Renewable magnetic ion-selective colorimetric microsensors based on surface modified polystyrene beads

Apichai, Sutasinee; Wang, Lu; Grudpan, Kate; Bakker, Eric

How to cite

APICHAI, Sutasinee et al. Renewable magnetic ion-selective colorimetric microsensors based on surface modified polystyrene beads. In: Analytica Chimica Acta, 2020, vol. 1094, p. 136–141. doi: 10.1016/j.aca.2019.10.011

This publication URL: https://archive-ouverte.unige.ch/unige:136735
Publication DOI: 10.1016/j.aca.2019.10.011

Renewable magnetic ion-selective colorimetric microsensors based on surface modified polystyrene beads

Sutasinee Apichai,[a,b,c] *Lu Wang,*[a] *Kate Grudpan,*[b,c] *Eric Bakker*[a]*

[a] Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva, Switzerland
[b] Center of Excellence for Innovation in Analytical Science and Technology, Chiang Mai University, Chiang Mai 50200, Thailand
[c] Department of Chemistry, Faculty of Science, Chiang Mai University, Chiang Mai 50200, Thailand
* e-mail: eric.bakker@unige.ch

Abstract

Magnetic ion-selective colorimetric microspheres based on surface modification of polystyrene beads (0.8 μm diameter) are reported for the first time. The common components of ion-selective optode sensing (chromoionophore, ion-exchanger and ionophore) and magnetic nanoparticles are adsorbed onto the surface of the polystyrene particles using a simple mixed solvent method. The average diameter of the magnetic microspheres is evaluated by dynamic light scattering as 0.79±0.06 μm. The reversible microsensors are circulated by flow and accumulated at a single spot by an applied magnet to become observable by digital camera. Hue signals are extracted from the recorded images to quantify the ratio of protonated and deprotonated form of the chromoionophore, which is the basis for optode response. The resulting magnetic microsensors respond to K^+ with excellent selectivity over the range of 10^{-6} M to 10^{-2} M and a response time of $t_{99} < 2.6 \pm 0.5$ min above 10^{-5} M. The use of solvatochromic dyes as pH independent transducers was not successful in this application~~.~~

Highlights

- Ionophore-based colorimetric sensors contain ionophore, chromoionophore, ion-exchanger, and magnetic nanoparticle on the surface of a polystyrene particle.
- Ion-selective colorimetric microspheres are formed using a simple mixed solvent procedure.
- The reversible microsensors are easily trapped and observed in an automatic flow system.
- The color change (hue value) of the microsensors monitored by a digital camera is used as signal.

Keywords: Ion-selective optical sensor; Microspheres; Colorimetry; Magnetic nanoparticle; Potassium ion, Polystyrene bead

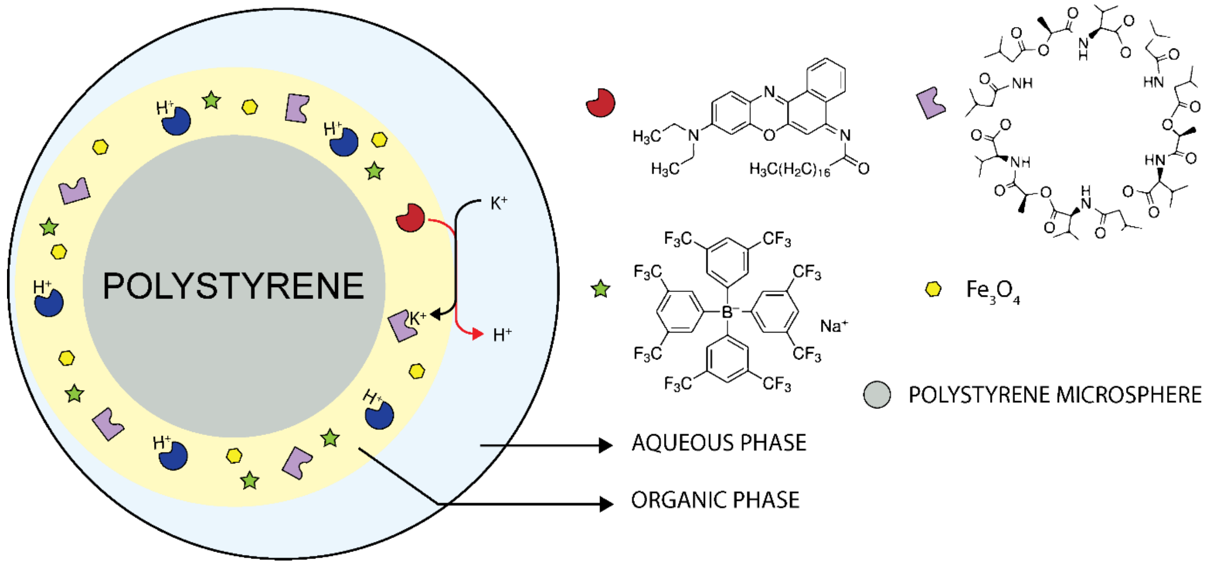
1. *Introduction*

The quantification of ionic species is necessary in many fields, including physiology, biochemical science, and environmental monitoring [1-7]. To achieve this, chemical sensors based on so-called ionophores, lipophilic ion receptors of high selectivity, are today well established. They are most widely used as potentiometric probes but increasingly also as optical sensors [8, 9]. While alternative readouts have recently been introduced [10-15], most ion-selective optode sensors are composed of a polymeric phase and contain the ionophore of choice, a lipophilic indicator (the so-called chromoionophore), and an ion exchanger [16]. Cation-selective optodes function on the basis of extraction equilibria between the analyte ion from the aqueous phase and hydrogen ions from the lipophilic sensing phase. The degree of the protonation of the chromoionophore in the sensing phase is used to determine analyte concentration. It is observable by several techniques, including UV-Vis absorbance and fluorescence spectroscopy, and more recently also by digital imaging techniques to give hue or saturation values [17, 18].

A magnetic separation from the sample after incubation is an attractive approach for colorimetric assays as it allows one to renew the detection chemistry and to additionally reduce spectral interferences arising from sample color and turbidity [18, 19]. Magnetic nanoparticles entrapped in polymer beads have been applied to biological diagnostic [20-24], pharmaceutical [25] and environmental work [21, 26-28] for separation, preconcentration and monitoring.

A number of approaches have been reported to fabricate microparticle-based ion-selective optodes, including the use of precipitation, spray coating, polymerization, sonic droplet casting, and the coating into particle templates [29-31]. Among these, the surface modification of polystyrene particles, a material well established in bioanalytical research [18,244 19], has recently been introduced as potentially attractive and simple method for the realization of optical ion sensors [10].

In this work, we report for the first time on the preparation and characterization of surface modified polystyrene (PS) particles that function as reversible ion selective optodes and that are modified with magnetic nanoparticles. Polystyrene beads containing superparamagnetic nanoparticles respond to an external magnetic field [32] and may therefore be trapped and focused at a desired location by application of an external magnet.



Scheme 1 Illustration of a cross-section of a K^+-selective magnetic microsensor bead and extraction between K^+ in the aqueous phase and H^+ in the bulk of the organic microsphere phase.

2. *Experimental*

Reagents. Magnetic iron oxide nanoparticles suspension, 0.8-1.4% solid material basis, 0.5-0.7% Fe basis (6.5±3.0 nm mean particle size, so-called magnetite particles), Latex beads (polystyrene, 0.8 µm mean particle size by DLS, without azide), potassium ionophore I (L, valinomycin), tetrahydrofuran (THF), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaTFPB), 3-octadecanoylimino-7-(diethylamino)-1,2-benzophenoxazine (Chromoionophore I), bis(2-ethylhexyl) sebacate (DOS), potassium chloride (KCl), calcium chloride $CaCl_2$), lithium chloride (LiCl), and magnesium chloride ($MgCl_2$) and Tris-HCl were obtained from Sigma-Aldrich. Solvatochromic dye ((E)-2-(4-(bis(2-(stearoyloxy)ethyl)amino)styryl)-3-ethylbenzo[d]thiazol-3-ium iodide) was synthesized in our laboratory as reported earlier [33].

Sensor preparation. To prepare the K^+-selective magnetic PS microsensors, 0.6 mg of NaTFPB, 1.0 mg potassium ionophore I and 6 mg of DOS, were dissolved in 800 µL of THF before being mixed with 30 µL of the magnetic iron oxide suspension and 400 µL of Chromoionophore I (0.33 mg Chromoionophore I was dissolved in 2.0 mL of THF) to form a homogeneous solution. 10 µL of commercial PS particle concentrate was diluted to 40 mL in H_2O. 0.5 mL of the mixture was pipetted and injected into 5.0 mL of the diluted PS particle suspension on a vortex with a spinning speed of 1000 r/min. The resulting clear solution was blown with compressed air over the surface for 20 min to remove THF. The K^+-selective magnetic microsensor based on solvatochromic dye (SD) contained 0.2 mg of solvatochromic dye, 0.6 mg of NaTFPB, 1 mg of potassium ionophore, 6 mg of DOS and 30 µL of magnetic iron oxide suspension. The mixture was prepared by dissolving those components in 800 µL of THF. A 125 µL volume of this mixture was then injected into 5.0 mL of the diluted PS particle suspension on a vortex with a spinning speed of 1000 r/min. Finally, the THF was removed by blowing compressed air for 20 min.

Instrumentation and measurement. The magnetic microsensors were attracted by an external magnet onto the inner surface of a flow cell built in house that served as detection zone. 20 µL of the K^+-selective magnetic PS microemulsion emulsion in 10 mL water was pumped through the flow-cell and re-circulated to the same reservoir for 30 min at a flow rate 0.9 mL/min. Subsequently, standard electrolyte solutions in 10 mM Tris-HCl buffer (pH 7.4) were circulated into the flow cell and made to equilibrate with the magnetically trapped microsensors. The resulting color of the microsensors was monitored with a digital camera (Canon EOS 5D Mark III) at an acquisition rate of 1 image every 30 s. For the calibration curve, the hue signals were extracted after automated cropping by Wolfram Mathematica software. The absorbance was measured with a UV-*vis* spectrometer (SPECORD 250 plus, Analytic Jena, AG, Germany) to characterize the selectivity of the K^+-selective magnetic microsensors. The size of the particles was measured on a ZetaSizer Nano ZS (Malvern Instruments) at 25 °C. The size measurements were conducted in dynamic light scattering mode at a 173° scattering angle. The size was obtained from the scattered light intensity using the Stokes-Einstein relationship. Scanning electron microscopic images were obtained under Jeol 6510LV Scanning electron microscope.

3. *Results and Discussion*

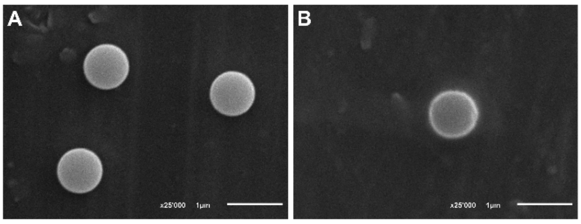


Fig. 1 Scanning electron microscope images of (A) unmodified PS and (B) modified PS for K^+-selective magnetic microspheres in H_2O.

Magnetite nanoparticles were doped with established ion selective optode sensing components (chromoionophore, ion-exchanger and ionophore) together with magnetic nanoparticles in an aqueous PS suspension, see Experimental. This resulted in functional K^+-selective microsphere decorated with sensing components on the outer polystyrene particle surface (Scheme 1) [10]. The sizes of sensors and adsorption of the ion selective optode components on the surface of PS beads were confirmed by both Scanning Electron Microscopy (SEM, Fig. 1) and Dynamic Light Scattering (DLS). DLS shows the diameters of the modified PS for K^+-selective magnetic microspheres and that of the unmodified PS beads were 0.79±0.06 μm and 0.86±0.02 μm respectively (Standard deviations were calculated from triplicates).

The magnetite nanoparticles embedded into the microparticle surface magnetized the K^+-selective microspheres, making it possible to remove them from suspension by an external magnet. Figure 2 shows that the blue magnetic microsensors can be efficiently separated from the aqueous phase and physically trapped onto the interior wall of the solution vial.

The colorimetric magnetic microsensor suspension was made to recirculate in a flow-cell by peristaltic pumping and subsequently trapped by the external magnetic field in the desired field of view (Fig. 3A). The magnetic microsensors were held onto the inner surface of the flow-cell wall and could be used without preconditioning of sensor. The process of magnetic microsensor accumulation was monitored by recording sequential images (Fig. 3B), where the progression of deeper color is clearly visible. In this work, hue value is used as the analytical signal. Ideally it would become independent of trapped microsensor quantity. Indeed, Fig. 3C shows that the corresponding hue value change for this accumulation experiment stabilize rapidly (3 min), indicating the time required before quantification can be performed. In contrast, the saturation value also shown in Fig. 3C takes about 30 min to stabilize, indicating the complete accumulation of the recirculating microspheres.

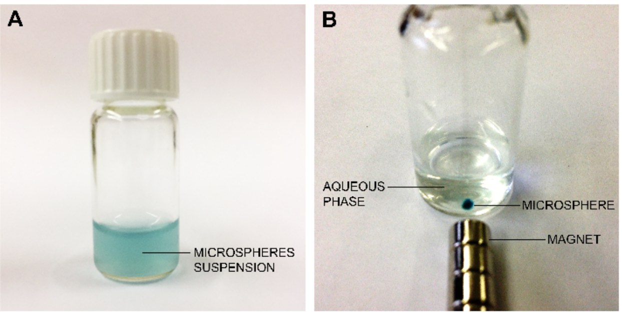


Fig. 2. Pictures of a microsphere suspension (A) before and (B) after trapping onto the inner wall of the vial by an applied magnetic field.

The response mechanism of the magnetic microsensors is the one based on equilibrium-based ionophore-based optical sensors (IBOS). Here, the ion exchange equilibrium can be expressed as Eq. (1), where (org) and (aq) are species in the magnetic microsensors and the sample phase, respectively.

$$\mathrm{IndH^+(org) + K^+(aq) + L(org) + R^-(org) \rightleftharpoons Ind(org) + LK^+(org) + R^-(org) + H^+(aq)} \qquad (1)$$

Before K^+ ion solution is pumped into the flow-cell, the microsensors contain predominantly hydrogen ions, protonated the chromoionophore ($IndH^+$) in the organic phase and resulting in a deep blue color of the magnetic microsensors. With increasing concentration of K^+ in solution, this ion is allowed to bind to valinomycin to form a stable complex (LK^+). The magnetic microsensors now express the red color of the deprotonated chromoionophore (Ind). One image was recorded every 30 s and the hue value of the sensor area extracted by software. Fig. 4A and 4B show the images and the hue values of the magnetic microsensors when exposed to increasing potassium ion concentrations.

The response times to 10^{-5}-10^{-3} M potassium ion concentrations (calculated as t_{99} values) was found to be less than 2.6±0.5 min. At higher potassium ion concentrations ($>10^{-2}$ M) the corresponding response time is <1.8±0.3 min. The signal was found to be fully reversible after exposure to potassium samples by continuously flowing potassium-free solution into the flow-cell. After exposure to 10^{-6}-10^{-4} M potassium, less than 5 min was required to reach the initial blue color while more than 5 min was needed for higher concentrations. Fig. 4C demonstrates the reproducibility of the K^+-selective magnetic microsensors to 0.1 mM K^+ concentrations and back to background buffer. The resulting magnetic microsensors responds to K^+ with excellent sensitivity in the range of 10^{-6} M to 10^{-2} M, as shown in Fig. 5. The sigmoidal response curve is as

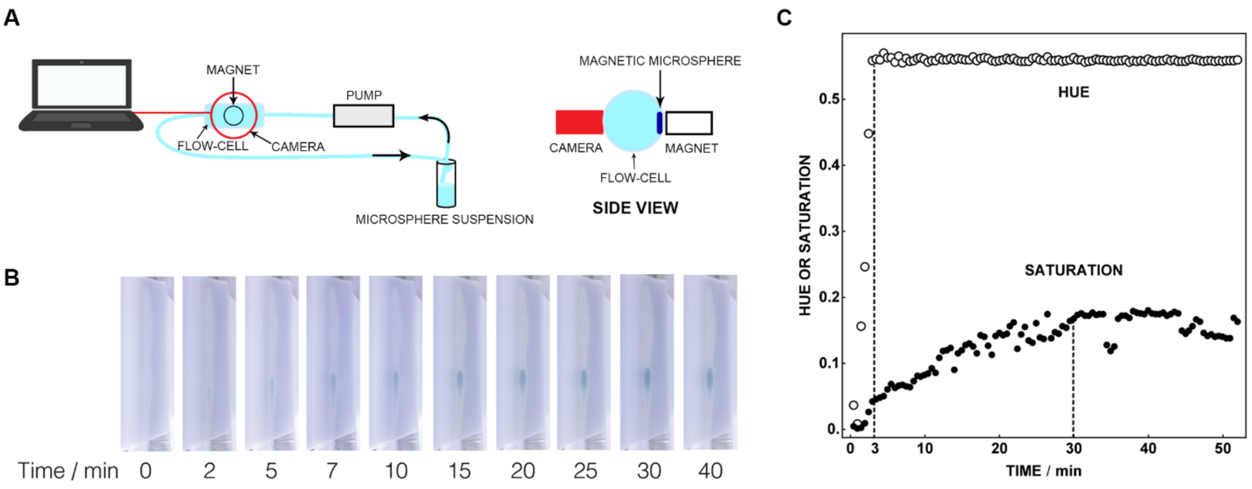


Fig. 3 (A) Setup for accumulation of magnetic microspheres on the inner surface of the flow cell wall, (B) recorded images and (C) hue and saturation values of the magnetic microspheres during accumulation.

expected for this class of sensors. The signal stability for a magnetically trapped sensing area was not extensively tested but was found to high for at least 21 sample injections. The LOD (limit of detection) is estimated as 2.5×10^{-5} M from a limiting sensitivity (slope of half the maximum value) [16]. The results in Figure 5 show that the common ions (Na^+, Li^+, Mg^{2+}, and Ca^{2+}) do not interfere in the activity range for K^+ and that they interfere only at very high concentrations. The horizontal distances of the logarithmic ion responses between potassium ion and other metal ions (Na^+, Li^+, Mg^{2+}, and Ca^{2+}) indicate logarithmic selectivity coefficients of about –3.3, –3.5, –4.4, –5.2, respectively, with standard deviations shown as error bars in Fig. 5.

The response and selectivity of K^+-selective magnetic microsensors was also confirmed by spectrophotometry. Experimental data points (error bars are standard deviations) and the theoretical dashed lines in Fig. 6 give the sensor response to separate solutions containing the indicated metal ions. Note that absorbance measurements show spectral interference from light scattering, which is

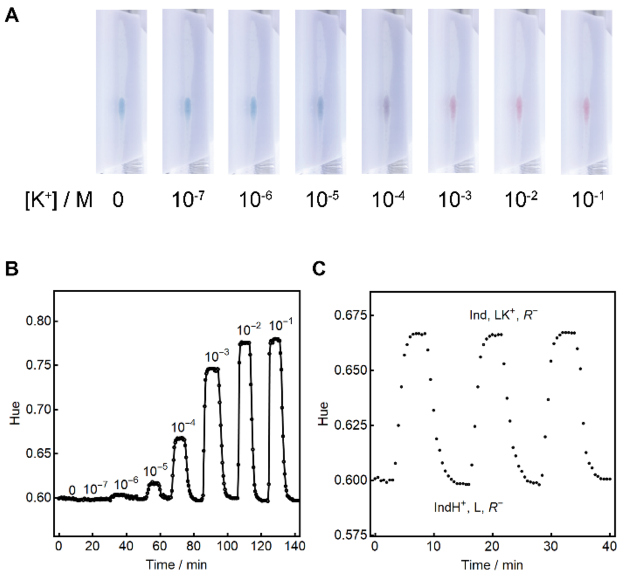


Fig. 4 (A) Recorded images and (B) hue value response of the K^+-selective magnetic microsensors for different concentrations of KCl at pH 7.4. Reversibility is demonstrated by an intermittent returning to potassium-free buffer solution background. (C) Reproducibility of the K^+-selective magnetic microsensors to 0.1 mM K^+ concentration at

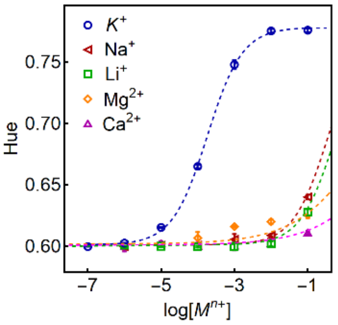


Fig. 5 Calibration curve for the K^+-selective magnetic microsensors on the basis of hue values. Error bars are standard deviations from triplicates and dashed curves are to guide the eye.

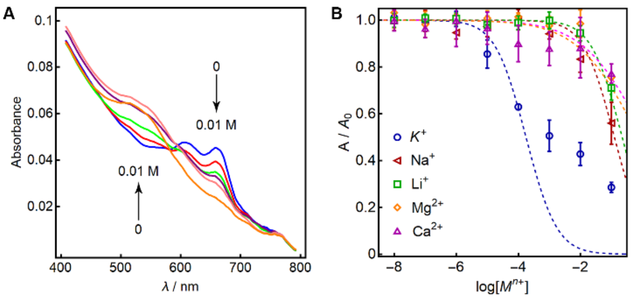


Fig. 6 (A) Absorbance change for the K^+-selective magnetic microspheres in H_2O with different concentrations of KCl at pH 7.4. (B) Interferences of different cations to the K^+-selective magnetic microsensors evaluated in absorbance mode at 663 nm (pH 7.4). Dashed curves are theoretical for traditional ion-selective bulk optodes.

absent with the colorimetric imaging otherwise used in this work (Figure 5). The corresponding logarithmic selectivity coefficients over Na^+, Li^+, Mg^{2+}, and Ca^{2+} were found as about –2.8, –3.1, –3.7, –3.8, and are somewhat inferior to the data in Figure 5. Quantitation by spectrophotometry is somewhat difficult because of the mentioned light scattering that distorts the spectra.

The application of the K^+-selective magnetic microsensors to practical sample measurement is intended to water samples such as drinking water, environmental water and human serum [34, 35]. Moreover, the renewable magnetic ion-selective colorimetric microsensors can be easily modified by using appropriate ionophores to detect other ions such as Na^+, Ca^{2+}, Pb^{2+}, Ag^{2+} *etc.* [7, 13, 35-37]. In all these cases, the samples need to be pretreated to avoid uncertainties of the sample pH to influence the results. Ion optodes have recently been developed to respond independently of sample pH by using solvatochromic dyes (SDs) instead of H^+-chromoionophores [38-40]. Here, the signal transduction is based on the exchange between the analyte cation in sample and the cationic SD in the sensing phase. More recently, hydrophobic SDs were introduced to achieve a localized ion-exchange at the sensor surface. In this approach, loss of SD is suppressed owing to its more hydrophobic tail anchored to the organic sensing phase while only the positive chromophore charge is released into the aqueous phase [29, 33]. Here, the surface of PS was modified with solvatochromic dye, ion-exchanger, ionophore, and magnetic nanoparticle for reversible pH-independent ion-selective sensors. The solvatochromic dye ((E)-2-(4-(bis(2-(stearoyloxy)ethyl) amino)styryl)-3-ethylbenzo[d]thiazol-3-ium iodide, SD 4) was synthesized as reported [33]. Unfortunately, a brief study showed that the SD-based sensor is indeed pH independent, unlike the systems based CH I described above that are pH cross-responsive. However, for sample concentrations $[K^+]>10^{-3}$ M, an irreversible sensing signal owing to aggregation was observed (Figure 7). The brown color is ascribed to the iron oxide, which is consistent with SD expelled from the sensor phase bulk. However, aggregation drastically reduces the available surface area that alters the local ion-exchange equilibrium. This effect may be caused by a sudden decrease of surface charge at high analyte concentration [41]. This hypothesis was confirmed by zeta potential measurements where an important decrease of surface charge at higher electrolyte concentrations was observed (Fig. 8). In principle, this may be overcome by surface functionalization or the use of adequate surfactant, but this was not further explored here.

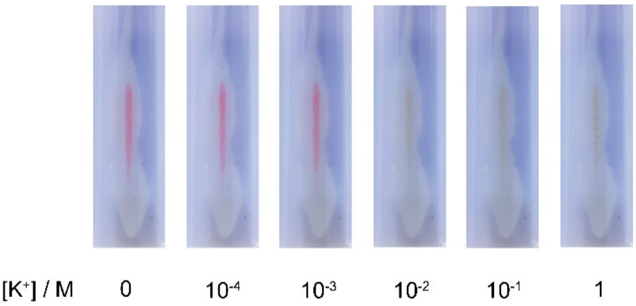


Fig. 7 Recorded images of the pH-independent K^+-selective magnetic microsensors for different concentrations of KCl, resulting in undesired aggregation.

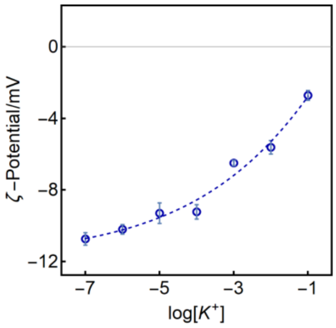


Fig. 8 Zeta potential change of the K -selective magnetic microsensors as a function of KCl concentration in 10 mM Tris-HCl pH 7.4. The dashed curve is to guide the eye.

4. *Conclusions*

It was shown that reversible ion-selective optical microsensors can be easily prepared by using commercial PS beads as a template to dope their outer surface with established ion selective optode components together with magnetite nanoparticles. The resulting K^+-selective magnetic microsensors respond to K^+ with adequate selectivity, reproducibility and a suitable response time, and give the expected sigmoidal response curve for such optodes. Importantly, the accumulation of the sensing beads onto the detection zone and subsequent characterization of optode response were realized in a flow system. The observation with an imaging camera eliminates the scattering interference observed with traditional absorbance measurements. Unfortunately, pH-independent ion-selective microsensors based on solvatochromic dyes gave unstable particle aggregates under the conditions used here. Overall, magnetic separation may be useful to achieve lower detection limits by a more efficient harvesting of the analyte ion, and might also offer advantages in physically separating the optode beads from the sample, thereby reducing matrix effects. These are topics for further study.

5. *Acknowledgment*

The authors thank the Swiss National Science Foundation for supporting this research and Jérôme Bosset, Christoph Ruediger Bauer and the Bioimaging Center of University of Geneva for the scanning electron microscopy. K.G. and S.A. thank the Thailand Research Fund (TRF) through the Research and Researchers for Industries (RRi) (Grant No. PHD56l0021) to support the stay of S.A. in Geneva.

6. *References*

[1] R.D. Johnson, L.G. Bachas, Ionophore-based ion-selective potentiometric and optical sensors, Anal. Bioanal. Chem. 376 (2003) 328-341.

[2] H.A. Clark, M. Hoyer, M.A. Philbert, R. Kopelman, Optical nanosensors for chemical analysis inside single living cells. 1. Fabrication, characterization, and methods for intracellular delivery of PEBBLE sensors, Anal. Chem. 71 (1999) 4831-4836.

[3] X. Xie, E. Bakker, Ion selective optodes: from the bulk to the nanoscale, Anal. Bioanal. Chem. 407 (2015) 3899-3910.

[4] E.V. Batrakova, A.V. Kabanov, Pluronic block copolymers: Evolution of drug delivery concept from inert nanocarriers to biological response modifiers, J. Control. Release 130 (2008) 98-106.

[5] J. Yin, Y. Hu, J. Yoon, Fluorescent probes and bioimaging: alkali metals, alkaline earth metals and pH, Chem. Soc. Rev. 44 (2015) 4619-4644.

[6] W.H. Tan, Z.Y. Shi, S. Smith, D. Birnbaum, R. Kopelman, Submicrometer Intracellular Chemical Optical Fiber Sensors, Science 258 (1992) 778-781.

[7] M. Lerchi, F. Orsini, Z. Cimerman, E. Pretsch, D.A. Chowdhury, S. Kamata, Selective optical sensing of silver ions in drinking water, Anal. Chem. 68 (1996) 3210-3214.

[8] S. Dai, Q. Ye, E. Wang, M.E. Meyerhoff, Optical detection of polycations via polymer film-modified microtiter plates: response mechanism and bioanalytical applications, Anal. Chem. 72 (2000) 3142-3149.

[9] A. Kisiel, K. Klucinska, Z. Glebicka, M. Gniadek, K. Maksymiuk, A. Michalska, Alternating polymer micelle nanospheres for optical sensing, Analyst 139 (2014) 2515-2524.

[10] X. Xie, G.A. Crespo, J. Zhai, I. Szilágyi, E. Bakker, Potassium-selective optical microsensors based on surface modified polystyrene microspheres, Chem. Commun. 50 (2014) 4592-4595.

[11] Y. Soda, D. Citterio, E. Bakker, Equipment-Free Detection of K^+ on Microfluidic Paper-Based Analytical Devices Based on Exhaustive Replacement with Ionic Dye in Ion-selective Capillary Sensors, Acs Sens. 4 (2019) 670-677.

[12] X. Wang, M. Mahoney, M.E. Meyerhoff, Inkjet-Printed Paper-Based Colorimetric Polyion Sensor Using a Smartphone as a Detector, Anal. Chem. 89 (2017) 12334-12341.

[13] D. Prabhakaran, H. Nanjo, H. Matsunaga, Naked eye sensor on polyvinyl chloride platform of chromo-ionophore molecular assemblies: A smart way for the colorimetric sensing of toxic metal ions, Anal. Chim. Acta 601 (2007) 108-117.

[14] H.R. He, H. Li, G. Mohr, B. Kovacs, T. Werner, O.S. Wolfbeis, Novel Type of Ion-Selective Fluorosensor Based on the Inner Filter Effect - an Optrode for Potassium, Anal. Chem. 65 (1993) 123-127.

[15] X.D. Wang, O.S. Wolfbeis, Fiber-Optic Chemical Sensors and Biosensors (2013-2015), Anal. Chem. 88 (2016) 203-227.

[16] E. Bakker, P. Bühlmann, E. Pretsch, Carrier-based ion-selective electrodes and bulk optodes. 1. General characteristics, Chem. Rev. 97 (1997) 3083-3132.

[17] K. Cantrell, M.M. Erenas, I. de Orbe-Payá, L.F. Capitán-Vallvey, Use of the hue parameter of the hue, saturation, value color space as a quantitative analytical parameter for bitonal optical sensors, Anal. Chem. 82 (2010) 531-542.

[18] M. Zhao, L. Josephson, Y. Tang, R. Weissleder, Magnetic sensors for protease assays, Angew. Chem. 42 (2003) 1375-1378.

[19] I. Koh, L. Josephson, Magnetic Nanoparticle Sensors, Sensors 9 (2009) 8130-8145.

[20] A.W. Zaibudeen, J. Philip, Magnetic nanofluid based non-enzymatic sensor for urea detection, Sens. Actuat. B-Chem. 255 (2017).

[21] G. Giakisikli, A.N. Anthemidis, Magnetic materials as sorbents for metal/metalloid preconcentration and/or separation. A review, Anal. Chim. Acta 789 (2013) 1-16.

[22] R.S. Karumanchi, S.N. Doddamane, C. Sampangi, P.W. Todd, Field-assisted extraction of cells, particles and macromolecules, Trends Biotechnol. 20 (2002) 72-78.

[23] J.B. Haun, T.J. Yoon, H. Lee, R. Weissleder, Magnetic nanoparticle biosensors, Wires. Nanomed. Nanobi. 2 (2010) 291-304.

[24] Y. Zhang, D.J. Zhou, Magnetic particle-based ultrasensitive biosensors for diagnostics, Expert Rev. Mol. Diagn. 12 (2012) 565-571.

[25] C.S. Brazel, N.A. Peppas, Modeling of drug release from swellable polymers, Eur. J. Pharm. Biopharm. 49 (2000) 47-58.

[26] I. Larraza, M. López-Gónzalez, T. Corrales, G. Marcelo, Hybrid materials: magnetite–polyethylenimine–montmorillonite, as magnetic adsorbents for Cr (VI) water treatment, J. Colloid Interface Sci. 385 (2012) 24-33.

[27] O. Philippova, A. Barabanova, V. Molchanov, A. Khokhlov, Magnetic polymer beads: recent trends and developments in synthetic design and applications, Eur. Polym. J. 47 (2011) 542-559.

[28] Z. Lin, Y. Zhang, Y. Chen, H. Qian, Extraction and recycling utilization of metal ions (Cu^{2+}, Co^{2+} and Ni^{2+}) with magnetic polymer beads, Chem. Eng. Commun. 200 (2012) 104-112.

[29] L. Wang, X. Xie, J. Zhai, E. Bakker, Reversible pH-independent optical potassium sensor with lipophilic solvatochromic dye transducer on surface modified microporous nylon, Chem. Commun. 52 (2016) 14254-14257.

[30] M. Bamsey, A. Berinstain, M. Dixon, Development of a potassium-selective optode for hydroponic nutrient solution monitoring, Anal. Chim. Acta 737 (2012) 72-82.

[31] O.S. Wolfbeis, M. Schäferling, A. Dürkop, Reversible optical sensor membrane for hydrogen peroxide using an immobilized fluorescent probe, and its application to a glucose biosensor, Microchim. Acta 143 (2003) 221-227.

[32] I. Csetneki, M.K. Faix, A. Szilágyi, A.L. Kovacs, Z. Nemeth, M. Zrinyi, Preparation of magnetic polystyrene latex via the miniemulsion polymerization technique, J. Polym. Sci. 42 (2004) 4802-4808.

[33] X. Xie, I. Szilágyi, J. Zhai, L. Wang, E. Bakker, Ion-Selective Optical Nanosensors Based on Solvatochromic

Dyes of Different Lipophilicity: From Bulk Partitioning to Interfacial Accumulation, ACS Sens. 1 (2016) 516-520.

[34] A. Lapresta-Fernández, R. Huertas, M. Melgosa, L.F. Capitán-Vallvey, Colourimetric characterisation of disposable optical sensors from spectroradiometric measurements, Anal. Bioanal. Chem. 393 (2009) 1361-1366.

[35] H. Hideaki, M. Nami, W. Kazuhiko, N. Eriko, Y. Noriko, S. Koji, Ion sensing film optodes: disposable ion sensing probes for the determination of Na^+, K^+, Ca^{2+} and Cl^- concentrations in serum, Sens. Actuat. B-Chem. 29 (1995) 378-385.

[36] K. Seiler, K. Wang, E. Bakker, W.E. Morf, B. Rusterholz, U.E. Spichiger, W. Simon, Characterization of sodium-selective optode membranes based on neutral ionophores and assay of sodium in plasma, Clin. Chem. 37 (1991) 1350.

[37] H. Shibata, Y. Hiruta, D. Citterio, Fully inkjet-printed distance-based paper microfluidic devices for colorimetric calcium determination using ion-selective optodes, Analyst 144 (2019) 1178-1186.

[38] X. Xie, J. Zhai, E. Bakker, Potentiometric Response from Ion-Selective Nanospheres with Voltage-Sensitive Dyes, J. Am. Chem. Soc. 136 (2014) 16465-16468.

[39] I. Murkovic, A. Lobnik, G.J. Mohr, O.S. Wolfbeis, Fluorescent potential-sensitive dyes for use in solid state sensors for potassium ion, Anal. Chim. Acta 334 (1996) 125-132.

[40] O.S. Wolfbeis, Fluorescence-Based Ion Sensing Using Potential-Sensitive Dyes, Sens. Actuat. B-Chem. 29 (1995) 140-147.

[41] L. Wang, S. Sadler, T. Cao, X. Xie, J.M. Von Filseck, E. Bakker, Simplified Fabrication for Ion-Selective Optical Emulsion Sensor with Hydrophobic Solvatochromic Dye Transducer: A Cautionary Tale, Anal. Chem. 91 (2019) 8973-8978.