

Bulk and Microfluidic-Based pH Sensors

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The determination of pH is of paramount importance in environmental, pharmaceutical, and medicinal sciences, etc., for accurate controlling, monitoring, and adjusting whole processes on microscale and macroscale. Therefore, the pH measurements have drawn continuous efforts from a great deal of research. The bulk pH determination can tackle part of the demands from laboratories and industrial applications.

Keywords: pH determination ; bulk pH sensing ; microfluidic-based pH sensing

1. Introduction

The determination of pH is of great significance in various types of inspections such as chemistry, biology, agriculture, architecture, and so on ^[1]. Since the first research on pH was announced in 1914 and the main role of the hydrogen ion concentration and its determination of H^+ in biology had been established ^[2], there has been a great historical development in pH measurement and different specific methods of determination have been used depending on diverse needs (different equipment, samples, analytically time or locations ^[3]) in the past few decade's years. In this case, pH measurements, the universal quality analysis, have been widely used in both laboratory level and industry because of reasonable prices, easy operations, efficiency, and so on. In the following parts, the definition, history, specific methods, and applications of pH are included.

2. Mechanism of pH Sensing

2.1. Specific pH Measurement

2.1.1. Cell for a Primary Method Measuring pH

Based on cell I (consisting of a platinum hydrogen gas electrode, a chosen buffer solution, and a silver/silver chloride reference electrode ^[4]), a new cell called the Harned cell is developed by Harned et al. ^[5] to measure the acidity of the sample in the 1930s. This cell was developed at the NBS (National Bureau of Standards, USA, now NIST) by Bates ^[6] and Hamer ^[7] to ensure the accuracy of pH determination in the next decades.

Adding the chloride ions to the chloride-free buffer solution at some different Cl molarities to keep the balance into the potential of the Ag/AgCl electrode. With the help of the Harned cell, it can solve the problem of the LJP and connection so that the cell potential only includes the disparity in the two electrode potentials.

To develop a battery without a liquid junction, it is certain to follow a convention that the single ion activity consisted of Equation (1) above. In this case, the leading method for pH based on this aim, the Bates–Guggenheim convention ^[8] is used and can be related to the Debye–Hückel theory of strong electrolytes but this convention only suits the solutions of low ionic strength, $I \leq 0.1 \text{ mol}\cdot\text{kg}^{-1}$.

If the expanded uncertainty relates to the other thermodynamic assumption, the traceability of the determined pH value to the SI can be described in terms of pH(S) values so that the Bates–Guggenheim convention can be considered. However, compared with the experimental expanded measurement uncertainty ($k = 2$) for a pH value of a selected primary buffer solution (0.003–0.004), the measurement uncertainty contribution growing from the used convention is 0.01. Fortunately, this convention is still common use for most of the applications ^[9].

2.1.2. The Differential pH Cell (Baucke Cell)

There is one specific drawback of Harned cell—long-time production to ensure accuracy, which leads to a less suitable economy for most of the conventional laboratories and determinations. Therefore, to meet the basic need of pH measurement, lots of cells with liquid junctions may be applied to measure the pH values of a secondary reference buffer

liquid by comparing that of a major buffer solution ^[10], which leads to a more popular application in the public and provides operators with critical reasonable methods.

Similar to the content of the primary standard, the secondary reference buffer solutions are developed, and the differential potentiometric cell is produced by Baucke first ^{[11][12][13][14]}. It is called a differential cell or Baucke cell, cell II, with the aim of standardizing pH buffers solution, is composited by two identical metal electrodes, Pt (1) and Pt (2), and two quasi-identical buffers solutions, S₁ and S₂, with pH values, pH(S₁) and pH(S₂).

Compared to cell I, cell II is employed to distribute pH(S₂) for a certified reference material (CRM) below so S₂ is a CRM buffer for the assignment of pH (S₂) and S₁ is considered a primary pH buffer ^[15]. S₁ is merely a small batch as a primary reference while S₂ is a larger batch for the same nominal construction of S₁. As the traceability of pH (S₂) for the CRM to the SI is measured from the Harned cell (from pH(S₁) to the SI) and from the differential measurement (from pH (S₂) to pH(S₁)), some uncertainty can be ignored and do not lower the accuracy of measurement.

As Baucke developed cell II, this cell is also called the “Baucke cell”. Contradistinguish the main determination of pH, the differential measurement of pH was easily operated and improves the efficiency of determination, which led to the wide usage in projects for the dissemination of pH measurement capability of a number of countries ^[16].

2.1.3. Ordinary pH Measurements: The Glass Electrode

The primary and differential measurements of pH are applied at NMIs (National Metrology Institutes) and authoritative laboratories to realize and publish the accurate quantity of pH because of their characteristics—complexity and restriction to specific buffers. So, there are some other routine pH measurements for most of the labs. The glass electrode might be one of the typical examples ^[17].

According to the 2002 IUPAC, the definition of the glass electrode is that a bulb or other suitable form of glass is always constructed into the hydrogen ion-responsive electrode contacted to a stem of high-resistance glass complete with an internal reference electrode and internal filling solution system. Choosing different geometrical forms of glass depends on different types of applications. For instance, for medical science, it is suitable for some special applications such as a capillary electrode for blood measurement ^[14].

The routine pH determinations consist of a pH test step including a pH meter and a pH electrode. As for the pH electrode, it is usually called a “glass electrode” while it is composed of two independent electrodes—the internal glass electrode and the external reference electrode having a liquid junction. The electrode paid is always considered to be designed as a combination or single rob. The representative electrode of this method is based on cell III:



The Ag|AgCl reference electrode and the KCl buffer solution on the left side of cell III include the external reference electrode. The diaphragm between the sample buffer liquid and KCl liquid offers electrical contact while minimizing the flow of the KCl solution into the sample buffer. An LJP rises at this boundary of solution phases.

Because of many uncertain and systematic influences, notably including the LJP, it is necessary to calibrate cell III concerning reference buffer solutions traceable to primary pH standards. The calibration processes can be divided into single-point, two-point, and multipoint calibrations ^[15].

During these three calibration procedures, it is important for the indeterminacies of the residual LJP and the buffer pH values to be contained in the calculation of the no determinacy of the pH of the sample.

As for single-point calibration, it uses one criterion. According to the measured potential of the standard and the thermodynamic (Nernstian) slope, k , there is an assumption of calibration function—a straight line defined according to the test potential of the standard and the thermodynamic (Nernstian) slope, k . Single-point calibration is of great benefit to acquiring an approximate pH value prior to achieving more accurate results due to the application of two-point or multipoint calibration. As for the two-point or bracketing process, it is adopted in most routine pH measurements as this calibration uses two standards with values that “bracket” the range where the uncharted lies.

For multipoint calibration, it is suggested that multipoint calibration is adopted because the large slope of the pH(X) value requires minimum uncertainty and maximum consistency. The pH of the reference buffer solution, which is different from the main standard buffer in composition and buffer capacity, is also tested by multipoint calibration. These pH reference

buffers often play the role of reference to technical buffers or ready-to-use buffers. Electrode calibration can be calculated in terms of linear regression of the cell potential difference of the least square line at the pH of each calibrator [17].

As the last two calibration procedures, the two-point and multipoint calibration protocols, the glass electrode typically produces a practical slope, k' which is slightly smaller than k . The main cause in this deviation is the variation in the LJP with pH [15]. However, Baucke et al. [18] stated that this deviation is due in part to shifts in the surface activity of the silanol groups on the surface of the glass film, which is therefore an inherent property of the glass electrode itself by comparing the response of glass and Pt|H₂ electrodes.

In conclusion, the electrochemical measurement includes a working electrode and the reference electrode of two electrodes to form a complete circuit. During the process of measurement, the reference electrode provides a constant potential effect, which leads to maintaining its potential under the concentration of the solution of the test. Therefore, the reference electrode must be requested with good reversibility, reproducibility, and stability. There are three main types of pH measurement (Harned Cell, Baucke Cell and the glass electrode) developed and provided for researchers to use for different requirements.

3. pH Sensors

On the basis of the study of pH determination, it is noticeable that pH sensors play a universal role in pH measurement techniques. The pH sensor is the earliest and with the help of these kinds of electrodes, the cells can be used as the pH sensors consisted of various types of electrodes. pH sensors, usually composed of a chemical part and a signal transmission part of electrodes, are commonly used for industrial measurement of solutions, water, and other substances. In most of the developed chemical sensors, the earliest application of pH electrodes is hydrogen electrodes. With the development of scientific research level, glass electrodes, hydroquinone electrodes, and metal/metal oxide electrodes have especially been developed successfully and the most common usage of pH sensors is glass electrodes. These electrodes' detection of their principles is similar, but the results of the determination are extraordinary and different.

3.1. Hydrogen Electrode

Prior to glass electrodes, the pH sensor is mainly a hydrogen electrode, which can be used in both aqueous solutions and non-aqueous solutions. The characteristic of the hydrogen electrode is that it is plated with spongy platinum black as the sensitive layer of H⁺ [19]. There are two types of hydrogen electrodes—standard and reversible hydrogen electrodes. In general, these two kinds of techniques have the same design and only two main systems based on the same principle (potential difference arises from different values of two variables—an (H⁺) and $f(\text{H}_2)$ [20][21] are commonly used in these years. The main difference between these two-compartment designs is the supply of hydrogen. As for the “open” system, the hydrogen can be achieved by the bottom a small opening and the “close” device can achieve hydrogen not only by the bottom small opening but also use negative potential as a cathode in water electrolysis to generate hydrogen. Devynck et al. [22] investigated the hydrogen electrode that served as a pH indicator in the hydrogen fluoride and superacid media by the means of voltammetric and potentiometric measurements in the acid ranges.

However, there are many disadvantages of hydrogen electrodes. Firstly, platinum black is prone to inactivation poisoning affected by mercury, and oxygen cyanide, which leads to loss of original activity of platinum black. In addition, the structure of the hydrogen electrode is complex and the use of high purity hydrogen (99.9999%), and the test environment is demanding, which brings a lot of inconvenience to the actual use and has little practical value. These kinds of hydrogen electrodes have good reversibility, stability, and reproducibility, so they are often used as reference electrodes to measure the standard electrode potential of other electrodes.

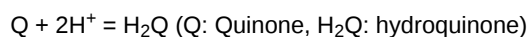
3.2. The Glass Electrode

According to the above introduction of ordinary pH measurements, the glass electrode is routinely used for pH measurements in a common lab setting. The glass electrode, the early use of pH sensors, is currently the most popular use of a hydrogen ion-selective electrode. Its sensitive structure is a hyaline membrane which is the common chemical, silica. This kind of chemical consists of a silica bond to form a mesh skeleton. In this case, alkali metal ions such as sodium–potassium, lithium, etc., can be saved in the mesh structure. When the glass electrode is immersed and activated, the metal ions existing in the mesh construction can generate hydration ions with water, and the reaction between metal ions and hydration ions occurs, resulting in a pH response. The silver/silver chloride or calomel electrodes are usually used as internal reference electrodes, and the saturated calomel electrode (SCE) is used as an external reference electrode during the measurement.

Although it has the advantages of sensitivity, accuracy (high measurement accuracy of 0.02 pH [23]), short reaction time and high stability, there are still many defects, such as fragility, high internal resistance, high film impedance, the difficulty of miniaturization and inconvenience for connection with other instruments [24], which leads to the limitation of their determination scope. Therefore, various pH sensors have been developed to address these problems.

3.3. Quinone Hydroquinone pH Electrode

Bulmnan et al. [25] firstly proposed the Redox reaction between hydroquinone and quinone, which can be used to measure the concentration of hydrogen ions. Quinone hydroquinone electrodes are composed of smooth platinum or gold electrodes immersed in a quinone hydroquinone saturated solution. Its electrode reaction:



The quinone hydroquinone electrode is dependent on the same Nernst equation for computing basis, hydrogen ion concentration of the solution is achieved by the potential difference. Additionally, the quinone hydroquinone electrode is not only simple to prepare but also has fast potential stability, low internal resistance, prevention from interference antioxidants and other substances. This technique can be used in a solution containing soluble gases or acetone formic acid with a carbonyl structure and other organic acids. However, the main disadvantage of the quinone hydroquinone electrode is the lack of understanding the complex interactions of structural types (various kinds of natural membranes or interfaces and the network of extra- and intracellular) [26]. In this case, with the help of basic and applied science, it is necessary to enrich different types of biomimetic interfaces on the surface of the nanomaterial [27].

The most common method to fabricate quinone hydroquinone sensors is self-assembly (SAM) because of simple operation, chemical availability, etc. [27]. There are different kinds of SAM surface reactions. For instance, Zhang et al. [28] demonstrated that a representative reaction, which is a modulated quinone hydroquinone transition and heterocyclization produced by benzoquinone and L-cysteine). Quinone hydroquinone can be used as the composition of nanomaterial to achieve biosensors. As the transform of dopamine and dopaquinone can be a symbol of pH changes, Medintz et al. [29][30] studied that the biosensor consisted of dopamine and quantum dots conjugates to detect whether cells undergo drug-induced alkalosis by measuring cytoplasmic pH.

3.4. Optical Fiber pH Sensor

The optical fiber pH sensor is the sensor with a very high sensitivity that appeared in the 1980s, and it can be continuously used to measure automatically. Different from other electrochemical measurement methods of pH electrodes, an optical fiber pH sensor using optical properties for pH measurement has been developed as the light electrode within the scope of different sections in the range of pH (from 1.0 to 8.0) for various needs in pH measurement. For instance, their accuracy reaches 0.1–0.05 pH unit when sample pH changes. As for the fabrication of optical sensors, the choice of platform is the key to designing relevant devices successfully. In these years, lots of absorption- and luminescence-based optical sensing techniques have been studied in these years [31][32][33][34][35][36]. The optical fiber sensor platforms are considered the traditional platforms and there have been lots of studies on their developments.

The mechanism of optical fiber pH sensor is to use chemicals, which is sensitive to hydrogen ions as sensitive element material, to produce different spectral characteristics by these chemicals to obtain the pH values. The sensor is composed of a light wave as energy transfer medium and optical fiber as a light transmission medium. The main drawback of the optical fiber sensor is its narrow linear range and long response time. The application is limited of this instrument because different pH testing scopes need to change different probes and cannot be used for suspension. To deal with the problems of optical fiber sensors, another platform, a planar waveguide-based sensor has been developed as they are not only more stable but also more attractive with the help of advanced manufacturing techniques [37].

According to the shifts of test optical signal characteristics generated by indicators and the interactions between the materials, fiber optic pH sensors can be divided into fluorescent light, absorption type, and reflection type. Peterson et al. [38] developed the first optical fiber pH sensor based on the principle of light absorption in the 1990s, and the optical fiber pH sensor based on light absorption has been continuously developing: Tzonkov et al. [39] improved the response time of the electrode to 30 s through the study of the dynamic model. As for technology, the invention of optical waveguide technology realized long-distance telemetry, and the invention of disappeared wave technology expanded the detection range, which leads to the development of optical absorption fiber pH sensors. Since the 1990s, lots of polymer films have been used on the surface of electrodes to enhance the reflected light, which can lead to improving the sensitivity of reflective fiber pH sensors. For instance, the PAN membranes were developed by radical polymerization: poly(acrylonitrile acrylic acid-2-vinylnaphthalene) and poly(acrylonitrile-methacrylic acid-2-vinylnaphthalene) [40]. Gu et al. [41] used

polyethylenimine (PEI) and sodium alginate (SA) to deposit on the side surface of the thin-core fiber modal interferometer (TCFMI) by self-assembly technique for the determination of pH values in biology. Alabbas et al. [42] describe the design of a reflection-type fiber-optic pH sensor for improved reproducibility, which can be used to measure the pH values of acidic and alkaline vapors. As fluorescence is a highly sensitive analysis method with a short response time, most of these fiber-optic pH fluorescence sensors use fluorescent reagents as stationary phases. Bastien et al. [43] used polymethylmethacrylate (PMMA) as optical fibers for on-body monitoring in biological solutions.

3.5. Ion Sensitive Field Effect Transistor (ISFET) pH Sensor

ISFET, a new type of pH-sensitive device invented by Bergveld in 1981 [44], the main material is a silicon chip. The structure of ISFET is similar to that of MOSFET (metal-oxide-semiconductor field effect transistor) but the ion-sensitive membrane is used to replace the metal gate of the MOSFET [45]. After the contact between the sensitive membrane and solution, the Nernst response to hydrogen ions occurs. Compared to other pH sensors, the ISFET pH electrode has good precision, repeatability, miniaturization, and short response time while the limitation of the large size of the ISFET sensor for further employment becomes the main disadvantage [46][47].

3.6. Metal/Metal Oxide pH Sensor

Metal/metal oxide pH sensor, as an important substitute system for pH glass electrodes, is also a major research direction of pH electrodes up to now. There are some characteristics of this technique—simple preparation, small internal resistance, quick response, high mechanical strength, and miniaturization. In addition, this type of sensor can not only adapt to the test environment of high temperature or strong agitation system but also can be used in the system containing F⁻ solution. Morishita et al. [48] used the sensor consisting of a lead electrode and an oxidized stainless steel electrode for oil deterioration based on the principle of pH value measurement. Researchers [48] used the sensor consisting of a lead electrode and an oxidized stainless steel electrode for the pH value measurement. With a good linear relationship of the sensor signal to the quasi-pH value of oil, the region where oil deterioration proceeded can be identified. In addition, the residual basic additives in the oil can be easily estimated from the sensor signal. Some achievements have also been made in the miniaturization development of metal/metal oxide pH sensors [49]. For example, with the help of the connection of carbon substrates and immobilized noble metal nanostructures [50], sensitive biosensors can be developed in medical products, instruments, and techniques [51][52][53] because of their positive effect on redox reactions.

The principle of metal/metal oxide electrode is based on redox reaction, the substance of reaction is the reduction reaction of metal oxide with the participation of hydrogen ions. At present, the study of this sensor mainly focuses on a few elements in the fourth, fifth, and sixth periods, and the most are the research on the platinum group elements in the sixth group. Metal/metal oxide electrode preparation methods include sputtering, electrochemical cycle voltammetry and thermal oxidation method, etc.

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