective medium under the application of electric current are commonly used for electrokinetic processes as on-chip ion concentration polarization (ICP) and bioparticle preconcentration to enhance biosensing. Herein, we demonstrate the ability to dynamically control the electrically driven ion transport by integrating individually addressable microvalves. The microvalves are located along a main microchannel that is uniformly coated with a thin layer of an ion-exchange membrane (IEM). The interplay of ionic transport between the solution within the microchannel and the thin IEM, under an applied electric current, can be locally tuned by the deformation of the microvalve. This tunability provides a robust and simple means of implementing new functionalities into lab-on-a-chip devices, e.g., dynamic control over multiple ICP layers and their associated preconcentrated molecule plugs, multiplex sensing, suppression of biofouling, and plug dispersion, while maintaining the well-known application of microvalves as steric filtration.

INTRODUCTION

Passage of an electric current through an ionic permselective medium (e.g., nanochannel or ion-exchange membrane) results in an electrokinetic phenomenon termed ion concentration polarization (ICP). Under application of a direct current electric field, the symmetry-broken transport of ions through the permselective medium triggers ionic depletion and enrichment diffusion layers at the two opposite interfaces of the permselective medium. This then leads to a non-linear current−voltage response consisting of three regimes. The first is of a linear Ohmic-like response (i.e., under-limiting regime) that later transitions to a plateau-like response (limiting regime) at the limiting current, and upon a further increase of the voltage it shifts to an over-limiting current that continuously increases (over-limiting regime). The interplay between the various microchannel-related resistances and the ionic permselective medium-related resistance determines the limiting current \( I_{\text{lim}} \). The transition to the limiting regime occurs due to the increased electrical resistance associated with the vanishing of the electrolyte ionic concentration at the depleted membrane−microchannel interface.

This ion depletion results in a strong electric field gradient, which traps and preconcentrates charged bioparticles into a plug through a mechanism known as field gradient focusing. The trapping occurs due to a force balance between the counter-acting advection and electro-migration at the edge of the depletion layer. The concentration of the target bioparticle (e.g., DNA, protein, and bacteria) at the plug can reach several orders of magnitude of the initial concentration, which significantly enhances its detection. Among other electrokinetic-based bioparticle preconcentration techniques, e.g., dielectrophoresis and isotachophoresis molecular trapping, ICP-driven preconcentration is regarded as one of the most efficient and common tools for enhancing the detection of charged bioparticles in microscale bioanalysis. The ionic depletion layer can be utilized also for separation of particles and enrichment based on coupling alternating current-driven dielectrophoresis with ICP effects. ICP-driven preconcentration is commonly realized within microfluidic channels with relatively high hydraulic permeability, either by employing the ionic permselective medium as a bridge between two microchannels or as a patterned thin surface coating embedded at the bottom of the main microchannel. The latter can be also realized using an electrode instead of an ionic permselective medium wherein the local ion concentration is modulated via electrochemical reaction (often termed faradic ICP). These microfluidic system designs maintain minimal hydrodynamic interference within the microfluidic channels and support a sufficiently high flow rate and flux of target bioparticles toward the plug.

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However, for robust preconcentration, aside from the requirement for high throughput to achieve rapid bioparticle accumulation, precise overlap of the plug with the sensing region (e.g., immobilized molecular probes as antibodies or electrodes for electrochemical sensing) is essential. One way of achieving such an overlap is via extensive precalibration involving an elaborate process of trial and error to define the optimal operation conditions (e.g., applied voltage and flow rate) as a function of the system parameters (e.g., ionic strength, geometry, and target molecules). Adding hydrodynamic pressure onto electro-osmotic flow in addition to geometry variations can assist in localizing the plug, although some precalibration is still required.

A more direct and precise approach involves the active control of plug location via powered electrodes. The electrodes are embedded within the microchannel for localized stirring of the fluid, driven by either alternating current electro-osmosis or electrothermal flow. These methods require electrode fabrication and are mostly limited to a relatively low ionic strength electrolyte (<2 mM). Recently, we developed a series of tunable nanochannels by using microvalves made of a soft elastomer (polydimethylsiloxane, PDMS). Microvalve enables tuning of the cross-sectional area of the main microchannel from the micro- to nano-meter scale, thereby switching the microchannel into an ionic permselective nanochannel. It was shown that a series of such tunable nanochannels can be used to generate multiple plugs in series, wherein the location of the multiple plugs can be dynamically controlled based on which microvalves were operated. However, the fact that the solution must flow through nanochannels with high hydrodynamic resistances results in a low throughput and correspondingly prolonged process, with a low preconcentration factor.

The present work combined the advantages of ICP using a thin cation exchange membrane (CEM) coating (acting as the ionic permselective medium), with the advantages of a tunable microchannel geometry achieved by utilizing multiple elastomeric microvalves. The use of microvalves eliminates the need to pattern the CEM during the chip fabrication process. Instead, a uniform CEM coating was deposited along the entire bottom surface of the microchannel. Despite the uniform CEM coating, a highly controlled ICP-driven preconcentration plug was dynamically formed around each individual microvalve. When a fixed voltage drop was applied from both ends of the microchannel with a sufficiently deformed microvalve, the interplay of ionic transport between the solution and the CEM led to generation of ICP and preconcentration plugs. Although the deformed microvalve did not fully block the microchannel, it could deflect sufficient ionic current through the CEM to trigger the ICP, while the remaining gaps of several microns allowed for moderate hydraulic permeability. This behavior was examined and optimized under various operation conditions (e.g., microvalve deformations, ionic strengths, and applied voltages) and verified with a numerical model. Integration of an array of individually addressable microvalves enabled control of the location of both the ICP region and the preconcentration plugs via interaction between multiple ICP regions. In contrast to other studies that were based on fixed system geometry and properties, the unique device presented here opens new opportunities, including real-time tuning of the overall performance, in particular the system’s ionic permselectivity, spatio-temporal control of ICP, and multiple preconcentration plugs.

**METHODS**

**Experimental Setup.** The chip consisted of a main microchannel (35-mm-long, 250-μm-wide, and 55-μm-high) uniformly coated with a CEM (Nafion) at its bottom surface (CEM thickness of ~2% of the microchannel height) and with several microvalves (3–7) embedded along the length of the top of the main microchannel. Each microvalve was individually controlled by a control channel (orthogonal to the main channel, 230-μm-wide, 320-μm-high) filled with pressurized deionized water (DI). Pressurization of the fluid inside the control channel deforms the ceiling of the main channel, which reduces its cross-sectional dimension. Precise control of the main channel cross-section can thereby be achieved by tuning the pressure inside the control channel (P). All channels comprise 1:10 (base: cross-linker) PDMS, while a deformable thin PDMS film (~60-μm-high) separates the bottom part of the control channel from the top part of the main channel (i.e., no flow or current crosses between the two channels). The fabrication process, chip geometry, and the experimental setup, including the pressure control system, are fully described in Supplementary Figures S1–S4. Two silver–silver chloride electrodes (Ag/AgCl, A-M system, 0.015” diameter) were immersed within the cathodic and anodic reservoirs at the opposite ends of the main microchannel to apply either a voltage drop or an electrical current using a source-meter (Keithley 2636). A low concentration analyte (relative to the electrolyte ion concentrations) of negatively charged fluorescent dye (Alexa 488, Thermo Scientific Inc.) was used as the target bioparticle for ICP-driven preconcentration within a 10 mM KCl aqueous electrolyte (1.6 mS/cm, unless otherwise is mentioned). The fluorescence intensity of the dye, visualized and captured using a spinning disk confocal system (Yokogawa CSU-X1), an inverted microscope (Eclipse Ti-U, Nikon), and a camera (Andor iXon3), was analyzed by normalizing the local fluorescent dye intensity by the initial intensity measured before electric field application and microvalve activation. The net flow was driven by a pressure difference between the reservoirs, and the velocity was measured by monitoring 1 μm polystyrene (green fluorescent protein (GFP)-labeled particles, Thermo Scientific Inc.). The method to reconstruct the 3D channel for the closure percentage evaluation is fully described in Supplementary Figure S5.

**Numerical Simulations.** The fully coupled Poisson–Nernst–Planck equations were solved along with the simplified Navier–Stokes equation (neglecting inertia and body forces) for an incompressible fluid using a two-dimensional time-dependent model (COMSOL Multiphysics 5.3). A microchannel (2 L-long) with a CEM embedded at the bottom surface (thickness of 2% of the microchannel height H), initially filled with a symmetric binary (εz = ± 1) electrolyte of equal ion diffusivities (D = Dz) and low analyte concentration (ελ, relative to the concentration of the dominating background electrolyte ions, ε0, was simulated). The following normalization was used to present the results: axial coordinate x = Lx, ion concentration εi = ε0εi, electrical potential φ = (RT F L)εi, electric field E = (RT F L)εi, ionic flux j = (Dz + L)εi, active current density i = F(εi − j) = (FDc0/L)εi.
average flow velocity \( u = \left( \frac{D}{T} \right) \), and time \( t = \left( \frac{L^2}{D} \right) \). Here, tilde notations denote nondimensional parameters, subscript \( i \) denotes the different electrolyte \( (i = +, -) \), for positively and negatively charged ions, respectively) and analyte \( (i = A) \) ionic species within the solution, \( R \) is the universal gas constant, \( T \) is the absolute temperature, and \( F \) is the Faraday number. A fixed volumetric charge density \( (N = e_0 N) \) was defined within the CEM, along with a solvent impermeability condition at the CEM surface. To account for microvalve actuation, the microchannel cross-section was narrowed (0.05 L long) at its center. For simplification, only a single microvalve was considered, and the shape of the narrowed section was modeled as a rectangular gap of uniform height that approximates the average realistic non-uniformly deformed gap height. The different deformation levels were implemented by tuning the closure percentage of the microchannel, from an open microchannel with 0% closure for the undeformed microvalve up to an almost completely closed microchannel with 98% closure for the fully deformed microvalve. For additional information, see Supplementary Figure S6.

### RESULTS AND DISCUSSION

**Working Principle.** The system response roughly divided into three modes, defined by the deformation level of the microvalve and the corresponding ICP response (i.e., Ohmic, ICP with/without an effective formation of a plug) (Figure 1). When a relatively low pressure is applied within the control channel \( (P_i) \), the microvalve is considered to be deactivated (i.e., not deformed) and the main microchannel, tens of microns in height, remains open (Mode [I]). Despite the deactivated microvalve, the uniform CEM coating on the microchannel bottom surface causes the electrically driven ion transport that supports the electrical current \( I_{\text{Tot}} \) to divide between the CEM \( (I_{\text{CEM}}) \) and the bulk solution \( (I_{\text{Sol}}) \). The ratio between the two currents is determined by the electrical resistance of each component. A simplified equivalent circuit of the system’s response for the initial times after application of an external electric potential/current (previously to the possible emergence of diffusion layers) was used to describe this behavior (Figure 1). The circuit consists of fixed anodic and cathodic microchannel resistors \( R_{\text{Anod}} \) and \( R_{\text{Cath}} \) external to the microvalve section. These are connected in series to the resistances within the microvalve section comprised of a geometry-dependent variable resistor of the solution, \( R_{\text{Sol}} \), and a fixed CEM resistor, \( R_{\text{CEM}} \), which are connected in parallel. Hence, in the case of a deactivated microvalve, the ratio of \( I_{\text{CEM}}/I_{\text{Sol}} \) is uniform along the entire channel due to the uniform cross-section geometry. If the electrical current passing through the edge of the CEM (closest to the anode electrode) is insufficient to generate ICP, there will be no generation of ICP along the entire microchannel (i.e., \( I_{\text{Tot}} < I_{\text{Lim}} \)). Unlike the electrical current, the solution fluid flow between the two inlets is through the main channel, due to the negligible hydraulic permeability of the CEM. A further increase of \( P \) deforms the microvalve, wherein at a certain threshold \( (P_{\text{th}}) \), the deformation is sufficient to divert enough electrical current through the CEM that exceeds \( I_{\text{Lim}} \) (Mode [II]), \( I_{\text{Tot}} > I_{\text{Lim}} \) to form a stable ICP. At this state, the valve deformation partially blocks the cross-sectional area of the microchannel while leaving gaps of several microns. This reduced cross-section modifies the local interplay between \( I_{\text{Sol}} \) and \( I_{\text{CEM}} \) by increasing \( R_{\text{Sol}} \) (while \( R_{\text{CEM}} \) is unaffected), which, in turn, leads to increased \( I_{\text{CEM}}/I_{\text{Tot}} \). Yet, these remaining gaps enable sufficient hydraulic permeability for moderate fluid flow. An even further increase of \( P \) \( (P_{\text{th}}) \) deforms the microvalve such that these gaps are further reduced to sub-micron sizes which substantially increase the hydrodynamic resistance (Mode [III]) and may result in electro-osmotic backflow and dispersion of the plug. For the purpose of developing an effective preconcentration plug with a high concentration factor, conditions of sufficient ion transport through an ion permselective medium together with comparatively high hydraulic permeability are essential. Mode II meets these requirements and thereby efficiently generates a plug with a high accumulation factor.

An experimental demonstration of on-demand local application of ICP and the development of the corresponding preconcentration plug by microvalve activation is shown in Figure 2. At times 0–10 s, despite the applied electric potential \( (\phi = 60 \text{ V}) \), when the microvalve was not active \( (P = 0 \text{ psi, Mode [I]}) \), the system did not exhibit any visual indication of development of ICP (i.e., uniform fluorescence intensity). Only upon deformation of the microvalve \( (t > 10 \text{ s, } P = 16 \text{ psi, Mode [II]}) \), did fluorescent molecules accumulate into a highly preconcentrated plug at the edge of the depletion layer. The plug propagated toward the anodic side as the depletion layer grew in size. Deactivation of the microvalve \( (P = 0 \text{ psi, Mode [I]}) \) resulted in immediate flushing downstream of the plug.
ICP Dependency on the Microvalve Deformation: Experimental Investigation. The system response was experimentally studied via visualization and electrical characterization of various microvalve deformations by gradually increasing $P$ [Figure 3 and Supp. M2]. Confocal imaging-based three-dimensional reconstruction of the cross-section shape of the main microchannel beneath the activated microvalve revealed non-uniform closure, with maximum deformation at the center of the microvalve and gaps at the sides of the cross-sectional area through which the solution can pass [Figure 3A]. This deformation evolves from the initial curved cross-sectional shape of the main channel [Figures S2 and S3]. To simplify the analysis, instead of considering the precise gap geometry, the approximated closure percentage of the main microchannel underneath the microvalve was considered. The relation between the applied $P$ to the closure percentage and the flow velocity is described in Figure S7. As discussed already, there was no visual indication (i.e., no changes in the fluorescence intensity) of ICP when the microvalve was deactivated ($P = 0$ psi) [Figure 3B]. In agreement, the chronoamperometric response (i.e., electric current resulting from a step-wise application of a constant voltage drop) exhibited a steady current over time ($I_{\text{tot}} \approx 2.75 \mu A$) that was proportional to the electrolyte Ohmic resistance as occurs in non-selective systems, justifying the negation of an induced ICP-related diffusion layer contribution to the resistance [Figure 3C–E]. Increasing $P$ beyond 18 psi switched the system behavior to a non-linear $I$–$V$ response (Mode [II]) typical to ion permselective systems with an approximated limiting current of $I_{\text{tot}} = 0.25 \pm 0.05 \mu A$ [Figure 3E]. When activating the microvalve with $P = 18$ psi, with partial microchannel closure (∼60% closure), fluorescence clearly showed ICP-related depletion and preconcentration plug development at its edge [Figure 3B]. Concurrently, the chronoamperometric measurement showed current reduction over time in conjunction to visualization of the continuous growth of the depletion layer [Figure 3C,D]. A further increase in the pressure (21 psi) resulted in faster development of the depletion layer and a larger current reduction. In contrast to a lower $P$, for $P > 21$ psi, the microvalve deformed with sub-micron gaps and blocked ∼92% of the main channel. The gap size was estimated by the fact that 1 μm polystyrene GFPs failed to pass through generating a sterically-based filtration (Figure S8). Such a considerable closure resulted in a significantly decreased flow rate (down to ∼8 μm/s, see Figure S7) and a negligible preconcentration factor (Mode [III]). Application of $P$ in the range of 13–16 psi resulted in an unstable ICP that appeared and disappeared in an uncontrolled manner. Taken together, a semi-closed microvalve with $P \approx 18 \pm 1$ psi provided the best conditions for robust and an effective molecule preconcentration. Of note, the cross-section reconstruction and the particle trajectories suggested that starting from 18 psi, the ceiling of the main microchannel underneath the microvalve had already partially collapsed onto the bottom surface at the center of the main channel while leaving gaps only at the sides of the microchannel cross-section. The partial contact between the ceiling and the bottom surfaces of the microchannel may have resulted in the formation of nanochannels. However, the contribution of these nanochannels to the developed ICP was ruled out by repeating the same experiments in an identical microchannel system without a CEM coating. Even for the maximum tested $P$ (32 psi), there was no indication of ICP, likely due to lack of ionic permselectivity of the obtained nanochannels at this relatively strong electrolyte ionic strength (∼10 mM) [Figure S9]. The classification of the system response into one of the

![Figure 2](https://doi.org/10.1021/acs.analchem.2c04600)
three modes depends not only on the applied \( P \) but also on the applied voltage drop. Increasing/decreasing the voltage drop shifted the transition between the under-limiting and over-limiting current regimes to a lower/higher \( P \) due to a higher/lower \( I_{\text{Tot}} \) that reached above/below \( I_{\text{Tot}}^{\text{Lim}} \), respectively [Figure S10].

**ICP Dependency on Microvalve Deformation: Numerical Simulation Investigation.** A study case of 94\% local closure of the microchannel (from its initial open state, \( \phi = 75\% \), \( u = 65 \)) was numerically analyzed (Figure 4). The electrolyte ion concentrations (\( c_\text{ES} \)) and the electrical field (\( \mathbf{E} \)) distributions indicated a local generation of ICP starting at the narrowed cross-section region (\( x = 1 \)) representing the activated microvalve. Plotting the analyte concentration (\( c_\text{A} \)) as well demonstrated the preconcentration plug development over time. At time zero (\( t = 0 \)), when voltage drop was applied (\( \phi = 75\% \)), both the electrolyte ions and analyte were initially uniformly distributed within the microchannel. Then, although the CEM layer (marked as a yellow rectangle) was uniformly coated on the bottom surface, at \( t > 0 \) depletion/enrichment layers of ions were generated only from the anodic/cathodic sides of the narrowed cross-section region (Figure 4A). The ionic current streamlines showed that the closure diverted the current streamlines from the solution toward the CEM. Within the depletion layer, the localized high electric fields induced strong electrophoretic forces on the negatively charged analyte molecules (Figure 4B), which, together with the counteracting background advection, resulted in accumulation of the analyte into a plug. Numerical calculation of the non-dimensionalized ionic current per unit width (\( \tilde{I}_{\text{Tot}} = I_{\text{Tot}}/(FDc_0H/L) \), \( I_{\text{Tot}} \) obtained via integration of the ionic current density, \( i_\text{ES} \), over the microchannel’s height including the CEM) as a function of time exhibited a current reduction, in agreement with the experimental results [Figure 4C]. Furthermore, the ionic currents passing through each region separately underneath the microvalve (\( I_{\text{Sol}} \) and \( I_{\text{CEM}} \)) were examined for each level of closure. With an open channel (0\% closure), \( I_{\text{CEM}} \) approached \( 10\% \) of \( I_{\text{Tot}} \) and gradually increased to \( >70\% \) for a channel

Figure 3. Experimental results of the effect of the microvalve deformation level on the electrically driven ion transport response. (A) Schematic description of the main microchannel deformation, in addition to optical reconstruction of the microchannel cross-section underneath the center of the microvalve (black and white colors represent solid surfaces, i.e., microvalve wall, and the fluid, respectively). (B) Fluorescence intensity over time in a system with a deactivated (\( P = 0 \) psi at \( t < 45 \) s and \( t > 190 \) s) versus activated microvalve (varied \( P \) at \( 45 < t < 190 \) s). Each column represents a different control channel pressure (\( P \)) which gradually increases from left (0 psi) to right (21 psi). The percentage of microvalve closure (estimated from (A)) and the average flow velocity (\( u \), calculated using GFPs, Figure S8) are indicated. A constant voltage drop (25 V) was applied throughout the entire operation period (0 < \( t < 250 \) s). (C) Chronoamperometric measurements of the total current response (\( I_{\text{Tot}} \)) in correspondence to the examined conditions in (B). (D) Assessment of the relative contribution of each resistance component on the overall electrical resistance (\( R_{\text{Tot}} \)) measured in (C). The resistance components are the Ohmic electrolyte (gray), Ohmic microvalve deformation (black), and ICP-related depletion layer (yellow). (E) Current–voltage response (scan rate 7.5 mV/s) with the estimated \( I_{\text{Tot}}^{\text{Lim}} \) (red dot).
with 97% closure (Figure 4D). In terms of ICP, the current−voltage curves showed that the limiting and the over-limiting regimes were reached at lower $I_{\text{Tot}}$ for higher degrees of closure (Figure 4E). Thus, tuning the closure adjusts the ratio of $I_{\text{CEM}}$ to $I_{\text{Tot}}$, which is responsible for triggering the over-limiting ICP at lower $I_{\text{Tot,Lim}}$. Accordingly, an analyte plug was only formed after crossing the limiting regime (Figure 4F). For example, application of a constant voltage of $\phi = 78$ fell within the under-limiting (Ohmic-like) regime for 90% closure without formation of a plug (Mode [I]). Increasing the closure to 94%, while maintaining the same voltage, switched the response to the over-limiting regime and provided the conditions required for plug formation (Mode [II]). However, although further closure of the cross-section led to a decrease of $I_{\text{Tot,Lim}}$, slower growth of the preconcentration factor was obtained due to the reduced flow rate.

Figure 4. Numerical simulation investigation of the effect of local closure percentage on the electrically driven ion transport response. A study case of 94% main channel closure (applied $\phi = 78$, $u = 65$) is presented, wherein the membrane is depicted as a yellow rectangle and has $\bar{N} = 7$. (A) Electrolyte concentration ($\bar{c}_{\text{aq}}$) distribution over non-dimensional time ($\bar{t} = 0,0.015,0.035,0.07,0.14$), wherein the black lines indicate the electrical current streamlines, and the colored contour lines denote the analyte concentration ($\bar{c}_{\text{A}}$). (B) Electric field ($\vec{E}$) distribution, flow streamlines (black lines), and analyte concentration (colored contour) for the same conditions as (A). (C) Ionic current ($I_{\text{Tot}}$) response over time. The effect of closure percentages on: (D) initial ($\bar{t} = 0$) ratio of $I_{\text{CEM}}$ and $I_{\text{Tot}}$ to that of $I_{\text{Tot}}$ (black lines), (E) Ionic current−voltage response (for each curve, $I_{\text{Tot,Lim}}$ is marked with a red dot), (F) Analyte plug location and preconcentration factor under $\phi = 78$ at $\bar{t} = 0.07$. The maximum analyte concentration ($c_{\text{A,MAX}}$) obtained at given time of $\bar{t} = 10^{-2}$ within the main channel as a function of (G) $\phi$ (examined range of $0 < \phi < 700$, $\bar{N} = 7$, $u = 65$) or (H) $\bar{N}$ ($\phi = 380,0 < \bar{N} < 20$, $u = 65$) for various closure percentages (0−96%). The response phase diagram is divided into regions (dashed white lines represent the borders) that enable microvalve-based controllability over the plug generation: Mode [I]-Ohmic, [II]-ICP with a plug, [III]-ICP with a negligible plug.
Plug even though the microchannel is fully open (for all closures). On the other hand, increasing the closure percentage needed to reach this optimum point of highest preconcentration factor is reduced with increasing percentage. Between these two limits, the closure percentage that provides for the highest preconcentration factor obtained within a given time interval (\( t = 10^{-5} \)) can be found. It can be seen that the closure percentage needed to reach this optimum point of highest preconcentration factor is reduced with increasing closure percentage.

Plug Manipulation Using an Array of Microvalves. After demonstrating the potential to dynamically control ICP and its associated plug using a single microvalve, controllability was extended to an array of microvalves. Owing to the uniform CEM coating, the number of plugs and their locations can be dynamically determined. While the choice of which microvalves are activated determines where ICPs are generated, the interaction between two adjacent ICPs prevents further propagation of the plug and sets its final location. The microvalves within the array can be operated simultaneously or in a certain sequence, dictated by the desired application. Such microvalve-based programmability replaces the need to pattern the CEM coating, e.g., into an array of individually addressable CEM pairs. For example, the dynamic operation sequence of two microvalves enabled control over the number of plugs formed and later merging them to a single plug, as shown in Figure 5A. The number of plugs can be increased by activating more microvalves (Figure S12). Yet, each activated microvalve contributes to the overall hydrodynamic resistance, and therefore activation of too many microvalves leads to a low accumulation rate of molecules and a significantly lower preconcentration factor of each plug. In addition to the use of microvalves for controlled ICP generation, we demonstrated the ability to capture an analyte plug between two activated microvalves for controlled ICP generation, we demonstrated the ability to capture an analyte plug between two activated microvalves long after turning the electric field off and with it, loss of the ICP (Figure S5B). Without such physical isolation of the plug, as soon as the electric field is turned off, the balance between the electro-migration and advection is disturbed with the plug being advected downstream (Supp. M3). The ability to form a stagnant plug without the need for a continuously applied electric field is of importance for various applications, e.g., electrochemical and immunoassay sensing as well as analyte separation.

CONCLUSIONS

To summarize, we have developed a method to tune the effective ion permselectivity and hydraulic permeability of a microfluidic system for on-demand ICP and preconcentration of a target analyte. By integrating a single microvalve on top of a microchannel with uniform CEM coating at its bottom, we...
have achieved a wide range of responses starting from a non-selective to highly selective ion transport behaviors. We have shown that controlling the deformation of the microvalve also enables one to dynamically control the interplay between the CEM and the solution resistances in the deformed microvalve region, thereby, to control the ionic current that passes through the CEM. However, increasing the microvalve deformation results in increased hydrodynamic resistance and decreased flow rate and accumulation of analytes within the plug. Hence, owing to the unique tuning capabilities mentioned above, we have found the optimal deformation level which enabled sufficient ion transport through the CEM for generation of ICP, while keeping a sufficiently large solution flow throughput for an effective and high concentration factor of the associated preconcentrated analyte plug. The deformation level can be retuned for any change in the operation condition and thus enabling an efficient operation without the need of redesigning and fabricating a new chip. Hence, such a microvalve could replace previously studied electrokinetic-based valving.\(^{8,9,46}\) Additionally, application of multiple microvalves in series introduces a robust and simple way to implement a variety of new functionalities into lab-on-a-chip devices, e.g., programable manipulation of multiple preconcentration plugs for sensitive multiplex sensing, suppression of biofouling, and plug dispersion, while maintaining the well-known application of microvalves as steric filtration.

**ASSOCIATED CONTENT**

*Supporting Information*  
The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.analchem.2c04600.

Schematic of the fabrication process of the microfluidic chip; microscopic images; numerical simulation; experimental setup; 3D reconstruction; particle trajectories and calculated average flow velocity; experimental system response without a Nafton coating; limitations and optimization of microvalve operation; and dynamic operation of multiple plugs (PDF)

Experimental and numerical demonstration of on-demand ICP-based preconcentration plug formation by dynamic microvalve activation (AVI)

Experimental results of the effect of the microvalve deformation level on the system response, including ICP generation, preconcentrated plug, and solution flow (AVI)

Experimental demonstration of preconcentrated plug manipulation and trapping using multiple microvalves (AVI)

**AUTHOR INFORMATION**

*Corresponding Author*

Gilad Yossifon — Faculty of Mechanical Engineering, Technion—Israel Institute of Technology, Haifa 3200003, Israel; School of Mechanical Engineering, Tel-Aviv University, Tel Aviv 69978, Israel; orcid.org/0000-0001-7999-2919; Email: gyossifon@tauex.tau.ac.il

*Authors*

Barak Sabbagh — Faculty of Mechanical Engineering, Technion—Israel Institute of Technology, Haifa 3200003, Israel

Sinwook Park — School of Mechanical Engineering, Tel-Aviv University, Tel Aviv 69978, Israel

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.analchem.2c04600

**Notes**

The authors declare no competing financial interest.

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**REFERENCES**

(1) Schoch, R. B.; Han, J.; Renaud, P. Rev. Mod. Phys. 2008, 80, 839.
(2) Mani, A.; Zangle, T. A.; Santiago, J. G. Langmuir 2009, 25, 3898–3908.
(3) Yossifon, G.; Mushenheim, P.; Chang, Y.-C.; Chang, H.-C. Phys. Rev. E 2009, 79, No. 046305.
(4) Kim, S. J.; Wang, Y.-C.; Lee, J. H.; Jang, H.; Han, J. Phys. Rev. Lett. 2007, 99, 44501.
(5) Yossifon, G.; Mushenheim, P.; Chang, Y.-C.; Chang, H.-C. Phys. Rev. E 2009, 79, No. 046305.
(6) Yossifon, G.; Mushenheim, P.; Chang, Y.-C.; Chang, H.-C. Phys. Rev. E 2009, 79, No. 046305.
(7) Yossifon, G.; Mushenheim, P.; Chang, Y.-C.; Chang, H.-C. Phys. Rev. E 2009, 79, No. 046305.
Anand, R. K.; Sheridan, E.; Knust, K. N.; Crooks, R. M. Anal. Chem. 2011, 83, 2351–2358.

Park, S.; Yossifon, G. Nanoscale 2019, 11, 9436–9443.

Louër, A. C.; Plecis, A.; Pallandre, A.; Haghiri-Gosnet, A. M. Pressure-Assisted Selective Electropreconcentration in a Straight Nanochannel. In 17th Int. Conf. Miniaturized Syst. Chem. Life Sci. MicroTAS 2013, 2013; 2, pp 763–765.

Wang, Y.-C.; Han, J. Lab Chip 2008, 392–394.

Choi, J.; Huh, K.; Jaesuk Moon, D.; Lee, H.; Young Son, S.; Kim, K.; Chan Kim, H.; Chae, J.-H.; Yong Sung, G.; Kim, H.-Y.; Hong, J. W.; Jae Kim, S. RSC Adv. 2015, 5, 66178.

Kim, K.; Kim, W.; Lee, H.; Kim, S. J. Nanoscale 2017, 9, 3466–3475.

Park, S.; Yossifon, G. Phys. Rev. E 2016, 93, No. 062614.

Park, S.; Yossifon, G. Anal. Chem. 2020, 92, 2476–2482.

Sabbagh, B.; Stolovichki, E.; Park, S.; Weitz, D. A.; Yossifon, G. Nano Lett. 2020, 20, 8524–8533.

Quist, J.; Trietsch, S. J.; Vulto, P.; Hankemeier, T. Lab Chip 2013, 13, 4810.

Kim, B.; Heo, J.; Kwon, H. J.; Cho, S. J.; Han, J.; Kim, S. J.; Lim, G. ACS Nano 2013, 7, 740–747.

Green, Y.; Yossifon, G. Phys. Rev. E 2015, 91, 63001.

Manzanares, J. A.; Murphy, W. D.; Mafé, S.; Reiss, H. J. Phys. Chem. 1993, 97, 8524–8530.

Dydek, E. V.; Zaltzman, B.; Rubinstein, L.; Deng, D. S.; Mani, A.; Bazant, M. Z. Phys. Rev. Lett. 2011, 107, No. 118301.

Yaroshchuk, A.; Zholtovskiy, E.; Pogodin, S.; Baulin, V. Langmuir 2011, 27, 11710–11721.

Choi, J. H.; Lee, H. J.; Moon, S. H. J. Colloid Interface Sci. 2001, 238, 188–195.

Sun, G.; Senapati, S.; Chang, H.-C. Lab Chip 2016, 16, 1171.

Sun, G.; Pan, Z.; Senapati, S.; Chang, H. C. Phys. Rev. Appl. 2017, 7, No. 064024.