



A Review on Voltammetry Potentiostat Devices to Detect Leptospirosis

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ABSTRACT

Electrochemical systems are becoming increasingly popular in recent years due to their ability to be small and interactive at a reasonable cost. This allows for large-scale concurrent work with other comparable experiments. However, Leptospirosis is an arising zoonotic sickness that is viewed as a reappearing irresistible illness. There has been an impressive increase in the number of cases reported as well as recurrence of episodes in South-East Asia. The number of leptospirosis cases in Malaysia is increasing in recent years. Malaysian weather with high humidity and warm temperatures allow *Leptospira* to survive longer in the environment. To reduce the risk of death, the disease should be diagnosed at an early stage. However, if the *Leptospira* bacteria can be detected in situ, human infections can be avoided. Many biosensors have been invented to detect *Leptospira*. Therefore, this study aims to review different kinds of portable *Leptospira* detectors using compact voltammetry potentiostat. This review paper includes a comprehensive overview of the miniaturized and potentiostat system, and materials used to detect Leptospirosis. Studies on detectors especially for electrochemical material detection have provided views about how wireless detectors interfaces with smart devices which help to save, analyze, and visualize data and transmit final information with proper protocol. This paper is intended to briefly study the development of voltammetry potentiostat as well as the new research in recent days. The review addresses the improvement of theoretical technique besides its application as well. In addition, this article discusses the future of mini potentiostat to determine diseases like Leptospirosis with electrochemical analysis using a potentiostat.

Keywords: Leptospirosis, Potentiostat, Electrochemical instruments, Portable, Voltammetry

1. Introduction

Leptospirosis is an arising zoonotic sickness above the range of one million around the world (Abdullah et al., 2021). It was viewed as a reappearing irresistible illness, especially in tropical countries including subtropic regions. There has been an impressive increase in the number of cases reported as well as recurrence of episodes in South-East Asia (Thailand, Malaysia, and Indonesia). As a result of misreporting in various regions of the world, leptospirosis in the jungle ranges from 0.1 to 10, with at least 100 of the one million people affected by flame retardants or high-risk areas. In any case, these are probably going to be disparaged due to transdiagnosis and deficient reconnaissance frameworks in numerous nations (Abdullah et al., 2021). The long-time scales need from starting appearance to determination and treatment for cutting-edge medical problems are being decreased by interfacing logical science and electronic designing (Windmiller et al., 2013). This leaves us with the likely ability to couple investigation with a solitary gadget equipped for applying for medicines because of real-time physiological estimations, giving a customized and suitable consideration.

Generally, Leptospirosis disease is spread by rodents (Ludwig et al., 2017). In Malaysia, the number of leptospirosis cases is increasing with each passing year, as is the number of deaths due to the disease (Soo et al., 2020). Figure 1 presents the total number of Leptospirosis cases in Malaysia from 2004 to 2012. Malaysian weather with high humidity and warm temperatures allow *Leptospira* to survive longer in the environment. To reduce the risk of death, the disease should be diagnosed at an early stage. However, if the *Leptospira* bacteria can be detected in situ, human infections can be avoided.

Many biosensors have been invented to detect *Leptospira*. However, these biosensors require lab analysis using a potentiostat (Bianchi et al., 2019). The electrochemical signal can be turned into a certain amount of electrical response, and something that bacteria can use to find nanocomposites. The biochemical reaction between the thin active surface and the target bacteria produces electrical signals that can be measured and counted. This is a reliable

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way to find bacteria. Currently, going to get rid of these bacteria takes a very long time. For example, the Microscopic Agglutination Test (MAT) needs at least 8 days to find out if these bacteria are present (Villumsen et al., 2012). The Enzyme-Linked Immunosorbent Assay (ELISA) method isn't good enough to find *Leptospira*, and it needs time to stabilize (Chalayon et al., 2011). The Polymerase Chain Reaction (PCR) method uses both urine and clinical blood samples in a test, which might also cause contamination (Yasouri et al., 2013). In the early stages of Leptospirosis, it can be hard to find because it requires specific tools, specific and sensitive samples, a large laboratory space, and experts with a lot of training. Because of the problems listed above, there is more interest in using nanocomposite thin film as a detector.

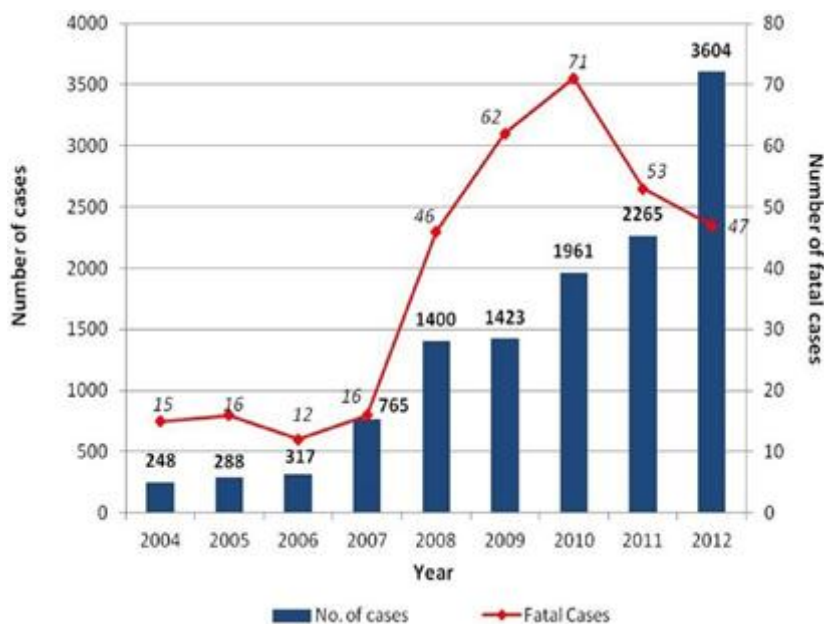


Figure 1. The number of Leptospirosis cases in Malaysia from 2004 to 2012.

Source: Azhari et al. (2019)

Voltammetry is one of the most important ways to study electrochemistry. In this method, a known potential is applied between two or more electrodes, and the current that flows through the cell is studied (Scholz et al., 2015). Voltammetry covers a wide range of techniques, such as linear sweep, square wave, alternating current, and cyclic voltammetry (Zanarini et al., 2011). A voltammetric system needs a computer, a potentiostat, and an electrochemical cell. Many scientists are already working on making computers and electrochemical cells that are smaller. This leaves only the precision potentiostat, which takes longer to make smaller than the others. This study provides an overview of the miniature and potentiostat system, and materials used to detect Leptospirosis by reviewing the present state of the miniature and potentiostat system.

2. Methodology

The present study follows a systematic review technique. The research investigates the present condition of the miniature and potentiostat system to detect Leptospirosis. To do the investigation, we reviewed 40 articles collected from Google Scholar and the Web of Science database. Based on the literature review, this article discusses the future of mini potentiostat to determine diseases like Leptospirosis with electrochemical analysis using a potentiostat.

3. Detection of Leptospirosis with Voltammetry Potentiostat devices

3.1. Ministate

The Ministate device was made to provide a typical range of potentials using a standard three-electrode configuration while accurately detecting currents in the micro to nano ampere range (Adams et al., 2019). The device was also made so that its key parameters can be tuned for a specific application with only a few changes to the circuit. The Ministate device was made to work with a single-cell, rechargeable lithium-polymer battery. However, any power source above 3.7V would work, including a 5V supply from a USB port. Instead of making a custom CMOS chip, the device was made to be as small as possible while still being easy to make. It does it by using low-cost discrete components. Figure 2 shows the Ministate plan for how it works and its full circuit diagram.

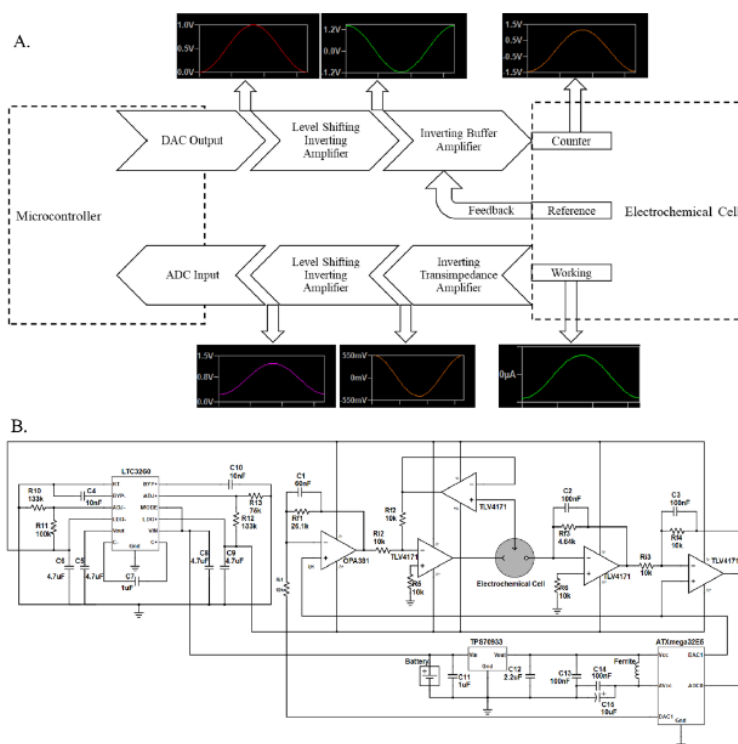


Figure 2. Operational MiniState Circuit diagram (A) The Digital to Analog Converting (DAC) operation (B) Component of ministate
Source: Adams et al. (2019)

3.2. Cyclic voltammetry validation

Cyclic voltammograms were made by sweeping the potential between -0.1V and 0.8V at different scan rates. The experiments were done on both the commercially available potentiostat and the MiniState, as shown in Figure 3, to make sure that both the current and the potential were measured correctly. To compare the two systems, even more, the diffusion coefficient of the ferricyanide system was measured with both systems. This measurement looks at how well the potentiostat works under a variety of conditions (scan rates and currents). The measurements were close: $1.25 \times 10^5 \text{ cm}^2/\text{s}$ for the commercial potentiostat and $1.26 \times 10^5 \text{ cm}^2/\text{s}$ for the MiniState. This shows that the MiniState is measuring currents and potentials correctly in cyclic voltammetry (CV) mode under a wide range of experimental conditions. The scans shown are the second CV from each set.

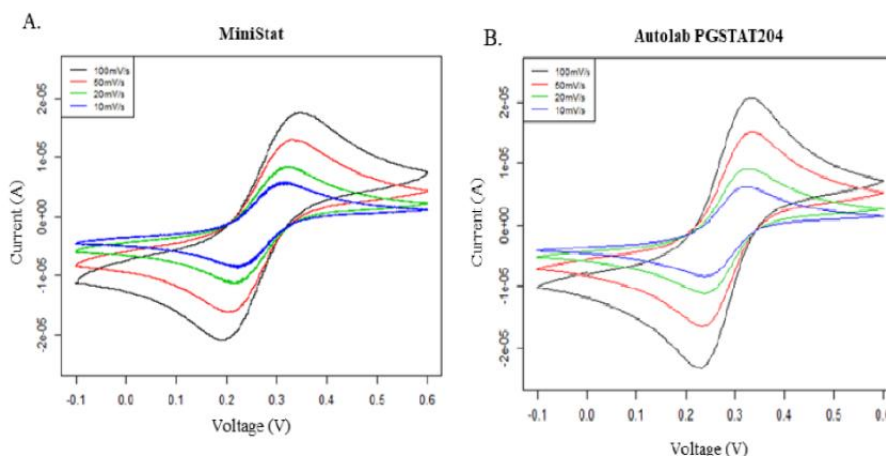


Figure 3. Voltammograms of Potassium Ferricyanide (1 mM in 1 M KCl, vAg/AgCl reference electrode, GC working electrode) on both the MiniState and the Auto lab PGSTAT204 sweeping the potential between -0.1V and 0.8V , at various scan rates.

A large portion of these plan choices is under the guise of making the activity simple by methods for a sun port-free and easy-to-use gear. However, they wind up forestalling the full utilization of the hardware capacities and genuine comprehension of the gathered information. Counting clinical diagnostics, natural, industrial petrochemistry is valuable for investigations in applications and food observing QC, and other gadgets for individual health issues. (Pedrero et al., 2014; Labib et al., 2016; Duffy et al., 2017). Various strategies also empowered the electrochemical recognition of analytes which includes proteins, DNA, particles, synapses, and much littler electroactive material (Wang et al., 2008, Bandodkar et al., 2015, Gumpu et al., 2015). Figure 4 shows the cyclic voltammogram of ferricyanide on a printed electrode where the insert represents the relation between the square root of scan rate and peak current. Furthermore, potentiostat instruments play an important role in the electro analysis to control and estimate the electrical flow and voltages. The figure presents the square wave voltammogram assessed by UWED and potentiostat. It illustrates a linear correlation between ferricyanide and peak amplitude.

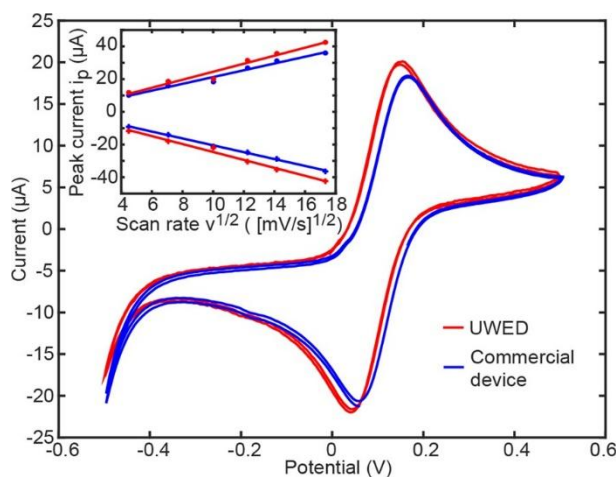


Figure 4. Cyclic voltammogram of ferricyanide on a printed electrode.
Source: Karikalan et al. (2017)

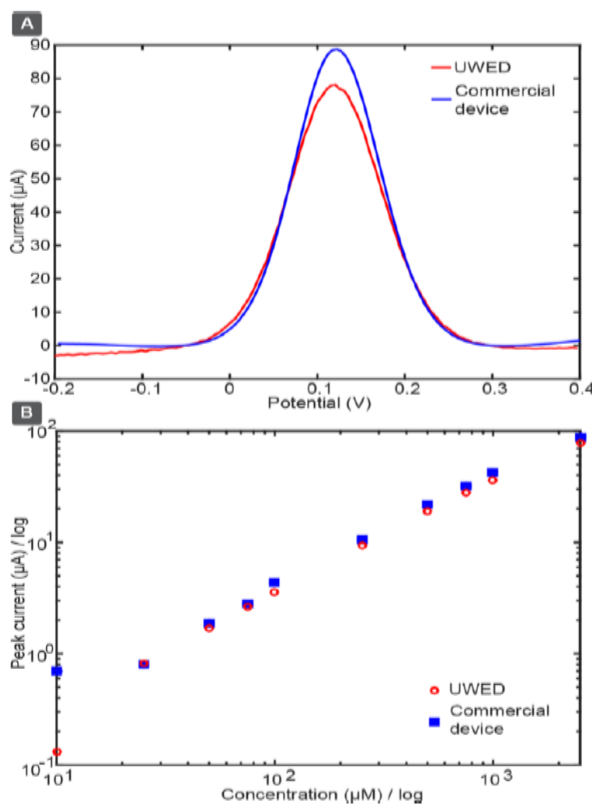


Figure 5. Represent square wave voltammogram assessed by UWED and potentiostat.
Source: Karikalan et al. (2017)

3.3. Hardware development

The hardware development and configuration frequently depend on a "discovery" development reasoning, driving the client far from the standards of activity of the machine and changing into an "information spitting" material (Mettakoonpitak et al., 2016). Figure 6 presents the (i) construction of the circuit board and (ii) analog circuit of the potentiostat with highlighted (A) amplifier for addition; (B) potential controlling amplifier; and (C) trans-impedance amplifier.

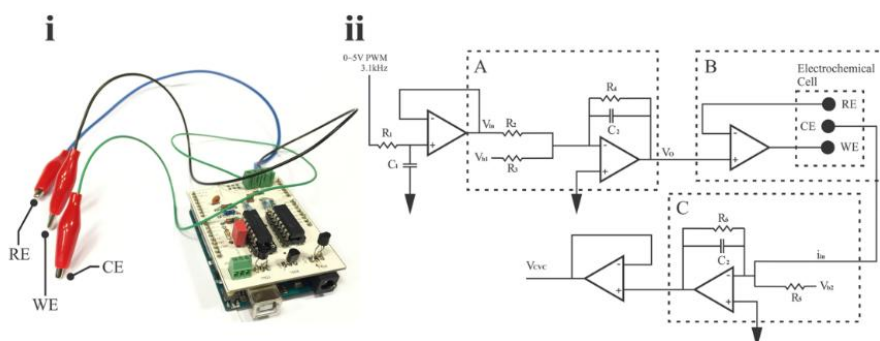


Figure 6. The construction of the circuit board and analog circuit of the potentiostat.

Source: Meloni et al. (2016)

Furthermore, advances in hardware have empowered improving the huge, substantial, and costly benchtop potentiostat to compact and ease electric peruses that are reasonable for investigation for utilization and in asset restricted or field settings (Izadyar et al., 2016). Figure 7 presents the panels illustrating the function of UWED and the main components of UWED.

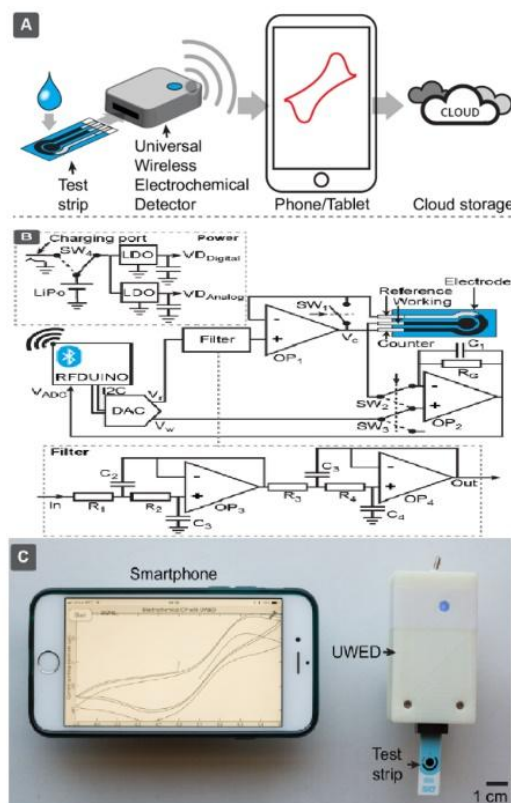


Figure 7. (A), (C) Panels illustrating the function of UWED (B) The main components of UWED

Source: Ainla et al. (2018)

3.4. Potentiometry and Ion-transfer stripping voltammetry

Anthraquinones is the foremost varied cluster of quinones gift in the food item. It performs as a secondary source of metabolic material which boosts the quality of applications of an internal organ (Izadyar et al., 2016). It also exhibits additional vital, antibacterial, biological, antiviral, and antifungal activities. Hydroxylated anthraquinones are synthetic compounds widely consumed as a form of drugs; because of their actively performing as biological compounds. For example, Quinzaine (1,4 dihydroxy γ -anthraquinone), anthrarufin (1,5 dihydroxy-anthraquinone), chrysalises (1,8 dihydroxy-anthraquinone), and theaflavin (2,6 dihydroxy-anthraquinone) enter this group. Those hydroxy Lateatha quinones that feature as a quinoid ring whereas two American state teams within their structure, dissent from one another by replacement of various carbon counts in those molecules. Hydroxy Lateatha quinones' prohibition of autophagy is also a good technique to beat the chemoresistance of sure therapy for the drug. A combination of medical care with anthraquinones like chrysalises and the antibiotic drug could give an efficient methodology for carcinoma dealing, even though some of them are ordinarily utilized as inhibitor compounds in food and health-related applications (Mirceski et al., 2017).

Due to their importance of independently measuring the constant of acidity of those structures, however, up to now the acidity constants of this set of hydroxy plateman phanquinones, as there is no report in liquid medium. During this task, values of pK_a and molecules in aqueous were reported for the very first time. Moreover, quinzaine is unique amongst anthraquinone dyes ordinarily utilized as fuel markers to differentiate their source of hail and quality, bearing vital applications in drugs because of its repressive impact on the human enteral bacterium. In the view from a pharmaceutical point, since it is a structural a part of antitumor drugs corresponding to daunomycin, antibiotic drugs, and mitoxantrone that move with desoxyribonucleic acid by the embolism methodology, the chemical science quantification of quinzaine in liquid media is additionally reported in presence of various anthraquinones as meddling agents, taking advantage of the inclusion complicated fashioned between quinzaine and (2-hydroxy)-propyl- β -Cyclodextrin (2HpbC D), the acidity constants in liquid media and thus the formation (Cláudio et al., 2011).

For ion transfer some distinctive voltammetric methodologies had been implemented for analysis, like linear sweep stripping voltammetry (LSSV), differential pulse stripping voltammetry, rectangular wave stripping voltammetry and chronoamperometry, cyclic voltammetry (CV), and scanning electrochemical microscopy (SECM). Stripping methods are more commonly used for huge error correction and overall, an impressive development in industrial sensors (Tiwana et al., 2012). Figure 8 presents stripping voltammograms to acquire potential sweep rate and ITS of 50 nM K^+ at 0.1 V/s with various preconcentration times. Furthermore, Figure 8 presents the background-subtracted stripping voltammograms and the background-subtracted stripping voltammograms of certiorari ion.

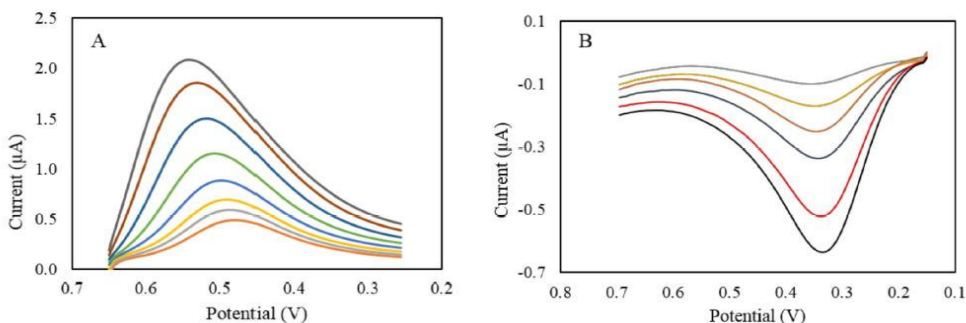


Figure 8. (A) Background-subtracted stripping voltammograms (B) Background subtracted stripping voltammograms of certiorari ion
Source: Izadyar et al. (2016)

Moreover, square-wave voltammetry (SWV) is an effective electrochemical way of task completion suitable for analytical activity (R), mechanistic observation of electrode Strategies, and electrokinetic measurements. In recent times, its miles have been taken into consideration as one of the maximum superior voltammetric methodologies, which unifies the benefits of pulse strategies (improved sensitivity), cyclic voltammetry (insight into the electrode mechanism), and impedance strategies (kinetic information of very speedy electrode tactics). Figure 9 presents the dependence of the peak potential separation of the potential-corrected SW polarograms on the SW amplitude and the kinetic parameters.

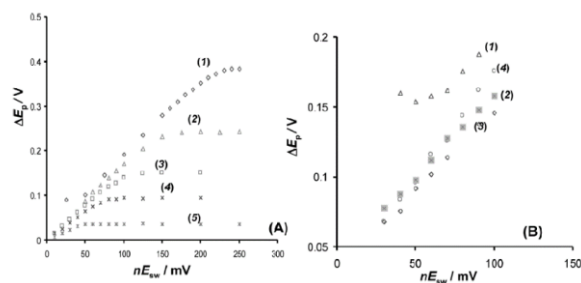


Figure 9. (A) The dependence of the peak potential separation $\Delta E_p = (E_p, aE_p, c)$ of the potential-corrected SW polarograms on the SW amplitude. The kinetic parameter for (A) is $wk = 0.05$ (1); 0.2 (2); 0.5 (3); 1 (4) and 3 (5), while for (B) it is $k = 0.1$ (1); 0.5 (2); 1 (3) and 10 (4) ($k = ks/(Df)$; 0.5: ks (cm/s) is the standard rate constant and D is the common diffusion coefficient (R))

In a historical context, it initiated from the Kalousek commutator and Banker's square-wave polar graph (Lee et al., 2010). Nowadays, the SWV included in virtual electrochemical material makes use of a combination of a staircase ability modulation and periodic square-formed tertial function, dispensed at a sedentary electrode (Das et al., 2011; Mukherjee et al., 2012). We tend to address the recent advances and application of SWV masking the period from 2007 up to date, i.e., the duration once the book of the treatise is devoted fully to the present technique.

4. Conclusion

Leptospirosis is a life-threatening disease caused by the bacteria *Leptospira*. Commonly, the disease is spread by rodents. In Malaysia, the number of leptospirosis cases is increasing with each passing year, as is the number of deaths due to the disease. Malaysian weather with high humidity and warm temperatures allow *Leptospira* to survive longer in the environment. To reduce the risk of death, the disease should be diagnosed at an early stage. However, if the *Leptospira* bacteria can be detected in situ, human infections can be avoided. Many biosensors have been invented to detect *Leptospira*. However, these biosensors require lab analysis using a potentiostat. In situ detection is not available because the potentiostat is not portable. This study aims to review different kinds of portable *Leptospira* detectors using compact voltammetry potentiostat.

The study described the design of a compact potentiostat. The amplifiers are integrated to construct a compact voltammetry potentiostat. A microcontroller is programmed to provide voltage to potentiostat for linear voltammetry and differential pulse voltammetry analysis. The microcontroller is also programmed to capture voltage obtained from the potentiostat and to determine the presence and concentration of *Leptospira* based on the voltage. The mini potentiostat and an LCD are connected to the microcontroller to construct a portable *Leptospira* detector. The LCD is used to display the results. The portable detector is integrated with polyaniline Fe-Al nanocomposite thin film biosensors and tested on live *Leptospira*. Finally, the system is implemented on a Printed Circuit Board (PCB). The review addresses the improvement of theoretical technique besides its application as well. This research is expected to provide insights on a portable *Leptospira* detection kit that can be used by authorities or individuals to rapidly detect the presence of *Leptospira* in situ. Thus, Leptospirosis disease infection in humans can be avoided.

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