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## Potentiometric sensing utilizing paper-based microfluidic sampling

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### Abstract

A new approach to potentiometric sensing utilizing paper-based microfluidic sampling is studied in this work. A solid-contact ion-selective electrode and a solid-contact reference electrode are pressed against a filter paper into which the sample solution is absorbed. The filter paper acts simultaneously as a sampling unit and as a sample container during potentiometric sensing. The paper substrates containing standard and sample solutions are disposable, while the sensors are used multiple times. The analytical method presented here opens new possibilities for economically and ecologically sound measurements of ions in various samples.

### Introduction

Paper is an inexpensive and readily available material which has become an interesting substrate for fabricating low-cost and flexible electronics.<sup>1-2</sup> Furthermore, the ability of paper to transport liquids via capillary forces has been utilized for the development of microfluidic

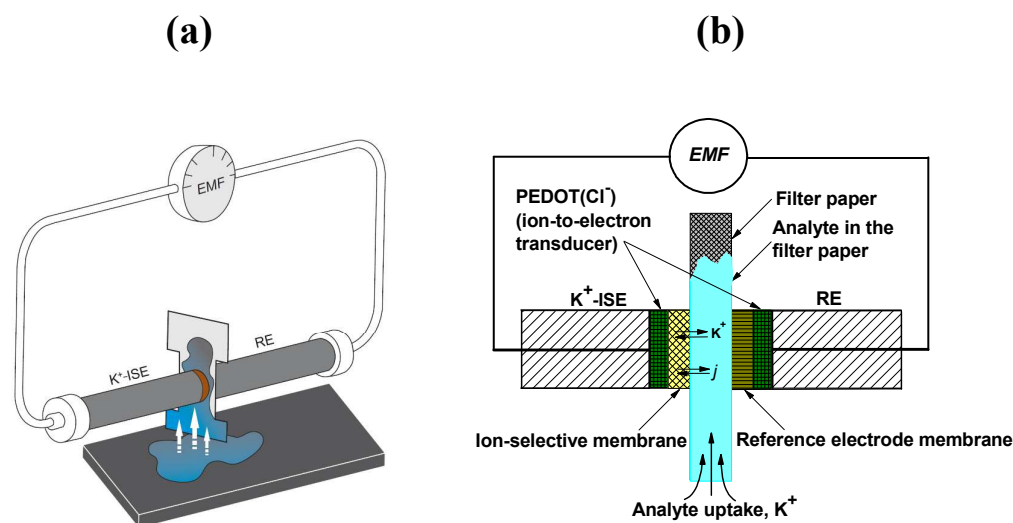
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3 paper-based analytical devices ( $\mu$ PADs).<sup>3-13</sup> The construction of  $\mu$ PADs commonly involves  
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5 patterning of the paper to form channels with hydrophobic walls that guide liquid transport in  
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7 the paper to the regions where detection takes place.<sup>3-5</sup> In addition to optical detection  
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9 methods, also electrochemical methods have been applied to paper-based microfluidic  
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11 devices.<sup>6-11</sup> However, among the electrochemical methods that have been applied so far in  
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13 microfluidic paper-based devices, very few are based on potentiometry.<sup>14</sup>  
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17 The simplicity of potentiometry, together with the possibility to fabricate ion-selective  
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19 electrodes (ISEs) in small sizes, create an opportunity to perform selective and low cost  
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21 analysis.<sup>15-17</sup> Among the different types of ISEs, the solid-contact design is attractive as it  
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23 gives durable ISEs that are relatively easy to maintain and use.<sup>17-22</sup> Combining solid-contact  
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25 ISEs with a solid-contact reference electrode can give rise to powerful analytical devices.<sup>23,24</sup>  
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27 Application of all-solid-state electrodes together with paper-based microfluidic sampling may  
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29 greatly simplify the analytical procedure, because the paper itself is used simultaneously as  
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31 sample transport medium and sample container (electrochemical cell). Additionally, paper-  
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33 based sampling may prevent larger particles from reaching the sensor surface, depending on  
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35 the pore size of the paper. For example, microfluidic paper-based sampling has been used to  
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37 separate red blood cells from plasma in the analysis of whole blood.<sup>25</sup>  
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43 In the present work paper-based microfluidic sampling using ordinary filter paper is employed  
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45 for the potentiometric detection of ions in small volumes. A solid-contact ISE and solid-  
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47 contact reference electrode are pressed against a disposable paper substrate acting as sampling  
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49 unit and sample container. The present work provides proof of concept for potentiometric  
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51 sensing utilizing paper-based microfluidic sampling by using a solid-contact  $K^+$  ion-selective  
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53 electrode and a solid-contact reference electrode to determine the concentration (activity) of  
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55  $K^+$  ions in samples absorbed into ordinary filter paper.  
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## Experimental

Solid-contact  $K^+$ -ISEs were fabricated by using poly(3,4-ethylenedioxythiophene) (PEDOT) as ion-to-electron transducer and plasticized PVC (containing valinomycin as ionophore) as ion-selective membrane, as described earlier.<sup>26</sup> The solid-contact reference electrode (SC-RE) was constructed in an analogous manner by using a non-selective plasticized PVC membrane containing tetrabutylammonium tetrabutylborate (TBA-TBB).<sup>23</sup> The potentiometric cell utilizing paper-based sampling is shown schematically in Fig. 1. The upper part of the filter paper was positioned between the  $K^+$ -ISE and the SC-RE electrodes and the lower part of the filter paper was in contact with the sample solution. The sample solution was then transported via capillary forces into the pores of the filter paper to the region in between the electrodes, thereby closing the electrical circuit. Further experimental details are available as electronic supplementary information.

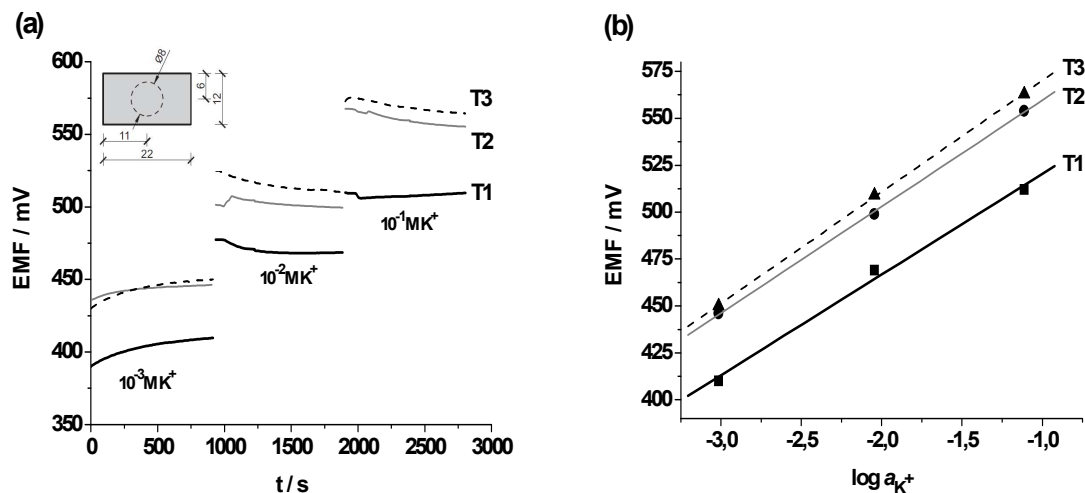


**Fig. 1.** Illustration of the potentiometric setup utilizing paper-based sampling: (a) general view, (b) close up of the electrodes and the cross-section of filter paper.

## Results and discussion

Before utilizing paper-based sampling, the potentiometric response of  $K^+$ -ISEs was investigated in a conventional set up, with KCl solutions ranging from  $10^{-1}$  M to  $10^{-3}$  M. After confirming that the electrodes had a close to Nernstian response (Slope  $\approx 57.0$  mV dec $^{-1}$ ) in the concentration range studied, the same electrodes were then pressed against the filter paper (in contact with the same KCl solutions) as shown in Fig. 1. The KCl solution moved upwards via capillary forces to the electrode contact area, and the potentiometric response of the  $K^+$ -ISE vs. SC-RE was attained. Fig. 2a shows the dynamic response of the  $K^+$ -ISE using three types of filter papers of shape B shown in Fig. S1 (in contact with  $10^{-1}$  –  $10^{-3}$  M KCl). The corresponding calibration curves are shown in Fig. 2b. During measurements, each filter paper was in constant contact with 15 mL of solution. The potentiometric measurement was run for 900 s in each solution (Fig. 2a). For all types of filter papers tested an initial potential drift was followed by relatively stable potentials in each solution. The SC-RE based on plasticized PVC containing TBA-TBB was previously found to have a relatively long response time (ca. 300 s).<sup>23</sup> To allow sufficient time for equilibration, the calibration curves were plotted from the potential values sampled after 900 s in each solution.

For the filter papers (shape B in Fig. S1) of type T1 (pore size = 12–25  $\mu$ m), T2 (pore size = 4–12  $\mu$ m) and T3 (pore size = 2  $\mu$ m) the calibration slopes were close to Nernstian (T1: 53.6, T2: 56.7 and T3: 59.4 mV dec $^{-1}$ ). For the filter papers (shape A in Fig. S1) of type T1 and T2 the calibration slopes were also close to Nernstian (T1: 55.2 and T2: 58.3 mV dec $^{-1}$ ) while a super-Nernstian response was obtained (67.8 mV dec $^{-1}$ ) for filter paper type T3 (results not shown). In all cases the linear fit was satisfactory,  $r^2 > 0.996$ .



**Fig. 2.** Potentiometric response of  $K^+$ -ISE utilizing all filter paper types (T1, T2, T3) in shape B (Fig. S1) as the sampling unit: (a) dynamic response at  $10^{-3} - 10^{-1}$  M  $K^+$ , (b) calibration curves after 900 s measurement time in each solution.

The influence of the measurement time was studied by obtaining the slope and the potential drift of the  $K^+$ -ISEs (vs. SC-RE) after various times (300, 450, 600 and 900 s). The drifts of potential were calculated in several time intervals: 300-450, 450-600, and 600-900 s. Results were calculated from three consecutive measurements and are presented in Table 1.

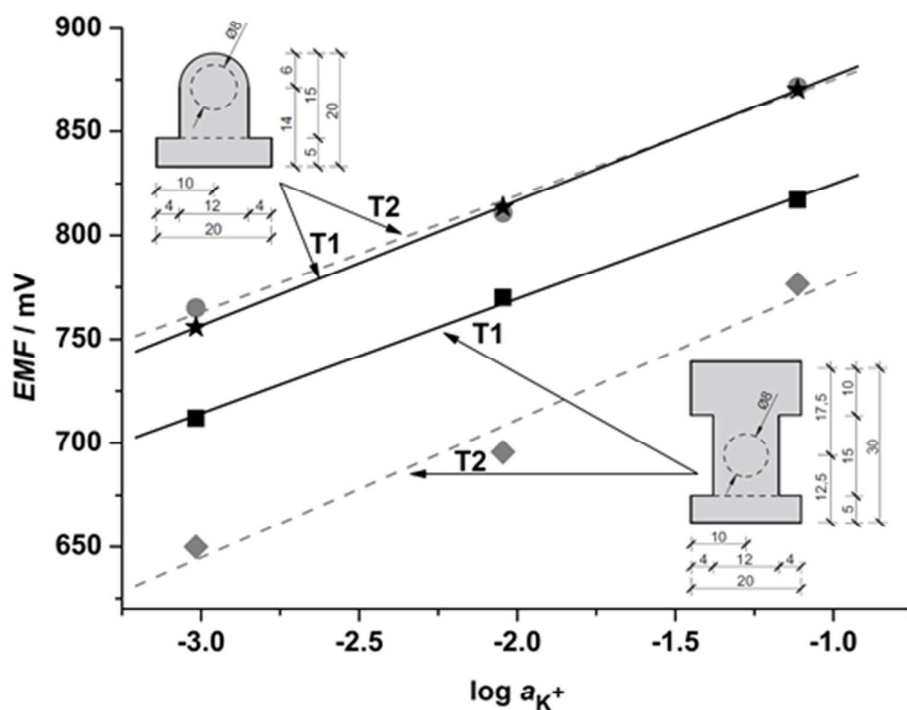
**Table 1.** The slope and the drift after different time intervals during the potentiometric measurement for filter papers of shape B (Figure 1).

Time / s	Filter paper, T1	Filter paper, T2	Filter paper, T3
	Slope / $mV \text{ dec}^{-1}$		
300	$53.0 \pm 6.8$	$60.1 \pm 5.9$	$65.1 \pm 9.1$
450	$53.7 \pm 3.6$	$61.1 \pm 4.6$	$65.6 \pm 5.4$
600	$54.3 \pm 2.4$	$61.4 \pm 4.2$	$64.0 \pm 6.2$
900	$54.7 \pm 2.1$	$61.4 \pm 4.2$	$63.1 \pm 5.8$
	Drift / $mV \text{ s}^{-1}$		
300-450	0.019	0.019	0.019
450-600	0.012	0.012	0.017
600-900	0.008	0.007	0.008

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3 The slopes after 300-900 s for all types of the applied filter papers were relatively close to  
4 Nernstian, but there is a significant increase in slope with decrease in pore size of the filter  
5 paper (Table 1). This result indicates that the filter paper affects the ionic equilibria and  
6 potential formation at the electrode/sample interface. This is a crucial point to consider in  
7 more detail upon further development of microfluidic paper-based sampling connected with  
8 potentiometric sensing.  
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11 Overall, there was a clear decrease in the potential drift with increasing measurement time  
12 (Table 1). The potential drift between 600 and 900 s for all three types of filter paper were  
13 smaller than  $0.01 \text{ mV s}^{-1}$ , while between 450 s and 600 s the drift was in the range  $0.01\text{--}0.02$   
14  $\text{mV s}^{-1}$ . Therefore, a measurement time of 600 s was deemed necessary. The super-Nernstian  
15 response observed for filter paper T3 does not necessarily limit its applicability in  
16 potentiometric determination of ions. However, in this communication, only filter paper types  
17 T1 and T2 were studied further to illustrate the possibilities offered by potentiometric sensing  
18 utilizing paper-based microfluidic sampling.  
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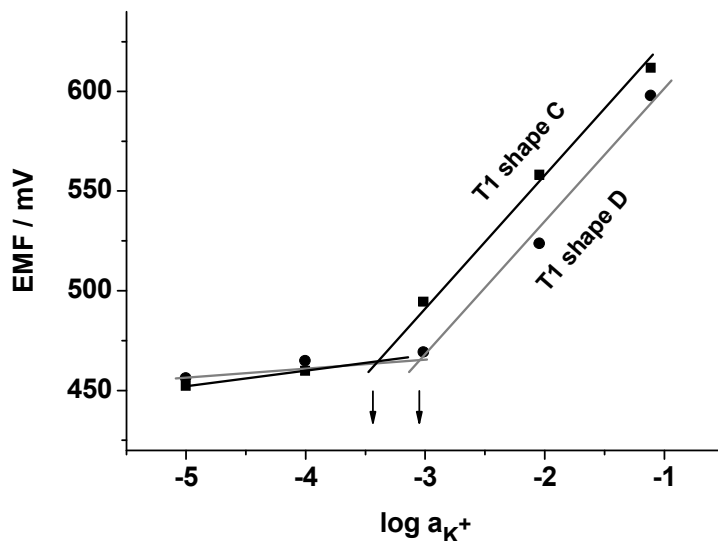
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21 Two alternative shapes of the filter papers were introduced and studied as well (shapes C and  
22 D in Fig. S1). In both cases the main body of the filter paper ( $12 \times 15 \text{ mm}^2$ ) was expanded in  
23 the lower part by a rectangular area ( $20 \times 5 \text{ mm}^2$ ), which increases the area of the filter paper  
24 that is in contact with the sample solution. On the other hand, in order to investigate whether  
25 the upper part of the filter paper may influence the analyte distribution when the paper was  
26 placed vertically, shape C was extended with a rectangular area ( $20 \times 10 \text{ mm}^2$ ) at the top while  
27 shape D was shortened (Fig. S1). The volume of solution which can be accommodated by the  
28 shapes C and D was measured by weighting the filter paper before and after the measurement.  
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30 It was found that less than  $200 \text{ }\mu\text{L}$  of the sample solution was taken up by the filter papers C  
31 and D. Therefore, in the further studies, only  $200 \text{ }\mu\text{L}$  calibration solutions were used to  
32 investigate the potentiometric response of  $\text{K}^+$ -ISEs.  
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**Fig. 3.** Calibration curves of  $K^+$ -ISE utilizing filter paper shape C and D (Fig. S1) types T1 and T2.

In Fig. 3, the calibration curves of  $K^+$ -ISEs (vs. SC-RE) taken after 600 s are shown for filter papers T1 and T2 with shapes C and D. The obtained potentiometric response for  $K^+$ -ISE using filter paper T1, shapes C and D were 55.2 and 56.0  $mV\ dec^{-1}$ , respectively. In both cases, the linear fit was satisfactory,  $r^2 > 0.995$ . On the contrary, the potentiometric response for  $K^+$ -ISE using filter paper T2 with shape C was 66.4  $mV\ dec^{-1}$ ,  $r^2 = 0.985$  and with shape D, 60.1  $mV\ dec^{-1}$ ,  $r^2 = 0.999$ . Filter paper T1 (pore size = 12–25  $\mu m$ ) was thus found to be less sensitive to the shape of the filter paper substrate, compared to filter paper T2 (pore size = 4–12  $\mu m$ ). Finally, the detection limit of the  $K^+$ -ISE was investigated when the filter paper T1 of shapes C and D was applied as sampling unit. The calibration curves are shown in Fig. 4.





**Fig. 4.** Detection limit of the  $K^+$ -ISE when utilizing filter paper shapes C and D (Fig. S1) type T1.

For both cases the detection limit was found to be relatively high, i.e.  $10^{-3.4}$ - $10^{-3.0}$  M  $K^+$ . Interestingly, the detection limit for a  $Ag^+$ -ISE was also found to be about three orders of magnitude higher in a nitrocellulose paper matrix compared to bulk solution.<sup>14</sup> A possible reason for the high detection limit is that the paper matrix in close vicinity of the electrode membrane influences the transport of primary ion that is released from the ion-selective membrane at low concentrations of the primary ion in the sample. This is an interesting problem that needs to be studied in more detail. In order to improve the response time and potential stability, further studies will also be conducted by using alternative solid-state reference electrodes that have recently been developed.<sup>27</sup>

## Conclusions

The results presented in this communication indicate that potentiometric measurements by using solid-contact ion-selective electrodes and a solid-contact reference electrode can be performed on samples absorbed into ordinary filter paper. In this way, selective electrochemical detection by ion-selective electrodes may be integrated with convenient sampling and sample handling offered by disposable filter papers. The proposed approach requires only 200  $\mu\text{L}$  of sample solution, which may be reduced further via miniaturization of the sensors. The pore size of the filter paper was found to influence the potentiometric response, which opens a topic for further studies. This communication serves as a proof of concept, but further work is clearly needed in order to clarify the factors influencing the detection limit, to shorten the measurement time and to evaluate ISEs for other ions than  $\text{K}^+$ .

## Acknowledgement

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