Tunable electrochemical pH modulation in a microchannel monitored via the proton-coupled electro-oxidation of hydroquinone

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Electrochemistry is a promising tool for microfluidic systems because it is relatively inexpensive, structures are simple to fabricate, and it is straight-forward to interface electronically. While most widely used in microfluidics for chemical detection or as the transduction mechanism for molecular probes, electrochemical methods can also be used to efficiently alter the chemical composition of small (typically <100 nL) microfluidic volumes in a manner that improves or enables subsequent measurements and sample processing steps. Here, solvent (H₂O) electrolysis is performed quantitatively at a microchannel Pt band electrode to increase microchannel pH. The change in microchannel pH is simultaneously tracked at a downstream electrode by monitoring changes in the *i*-*V* characteristics of the proton-coupled electro-oxidation of hydroquinone, thus providing real-time measurement of the protonated forms of hydroquinone from which the pH can be determined in a straightforward manner. Relative peak heights for protonated and deprotonated hydroquinone forms are in good agreement with expected pH changes by measured electrolysis rates, demonstrating that solvent electrolysis can be used to provide tunable, quantitative pH control within a microchannel. © 2014 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4894275>]

INTRODUCTION

Recently, the advantages of performing chemical analysis in ultrasmall (fL–nL) volumes have been demonstrated in a variety of systems including microchannel electrodes,^{1–5} nanogap electrodes,^{6,7} nanoscale electrodes,^{8,9} and nanopores.^{10–12} In general, the principal benefits afforded by miniaturization arise from: (1) the ability to perform multiple measurements simultaneously in an array format, and (2) rapid diffusive transport across small characteristic length scales. The latter benefit, rapid diffusive transport, enables fundamentally different sensor strategies compared to macro-scale systems and motivates the study of novel techniques at these smaller length scales. The ability to rapidly and precisely modify small volumes (10^{–15}–10^{–9} L) *in situ*, which is explored in this work, is uniquely available in microfluidic (and smaller) systems and will be an important factor enabling the realization of next generation methods in micro-scale chemical analysis.

Electrochemical methods are particularly well-suited for *in situ* modification of the chemical characteristics of small volumes, because of the relative ease of fabrication and control of μ m-scale electrodes.¹³ In the absence of other electro-active starting materials, solvent electrolysis can be used to alter the chemical content of small sample volumes, e.g., in aqueous samples, the electrochemical reduction of water generates OH[–] anions and H₂ gas. In macro-scale

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systems, this simple electrolysis reaction is used reliably as a source of $\text{H}_2(\text{g})$ for catalytic hydrogenation.¹⁴ Direct H_2O electrolysis has also been demonstrated on the micro/nano-scale in nanochannels,¹⁵ microgap electrodes,¹⁶ and water droplets¹⁷ in order to manipulate solution pH and H_2 content to improve chemical analysis/processing. The electrolysis of H_2O also plays an important role in many microfluidic devices. For example, electrolysis at bipolar electrodes is used for molecular separation/enrichment in both microchannels and capillaries,^{18,19} and electrolysis products are inevitably formed at the electrodes used to drive electroosmotic flow.²⁰ It should be noted that the pH of microfluidic volumes can also be manipulated without direct H_2O electrolysis. Cheng *et al.* and Gabrielsson *et al.* both demonstrated microchannel pH control by driving H_2O dissociation at the interface between an aqueous solution and a bipolar membrane.^{21–23} While this technique has the significant advantage of not resulting in gas formation, the use of relatively large DC biases to drive H_2O dissociation is not readily amenable to concurrent in-channel electrochemical measurements.

Microchannels offer highly controlled device geometries and flow rates for the study of electrochemical processes. Building on the well-established theoretical knowledge of planar microchannel electrode behavior,^{24,25} microchannels containing dual electrodes have been used for the study of oxygen reduction catalysis²⁶ and homogeneous reaction rates.²⁷ In the work presented here, we employ a similar dual electrode microchannel flow cell device for the characterization of electrochemically mediated pH modulation in a microchannel. The device, depicted in Fig. 1, consists of a single $200\ \mu\text{m} \times 55\ \mu\text{m} \times \sim 1\ \text{cm}$ ($w \times h \times l$) microchannel with two underlying Pt thin-film electrodes, a $100\ \mu\text{m}$ wide pH modulating electrode (PME) and a $10\ \mu\text{m}$ wide detection electrode (DE), separated by 2.3 mm. A Pt thin-film counter electrode (CE) and Ag/AgCl reference electrode (RE) are located in the microchannel outlet reservoir. While pH is modified at the PME, the proton-coupled electro-oxidation of hydroquinone (QH_2) is altered, allowing QH_2 to act as a model analyte and pH indicator through the pH dependence of its cyclic voltammetry waveshape. Special attention is given to the faradaic processes occurring at the PME and the efficiency with which the PME titrates (deprotonates) QH_2 , demonstrating tunable and quantitative downstream pH control.

METHODS

Materials

Microchannel masters were created using SU-8 2050 photoresist and SU-8 developer (Microchem) on p-type $\langle 100 \rangle$ silicon wafers (Montco Silicon Technology). Microchannels were formed in poly(dimethylsiloxane) (Sylgard 184, Dow Corning). Electrode patterning was accomplished using AZ-5214E (AZ Electronic Materials), using standard microscope slides as substrates. Hydroquinone was purchased from Alfa Aesar, and potassium nitrate was purchased from Fisher Scientific. Sodium hydroxide was used to adjust the pH of solutions. All aqueous solutions were prepared in filtered deionized (DI) water (Millipore), and all hydroquinone (QH_2) solutions were prepared immediately before use to prevent spontaneous oxidation in solution. All reagents were used as received.

FIG. 1. Schematic depiction of device used to study electrochemical pH manipulation in a microchannel. The pH of a flowing solution is increased via reduction reactions at the PME. The darker blue region depicts the volume exhibiting increased pH. This high pH region extends from the PME to the microchannel outlet at which point the solution is rapidly diluted in the large reservoir volume. The pH change subsequently alters the characteristic i - V curve of a probe electrochemical oxidation reaction occurring at the DE.

Device fabrication

Poly(dimethylsiloxane) (PDMS) microchannels were fabricated using the rapid prototyping method.²⁸ In brief, this method consists of spinning a layer of SU-8 2050 to the desired thickness, *ca.* 55 μm in this case, and processing this film according to the manufacturer's instructions for UV exposure and development to create a microchannel master mold, containing features 55 μm high, 200 μm wide, and 12 mm long. Microchannels were then achieved by pouring PDMS over the master mold and curing at 75 °C for at least 30 min. The channels were then cut from the mold, and circular reservoirs were cut at each end. Plastic tubing (2 mm O.D.) was sealed to the inlet side of the channel in order to allow coupling to a syringe pump.

Electrodes were patterned and deposited on a glass slide using photolithography and thermal evaporation. Three electrodes were defined using negative-tone AZ-5214E on a glass slide. The electrode pattern included one 100 μm wide pH modulating electrode, one 10 μm wide detection electrode and one $\sim 5\text{ mm} \times 5\text{ mm}$ counter electrode and the necessary contact pads needed to make electrical connections, as depicted in Fig. 1. Prior to metal deposition, a low power O_2 plasma was used to remove any residual photoresist from the patterned regions. A 10 nm Cr adhesion layer was then thermally evaporated on the patterned substrate. Following the deposition of this adhesion layer, the substrate was immediately moved to a plasma sputterer, in which a 60–80 nm thick Pt layer was deposited. After metal deposition, the remaining photoresist was removed in an agitated acetone bath. The substrate was then sequentially rinsed in acetone, isopropanol, and DI water before being cleaned in a high power O_2 plasma. The PDMS microchannel and electrode-containing glass substrate were then exposed to air plasma for ~ 1 min, aligned, and bonded together.

Electrochemistry and flow control

The potentials of the PME and DE were controlled using a CHI bipotentiostat (842c, CH Instruments). A commercial Ag/AgCl reference electrode (69–0053, Warner Instruments) was placed in the outlet reservoir of the microchannel, while the counter electrode was a Pt disk on the glass slide defined by the size of the outlet microchannel reservoir ($d \approx 3\text{ mm}$). Constant negative potentials were applied at the PME in order to induce OH^- generation, while cyclic voltammetry was performed at the downstream DE. Flow in the channel was controlled with a syringe pump.

RESULTS AND DISCUSSION

Electrochemical pH manipulation

Solution pH can readily be manipulated by applying a constant negative potential at the PME in order to drive OH^- production through the reduction of O_2 and H_2O , which proceed through reactions (1) and (2),

Reactions (1) and (2) are expressed for a solution with a neutral/basic pH, which is characteristic of the chemical systems addressed here. The current at the PME, i_{PME} , was measured in 0.1M KNO_3 as a function of PME potential, E_{PME} , under different flow conditions. The corresponding plots of i_{PME} vs. E_{PME} are shown in Fig. 2. The magnitude of E_{PME} is limited by the nucleation of H_2 bubbles at very negative potentials ($\leq -2.0\text{ V}$); however, the convective removal of H_2 away from the PME and ability of H_2 to rapidly permeate through PDMS²⁹ precludes bubble nucleation under the conditions used here. Interestingly, i_{PME} has negligible flow rate dependence, suggesting that electron transfer is not mass-transport limited. This is surprising

FIG. 2. Plot of i_{PME} vs. E_{PME} for the reduction of O_2 and H_2O at the Pt PME at various values of V_f ranging from 2.8 to 28 $nl\ s^{-1}$, which are identified by the symbols defined in the legend. (Inset: Magnified view of the data at $E = -1.0\ V$). Error bars show ± 1 standard deviation.

given the low linear flow velocities studied, ranging from 2.8×10^{-2} to $2.8 \times 10^{-1}\ cm\ s^{-1}$; however, the E_{PME} range used can support Reactions (1) and (2) simultaneously.

It is informative to consider what portion of i_{PME} is mediated through O_2 (Reaction (1)) vs. H_2O (Reaction (2)) reduction. The maximum transport limited current associated with the reduction of O_2 , i_{lim,O_2} , can be estimated using the Levich equation³⁰

$$i_{lim,O_2} = 0.925nFC_{O_2}(D_{O_2}wx_e)^{2/3}\left(\frac{4V_f}{h^2}\right)^{1/3}, \quad (3)$$

where $n=4$ is the number of electrons transferred, F is Faraday's constant ($96485\ C\ mol^{-1}$), C_{O_2} is the concentration of O_2 ($\sim 0.25\ mM$),³¹ D_{O_2} is the O_2 diffusion coefficient ($\sim 2.5 \times 10^{-5}\ cm^2\ s^{-1}$),³² w is the channel width ($200\ \mu m$), x_e is the electrode length ($100\ \mu m$), h is the channel height ($50\ \mu m$), and V_f is the volumetric flow rate. The maximum current attributed to the convective delivery of dissolved O_2 under the slowest mass transport conditions, $V_f = 2.8\ nl\ s^{-1}$, is $i_{lim,O_2} \approx 0.20\ \mu A$, which is approximately an order of magnitude lower than the maximum currents observed at the PME. However, unexpectedly large oxygen reduction currents have been reported at microchannel electrodes previously, owing to the flux of O_2 through the gas-permeable PDMS microchannel material.³³ Thus, finite element simulation calculations were used to determine the maximum possible O_2 reduction current at a micro-channel band electrode under two sets of hydrodynamic conditions in which O_2 is either available or unavailable, from permeation through the channel material. Details of the simulation methods and results are available in the supplementary material.³⁴ Under the flow conditions used in these experiments, the additional flux of O_2 through the PDMS channel material has a negligible impact on the O_2 reduction current with only $\sim 7\%$ increase in current at the lowest flow rate studied, $V_f = 2.8\ nl\ s^{-1}$, and no increase under other conditions (Table S2 of the supplementary material³⁴).

Since the experimentally observed values of i_{PME} are too large to be the result of O_2 reduction alone, the majority of i_{PME} must be supplied by the reduction of H_2O (Reaction (2)). The onset of H_2O reduction must begin at $E \leq -0.8\ V$ vs. Ag/AgCl, because i_{PME} exceeds i_{lim,O_2} at potentials more negative of $-0.8\ V$. Although $-0.8\ V$ vs. Ag/AgCl is insufficient to drive H_2O reduction for most electrochemical systems, Pt is known to catalyze hydrogen evolution (i.e., Reaction (2)),³⁵ explaining the apparently kinetic-limited reaction occurring at the PME. The very small flow rate dependence of i_{PME} vs. E_{PME} shown in the inset of Fig. 2 is likely caused by contributions from mass-transport limited O_2 reduction. The expected magnitude of this O_2 reduction current, obtained either from Eq. (3) or from finite element calculations,³⁴ changes by approximately $0.05\text{--}0.1\ \mu A$ with changing flow rate (see Table S3 of the supplementary material³⁴), in good agreement with the observed flow rate variations shown in Fig. 2.

pH-dependent hydroquinone/benzoquinone (QH₂/Q) redox couple

The hydroquinone/benzoquinone redox couple is both a good model system for pH studies and is of practical importance due to the deleterious impact of QH₂/Q in the environment.^{36,37} The overall reaction for the oxidation of hydroquinone (QH₂) to benzoquinone (Q) is

However, the mechanism is a complex combination of two one-electron transfer processes and up to two deprotonation steps, for which there are nine possible oxidation and protonation states among the reactants, intermediates, and products.³⁸ Fortunately, in the pH range of ~4–11, the available pH-dependent reaction pathways can be greatly simplified.³⁸ Figure 3(a) shows the primary reaction pathways that are relevant to the experimental conditions used here.

To investigate the effect of pH on the *i*-*V* characteristics of the oxidation of QH₂, cyclic voltammetry was performed at the DE under hydrodynamic conditions (*V_f* = 28 nl s⁻¹) in 5 mM QH₂ and 0.1M KNO₃ solutions with different concentrations of KOH. The positive sweep portion of the background-subtracted *i*-*V* curves is shown in Figure 3(b). In the absence of KOH, the onset of QH₂ oxidation begins positive of +0.3 V with a half wave potential, *E*_{1/2} ~ 0.55 V. In 1 mM KOH, a small oxidation peak is observed beginning at -0.2 V, which reaches a steady state value near 20 nA. A second oxidation peak then occurs with a similar onset to the peak observed in the absence of KOH, *E*_{1/2} ~ 0.53 V. In 5 mM KOH, the *i*-*V* curve has a completely different shape with a larger initial oxidation peak near -0.2 V (~100 nA vs. ~20 nA), immediately followed by a broad, slowly increasing oxidation current. Clearly, as the pH of the solution increases, the electro-oxidation of QH₂ can occur at more negative potentials, as expected for proton-coupled electron transfer.³⁸ The appearance of multiple oxidation peaks also suggests that different protonated species are present in solution, explaining the two current peaks. For example in 1 mM KOH, the oxidation of singly-protonated hydroquinone, QH⁻, occurs near -0.2 V, with a magnitude of *i*_{-H}, where *i*_{-H} is used to denote the current associated with deprotonated forms of QH₂. The second peak, beginning near 0.3 V, contains the total current, *i*_t, with contributions from both QH₂ and QH⁻. In more alkaline solution (5 mM KOH), a larger fraction of QH₂ is deprotonated, causing the *i*-*V* curve to condense into a more complex single waveshape (blue curve, Figure 3(b)), which potentially contains contributions from QH₂, QH⁻ and Q²⁻.

Manipulation of pH during electro-oxidation of QH₂ in a microchannel

A solution of 0.1M KNO₃ and 5 mM QH₂ was introduced to the microchannel at various flow rates ranging from 2.8 to 28 nl s⁻¹ using a syringe pump. Cyclic voltammetry was

FIG. 3. (a) Reaction routes for electron transfer and protonation/deprotonation reactions for the QH₂/Q redox couple. (b) Background subtracted *i*-*V* curves recorded in 5 mM QH₂ and 0.1M KNO₃ at the platinum detection electrode with different concentrations of KOH added to the test solution. Background measurements were performed in the same electrolyte mixture in the absence of QH₂. Only positive sweep portions of CV scans are shown for clarity. *V_f* = 28 nl s⁻¹, *v* = 100 mV s⁻¹.

FIG. 4. Anodic portion of i - V curves recorded at the DE, while the PME is held at various negative potentials at different flow rates: V_f =(a) 28, (b) 14, (c) 5.6, and (d) 2.8 nl s⁻¹. Solutions contained 0.1M KNO₃ and 5 mM QH₂. Background measurements were performed in 0.1M KNO₃ under the same flow conditions. Only positive sweep portions of CV scans are shown for clarity. $v = 100$ mV s⁻¹. E_{PME} is left floating before being stepped to potentials from -0.4 V to -1.4 V in increments of 0.2 V, as indicated in the legend and by the diagonal arrow labeled E_{PME} in each panel.

performed at the DE while the PME was either floated or held at various negative potentials in order to generate OH⁻ electrochemically. Because of the relatively large, 2.3 mm, separation between PME and DE, a homogeneous pH distribution develops in the microchannel through diffusion before reaching DE, as indicated schematically by the dark blue shading in Figure 1. The resulting i - V curves, shown in Fig. 4, are all background-subtracted, using data collected under the same hydrodynamic and potentiostatic conditions, to remove signal not associated with the electro-oxidation of QH₂. With no potential applied to the PME, QH₂ oxidation occurs at potentials >0.3 V vs. Ag/AgCl with a sigmoidal i - V shape, which is characteristic of transport limited hydrodynamic voltammetry at a channel band electrode.^{24,25} The peak current magnitudes for QH₂ oxidation (for E_{PME} =floating, E_{DE} =0.9 V) at each flow rate are i_t =420, 380, 320, and 290 nA at V_f =2.8, 5.6, 14, and 28 nl s⁻¹, respectively. The magnitude of i_t does not follow the $V_f^{1/3}$ dependence characteristic of the Levich equation (Eq. (3)), because experiments were performed at relatively low Péclet numbers, characteristic of a transport regime intermediate between thin layer and Levich behavior.²⁵

At the highest flow rate of 28 nl s⁻¹, the i - V curves shift slightly to more negative potentials as E_{PME} is poised at progressively more negative potentials from -0.4 to -1.4 V, as shown in Fig. 4(a). At the most negative value of $E_{PME} = -1.4$ V, a small, additional QH₂ oxidation wave appears related to the oxidation of deprotonated QH₂, beginning near -0.15 V and reaching a steady-state current of $i_H \approx 40$ nA at $E_{DE} = 0.2$ V. This oxidation wave at i_H is qualitatively similar to that observed in 1 mM KOH (black curve, Figure 3(b)), supporting the hypothesis that this oxidation wave is caused by pH changes induced by the PME. The total maximum current at 0.9 V, i_t , is largely unaffected by the value of E_{PME} .

At a lower flow rate of 14 nl s⁻¹, i_H is larger than at $V_f = 28$ nl s⁻¹, as shown in Fig. 4(b). At $E_{PME} = -1.4$ V, $i_H \approx 70$ nA. This trend of increasing i_H with decreasing flow rate continues at $V_f = 5.6$ nl s⁻¹, where $i_H \approx 130$ nA for $E_{PME} = -1.4$ V, cf. Fig. 4(c). At both intermediate flow rates, i_t does not change significantly as E_{PME} becomes more negative. Since i_t contains contributions from all forms of QH₂, it is determined by the formal concentration of QH₂, so its insensitivity to pH changes caused by the PME is reasonable.

At the lowest flow rate studied, 2.8 nl s⁻¹, i_H continues to increase as E_{PME} becomes more negative until the i - V curve shape changes to a single, broad wave at $E_{PME} \leq -1.2$ V, as shown

in Fig. 4(d). i_t also decreases in Fig. 4(d) for $E_{PME} < -1.0$ V at 2.8 nl s^{-1} . The decrease in i_t and the increase in complexity of the oxidation wave shapes at $E_{PME} < -1.0$ V are very similar to those observed in the presence of 5 mM KOH (blue curve, Figure 3(b)). While the detailed shapes of these i - V curves are not fully understood, the decrease in i_t might be caused by the formation of reversible adducts with OH^- .^{38,39} The complexity of the wave shape is the result of the concurrent oxidation of up to three forms, i.e., QH_2 , QH^- , and Q^{2-} .

As observed in Fig. 4, i_{-H} increases as E_{PME} becomes more negative, especially at low flow rates. The relative magnitude of i_{-H} provides a direct measure of the protonation state of QH_2 species in the microchannel, such that the alpha fraction, the fraction of total QH_2 in a given protonation state, of both deprotonated forms of QH_2 , α_H , can be calculated from the ratio of i_{-H} to i_t according to

$$\alpha_H = \frac{i_{-H}}{i_t} = \alpha_{\text{QH}^-} + \alpha_{\text{Q}^{2-}}, \quad (5)$$

where α_{QH^-} and $\alpha_{\text{Q}^{2-}}$ are the alpha fractions of QH^- and Q^{2-} , respectively. The potentials at which i_{-H} and i_t are evaluated are indicated in Figs. 4(a)–4(d) for clarity. A plot of α_H vs. i_{PME} for different flow rates, Fig. 5(a), shows that α_H increases as i_{PME} becomes more negative in all cases, but at low flow rates α_H increases more as i_{PME} decreases, as was already noted in Figure 4.

Given the 1:1 stoichiometry of electrons transferred to OH^- generated in Reactions (1) and (2), the local concentration of OH^- generated at the PME, $[\text{OH}^-]_{\text{gen}}$, can be approximated as

$$[\text{OH}^-]_{\text{gen}} = -\frac{i_{PME}}{FV_f}. \quad (6)$$

Figure 5(b) is a plot of α_H vs. $[\text{OH}^-]_{\text{gen}}$ for each flow rate studied. Interestingly, the values of α_H measured at different flow rates all fall onto the same master curve after normalizing to the total concentration of OH^- added to the system, strongly supporting the view that the addition of OH^- at the PME causes the observed changes in electrochemical behavior at the DE.

The titration efficiency, $\eta_{\text{titration}}$, measures the percentage of $[\text{OH}^-]_{\text{gen}}$ that is available for changing the protonation state of QH_2 . Departures from ideal behavior are caused by competing faradaic and homogeneous reactions. For example, a fraction of i_{PME} not associated with reactions 1 and 2 either does not generate OH^- at all or generates it at a stoichiometric ratio of $<1 \text{ OH}^-/e^-$. In addition, the current can be augmented by the reduction of sample impurities or the adsorption/desorption of electrolyte ions or the reduction of surface oxides. Alternatively, some of the OH^- generated at the PME are inevitably consumed by competing homogeneous equilibrium processes like reaction with dissolved CO_2 species, titration of the silanol surface of the PDMS microchannel, or consumption by sample impurities. Ultimately, a knowledge of $\eta_{\text{titration}}$ allows the effective concentration of OH^- generated, $[\text{OH}^-]_{\text{eff}}$, to be evaluated as

$$[\text{OH}^-]_{\text{eff}} = \eta_{\text{titration}} [\text{OH}^-]_{\text{gen}}. \quad (7)$$

FIG. 5. Plot of α_H vs. (a) i_{PME} and (b) $[\text{OH}^-]_{\text{gen}}$ for flow rates 2.8, 5.6, 14, and 28 nl s^{-1} . α_H is calculated from Eq. (5), while $[\text{OH}^-]_{\text{gen}}$ is calculated with Eq. (6). Solid lines are included as a guide to the eye.

FIG. 6. Plot of α_H vs. calculated pH for flow rates 2.8, 5.6, 14, and 28 nl s^{-1} . The calculation of the pH from $[\text{OH}^-]_{\text{eff}}$ and the various alpha fractions is described in the supplementary material.³⁴

A value of $\eta_{\text{titration}} = 0.7$ was determined by fitting the experimentally determined α_H values to the pH calculated from Eq. (7) and the Henderson-Hasselbalch equation for the $\text{QH}_2/\text{QH}^-/\text{Q}^{2-}$ system (see supplementary material³⁴). Figure 6 shows α_H plotted as a function of pH along with the alpha fractions of the various QH_2 species for comparison. Overall, the data are in good agreement with theory. The PME was able to accomplish pH changes of several decades in 5 mM QH_2 , although pH calculations at $\alpha_H \approx 1$ are outside the resolution window of the QH_2 system, which becomes saturated at $\text{pH} \gtrsim \text{pK}_a = 11.4$.

CONCLUSIONS

The behavior of an upstream pH modulating electrode, investigated by characterizing a pH-sensitive model system (QH_2), is determined by a combination of hydrodynamic conditions (volumetric flow rate) and electrochemical driving force at the PME. Under low flow conditions, the PME was able to deprotonate 100% of the initially present diprotic species, QH_2 , creating an approximately 50:50 mixture of QH^- and Q^{2-} as evidenced by changes in the i - V characteristics of QH_2 . The magnitude of pH modulation is readily tuned through control of the rate of the electrolysis (through E_{PME}) and the flow rate. With the ability to titrate even a relatively high concentration (5 mM) of protonated species, the microchannel PME is a promising tool for improving microfluidic electroanalysis of pH-sensitive biomolecular systems, such as enzyme-catalyzed or affinity based sensors or the direct electrochemical detection of electroactive species like dopamine and ascorbic acid. Dynamic pH changes should also be accessible to the PME through the generation of OH^- -rich plugs of solution, although limitations will be imposed by axial dispersion. Furthermore, the general strategy developed here, using an upstream PME for solvent electrolysis, could equally well be applied to produce O_2/H^+ , thereby accessing the acidic end of the pH range. Thus, this simple electrochemical method for direct, *in situ* microfluidic pH control can be used for other valuable biological applications like on-chip cell culture or high-throughput investigations of other pH sensitive bioprocesses.

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