Universal mobile electrochemical detector designed for use in resource-limited applications

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Introduction

- This paper describes an inexpensive, handheld device that couples the most common forms of electrochemical analysis directly to “the cloud” using any mobile phone, for use in resource-limited settings.
- It is designed to operate with a wide range of electrode formats, performs on-board mixing of samples by vibration, and transmits data over voice using audio
- The electrochemical methods that are demonstrated enable quantitative, broadly applicable, and inexpensive sensing with flexibility based on a wide variety of important electroanalytical techniques

The electrochemical methods utilised are

- Chronoamperometry,
- Cyclic Voltammetry,
- Differential Pulse Voltammetry
- Square Wave Voltammetry,
- Potentiometry, each with diffe t uses.

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Four applications demonstrate the analytical performance of the device:
these involve the detection of

(i) glucose in the blood for personal health,

(ii) trace heavy metals (lead, cadmium, and zinc) in water for in-field environmental monitoring,

(iii) sodium in urine for clinical analysis, and

(iv) a malarial antigen (Plasmodium falciparum histidine-rich protein 2) for clinical research.

Innovative

- The parallel development of two successful technologies—mobile health (mHealth) and point-of-care (POC) diagnostics
- For communication of data, they have exploited the ubiquity of the hands-free audio port, a nearly universal interface to mobile phones
- Designed a protocol to transmit digital data over a live voice connection.
- This approach guarantees that

(i) Any phone can function as a modem to link the results of testing to a remote facility through any available mobile network (2G, 3G, or 4G),

(ii) The device does not require any specific software application,
operating system, or connector (beyond an audio cable).

- Detection of Glucose in Blood – chronoamperometry, glucose test strips, whole blood samples
- Detection of Heavy Metals in Water (Zn(II), Pb(II), Cd(II)) – SWASV, SPEs(DRP 110-CNT), (i) a WE consisting of carbon ink modified by carbon nanotubes, (ii) a counter electrode consisting of carbon ink, and (iii) an RE consisting of Ag/AgCl ink
- Detection of Sodium in Urine – Potentiometry, ISE
- Detection of Malaria – chronoamperometry and sandwich ELISA

(i) A custom-made, three-electrode potentiostat, formed from two operational amplifiers, to perform electrochemical measurements

(ii) Three digital switches to reconfigure the potentiostat between two- and three electrode operation and between amperometric or potentiometric measurement

(iii) A small vibration motor to mix fluid samples

(iv) A dualchannel, 16-bit, digital-to-analog converter (DAC) to set the potentials of the reference electrode (RE) and working electrode (WE)

(v) A single-channel, 16-bit analog-to-digital converter (ADC) to sample data at high resolution

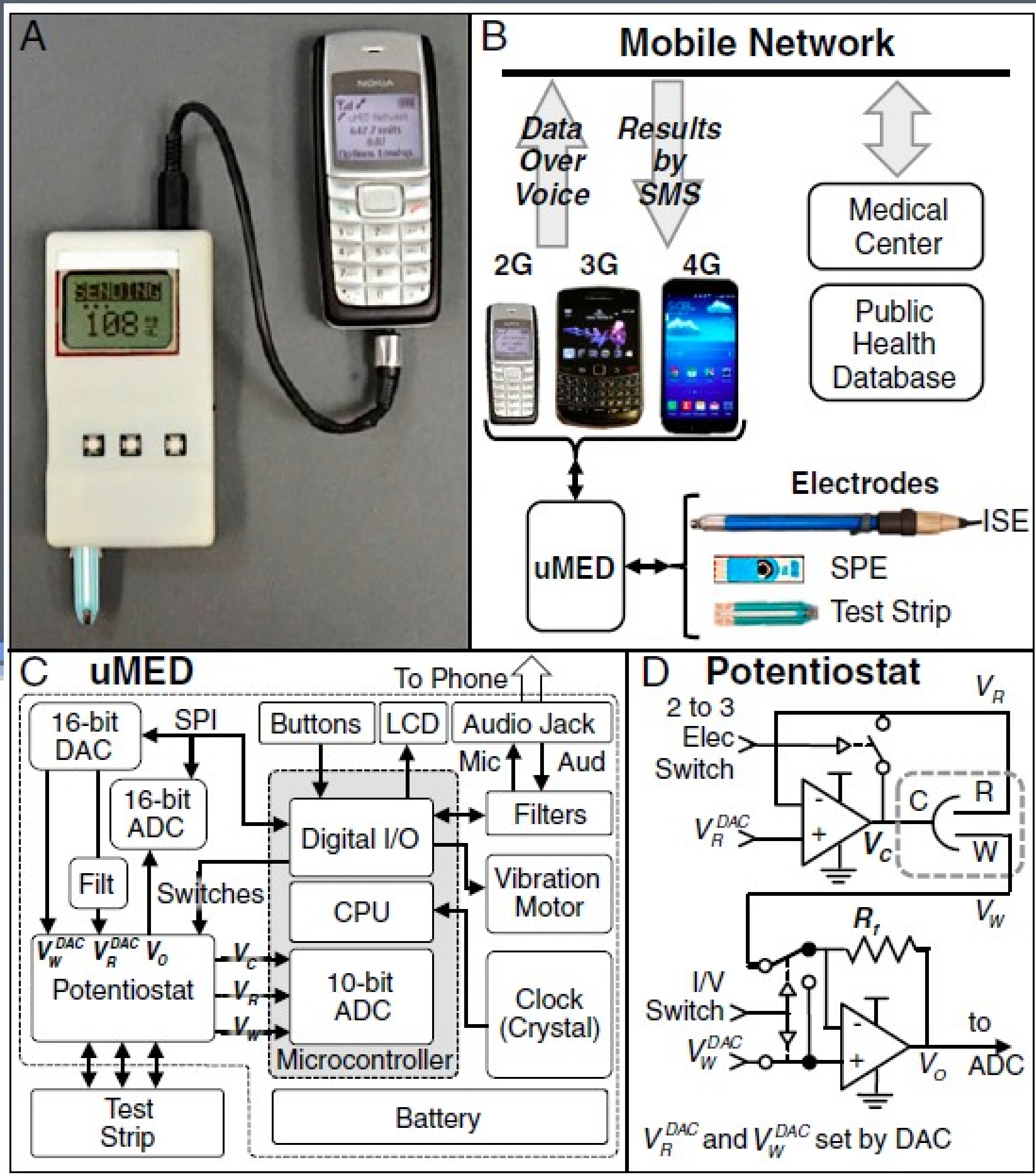
(vi) A pair of sockets to interface with various electrodes

(vii) A liquid crystal display (LCD) and three buttons to interface with the user

(viii) An audio port to communicate data

(ix) A microcontroller to operate the device

(x) A serial port to program the microcontroller



(A) An image of the uMED interfaced to a commercial glucose test
strip and a low-end mobile phone through a standard audio cable, for transmission of data over voice.
(B) A schematic of the connections and flow of data from the

(C) A block diagram of the hardware and interconnections of the device. (D) The circuit design for the reconfigurable potentiostat. CPU, central processing

Detection of Glucose in Blood

- For each measurement, glucometry from the uMED menu is selected, the test strip is inserted, and applied a droplet of blood (~5 μL , a volume easily obtained from a finger prick) to the test strip.
- Application of the sample triggered the chronoamperometry sequence, which began with an incubation period of 5 s at E = 0 followed by a measurement period of 10 s at E = 0.5 V.
- The uMED samples the output signal at 8 Hz and digitally averages the transient signal over the last t = 5 s of the measurement.

Detection of Heavy Metals in Water

This procedure requires a four-step pulse sequence

(i) Cleaning, where a positive potential (Eclean = 5 V, 120 s) applied to the WE oxidizes any impurities from the electrode surface to prepare it for the measurement.

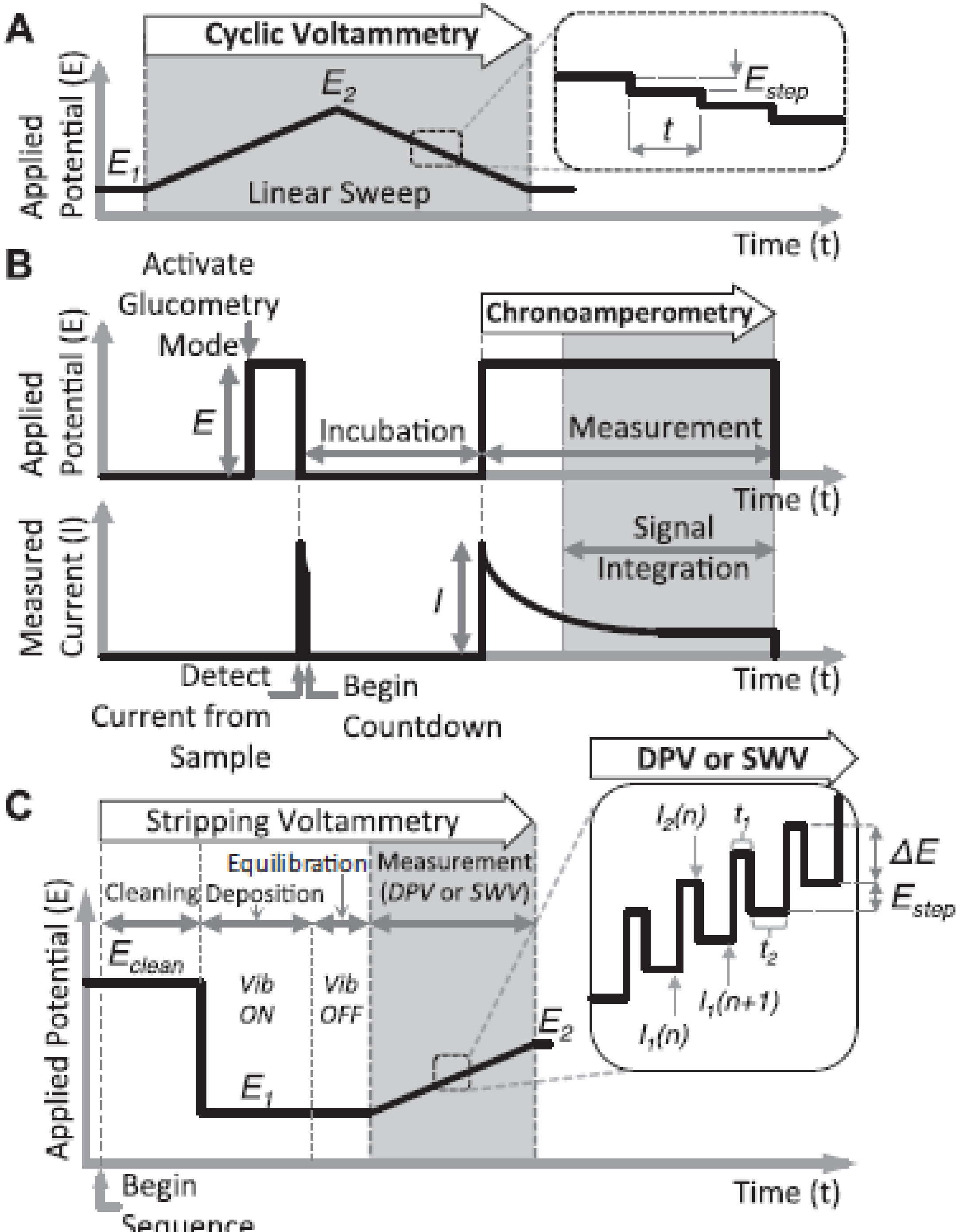
(ii) Deposition, where a negative potential (E1 = −1.4 V, 120 s) applied to the WE causes metal ions in solution to reduce onto the electrode surface if the potential is more negative than the reduction potential of the metal. The solution must be agitated during these first two steps, so that the kinetics are not limited by the rate of diffusion.

(iii) Equilibration, which is the potential maintained at E1 with no agitation for a short time (30 s) to ensure equilibration of the solution.

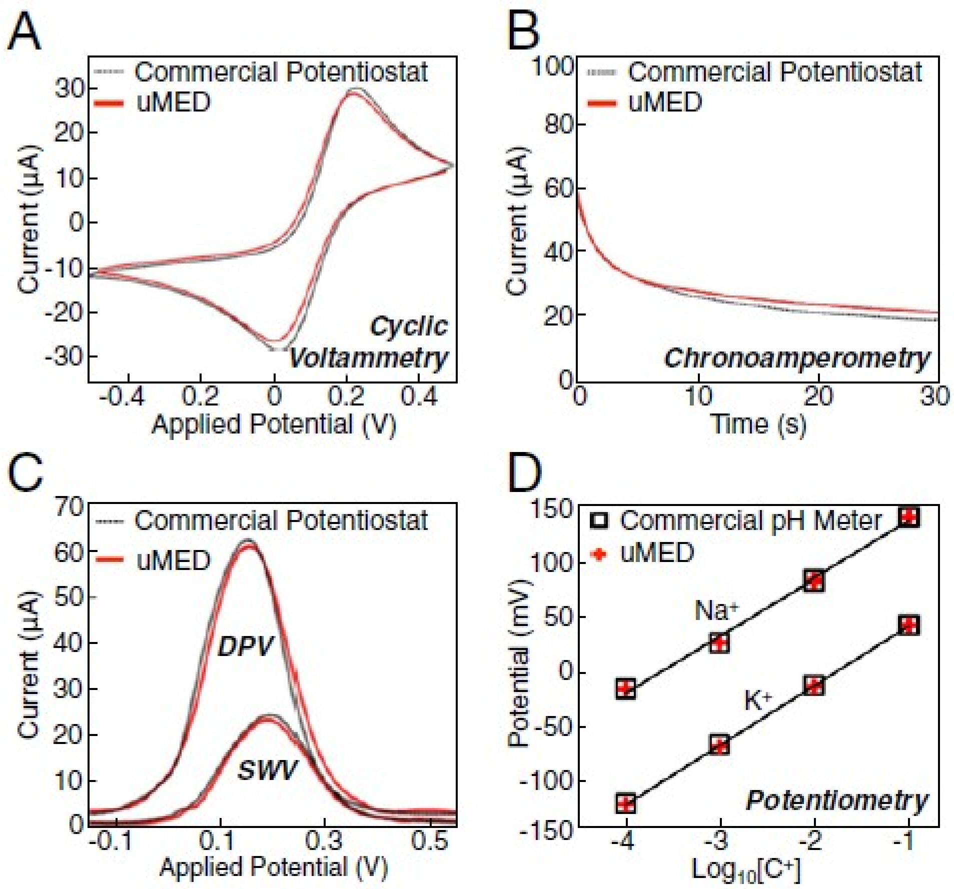
(iv) Measurement, where SWASV (SWV sequence from E1 to E2 = −0.1 V, at ΔE = 50 mV, Estep = 5 mV, f = 20 Hz) causes the metals deposited on the electrode surface to reoxidize and redissolve into the solution. The reoxidation occurs when E matches the oxidation potential of the metal, so that the measured current exhibits a different

Detection of Malaria

- To perform a malaria immunoassay, chronoamperometry to measure the concentration of PfHRP2 through a sandwich ELISA that was augmented for electrochemical detection was used.
- The detecting antibody was conjugated to horse radish peroxidase (HRP), which oxidizes 3,3′,5,5′-tetramethylbenzidine (TMB), a widely used chromogenic substrate.
- This reaction was performed in a 96-well plate and then a drop of solution was pipetted onto a commercial SPE (DRP110-CNT; DropSens).
- The uMED detects the oxidized product by performing chronoamperometry for 20 s at $\Delta E = 0.2$ V, sampling the output signal at 20 Hz, and digitally averaging the transient signal over the last $t = 8$ s of the measurement.

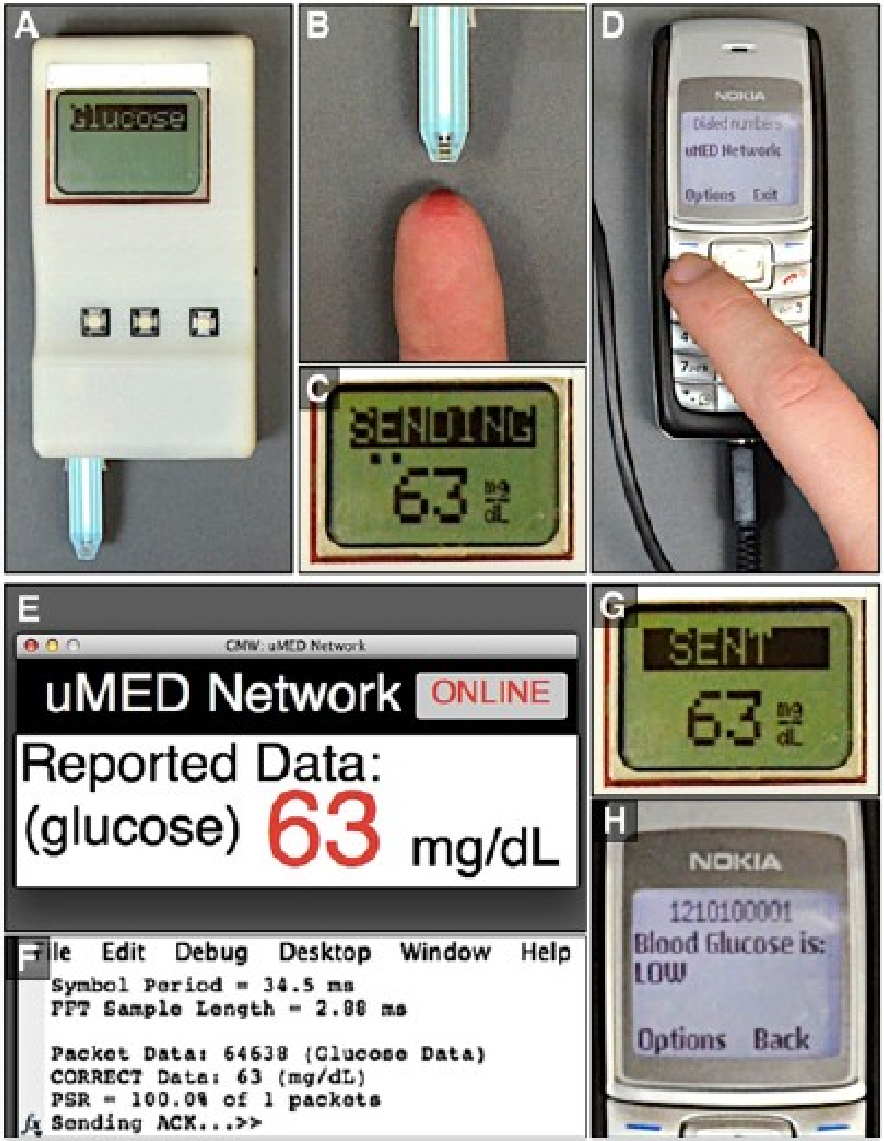


Examples of the timed sequence of applied potentials and measurement for a representative sample of possible pulse sequences.
(A)CV.
(B) Chronoamperometry in the context of glucometery.
(C) SWV and DPV in the context of ASV.
The shaded regions are used to indicate the times when the current is recorded.



(A) A cyclic voltammagram of 2.5mM ferricyanide/ferrocyanide in 0.1 M KCl.
(B) The measured current versus time for chronoamperometric detection of 1 mM ferrocyanide in 0.1 M KCl.
(C) Differential pulse and square wave voltammagrams of 1 mM 1-naphthol in 100 mM Tris, 100 mM NaCl.
(D) Detection of [K+] and [Na+] with potentiometry in an ionic strength adjuster

Differences between the commercial device and uMED were primarily caused by variations between test strips and electrochemical fluctuations during measurements, and not by differences in the



A demonstration of the uMED network in operation.
(A and B) The local user made a blood glucose measurement with the uMED.
(C) Upon completion, the device automatically began to transmit repeated packets
containing the measured value.
(D) The user then connected the device to
a mobile phone and placed a call to a remote Skype number.
(E and F) The remote application (i) automatically recorded the
audio-based data, (ii) extracted the encoded value, (iii) verified that it was error free, (iv) sent an acknowledgment tone back to the uMED, and (v) sent an SMS message (with
relevant information) back to the local user’s mobile phone.

Conclusion

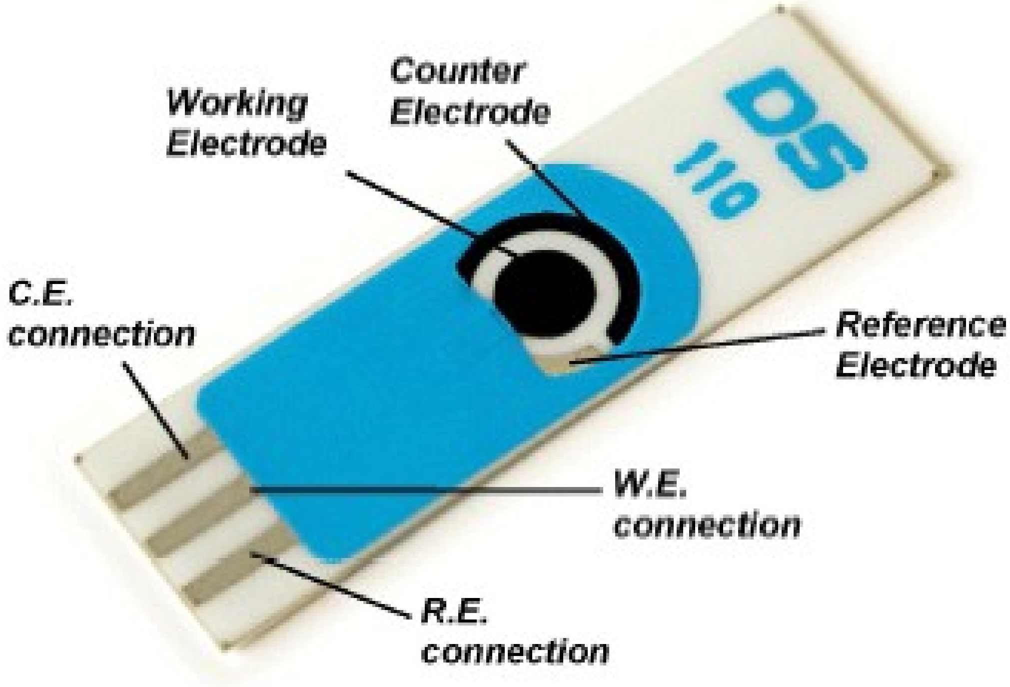
- They have demonstrated the broad electroanalytical capabilities of the device within a variety of important applications and contexts
- The linearity and precision of the uMED is equivalent to that of bench top instruments and can be used in field.
- The use of commercially available SPEs and test strips ensures reproducibility, guarantees that the device is useful immediately, and reduces the cost per test by decreasing the required sample volume to a single droplet
- The handheld, stand-alone format of the uMED, and use of lowpower, commercial electronic components offer several important benefits.

(i) The uMED can be used to collect data by someone who does not own a mobile phone.

(ii) The device can last for months to years on a single battery charge

(iii) The electronic components used are specified to operate stably over a broad range of temperatures (−40 to 85 °C); this stability makes the uMED well suited for use in a variety of climates around the world.

Prospectives



Thank you...