Heavy metals detection with paper-based electrochemical sensors

Ruiyu Ding†‡, Yi Heng Cheong†‡, Ashiq Ahamed‡∥, Grzegorz Lisak*†,‡

†College of Engineering, School of Civil and Environmental Engineering, Nanyang Technological University, 50 Nanyang Avenue, Singapore 639798, Singapore

‡Nanyang Environment and Water Research Institute, Residues and Resource Reclamation Center, 1 Cleantech Loop, Cleantech, Singapore 637141, Singapore

∥ Laboratory of Molecular Science and Engineering, Johan Gadolin Process Chemistry Centre, Åbo Akademi University, FI-20500 Turku, Finland

ABSTRACT: This feature article summarizes recent works in paper-based potentiometry and voltammetry in heavy metal determination. Interactions of paper substrates with heavy metals, influence on the sensing response, and modification methods applied to paper substrates to improve the performance of recently developed electrochemical sensors are discussed. Since the rekindling of interest in paper-based analytical devices, methodologies and electrode designs for heavy metal determinations are highlighted. Promising aspects of the use of these sensors for samples containing solids, and the increased versatility of the use of paper in analytics offers the possibility of increased acceptance of these low-cost platforms.

HEAVY METALS IN THE ENVIRONMENT

Heavy metals are some of the most challenging pollutants due to their toxic and non-biodegradable nature and their bioaccumulation in ecological systems.[1–6] The determination of heavy metals hence is of vital importance in monitoring environmental quality, which is currently under pressure from increased pollution caused by industrial, agricultural, and domestic activities.[7–12] As heavy metals enter and accumulate in the environment, they can be absorbed by plants and animals that live in the contaminated areas leading to bioaccumulation. Through the food chain, these eventually biomagnify inside the human body through the consumption of bioaccumulated plants and animals, or contaminated water. Currently, a natural mechanism for controlled removal of heavy metals from the human body is unknown.[13,14] Hence, even trace levels of toxic heavy metals, e.g. lead, cadmium, mercury, and arsenic may have detrimental effects on the environment and human health, including damage to multiple organs and nervous system.[7,15]

Standard analytical methods have hence been developed to quantify heavy metals in food and environmental samples. These include cold vapor atomic fluorescence, atomic absorption and emission spectroscopy, and inductively coupled plasma techniques (operable either through optical or mass discrimination). These are highly established for various samples and routinely offer high accuracy when performed in centralized laboratory facilities.[16–19] However, these require infrastructure, time, and manpower. Samples must be stored and transported without contamination and only trained personnel with specialized knowledge are able to obtain meaningful results. Furthermore, storage containers need to be scrutinized to prevent the deviation of heavy metals concentration in samples.[20] While standard procedures for sample handling are available, e.g. BS EN ISO 5667, requiring accreditation only further increases costs of operating the heavy metals testing facility. Hence, problems caused by heavy metal pollution are especially pronounced in countries with low gross domestic product per capita. Widespread poverty that encourages the use of cheap, polluting technologies[21] can lead to the increased prevalence of diseases such as cancer in regions where heavy metals are present in the food and environment.[22] Therefore, a cheap, fast, and easy measurement protocol that can be performed *in-situ* could introduce widespread testing of heavy metals pollution. Methods need to address challenging environmental and food samples with a high solid to liquid content or are difficult to collect e.g. sludge or wet soil. To communicate the goals for suitable sensing techniques, the World Health Organization (WHO) has formalized the ASSURED criteria (Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment-free and Deliverable to end-users). These serve as a benchmark for proposed sensors in resource-limited environments and feature strongly when evaluating their application to real situations.[23,24]

Electrochemical heavy metal detection. Figure 1 presents a variety of analytical techniques used to quantify heavy metals in different sample types. The wide variety of samples and concentration ranges imply that no single technique is universal. Instead, the most appropriate technique should be used for quantification. This is especially important for heavy metals that need to be detected at trace levels in substances that are either ingested or come into direct contact with humans. These limits are typically represented in parts per billion (ppb), e.g. WHO limits for Pb, Cd, Hg, As and Cr in drinking water are 10, 5, 1, 10 and 50 ppb, respectively. This corresponds to approx. 10^{-8} M concentration. Hence, many of the reviewed works are based on anodic stripping voltammetry, as the initial pre-concentration of analyte before stripping is required to reach such detection limits.[25] and this technique remains heavily featured in many recent reviews of heavy metal detection.[25–29]

An alternative electrochemical technique is potentiometry, which is a cheap, simple, and rapid method for direct measurements that does not usually require additional sample pretreatment, e.g. filtration, dilution and buffering.[30–32] Potentiometric sensors display a wide linear range (between 10^{-7} and 10^{-1} M) and can determine metal ions in a variety of samples. For example, in industrial wastewater and sludge, relatively high concentrations and a wide range of heavy metals are present (tens to hundreds of ppm of heavy metals)[33–35], thus, can be assessed by potentiometry.[36] Furthermore, efforts have been made to improve the lower detection limits (LDLs) of ion-selective electrodes (ISEs) for heavy metal sensing at the subnanomolar range.[37] For conventional ISEs with inner filling solutions, tailoring the inner filling solution concentration to reduce transmembrane ion fluxes has been investigated.[38] For all-solid-state ISEs without inner filling solutions, (i) investigations of conducting polymer doped with primary ion-complexing agents to reduce the primary ions leaching and contamination at membrane | sample interface,[39] (ii) use of hydrophobic materials to avoid water layer formation,[40] and (iii) application of a galvanostatic current to establish a primary ion transport gradient from the sensing membrane into the conducting polymer, thereby, reducing primary ion transport into the sample.[41] Furthermore, novel membranes[42] and conditioning methods were also proposed.[43] Some works also have demonstrated applicability to samples such as drinking water. Hence, ISEs with improved LDL show promise for translation to low-cost systems, if the inherent challenges, such as measurements in a non-equilibrium state can be addressed.[44,45]

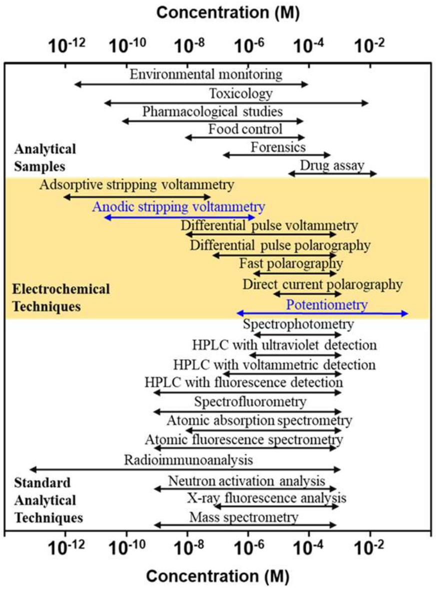


Figure 1. Analytical working ranges of various analytical techniques in respect of applicability of these techniques in various samples. Reproduced with permission from ref. 46. Copyright (2001) Taylor and Francis.

PAPER USE IN ANALYTICS

Paper use in various analytical systems. In the last ten years, the use of paper has been profoundly investigated for its applications in sensors.[46–48] Numerous detection methods have been adapted including colourimetric, fluorescent, electrochemical and (electro)chemiluminescent.[1,49] Some of these methods have also been used to detect heavy metal ions in paper-based analytical devices.[1,50,51] Colourimetry is commonly used, and some recent advances with nanomaterials and ion-imprinted technology have yielded devices with excellent limits of detection in the ppb range.[52] However, most devices still show low sensitivity and selectivity with poor LDLs of > 10 $\mu g\ L^{-1}$ which remain the main drawbacks of such an approach.[1,53] In comparison, electrochemical sensing methods yield better response times and sensitivities[54] that can quantify readings with less background noise.[1] While earlier paper-supported electrochemical devices exist, interest in sample-soaked paper as a medium was reignited by the Whitesides group in 2009.[55] One of their pioneering papers featured the sensing of heavy metals through anodic stripping voltammetry, and since then others have further investigated the advantages and challenges introduced by paper wicking of the sample. Interactions of positively charged heavy metals with cellulose groups in the paper can cause deviations from the expected behavior of electrodes, compared to similar measurements in solution. Hence, this work aims to link these interactions to the challenges encountered. With greater understanding, new approaches that can mitigate their negative impact can be developed.

Paper-heavy metals interactions. Cellulose, a large component of paper contains numerous hydroxyl and carboxyl groups, hence, the surface of commonly-used filter papers contains negatively charged adsorption sites.[56] These papers hence exhibit sorption potential for heavy metals,[57] and the removal of heavy metals via adsorption onto modified cellulose-based substrates has been widely reported.[58] The adsorption process demonstrates first order reversible kinetics and the isotherms followed both Freundlich and Langmuir models.[57,58] The adsorption potential increases with increasing ion concentration and has been found to be an exothermic process.[59]

Thus, for samples in contact with paper, initial concentrations of heavy metal ions can be perturbed due to adsorption. Frew and Pickering[60] studied the adsorption of Cu^{2+} ions in Whatmann 41 filter paper. An ion exchange reaction based on the Donnan membrane theory was dominated at low copper concentration, while after saturation of the exchange sites at high concentration, ingestion of the salts into fibers were reported. Types of functional groups were found to be equally divided between the carboxyl groups attached to the cellulose and acid-soluble impurities. Pickering[61] reported that the adsorption capacity of the divalent metal ions by the Whatman 1 filter paper was 4×10^{-6} g ions g^{-1} of paper. The adsorption of divalent ions was considerably reduced in the presence of competing electrolytes or at higher concentrations of acid, which could possibly lead to zero adsorption. At low pH, H^+ competes with metal ions for negatively charged sites onto the paper. Engin et al.[62] reported the effect of the adsorptive property of filter papers on the determination of heavy metal ion concentrations. Running samples through filter paper caused systematic errors especially for the detection of lower concentrations in aqueous solution. The study also reported an increased degree of adsorption with increasing pH, indicating the significance of the ion-exchange mechanism in the adsorption process.

Novel electrochemical devices enabled with paper. If the impact of ion interactions with paper can be addressed, the favourable physical and chemical properties of paper can be utilized. These include being flexible, porous, hydrophilic, wettable, thin, lightweight, customisable with functional group modification, and generation of flow with capillary action.[1,49,63,64] Paper is also an economical and environmentally-friendly substrate, and can be folded, crumpled, cut, perforated, biodegraded, and renewed, making it highly suited for flexible electronics.[50,65] Paper-based devices have also been evaluated for their ability to meet the WHO ASSURED criteria, and its physical and chemical properties can help in designing compliant devices. However, fully functional, paper-based individual components are not well-developed,[46] making fully ASSURED-compliant, electrochemical devices impractical at present, as some form of instrumentation is still required for any signal quantification to be achieved. Hence, a more practical approach to electrochemical measurement may be to use it with cheap and available devices like glucometers or smartphones.[66]

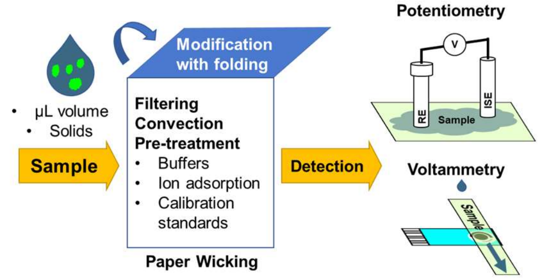


Figure 2. Increased functionality of electrodes using paper, and depictions of potentiometry and voltammetry experiments using paper as a sample medium.

Some of the reviewed works use paper purely as a substrate for the sensor.[67] Beyond electrochemical ion determination commonly performed in milliliters of sample solutions, wicking sample solutions through paper offers the opportunity to perform measurements on microliter volume samples. A further advantage of low-volume sampling is that the consumption of buffers, electrode modification and calibration solutions similarly can be reduced. This may hence extend the usage time of reagents that are applied together with these devices during operation. Depiction of paper as a microliter volume sampling medium for the potentiometry and voltammetry techniques is shown in Figure 2. Capillary forces drive the flow of solution through the porous structure of the paper, in which an interdiffusion mixing is characterized by mechanical dispersion and molecular diffusion.[68] The size of the spaces between the pores has resulted in paper being investigated alongside other microfluidic devices,[53] however, they differ from conventional microfluidic devices, where the flow is generated through hydrodynamic pressure or electroosmotic flow.[69] Electrodes, either conventional glassy carbon, ion selective, or screen-printed flat electrodes, can then be pressed against the paper surface for analytical reading. This has been performed under static or dynamic conditions of the sample, for both potentiometry and voltammetry measurements.[55,70,71] Other advantages of using paper are its ability to sample on uneven surfaces[72] and disposability which can reduce contamination and biofouling between each measurement.[73] Moreover, samples with high solid to liquid ratios can be filtered and pretreated with necessary buffer or calibration standards before determination. This can result in devices well-suited to taking measurements in real samples.[70,72,74,75] Additionally, paper can transport the sample around the device, and additional tests can be simultaneously performed. Paper devices can be folded to achieve electrode modification,[74] or to store reagents with techniques from origami.[76] In the following sections, this feature examines the possible influence on sample concentrations that pose difficulties in sensing, as well as proposals for mitigating their impact on the detection of heavy metals. In addition, the induced flow of samples through paper wicking as well as its filtering and substrate properties have been creatively used, and works with novel methodologies for ion determinations are highlighted.

PAPER-BASED POTENTIOMETRY AND VOLTAMMETRY

Paper as the electrode substrate. As paper-based electrochemical devices have become established tools in the field of sensing, the techniques for device fabrication have concurrently developed. The requirements for printing electrodes onto paper substrates and recommendations for designing new devices have recently been reviewed by Mazurkiewicz and coworkers.[77] The most basic use of paper as a substrate in sensor design is by substitution of more expensive support material, with electrodes printed. Commercially available low-cost, printed electrodes for detection of heavy metals was first demonstrated in 1992[78] with voltammetry. Subsequently, lab-made electrodes printed on paper supports have been proven in heavy metal sensing through potentiometry[79,80] and voltammetry.[81,82] In comparison to previously tested systems, potentiometric ISEs made using carbon nanotube (CNT) modified paper as a solid contact showed comparable stability and detection limits to similar ISEs made with glassy carbon electrodes.[83] Small batch manufacturing has also been reported for screen printed electrodes on paper, which showed comparable performance to commercially available electrodes from the Dropsens brand.[81]

Consistent and satisfactory detection results require printing electrodes with high reproducibility. Hence, using commercially available screen-printing inks for various electrodes is widespread, as these have been optimized for ink stability during the printing process. The most commonly used ink for voltammetric detection are carbon and Ag/AgCl[55,74,82,84,85] for the working, counter, and reference electrodes. Deviations of voltammetric peak areas between electrodes can be below 5% for Pb^{2+} and Cd^{2+} in the ppb range,[85] making such an approach highly established in voltammetry. Screen-printed carbon has also been used as a solid contact electrode for the production of potentiometric ISEs on a polyethylene terephthalate substrate for Pb^{2+} detection.[86] However, materials requirements differ significantly for electrodes designed for potentiometry when compared to voltammetry. Screen-printed carbon electrodes used in voltammetry directly contact the sample solution, and are designed to be wetted by aqueous solution.[87] In contrast, the substrate electrode used for solid-contact ISEs is buried under a polymeric ion-selective membrane (ISM), and if the underlying electrode is hydrophilic, a thin layer of water can form between the ISM and the electrode. As analyte ions can be trapped in this layer, transmembrane ion fluxes to the solution | ISM interface can lead to poor LDL[21] and poor stability.[90,91] Hence, commercially available screen-printing electrode inks may not be well-suited for potentiometry, and the development of solid contacts remains an ongoing field of research.[92]

Using hydrophobic solid contact materials such as CNTs can prevent water layer formation.[93] Modification of hydrophilic conventional solid contact materials like Poly(3,4-ethylenedioxythiophene)/polystyrenesulfonate (PEDOT/PSS) has also been proposed for solid-contact ISEs supported on paper. Ruecha et al.[94] investigated the mixture of PEDOT/PSS and graphene, producing highly hydrophobic electrode surfaces to prevent water layer formation. This was also demonstrated with other lipophilic solid contacts. For example, in Mensah et al.'s work, the paper substrate was first coated with a CNT suspension, then a barrier of sputtered gold. Subsequently, highly lipophilic conducting polymer poly(3-octylthiophene) was inserted between the gold layer and ISM.[95] In Hassan et al.'s research, polyaniline with high hydrophobicity was deposited between carbon printed paper strips and the ISM.[96] Both works demonstrated successful prevention of water layer formation due to the lipophilic conducting polymers. In addition to hydrophobic solid contacts, paper-strip ISEs with LDL of 1.2 nM for Cd^{2+} were reported when an ISM with a lower coefficient of diffusion (MMA-DMA) than the conventional plasticized polyvinyl chloride was used.[95]

Novel or modified printing inks need to be compatible with the properties of the paper substrate. In a work by Ruecha et al.,[97]commercial carbon ink modified with graphite powder (< 20 µm) was screen-printed on Whatman 1 filter paper as a working electrode. Using optical profilometry, much of the carbon ink was shown to have soaked into the cellulose matrix. This resulted in greater peak to peak separation of the paper electrodes when used in cyclic voltammetry in ferro/ferricyanide solutions compared to those on polymer substrates. Stripping voltammetry peaks were also poorly defined for paper substrate electrodes when analysing a sample containing Zn^{2+}, Cd^{2+} and Pb^{2+}.[97] Considering the 11 µm pore size of Whatman 1 filter paper, much of the solid carbon may have been inaccessible to ions in solution. This may require either repeated depositions or increased concentration of solid carbon in printing ink[77]. In contrast, some groups have reported success in printing electrodes with nanoscale materials. Figueredo and coworkers produced a highly reproducible device with a CNT ink. With the nanoscale feature size of the CNTs, a stable film was formed with the use of sodium-dodecyl-sulfate (SDS) surfactant in combination with chitosan (CS), but not with SDS alone.[98] Cationic CS was attracted to the negatively charged surface of the cellulose. By deprotonating the CS with each deposition, subsequent layers were able to be deposited with excellent coverage. This was verified with SEM images that showed pores in the CNT-SDS films but not in the CNT-CS-SDS films. LDL of 6.74 ppb for the determination of Pb^{2+} was achieved with their paper-based electrodes.

Aside from electrode materials, hydrophobic barriers have been used to control transport in the device.[73,99–101] Paper-based potentiometric ISEs showed better performance with controlled transport by avoiding direct contact between the ISM and paper. Selecting well-suited printing methods can also improve mechanical stability, form separate electrode zones, and facilitate microfluidic channels reducing sample volume required, and act as barriers against liquid penetration.[94,102] Paper treated with wax was investigated by Nery et al,[102] where higher sensitivity was shown with untreated paper, ascribed to its larger surface area. For paper treated with wax, rapid signal stabilization and lower drift in signal was observed, and ascribed to the reduction of interference from the residual soaking of paper through silver paint.[73] If separate hydrophobic treatment of paper is not desirable, photo paper due to its polymer film properties[82] can inherently resist the ingress of water.

Paper as a microfluidic sampling platform in potentiometry Paper can be applied as microfluidic sampling platforms[70] by placing an ISE and RE directly onto the paper substrate impregnated with sample solution (Figure 2). Paper substrates can hence protect the ISM from mechanical damage by hard solid sample surfaces. The ISEs and REs used for analysis are also exactly analogous to those used for taking measurements in beakers of sample solution, which sometimes differs for voltammetric measurements.

One problem identified by using paper as the sampling medium was the 1000, and 100 times higher LDL compared to conventional beaker-based measurements for Ag^{+} and Cd^{2+} respectively.[70,103] For clinically relevant metal ions analysis, e.g. Na^{+} and K^{+}, around tenfold higher LDL was found than sampling in beakers.[71,72] In contrast, comparable LDLs were registered for chloride sensitive ISEs coupled with paper-based sampling.[70] From the earlier examined interactions of paper and heavy metal ions, anionic carboxylate and hydroxyl groups in cellulose paper substrates would preferentially sorb positively charged metal cations through chemical or physical means, depleting the primary ion concentration at the ISE surface.[56,104,105] This results in a deviation from Nernstian slopes due to recorded potentials that are lower than expected at dilute primary ion concentrations. Anions conversely fail to sorb on the paper due to the electrostatic repulsion of like charges, and hence the concentration of anions in the paper is relatively unaffected.[106]

The unfavorable potentiometric response of sensing in the sample-soaked paper is characteristically super Nernstian.[70] This can be due to the depletion of the primary ion, due to parasitic side reactions/processes, at the solution | ISM interface[107] from binding to paper substrates.[108] For example, the super Nernstian response was observed for Pb^{2+}-ISEs by Bobacka et al.[70] as well as for Cd^{2+}- and Pb^{2+}-ISEs by Lisak et al.[64] at concentrations of 10^{-4} to 10^{-3} M $Cd(NO_3)_2$ and $Pb(NO_3)_2$. The concentration of bound lead and cadmium per gram of cellulose paper at 10^{-4} and 10^{-3} M $Pb(NO_3)_2$ was around 320 and 430 ppm, while for 10^{-4} and 10^{-3} M $Cd(NO_3)_2$ was around 100 and 130 ppm, respectively.[64] Pb^{2+} showed stronger binding affinity onto paper substrates than Cd^{2+}, consistent with previous studies.[57,109] Thus a higher potential difference due to the super Nernstian response was observed for Pb^{2+} than Cd^{2+}, resulting from greater depletion at the solution | ISM interface. The elimination of super Nernstian responses by pre-treatment of paper with primary ions was investigated. Papers were pre-soaked for 0.5-1 hour in calibration standard solutions, to saturate the negative sites on the paper surface.[64,70] This was able to extend the Nernstian response range to $10^{-1.35}-10^{-5.0}$ M for measurements of Pb^{2+} and Cd^{2+}. Pretreatment was also achieved by soaking, then drying papers with certain concentrations of primary ion solutions.[64] A similar extension of the Nernstian range was obtained by pretreating, then drying with higher concentrations of 10^{-3} to 10^{-4} M primary ion solutions. However, this effect disappeared when using lower concentrations of 10^{-5} to 10^{-6} M, possibly due to uncomplexed sites on the paper surface. Furthermore, pretreatment with a cation different from the primary ion was investigated. This was found depend on the relative binding affinities of the specific ions to paper. The stronger binding affinity for Pb^{2+} to paper compared to Cd^{2+} allowed for an extended Nernstian response for Cd^{2+} measurements with substrates pretreated with only a dilute 10^{-6} M $Pb(NO_3)_2$ solution. However, different concentrations of $Cd(NO_3)_2$ were unable to achieve the same effect on Pb^{2+} measurements which retained the super Nernstian response. Overall, the Nernstian response range was able to be extended to a low of 10^{-5} M, higher than the 10^{-6} LDL seen in beaker based measurements which may be due to ion desorption at lower sample concentrations.[110] However, the extended range may still be useful for measurements taken in environmental samples, including on-site heavy metal detection from industrial effluents and sludge

A deeper understanding of the ionic interaction between the sample and functional groups on the surface of the paper-substrate would aid in better modification strategies for the paper to suit any sort of ion-sensing application. For instance, paper modified by primary ions may still undergo cation desorption from the pretreated paper substrate into sample solutions. Alternative modification methods such as using organic salts to block ion exchange sites on paper substrates can also be explored, or acidifying the paper to diminish heavy metal binding can be investigated. Moreover, finding alternative specially manufactured/designed paper with fewer negative adsorption sites may thereby lead to negligible interaction with metal ions. Also, other strategies such as doping chemical agents into the ISM to reduce paper effects on paper | ISM interface and optimization of the potential reading time can be explored.

Paper as a microfluidic sampling platform in voltammetry In contrast to potentiometric sensing, the use of paper in voltammetry as a sampling medium need not incorporate electrodes that are equivalently used in beaker-based sampling. Some form factors may be more self-contained, like electrodes printed directly on the sample area, making them physically inseparable. While electrodes from commercial carbon inks are common,[55] other materials like boron doped diamond,[111] unmodified graphite,[112] or screen-printed carbon electrodes have also been used.[113]

Voltammetric sensing also diverges significantly from potentiometric sensing through sample modification steps. Many works reviewed here use pH 4, 0.1 M acetate buffer to adjust the pH of samples. This is common practice to prevent hydrolysis of ions in the sample. When using paper as a sampling medium, these buffers may also reduce the interaction of metal ions with the paper substrate. This corroborates with earlier work by Pickering, where absorption of divalent cations onto paper was greatly reduced at acidic pH, and competing electrolyte.[61] As buffer concentrations of 0.1 M far exceed those of sample ions ($10^{-7} – 10^{-8}$ M) in the reviewed voltammetric works, the impact of interactions between sample ions and paper may be sufficiently insignificant. Mitigating this problem has hence allowed investigation of other aspects, such as additional functionality of devices, or the generation of sample flow.

Transport of sample through paper upon contact generates convective flow at the paper | electrode interface. The constant renewal of sample at the electrode surface allows greater accumulation of ions during the pre-concentration step, as the process is diffusion-limited.[114] This produces an enhanced stripping current, compared to an identical procedure in static solution. The effect is similar to the impact of convection through stirring,[115] but with the additional benefit of sampling low volumes. In comparison to the same electrodes immersed in the solution, Nie et al. reported an improvement of the peak height by a factor of 5 for their screen-printed carbon electrodes for detection of 25 ppb of Pb^{2+}. An increase of peak height was also reported by Shi et al. for detection of 50 ppb Pb^{2+} and Cd^{2+} with screen printed electrodes,[113] but this was not quantified. For the boron-doped diamond paste electrodes investigated by Nantaphol et al., the peak heights of 50 ppb Cd^{2+} and Pb^{2+} were improved by factors of 4.3 and 3.1,[116] approaching the degree of improvement reported by Nie et al. The reported factors of improvement approach the impact of the stirring of a static liquid sample.[115] Wicking speed under capillary systems is commonly approximated by the Lucas−Washburn equation, and the theoretical treatment and recent alternative approaches have been separately reviewed.[117] To overcome the flow speed limitation of capillary flow, using a paper channel with multiple layers of paper has demonstrated improved flow rate and correspondingly the peak height. [118]

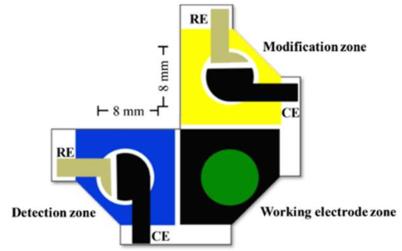


Figure 3. Paper device divided into 3 zones. For each step of 1: modification and 2: detection, the named zone is folded over the working electrode zone to introduce modifier or sample. Reproduced with permission from ref. 75. Copyright (2018) Springer Nature.

Measurements with static sample in the paper may conversely diminish characteristic stripping peaks. Nie et al. found a 30% reduction in peak current in cyclic voltammetry of ferrocenecarboxylic acid in comparison to electrodes immersed in a solution of the same concentration.[55] Transport of sample to the electrode surface remains controlled by diffusion even with a sheet of paper pressed against the electrode. This was confirmed by varying the scan rate in the setup and corroborates with earlier work.[111,119] Hence, reduced oxidation and reduction currents were ascribed to blocking of the space accessible by diffusion by the cellulose fibres. Poorly defined voltammetric peaks may lead to narrower linear ranges of measurement, and several works that employ testing of static samples wicked with paper show linear ranges that end just at or above safe levels of heavy metals as recommended by the WHO.[74,120,121]

Capillary forces have also been used to move the sample through the paper-based device. Other techniques apart from square wave anodic stripping voltammetry (SWASV) can then be applied simultaneously for the detection of more analytes. For example, Rattanarat et al. successfully combined optical and electrochemical techniques in a single device. In addition to SWASV detection of Pb and Cd with detection limits of 1 ppb, colourimetric detection of Fe, Ni, Cr, and Cu was achieved concurrently with the same sample.[122] A similar practice was also demonstrated by Chaiyo et al., where Cd^{2+} and Pb^{2+} were detected by SWASV down to a detection limit of 0.1 ppb, while simultaneously detecting Cu^{2+} with colourimetry.[85] In both cases, the sample was transported to different electrochemical and colourimetric detection zones and both methods were activated simultaneously.

Like in potentiometry, paper can be pre-treated to improve the measurement protocol. Modifying screen-printed carbon electrodes with Bi[29] or Au[123] nanoparticles in SWASV can improve the sensitivity of the measurement, while avoiding the use of toxic mercury. Deposition of these nanoparticles can occur before the pre-concentration step,[118] and Pungjunun et al. proposed folding of the paper device as a modification step. The electrode was divided into three parts; a modification, working electrode, and detection zone, as shown in Figure 3. By folding the modification over the working electrode zone, the working electrode was first modified with a solution of $AuCl_3$ containing 1 wt% Au^{3+} in 1 M HCl. Unfolding the modification zone and replacing it with the detection zone allowed for the time of introduction of the sample to be unambiguous.

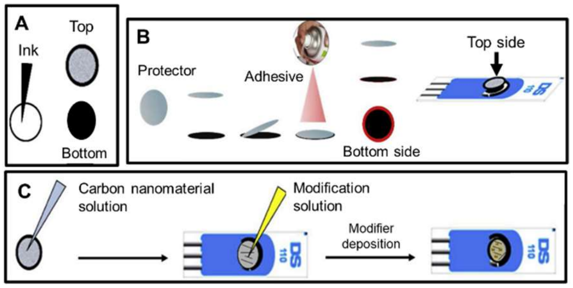


Figure 4. Porous carbon electrodes modified with Au nanoparticles. Screen-printed electrodes were made reusable by only replacing the carbon working electrode with each sample. Adapted with permission from ref. 125. Copyright (2019) Elsevier.

Pre-treatment of sample pH for SWASV was also achieved using paper as a medium. pH control of the sample is important as at low pH levels, H^+ ions compete with heavy metal ions for active sites at the working electrodes.[124] Conversely at high pH levels, the tendency for heavy metal ions to hydrolyze also increases, lowering the detection peak. In addition, modifiers like Bi^{3+} ions may hydrolyze above pH 5.[112] A well-chosen buffer can hence improve stripping peak currents, many works hence use 0.1 M acetate buffer to control the pH to be from 4 to 5. Tan et al. proposed pretreated paper with 0.1 M acetate buffer, 60 ppb Zn^{2+} solution, and 500 ppb Bi^{3+} solution in sequence. After the solutions had dried, 10 µL of the sample was directly deposited on the paper sampling medium, and determination of Pb^{2+} with a LDL of 2 ppb was achieved.[125]

Paper has also been shown to be highly suited to real sample testing. Samples with solids are filtered through pores as they are wicked. This can efficiently separate the liquid from solids. Medina-Sánchez et al.[126] demonstrated the filtering capability of their paper-based electrodes by depositing mud-spiked Pb^{2+} samples. SWASV distinguished between 75, 50, and 20 ppb concentrations of Pb^{2+}.[126] Stripping peaks of samples spiked with graphite powder or dirt at 8 ppb Pb^{2+} were indistinguishable from those without solids.[125] Food samples have also been investigated across some groups. Recovery of As^{3+} from unfiltered rice samples at concentrations of 1−5 µg ml^{-1} resulted in the recovery of 87.8–107.8%.[74] SWASV conducted with pyrolyzed rice ash with Cd^{2+} agreed well with ICP-MS results across 340−590 µg kg^{-1}.[75] Other groups have also shown success with investigating real samples but have used protocols with a separate filtering step. Chaiyo and coworkers with acid digested rice and fish[85] obtained acceptable recoveries for 5−60 ppb of Pb^{2+} and Cd^{2+}. Feng et al. were also able to obtain comparable detection of Pb^{2+} between their carbon tape electrodes and atomic absorption spectroscopy at concentrations of 300 to 425 ppb from the digestion of crushed toys.[120]

Instead of forming a whole electrochemical cell on paper, reusing the counter and reference electrodes with a replaceable working electrode may reduce costs even further. Costa-García proposed circular pieces of paper functionalized with carbon ink on one side. This side was connected to the carbon working electrode of a screen-printed electrode. The other side of the paper was modified with gold nanoparticles,[127] carbon nanofibers, graphene oxide and gold nanoparticles,[128] or mercury or bismuth films.[129] A schematic of the process is shown in Figure 4. It was found that measurements could be repeated 7-8 times without changing the screen-printed electrode used.[128] With their platform, they were able to detect As^{3+}, Hg^{2+}, Cd^{2+}, Pb^{2+}, and In^{3+} to 2.2, 6.0, 400, 100, and 40 ppb, respectively.

CONCLUSION AND PROSPECTS

In this feature article, the usefulness of paper in the design of cheap and convenient devices has been shown across multiple studies. Designs of paper-based potentiometric and voltammetric devices have established highly portable methods of heavy metal ion determination. The use of paper has also made sampling in complicated environmental situations, e.g. samples with low liquid and high solid content, possible. Additionally, modifying paper substrates can improve the sensitivity, accuracy of devices. However, the feasibility of paper-based devices currently remains limited. The instrument-free criterion is the greatest challenge facing paper-based devices in fully complying with the ASSURED criteria, and such a requirement rules out their use in locations where instrumentation is completely unavailable. The user-friendliness of operation also remains a challenge. In comparison to the ease of sampling with paper devices, the preparation of samples is still a laborious process that may require high temperatures, or unsafe reagents that are not easily obtainable by the general population. These may limit implementation for heavy metal determination. It is hence expected that future works may develop simple sample preparation techniques that show a similar ability to extract heavy metals from samples as established ones. It should also be mentioned that the ASSURED criteria were developed in the context of diagnosing sexually transmitted infections in resource-limited settings. As stated by Whitesides et al., these guidelines may impose unrealistic limitations, and hence the success of novel devices should rather be determined by how well a particular problem can be addressed by the actual resources available. [130]

Additionally, the use of paper can result in improved device performance but devices remain constrained by limitations of potentiometry and voltammetry. These include goals such as achieving stable and reproducible potentials comparable to liquid contact ISEs for potentiometric sensing and reducing the problems of interference and detectable ions in voltammetric sensing. Paper has been proven as a useful platform to quickly implement advances in these areas but does not contribute significantly to addressing more fundamental limitations of these techniques. Alternatively, the costs of using these sensors in a laboratory setting are estimated to be reduced by a factor of 10 when compared to conventional techniques, as shown by Bi et al.[75] The improved economic viability simply by translation onto paper may make heavy metal determination in food and environmental samples sufficiently attractive. Alongside protocols that can be easily replicated in a home or low-resource setting, the availability of both may be a significant step in truly bringing these devices to the people who need them the most.

AUTHOR INFORMATION

Corresponding Author

* Email: g.lisak@ntu.edu.sg; phone: +65-6592-1765.

Author Contributions

The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript. / ‡These authors contributed equally. (match statement to author names with a symbol).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The authors thank NEWRI (Nanyang Environment and Water Research Institute) and Singapore's Economic Development Board (EDB) for their financial support of this research.

REFERENCES

(1) Lin, Y.; Gritsenko, D.; Feng, S.; Teh, Y. C.; Lu, X.; Xu, J. *Biosens. Bioelectron*. 2016, 256–266.

(2) López Marzo, A. M.; Pons, J.; Blake, D. A.; Merkoçi, A. *Anal. Chem.* **2013**, *85* (7), 3532–3538.

(3) Hazrati, S.; Farahbakhsh, M.; Cerdà, A.; Heydarpoor, G. *Chemosphere* **2020**, 128767.

(4) Li, Z.; Huang, P.; Hu, H.; Zhang, Q.; Chen, M. *Chemosphere* **2020**, *258*, 127275.

(5) Slijepčević, N.; Pilipović, D. T.; Kerkez, Đ.; Krčmar, D.; Bečelić-Tomin, M.; Beljin, J.; Dalmacija, B. *Chemosphere* **2021**, *263*, 127816.

(6) Zhou, C.; Wang, X.; Song, X.; Wang, Y.; Fang, D.; Ge, S.; Zhang, R. *Chemosphere* **2020**, *253*, 126661.

(7) Tchounwou, P. B.; Yedjou, C. G.; Patlolla, A. K.; Sutton, D. J. *Exs*. 2012, 133–164.

(8) Cudjoe, D.; Acquah, P. M. *Chemosphere* **2021**, *265*, 129186.

(9) Tucker, E. L.; Chickering, G. W.; Spreadbury, C. J.; Laux, S. J.; Townsend, T. G. *Chemosphere* **2020**, *260*, 127524.

(10) Egbosiuba, T. C.; Abdulkareem, A. S.; Kovo, A. S.; Afolabi, E. A.; Tijani, J. O.; Roos, W. D. *Chemosphere* **2020**, *254*, 126780.

(11) Yuan, Y.; Zhan, W.; Jia, F.; Song, S. *Chemosphere* **2020**, *251*, 126369.

(12) Zhang, W.; Zhao, L.; Yuan, Z.; Li, D.; Morrison, L. *Chemosphere* **2020**, 128926.

(13) Draghici, C.; Jelescu, C.; Dima, C.; Coman, G.; Chirila, E. In *NATO SCI PEACE SECUR*; 2011; Vol. 1, 145–158.

(14) Vieira, C.; Morais, S.; Ramos, S.; Delerue-Matos, C.; Oliveira, M. B. P. P. *Food Chem. Toxicol.* **2011**, *49* (4), 923—932.

(15) Nordberg, G. F.; Fowler, B. A.; Nordberg, M.; Friberg, L. T. *Handbook on the Toxicology of Metals*; 2007.

(16) Appenroth, K.-J. *Crossroads* **2010**, *19* (Im), 1–18.

(17) Bradl, H.; Kim, C.; Kramar, U.; StÜben, D. *Interface Sci. Technol.* **2005**, *6* (C), 28–164.

(18) Furness, R. W.; Rainbow, P. S. *Heavy Metals in the Marine Environment*; 2018.

(19) *Case Studies in Food Safety and Environmental Health*; Ho, P., Vieira, M. M. C., Eds.; Integrating Safety and Environmental Knowledge Into Food Studies towards European Sustainable Development; Springer US: Boston, MA, 2007; Vol. 6.

(20) Borrill, A. J.; Reily, N. E.; Macpherson, J. V. *Analyst* **2019**, *144* (23), 6834–6849.

(21) Alloway, B. J.; Jackson, A. P. *Sci. Total Environ.* **1991**, *100* (C), 151–176.

(22) Onakpa, M. M.; Njan, A. A.; Kalu, O. C. *Annals of Global Health*. 2018.

(23) Mabey, D.; Peeling, R. W.; Ustianowski, A.; Perkins, M. D. *Nat. Rev. Microbiol*. 2004.

(24) Mayer, M.; Baeumner, A. J. *Chem. Rev.*. 2019, 7996–8027.

(25) Ariño, C.; Serrano, N.; Díaz-Cruz, J. M.; Esteban, M. *Anal. Chim. Acta* **2017**, *990*, 11–53.

(26) Wang, T.; Yue, W. *Electroanalysis* **2017**, *29* (10), 2178–2189.

(27) Nsabimana, A.; Kitte, S. A.; Fereja, T. H.; Halawa, M. I.; Zhang, W.; Xu, G. *Curr. Opin. Electrochem.* **2019**, *17*, 65–71.

(28) Zhao, G.; Wang, H.; Liu, G. *Int. J. Electrochem. Sci.* **2017**, *12* (9), 8622–8641.

(29) Wang, J.; Lu, J.; Hocevar, S. B.; Farias, P. A. M.; Ogorevc, B. *Anal. Chem.* **2000**, *72* (14), 3218–3222.

(30) Hassan, S. S. M.; Sayour, H. E. M.; Al-Mehrezi, S. S. *Anal. Chim. Acta* **2007**, *581* (1), 13–18.

(31) Paczosa-Bator, B.; Cabaj, L.; Raś, M.; Baś, B.; Piech, R. *Int. J. Electrochem. Sci.* **2014**, *9* (6), 2816–2823.

(32) Azmi, A.; Azman, A. A.; Ibrahim, S.; Yunus, M. A. M. *Int. J. Smart Sens. Intell. Syst.* **2017**, *10* (2), 223–261.

(33) Xu, L.; Xu, X.; Cao, G.; Liu, S.; Duan, Z.; Song, S.; Song, M.; Zhang, M. *J. Environ. Manage.* **2018**, *218*, 129–138.

(34) Mansoorian, H. J.; Mahvi, A. H.; Jafari, A. J. *Sep. Purif. Technol.* **2014**, *135*, 165–175.

(35) Šćiban, M.; Radetić, B.; Kevrešan, Ž.; Klašnja, M. *Bioresour. Technol.* **2007**, *98* (2), 402–409.

(36) Macchi, G.; Marani, D.; Pagano, M.; Bagnuolo, G. *Water Res.* **1996**, *30* (12), 3032–3036.

(37) Chumbimuni-Torres, K. Y.; Rubinova, N.; Radu, A.; Kubota, L. T.; Bakker, E. *Anal. Chem.* **2006**, *78* (4), 1318–1322.

(38) Sokalski, T.; Ceresa, A.; Zwickl, T.; Pretsch, E. *J. Am. Chem. Soc.* **1997**, *119* (46), 11347–11348.

(39) Bühlmann, P.; Yajima, S.; Tohda, K.; Umezawa, K.; Nishizawa, S.; Umezawa, Y. *Electroanalysis*. 1995, 811–816.

(40) Veder, J. P.; De Marco, R.; Clarke, G.; Chester, R.; Nelson, A.; Prince, K.; Pretsch, E.; Bakker, E. *Anal. Chem.* **2008**, *80* (17), 6731–6740.

(41) Lindner, E.; Gyurcsányi, R. E.; Buck, R. P. *Electroanalysis* **1999**, *11* (10–11), 695–702.

(42) Boswell, P. G.; Szíjjártó, C.; Jurisch, M.; Gladysz, J. A.; Rábai, J.; Bühlmann, P. *Anal. Chem.* **2008**, *80* (6), 2084–2090.

(43) Mendecki, L.; Fayose, T.; Stockmal, K. A.; Wei, J.; Granados-Focil, S.; McGraw, C. M.; Radu, A. *Anal. Chem.* **2015**, *87* (15), 7515–7518.

(44) Ceresa, A.; Bakker, E.; Hattendorf, B.; Günther, D.; Pretsch, E. *Anal. Chem.* **2001**, *73* (2), 343–351.

(45) Hu, J.; Stein, A.; Bühlmann, P. *TrAC - Trends in Anal. Chem*. 2016, 102–114.

(46) Smith, S.; Korvink, J. G.; Mager, D.; Land, K. *RSC Advances*. 2018, 34012–34034.

(47) Yang, Y.; Noviana, E.; Nguyen, M. P.; Geiss, B. J.; Dandy, D. S.; Henry, C. S. *Anal. Chem*. 2017, 71–91.

(48) Sharma, N.; Barstis, T.; Giri, B. *Eur J Pharm Sci*. 2018, 46–56.

(49) Kung, C. Te; Hou, C. Y.; Wang, Y. N.; Fu, L. M. *Sens. Actuators B Chem*. 2019.

(50) Almeida, M. I. G. S.; Jayawardane, B. M.; Kolev, S. D.; McKelvie, I. D. *Talanta* **2018**, *177*, 176–190.

(51) Meredith, N. A.; Quinn, C.; Cate, D. M.; Reilly, T. H.; Volckens, J.; Henry, C. S. *Analyst*. 2016, 1874–1887.

(52) Ozer, T.; McMahon, C.; Henry, C. S. *Annu. Rev. Anal. Chem.* **2020**, *13* (1), 85–109.

(53) Li, S.; Zhang, C.; Wang, S.; Liu, Q.; Feng, H.; Ma, X.; Guo, J. *Analyst* **2018**, *143* (18), 4230–4246.

(54) Yetisen, A. K.; Akram, M. S.; Lowe, C. R. *LAB CHIP*. 2013, 2210–2251.

(55) Nie, Z.; Nijhuis, C. A.; Gong, J.; Chen, X.; Kumachev, A.; Martinez, A. W.; Narovlyansky, M.; Whitesides, G. M. *Lab Chip* **2010**, *10* (4), 477–483.

(56) Kong, F.; Hu, Y. F. *Anal. Bioanal. Chem.* **2012**, *403* (1), 7–13.

(57) El-Araby, H. A.; Ibrahim, A. M. M. A.; Mangood, A. H.; Abdel-Rahman, A. A.-H. *J. Geosci. Environ. Prot.* **2017**, *05* (07), 109–152.

(58) O'Connell, D. W.; Birkinshaw, C.; O'Dwyer, T. F. *Bioresour. Technol*. 2008, 6709–6724.

(59) Wan Ngah, W. S.; Kamari, A.; Koay, Y. J. *Int. J. Biol. Macromol.* **2004**, *34* (3), 155–161.

(60) Frew, R. G.; Pickering, W. F. *J. Chromatogr. A* **1970**, *47* (C), 86–91.

(61) Pickering, W. F. *J. Chromatogr. A* **1960**, *4* (C), 481–484.

(62) Engin, M. S.; Uyanik, A.; Cay, S.; Icbudak, H. *Adsorpt. Sci. Technol.* **2010**, *28* (10), 837–846.

(63) Jang, I.; Song, S. *Lab Chip* **2015**, *15* (16), 3405–3412.

(64) Ding, R.; Krikstolaityte, V.; Lisak, G. *Sens. Actuators B Chem.* **2019**, *290*, 347–356.

(65) Balde, M.; Jacquemoud-Collet, F.; Vena, A.; Sorli, B. *Sens. Actuators, A Phys.* **2016**, *240*, 118–125.

(66) Paschoalino, W. J.; Kogikoski, S.; Barragan, J. T. C.; Giarola, J. F.; Cantelli, L.; Rabelo, T. M.; Pessanha, T. M.; Kubota, L. T. *ChemElectroChem* **2019**, *6* (1), 10–30.

(67) Krikstolaityte, V.; Ding, R.; Hui, E. C.; Lisak, G. *TrAC Trends Anal. Chem.* **2020**, 116070.

(68) Jang, I.; Kim, G.; Song, S. *Int. J. Heat Mass Transf.* **2018**, *120*, 830–837.

(69) Carrell, C.; Kava, A.; Nguyen, M.; Menger, R.; Munshi, Z.; Call, Z.; Nussbaum, M.; Henry, C. *Microelectron. Eng.* **2019**.

(70) Lisak, G.; Cui, J.; Bobacka, J. *Sens. Actuators B Chem.* **2015**, *207* (PB), 933–939.

(71) Cui, J.; Lisak, G.; Strzalkowska, S.; Bobacka, J. *Analyst* **2014**, *139* (9), 2133–2136.

(72) Ding, R.; Fiedoruk-Pogrebniak, M.; Pokrzywnicka, M.; Koncki,

R.; Bobacka, J.; Lisak, G. *Sens. Actuators B Chem.* **2020**, *323*, 128680.

(73) Lan, W. J.; Zou, X. U.; Hamedi, M. M.; Hu, J.; Parolo, C.; Maxwell, E. J.; Bühlmann, P.; Whitesides, G. M. *Anal. Chem.* **2014**, *86* (19), 9548–9553.

(74) Pungjunun, K.; Chaiyo, S.; Jantrahong, I.; Nantaphol, S.; Siangproh, W.; Chailapakul, O. *Microchim. Acta* **2018**, *185* (7).

(75) Bi, X.; Wang, H.; Ge, L.; Zhou, D.; Xu, J.; Gu, H.; Bao, N. *Sens. Actuators B Chem.* **2018**, *260*, 475–479.

(76) Yakoh, A.; Chaiyo, S.; Siangproh, W.; Chailapakul, O. *ACS Sensors* **2019**, *4* (5), 1211–1221.

(77) Mazurkiewicz, W.; Podrażka, M.; Jarosińska, E.; Kaalakandy Valapil, K.; Wiloch, M.; Jönsson-Niedziółka, M.; Witkowska Nery, E. *ChemElectroChem* **2020**, *7* (14), 2939–2956.

(78) Wang, J.; Tian, B. *Anal. Chem.* **1992**, *64* (15), 1706–1709.

(79) Novell, M.; Guinovart, T.; Blondeau, P.; Rius, F. X.; Andrade, F. J. *Lab Chip* **2014**, *14* (7), 1308–1314.

(80) Rius-Ruiz, F. X.; Bejarano-Nosas, D.; Blondeau, P.; Riu, J.; Rius, F. X. *Anal. Chem.* **2011**, *83* (14), 5783–5788.

(81) Yu, P.; Heist, C. A.; Remcho, V. T. *Anal. Methods* **2017**, *9* (11), 1702–1706.

(82) Zheng, H.; Ntuli, L.; Mbanjwa, M.; Palaniyandy, N.; Smith, S.; Modibedi, M.; Land, K.; Mathe, M. *Electrocatalysis* **2019**, *10* (2), 149–155.

(83) Novell, M.; Parrilla, M.; Crespo, G. A.; Rius, F. X.; Andrade, F. J. *Anal. Chem.* **2012**, *84* (11), 4695–4702.

(84) Smith, S.; Madzivhandila, P.; Ntuli, L.; Bezuidenhout, P.; Zheng, H.; Land, K. *Electrocatalysis* **2019**.

(85) Chaiyo, S.; Apiluk, A.; Siangproh, W.; Chailapakul, O. *Sens. Actuators B Chem.* **2016**, *233*, 540–549.

(86) Radu, A.; Anastasova, S.; Fay, C.; Diamond, D.; Bobacka, J.; Lewenstam, A. In *Proceedings of IEEE Sensors*; 2010; 1487–1490.

(87) Alkire, R. C.; Bartlett, P. N.; Lipkowski, J. *Adv. Electrochem. Sci. Eng.*, 2016; Vol. 16, 1–449.

(88) Fibbioli, M.; Morf, W. E.; Badertscher, M.; De Rooij, N. F.; Pretsch, E. *Electroanalysis* **2000**, *12* (16), 1286–1292.

(89) De Marco, R.; Veder, J. P.; Clarke, G.; Nelson, A.; Prince, K.; Pretsch, E.; Bakker, E. *Phys. Chem. Chem. Phys.* **2008**, *10* (1), 73–76.

(90) Michalska, A. *Anal. Bioanal. Chem.* **2006**, *384* (2), 391–406.

(91) Bobacka, J.; Ivaska, A.; Lewenstam, A. In *Electroanalysis*; 2003; Vol. 15, 366–374.

(92) Shao, Y.; Ying, Y.; Ping, J. *Chem. Soc. Rev.* **2020**, *49* (13), 4405–4465.

(93) Crespo, G. A.; Macho, S.; Rius, F. X. *Anal. Chem.* **2008**, *80* (4), 1316–1322.

(94) Ruecha, N.; Chailapakul, O.; Suzuki, K.; Citterio, D. *Anal. Chem.* **2017**, *89* (19), 10608–10616.

(95) Mensah, S. T.; Gonzalez, Y.; Calvo-Marzal, P.; Chumbimuni-Torres, K. Y. *Anal. Chem.* **2014**, *86* (15), 7269–7273.

(96) Hassan, S. S. M.; Kamel, A. H.; Amr, A. E. G. E.; Abdelwahab Fathy, M.; Al-Omar, M. A. *Molecules* **2020**, *25* (3).

(97) Ruecha, N.; Rodthongkum, N.; Cate, D. M.; Volckens, J.; Chailapakul, O.; Henry, C. S. *Anal. Chim. Acta* **2015**, *874*, 40–48.

(98) Figueredo, F.; Jesús González-Pabón, M.; Cortón, E. *Electroanalysis* **2018**, *30* (3), 497–508.

(99) Sjöberg-Eerola, P.; Bobacka, J.; Lewenstam, A.; Ivaska, A. *Sens. Actuators B Chem.* **2007**, *127* (2), 545–553.

(100) Lou, B.; Chen, C.; Zhou, Z.; Zhang, L.; Wang, E.; Dong, S. *Talanta* **2013**, *105*, 40–45.

(101) Hu, J.; Ho, K. T.; Zou, X. U.; Smyrl, W. H.; Stein, A.; Bühlmann, P. *Anal. Chem.* **2015**, *87* (5), 2981–2987.

(102) Nery, E. W.; Kubota, L. T. *Anal. Chim. Acta* **2016**, *918*, 60–68.

(103) Szucs, J.; Gyurcsányi, R. E. *Electroanalysis* **2012**, *24* (1), 146–152.

(104) Pelton, R. *TrAC - Trends in Anal. Chem*. 2009, 925–942.

(105) Alila, S.; Boufi, S.; Belgacem, M. N.; Beneventi, D. *Langmuir* **2005**, *21* (18), 8106–8113.

(106) Ota, R.; Yamada, K.; Suzuki, K.; Citterio, D. *Analyst* **2018**, *143* (3), 643–653.

(107) Lisak, G.; Bobacka, J.; Lewenstam, A. *J. Solid State Electrochem.* **2012**, *16* (9), 2983–2991.

(108) Mahadeva, S. K.; Walus, K.; Stoeber, B. *ACS Appl. Mater. Interfaces* **2015**, *7* (16), 8345–8362.

(109) Denizli, A.; Say, R.; Arica, Y. *Sep. Purif. Technol.* **2000**, *21* (1–2), 181–190.

(110) A., M. In *Thermodynamics - Interaction Studies - Solids, Liquids and Gases*; 2011.

(111) Nantaphol, S.; Channon, R. B.; Kondo, T.; Siangproh, W.; Chailapakul, O.; Henry, C. S. *Anal. Chem.* **2017**, *89* (7), 4100–4107.

(112) Shen, L. L.; Zhang, G. R.; Li, W.; Biesalski, M.; Etzold, B. J. M. *ACS Omega* **2017**, *2* (8), 4593–4603.

(113) Shi, J.; Tang, F.; Xing, H.; Zheng, H.; Bi, L.; Wang, W. *J. Braz. Chem. Soc.* **2012**, *23* (6), 1124–1130.

(114) Brainina, K. Z. *Talanta* **1971**, *18* (5), 513–539.

(115) Rico, M. Á. G.; Olivares-Marín, M.; Gil, E. P. *Electroanalysis* **2008**, *20* (24), 2608–2613.

(116) Nantaphol, S.; Chailapakul, O.; Siangproh, W. *Anal. Chim. Acta* **2015**, *891*, 136–143.

(117) Cate, D. M.; Adkins, J. A.; Mettakoonpitak, J.; Henry, C. S. *Anal. Chem.* **2015**, *87* (1), 19–41.

(118) Channon, R. B.; Nguyen, M. P.; Scorzelli, A. G.; Henry, E. M.; Volckens, J.; Dandy, D. S.; Henry, C. S. *Lab Chip* **2018**, *18* (5), 793–802.

(119) Nantaphol, S.; Chailapakul, O.; Siangproh, W. *Anal. Chim. Acta* **2015**, *891*, 136–143.

(120) Feng, Q.-M.; Zhang, Q.; Shi, C.-G.; Xu, J.-J.; Bao, N.; Gu, H.-Y. *Talanta* **2013**, *115*, 235–240.

(121) Kokkinos, C.; Economou, A.; Giokas, D. *Sens. Actuators B Chem.* **2018**, *260*, 223–226.

(122) Rattanarat, P.; Dungchai, W.; Cate, D.; Volckens, J.; Chailapakul, O.; Henry, C. S. *Anal. Chem.* **2014**, *86* (7), 3555–3562.

(123) Dai, X.; Nekraseova, O.; Hyde, M. E.; Compton, R. G. *Anal. Chem.* **2004**, *76* (19), 5924–5929.

(124) Afkhami, A.; Soltani-Felehgari, F.; Madrakian, T.; Ghaedi, H.; Rezaeivala, M. *Anal. Chim. Acta* **2013**, *771*, 21–30.

(125) Tan, S. N.; Ge, L.; Wang, W. *Anal. Chem.* **2010**, *82* (21), 8844–8847.

(126) Medina-Sánchez, M.; Cadevall, M.; Ros, J.; Merkoçi, A. *Anal. Bioanal. Chem.* **2015**, *407* (28), 8445–8449.

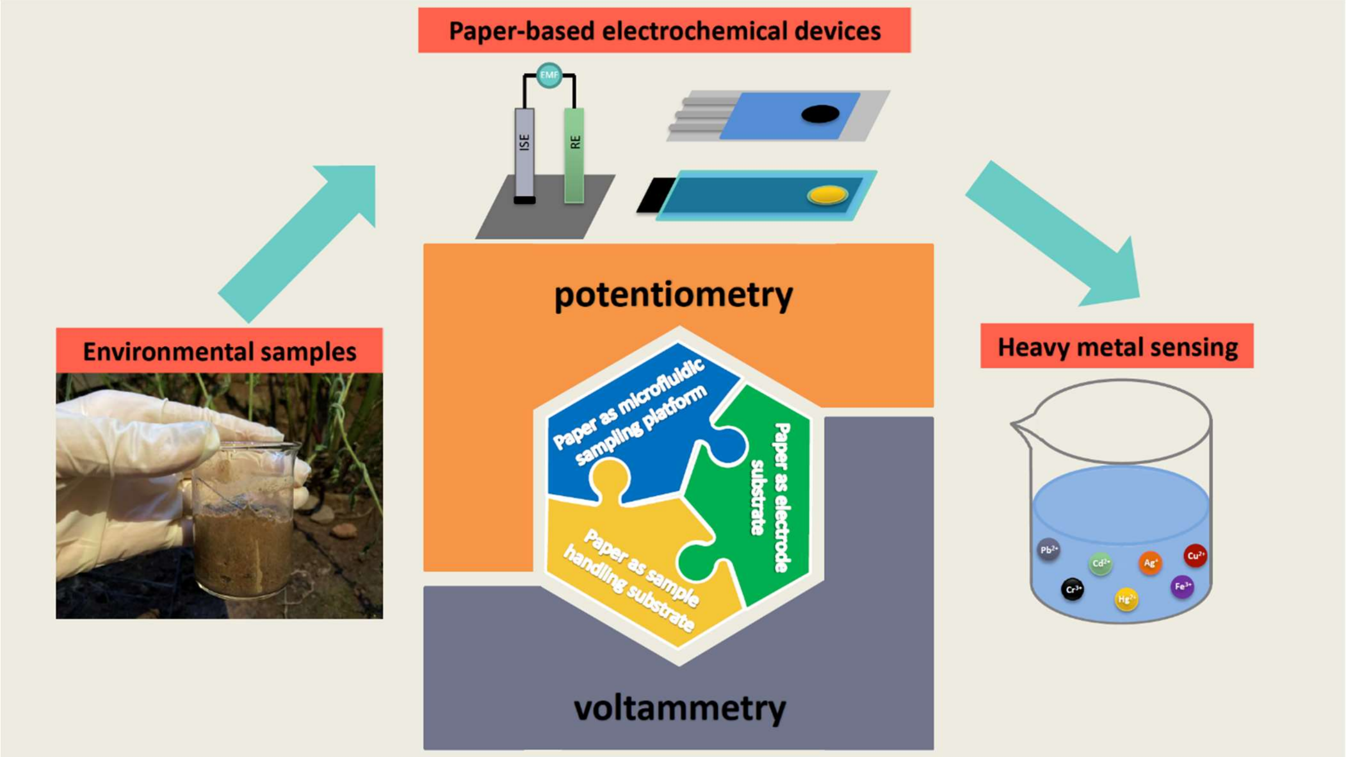
(127) Nunez-Bajo, E.; Blanco-López, M. C.; Costa-García, A.; Fernández-Abedul, M. T. *Anal. Chem.* **2017**, *89* (12), 6415–6423.

(128) Sánchez-Calvo, A.; Fernández-Abedul, M. T.; Blanco-López, M. C.; Costa-García, A. *Sens. Actuators B Chem.* **2019**, *290*, 87–92.

(129) Sánchez-Calvo, A.; Blanco-López, M. C.; Costa-García, A. *Biosensors* **2020**, *10* (5), 52.

(130) Kumar, A. A.; Hennek, J. W.; Smith, B. S.; Kumar, S.; Beattie, P.; Jain, S.; Rolland, J. P.; Stossel, T. P.; Chunda-Liyoka, C.; Whitesides, G. M. *Angew. Chemie Int. Ed.* **2015**, *54* (20), 5836–5853.

TOC


Paper-based electrochemical devices
EMF
ISE
RE
Environmental samples
potentiometry
Paper as microfluidic sampling platform
Paper as electrode substrate
Paper as sample handling substrate
voltammetry
Heavy metal sensing
Pb^{2+}
Cd^{2+}
Ag^{+}
Cu^{2+}
Cr^{3+}
Hg^{2+}
Fe^{3+}