Electrochemistry

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Thin-Layer Chemical Modulations by a Combined Selective Proton Pump and pH Probe for Direct Alkalinity Detection**

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Abstract: *We report a general concept based on a selective electrochemical ion pump used for creating concentration perturbations in thin layer samples (~40 μL). As a first example, hydrogen ions are released from a selective polymeric membrane (proton pump) and the resulting pH is assessed potentiometrically with a second membrane placed directly opposite. By applying a constant potential modulation for 30 s, an induced proton concentration of up to 350 mM may be realized. This concept may become an attractive tool for in situ titrations without the need for sampling, because the thin layer eventually re-equilibrates with the contacting bulk sample. Acid–base titrations of NaOH and* Na_2CO_3 *are demonstrated. The determination of total alkalinity in a river water sample is carried out, giving levels (23.1 mM) comparable to that obtained by standard methods (23.6 mM). The concept may be easily extended to other ions (cations, anions, polyions) and may become attractive for environmental and clinical applications.*

The thin layer confinement of liquids has recently attracted the attention of diverse chemical domains that include energy storage,[1] engineered microfluidics,[2] separation techniques,[3] material science,[4] and fundamental as well as applied electrochemistry.[5] On the one hand, major uses of thin-layer solutions or other thin-layer materials (i.e., insulators, conductive materials, membranes, etc.) have been intrinsically connected with the idea of less consumption of reagents, materials, and samples.[6] This latter aspect becomes a crucial factor when it comes to the monitoring of human fluids such as blood and plasma.[7] Thin layers are also suitable to an external stimulus or trigger. Once an external force (i.e., light, current, potential, concentration gradient, pressure, heat, etc.)[8] is applied to a confined layer, it provokes an exhaustive transformation of the layer (100% conversion). If this conversion/transformation is generated by the injection of charge (i.e., ions), it can be integrated over time and result in a coulometric methodology. Evidently, this is not the case for systems with large volume-to-surface ratios[9] or expandable volumes[10] in which only local variations are observed at short time scales. The latter approach is also accompanied by a time-dependent signal that is influenced by variations of diffusion coefficients.[9,10] Naturally, the rate of the process is dependent on the magnitude of the force as well as its rate of propagation into the thin-layer solution.

Concentration gradients can be modulated in the entire thin-layer sample, by applying either an external current or potential to an appropriate ion-transferring element (i.e., ion-selective membrane) placed in contact with the solution. Aiming to demonstrate this idea, we report here on a new concept that imposes a controlled and selective proton release on a thin-layer sample with subsequent potentiometric read-out. The thin layer eventually re-equilibrates with a solution of larger volume, allowing one to achieve repeated localized titrations without sampling or volumetric delivery.

Scheme 1 schematically shows the thin-layer titration concept for a sample containing strong base. The electrochemical cell is composed of two key elements, the hydrogen ion generator and the pH detector (Scheme 1a, Figure S1). The thin-layer solution (40 ± 5 μL) is delimited by the flat geometry of both elements (see the Supporting Information). The proton pump is a fast diffusive hydrogen ion-selective membrane (M1, see composition) that acts as a working electrode (WE) in a three-electrode cell with the respective counter (CE) and reference electrode (RE_1) placed outside of the thin layer. The applied potential or the applied current is controlled by a potentiostat/galvanostat that allows the current to flow between the working and the counter electrode while the potential is simultaneously measured between the working and the reference electrode. Opposite to the proton pump, a less diffusive pH-responsive membrane based on poly(vinylchloride) (M2, see composition) is located. This membrane is measured at zero current against a second reference electrode (RE_2) in the outside solution. Note that any possible contribution of co-extracted chloride and proton from the inner filling solution must not affect the thin-layer composition in the experimental time scale (thick membrane and low ion-diffusion coefficient[11]). As expected for a pH probe, the potential readout is linear with pH according to the Nernst equation.[11] This electrochemical configuration combines dynamic and equilibrium electrochemistry bridged by a thin-layer sample.

The electrochemical processes that take place during the experiment are illustrated in Scheme 1b. It begins by electrochemical polarization (current or potential) of the proton pump membrane, imposing a hydrogen ion flux of defined duration, and hence of defined charge, from the inner compartment (IFS, inner filling solution, 0.01 M HCl) across the membrane to the thin layer. The membrane (M1) contains an elevated amount of ionophore (L, 120 mM), resulting in a high hydrogen-ion-releasing capacity.[9] The concentration

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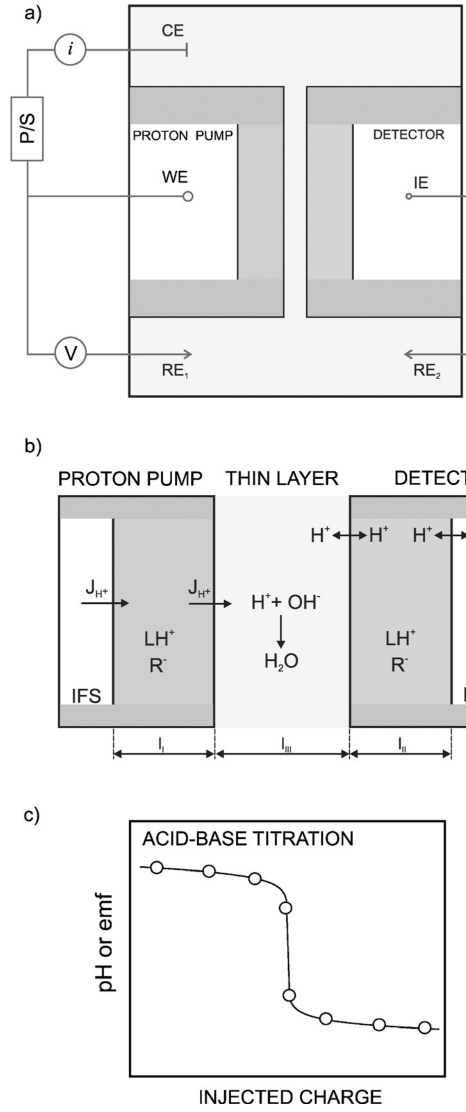

Scheme 1. Illustration of the reported concept. a) Electrochemical cell composed of a proton pump and a detector proton-selective membrane M1 (orange) and M2 (purple), respectively. WE: working electrode, RE$_1$ and RE$_2$: commercial reference electrode, CE: Pt rod, IE: indicator electrode, V: potential reader, i: current reader, P/S: power supply, emf: potentiometer. b) Magnification of the thin layer and electrochemical process that occurs once the proton pump is turned on ($l_I = 25$ μm, $l_{II} = 200$ μm, and $l_{III} = 100$ μm); L: ionophore; R$^-$: cation exchanger; J$_{H+}$: proton flux; IFS: inner filling solution. c) Acid–base titration output signal.

of the base decreases in the thin layer as a consequence of the released quantity of hydrogen ions. Eventually, any initially present base is consumed in the entirety of the thin layer and the neutralization process can be monitored with the detection membrane (M2) (L concentration, 15 mM) placed opposite of the thin layer. A titration curve is expected that is a function of injected charge (Scheme 1c).

The assembly consisting of proton pump and detector, along with the remaining electrodes (CE, RE$_1$, and RE$_2$), were placed in a 200 mL sample solution. Between each charge injection measurement, convection was forced by vigorous stirring of the reservoir, recovering the initial concentrations in the thin layer within 120 s. As the thin layer volume is five thousand times smaller than the volume of the contacting solution, no appreciable changes in the final concentration are expected after stirring the solution.

The proton release and detection process described above was established in initial experiments with MilliQ purified water (pH 5.5 after CO$_2$ equilibration). The first step of the characterization consists of selecting an appropriate proton-transfer potential (i.e., 300 mV relative to the reference electrode) and the associated release time. Figure 1a shows the potentiometric detection of protons at the membrane surface for several release times at that anodic potential. Eight constant potential steps with a gradual increment of the time period (from 30 s to 210 s) were applied to the proton pump membrane. As expected, longer applied potential steps resulted in lower detected pH. Similar experiments were performed with a defined time period and varying the applied potential or the current (Figure S2).

The transient proton profile is visualized in Figure 1b and is the result of the different processes that occur in the thin

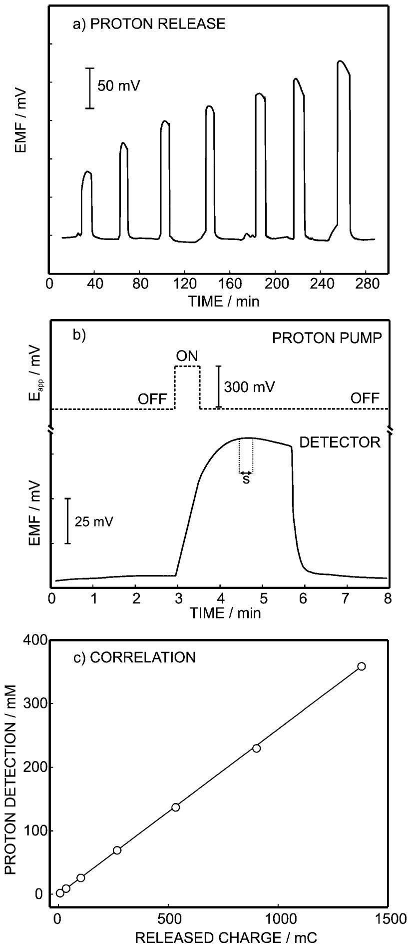

Figure 1. a) Potentiometric response as a function of time duration of the excitation pulse (between 30 to 210 s in steps of 30 s from left to right at 300 mV) at the proton pump membrane. b) Transient potential readout at the pH responsive membrane, with *s* the time interval used for recording the potentiometric response (excitation pulse of 30 s). c) Correlation between released charge and detecting hydrogen ion concentration in the absence of added base.

layer. The applied potential imposed a concentration gradient at the proton pump membrane surface that extends to the entire thin layer by mass transport. As the hydrogen ions reach the detection membrane, a potentiometric response starts to be observed. At this point, the proton source is turned off (to open circuit), resulting in a local equilibration of pH between the two opposing electrodes. As the thin layer is in direct contact with the outside solution (see Scheme 1 a), hydrogen ions diffuse laterally away, resulting in a gradual reversal of the hydrogen ion perturbation. A sufficiently long period of ca. 30 s is observed between the point of equilibration and the starting point of appreciable hydrogen ions loss that is used to record the pH.

Figure S3 shows an experimental comparison between the readout signal when considering passive diffusion and forced convection by stirring the outside solution. The latter allows one to reach the baseline signal five times faster than by passive diffusion, resulting in a reproducibility of pH readings for repetitive pulses of 2 % RSD for 30 s at 300 mV as shown in Figure 4S.

In the absence of added base, a linear correlation between injected charge and the hydrogen ion concentration readout is found (Figure 1 c). For this purpose, the detecting membrane was precalibrated with standard pH buffers, allowing one to convert the potential readings to hydrogen ion concentration. The injected charge was calculated as the integration of the output current over the pulse time. This linear correlation demonstrates that a reproducible and quantitative hydrogen ion flux into a thin layer sample can be established.

We further characterized the system by introducing a defined concentration of a base in solution. The strong base NaOH was titrated as a first application (Figure 2 a). As expected, the base concentration gradually diminished before the equivalence point with increasing injected charge. Once the base was consumed, the pH decreased rapidly to about 2. The titration curve was obtained by applying a constant potential (300 mV) to the proton source for different time intervals (6 s to 240 s, about 20 points). Between each pulse, the sample was stirred for 120 s to return the system to baseline. The titration was repeated at 25 mM, 50 mM, and 75 mM NaOH. Figure 2 a shows the experimental data points along with the expected titration curve in a confined sample. Injected charge is used instead of volume of added titrant and 91.6, 183.3, and 274.9 mC are required to titrate 25, 50, and 75 mM of NaOH. With an established thin-layer volume (40 μL), the injected charge is easily converted to released hydrogen-ion concentration. Note that spontaneous exchange of hydrogen ions with sodium ions at high pH must be avoided. The assessment of NaOH samples therefore requires membranes of adequate selectivity, which can be confirmed potentiometrically (Nernstian electrode slopes).

In a second example, the analysis of the diprotic weak base Na_2CO_3 ($pK_{a1} = 6.3$ and $pK_{a2} = 10.3$) is demonstrated with the methodology. Two equally spaced equivalence points are observed, confirming the localized titration of the carbonate and bicarbonate species (Figure 2 b). A roughly double amount of proton charge is required for titrating bicarbonate compared to carbonate (for 10 mM of Na_2CO_3, 48.2 mC is used for the first and 94.8 mC for the second endpoint). Three other concentrations of Na_2CO_3 (20, 30, and 40 mM) were also analyzed and showed the expected results.

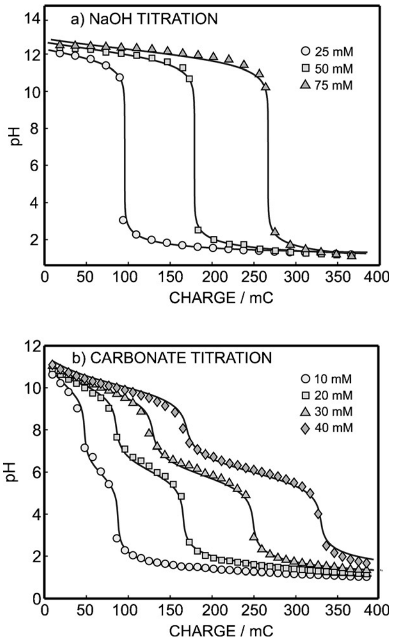

Figure 2. Thin-layer electrochemical titration of solutions containing a) NaOH and b) Na_2CO_3 at the indicated concentrations.

The amount of bicarbonate (and to a minor extent carbonate) in natural water sources such as rivers, lakes, and oceans has a noticeable effect on pH, water hardness, and indirectly in other processes that trigger ecosystem growth.[12] Total alkalinity (sum of titratable carbonate and hydroxide concentrations) is an important assessable parameter of natural ecosystems.[13]

The usefulness of the proposed concept was demonstrated here with the direct alkalinity detection in an unmodified natural river sample (Arve river in Geneva). In contrast, previous work[14] using proton release by an electrochemical splitting of water resulted in a poorly defined titrimetric analysis in synthetic samples (5 mM acetic acid, HCl mixture). Presumably, nonspecific oxidation/reduction of sample components, generation of undesired gases (O_2 and H_2) and the use of metallic electrodes (i.e., passivation) incompatible with biomedical or environmental samples, imposed important practical limitations on this otherwise elegant concept.

Figure 3 shows the titration curve as a function of injected charge. The major titratable species is bicarbonate at an observed concentration of 23.1 mM (92.6 mC), calculated as the maximum of the first derivative of (pH/charge) versus injected charge. This value was reasonably confirmed by volumetric titration (23.6 ± 0.2) mM. It is anticipated that the microfabrication of a more precise and thinner layer may further reduce the uncertainty (from 2 % to at least 1 %) and the response time of each titration down to seconds. The concept introduced here suggests that the electrochemical thin-layer proton pump is capable of assessing parameters in situ without sampling, standardization, and volumetric analysis. It is anticipated that this concept may serve as the

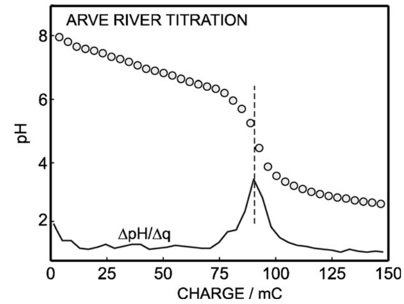

Figure 3. Titration of an unmodified Arve river sample by thin-layer electrochemistry (circles), along with the first derivative to visualize the endpoint.

fundamental basis for a new generation of calibration-free chemical sensors in a variety of applications.

Experimental Section

Potassium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (KTFPB), tetrakis(4-chlorophenyl)borate tetradodecylammonium salt (ETH 500), chromoionophore I, 2-nitrophenyloctylether (o-NPOE), tris-(hydroxymethyl)aminomethane (Tris), acetic acid, sodium acetate, sodium chloride, sodium hydroxide (1 M), and tetrahydrofuran (THF) were purchased from Sigma–Aldrich (analytical grade). M_1 is based on porous polypropylene (PP) membranes (Celgard, 0.237 cm^2 surface area, 25 μm thickness, and kindly provided by Membrane Wuppertal, Germany) and was used as supporting material (see membrane preparation and composition in the Supporting Information). All solutions were prepared in 10 mM of NaCl background electrolyte (note that 1 mM NaCl background gave the same results). River samples show an ionic strength in the range of 4–6 mM The fully automated (NOVA software, Autolab) method consisted of three steps: i) open circuit potential determination for 5 s at a sampling rate of 10 Hz (no current flow through the electrochemical cell), ii) anodic potential pulse at different times (from 30 s to 210 s) at a sampling rate of 500 Hz; iii) simultaneous potentiometric determination with M2.

Keywords: alkalinity · coulometry · proton pump · thin-layer systems · titration

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