Review Article

Different Techniques and Ionophores Used For Sensing Sodium Ion

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ABSTRACT

Sodium ion is one of the essential elements of human body; mostly exist in blood and extracellular fluid. Sodium ions along with potassium ions maintain the osmotic pressure of the cell and participate in the normal functioning of nerves, heart and muscles. The optimum concentration range sodium ion required for normal physiological functioning of human body is 134-145 mM/L, above which it causes hypernatremia and sodium level below 135 mM/L causes hyponatremia. Present day, with the point-of-care in health sector, monitoring sodium ion concentration in real time with high selectivity is of great interest. Analytical techniques led to the developments of portable devices in the form of optical sensors/optodes, ion-selective electrodes (ISEs), electrochemical sensors, ion selective field effect transistors (ISFETs) and surface plasmon resonance (SPR) based sensors. A variety of crown ethers, cryptands and calixarenes based sodium ion specific ionophores have been employed in construction of sodium sensors. Evolution of sodium ion sensors employing different techniques and variety of ionophores has been summarized in present review article.

Keyword: Sodium; Ion-Selective Electrodes; sensors; crown ethers; cryptands; ionophores

INTRODUCTION

Alkali metal cations are of great significance in clinical chemistry, biochemistry and environmental studies. Monitoring blood electrolytes especially sodium, potassium and lithium has been quite challenging due to their quite similar chemical properties. Sodium and potassium are required for the proper functioning of our nerves and the contraction of our muscles. Sodium ions predominate in the extracellular fluid of body whereas potassium is found mainly in the inside of the cells, the intracellular fluid. These two electrolytes need to be in constant dynamic balance for movement of nutrient and waste across the cell membranes. Sodium is necessary to maintain fluid balance,

electrolyte balance and pH (acid/alkaline) balance in the body [1-5].

In fact, sodium ions are so important, that humans have a specific sensor on the tongue that can detect the sodium salt. Thousands of years ago, when the diet of humans was potassium-rich and sodium-poor, this sensor for salt was a crucial survival tool. Nature, in her infinite wisdom, devised a way to help humans and animals to seek out salty foods so they could be assured of receiving adequate sodium from their diets. However, our body requires a fixed concentration of sodium ion (135 to 145 mM/L), the increase in Na^+ concentration above 145 mM/L causes hypernatremia and concentration below 135mM/L causes hyponatremia. The

danger is not excess, rather a lack of sodium. Excess sodium will raise blood pressure but will be excreted in the urine. A person suffering from a lack of sodium or hyponatremia can die quickly from the brain swelling or the heart stopping [6-9]. Therefore, Na+ ions need to be in constant dynamic balance, for which it is important to monitor the concentration of sodium ions accurately. Na+ needs to be in constant dynamic balance. If Na+ ion concentration is deficient or in excess, cell permeability is affected and the health of the cells suffers. Hence it is important to monitor its concentration accurately.

Number of analytical methods for sodium ion detection and quantitation have been developed and evaluated for their practical applicability [10-13], including flame photometry, enzymatic assay, electrophoresis, potentiometry, optical techniques, amperometry, surface plasmon resonance spectroscopy etc. Analytical techniques led to the developments of portable devices in the form of optical sensors/optodes, ion-selective electrodes (ISEs), electrochemical sensors, ion selective field effect transistors (ISFETs) and surface plasmon resonance (SPR) based sensors. A variety of crown ethers, cryptands and calixarenes based ionophores listed in table 1 have been employed in construction of sodium ion sensors. Present review paper gives an updated account of various ionophores used in the fabrication of sodium ion selective electrodes and sensors of different categories.

Table 1: List of Ionophores used for development of sodium ion sensors

POTENTIOMETRY & FET Techniques								
Ionophores	**Detection Range, M**	**LOD, M**	**Slope, mV.decade^{-1}**	**Selectivity**				
				Li+	**K+**	**Cs+**	**Rb+**	**NH4+**
Di(o-methoxy)stil benzo -24-crown- 8 [38]	9×10^{-6}- 1×10^{-2}	-	-	-3.69	-0.74	-	-	-1.60
Methyl p-t-butyl calix [4]aryl acetate [40]	10^{-4} - 10^{-1}	10^{-4}	60	-2.94	-2.59	-1.57	-3.1	-
bis[(12-crown-4)-2-ylmethyl]-2- dodecyl -2-methyl malonate [41]	-	$>10^{-5}$	-	-2.94	-2.59	-1.57	-3.15	-
Cryptand derivative [42]	10^{-4}- 10^{-3}	5.5×10^{-6}	59.4	-3.24	-3.66	-4.84	-4.3	-3.45
Bis(10-crown-3)-hexamethylenebis (3,6,10-trioxa cycloundecane) [43]	1×10^{-5} - 1	$6\pm0.5\times10^{-6}$	-	-	-	-	-	-
Molybdenum oxide bronze [44]	10^{-4}- 1	-	52	-	-	-	-	-
16-Crown-5 derivative [45]	-	$> 10^{-4}$	-	-2.5	-2.0	-3.5	-3.5	-2.8
4-*tert*-butylcalix[4] arene-tetraacetic acid tetraethyl ester [46]	1.3×10^{-5}- 2.3×10^{-1}	1.3×10^{-5}	59.4	-3.1	-2.5	-4.5	-	-4.8
p-tert-butylcalix[4] areneethyl ester [47]	3.0×10^{-6} - 1.0×10^{-1}	1.45×10^{-6}	58.65	-2.97	-2.20	-3.04	-	-
Phenytoin sodium with tungstosilicic acid [48]	5×10^{-6}— 5×10^{-3}	1.3×10^{-6}	30.9±0.1	-	-	-	-	-
B12C4 with anodised Indium Tin Oxide [50]	10^{-4} - 1	-	29.96	-	-3.11	-	-	-4.06
Bis(12-crown-4) [51]	-	1.3×10^{-6}	50	-	-	-	-	-

Ionophore	Detection range	LOD	Slope					
p-tert- butyl calix[4] arene [53]	10^{-3}-10^{-2}	10^{-5}	59.2	-2.5	-1.9	-1.6	-	-
1-methyl-1-vinyl-14-crown-5 [55]	$3.16 \times 10^{-}$ - 1.0×10^{-1}	2.81×10^{-6}	55.0	-3.20	-3.35	-	-	-3.22
Electrically neutral ligand [58]	10^{-1} - 5×10^{-5}	-	-57.1	-0.036	-0.19	-0.03	-0.67	-0.01
Chalcogenide glass electrodes [59]	10^{-3} - 1	10^{-4}	50	-1.95	0.04	-0.74	-	0.24
CCD-type semiconductor [60]	10^{-5} - 10^{-1}	$<10^{-2}$	31.5	-2.5	-2.2	-2.4	-2.1	-
Na $_{0.44}$ MnO$_2$ powder [61]	$1 - 2 \times 10^{-4}$	-	55	-2.26	-3.02	-	-	-
Dibenzopyridino-18-crown-6 [63]	10^{-1} - 10^{-4}	9.0×10^{-5}	58.5 ± 0.5	-2.41	-0.67	-1.22		-1.40
Cahx[4]arene derivative[88]	-	0.1	58	-2.5	-1.9	-3.3	-3.1	-
15-crown-5 functionalized with dithiolane [78]	10^{-3}- 1	-	44	-	-	-	-	-
Calix[4]arene [92]	$10^{-1} – 10^{-4}$	-	59	-3.1	-2.5	-	-	-4.8

OPTICAL METHOD

Ionophore	Detection range/ LOD (M)	Wavelength (nm)	Interfering Ions
N,N',N''-triheptyl-*N,N',N''*-trimethyl-4,4',4''-propylidyne-tris(3-oxabutylamide [15]	$20 – 200 \times 10^{-3}$	460	K^+, Ca^{+2}, Mg^{+2}
N,N'-dibenzyl-N,N'-diphenyl-1,2-phenylene-dioxy-diacetamide [16]	$1 -100 \times 10^{-3}$	540	K^+, Ca^{+2}
Calix[4]arene [17]	10^{-4} - 10^{-7}	480	Li^+, K^+
sodium binding benzofuran isophthalate acetoxy - methylester [18]	2×10^{-5} - 1×10^{-1}	455	Li^+, K^+
Ru(bpy)$_2$(15-C-5-bpy)$^{2+}$ [19]	$< 1 \times 10^{-3}$	450	-
Calix[4]arene derivative [20]	0.01 - 2.0	583	K^+
Benzo-15-crown-5 ether [21]	$< 0.4 \times 10^{-3}$	480	Na^+, Ca^{+2}
1-aza-15-crown-5 [22]	$< 5 \times 10^{-3}$	550	-
Calix[4]arene [23]	10^{-4}	320	Li^+, K^+
(bis[(12-crown-4)methyl] dodecylmethylmalonate [24]	10^{-4} - 10^{-1}	-	Li^+, K^+, Ca^{+2}, Mg^{+2}
Calix[4]arene [25]	10^{-2}	950	K^+
C14-DD16-Crown-5 [26]	10^{-5} - 10^{-1}	510	K^+

VARIOUS IONOPHORES AND TECHNIQUES EMPLOYED FOR CONSTRUCTING SODIUM ION SENSOR

Optical Sensors

Optical techniques are methods that use light to probe the matter. One prominent example is optical spectroscopy, which includes pump–probe spectroscopy, Raman spectroscopy and photoemission spectroscopy. Other examples of optical techniques are interferometry, ellipsometry, optical tweezers, imaging and sensing [14]. Zhujun et al. [15] developed an

optical sensor for sodium ion based on ion-pair extraction and fluorescence, where-in a sodium-selective ionophore [N,N',N''-triheptyl-N,N',N''-trimethyl-4,4′,4″-propylidyne-tris(3-oxabutyramide)] was immobilized on silica. The selectivity of sodium ion is in the range of 20 to 200 X 10-3M. Schaffar et al. [16] have developed an ion selective optrode for selective determination of sodium ion based on a potential-sensitive dye Rhodamine BC-18 ester together with sodium selective ionophore ETH 157. The detection limit of sensor was 1 to 100 × 10-3M. Jin et al. [17] have used calix[4]arene for Na+ sensor based on change in fluorescent characteristics specifically when complex is formed with Na+, the selectivity range was found to be 10-4 to 10-7M. Buchholz et al. have [18] developed a new fibre-optical sodium sensor based on an immobilized fluorescent sodium ion carrier. The sodium selectivity was in the range from $2 × 10^{-5}$ to $1 × 10^{-1}$M. Lai et al. [19] employed electrogenerated chemiluminescence method for the detection of sodium ion using 15-crown-5 ether derivative as a sodium ion selective ionophore. The detection limit of this sensor was found to be < 1× 10-3M. Benco et al.[20] have used calix[4]arene for the development of sodium ion sensor. This sensor works in the concentration range of 0.01 to 2.0 M. Ramachandran et al. [21] have used benzo-15-crown-5 ether as ionophore for sodium ion to construct a fluorescence based Na ion sensor, with detection limit as < 0.4 × 10-3M. Poronik et al. [22] have developed a probe which exhibits high sensitivity and good selectivity for Na+, based on the complexation of the Na+ by ionophore 1-aza-15- crown-5, which induces a prominent fluorescence enhancement via quenching of electron-transfer. The detection limit of sensor was < 5 × 10-3M. Leray et al. [23] have used calix[4]arene derivative as a ionophore because of its selective complexing property towards sodium ion. Wang et al. [24] described an ionophore-based ion-selective optode platform on paper for the first time with a sodium optode by Cellulose paper is shown to be an excellent substrate for adsorption of the required chromoionophore, ionophore, and ion-exchanger species. These adsorbed components form a hydrophobic phase that enables heterogeneous optical ion sensing in the absence of any plasticizer or organic polymer phase. They used

sodium ionophore VI for this purpose. Shortreed et al. [25] described a micrometer-size, fluorescent fiber-optic sodium sensor, based on a highly sodium-selective, calix[4]arene as ionophore. The optode have excellent sodium selectivity, with other physiologically relevant cations (e.g., potassium, calcium, and magnesium). Hisamoto et al. [26] have developed a rapid flow-through analysis system for sodium ion which was based on ionophore C14-DD16C5. The ionophore exhibits high selectivity for sodium ion over potassium ion. The selectivity range was from 10^{-5} to 10^{-1} M. Zha et al. [27], developed a novel sodium ion sensor.

Ion-Selective Electrodes

Development of ion selective electrodes (ISE) was a breakthrough discovery specially for alkali metal monitoring. ISEs are based on potentiometric methods have advantages such as good selectivity and give results in short time. Electrodes can simply be produced with a very low cost and above all they allow to analyze the solution without pre-treatments. Some of them are in solid state such as selenite, sulfate and hydroxide electrodes [28-30], some of them are prepared using PVC membrane such as iodide and glucose electrodes [31,32]. An ion-selective electrode (ISE), also known as a specific ion electrode (SIE), is a transducer (or sensor) that converts the activity of a specific ion dissolved in a solution into an electrical potential. The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation. Ion-selective electrodes are used in analytical chemistry and biochemical/biophysical research, where measurements of ionic concentration in an aqueous solution are required [33,34]. Direct and indirect are two methods commonly used in biochemistry laboratories in order to measure the electrolytes employing ion selective electrodes [35]. In direct method samples are not diluted while in indirect method samples are diluted. In the clinical practice, it's the sodium concentration in plasma water -measured by direct ISE- which is important to consider as it is responsible of water movements between the liquid compartments. Knowing the difference between direct and indirect ISE, especially with sodium and inappropriate therapeutic decisions could be taken if the clinician is not aware of

this difference. The increase and the decrease in plasma water volume are the situations that distort the results of the indirect ISE because this method, after a dilution step, does not take into account the real percentage of plasma water of the patient in the determination of the concentrations leading to pseudohyponatremia, pseudonormonatremia or pseudohypernatremia. In the direct ISE, the sample is not diluted and the results are correct even if the volume of plasma water is modified.

Moore et al. [36] determined sodium in body fluids by using sodium aluminium silicate glass electrode. The reported electrode produces highly accurate and reproducible results. The sample need not require further dilutions. The LOD was 0.01M. Levy [37], worked on determination of sodium ion in serum with ion-selective electrode, the selectivity of this electrode was found to be 145 X 10-3 M. Zhou et al. [38] prepared Sodium ion-selective electrode which was based on ionophore di(o-methoxy)stilbenzo-24-crown-8 ether. The lower detection limit of this sensor is $9×10−6 – 1×10−2$ M. Ladenson [39] proposed a direct potentiometric method for determination of sodium and potassium in whole blood. Diamond et al. [40] have developed sodium ion-selective electrode based on methyl p-t-butyl calix[4]aryl acetate as the ionophore. The electrode works in the range $10−4−10−1M$. Moody et al. [41] developed an potentiometric sensor employing bis[(12- crown-4)-2-ylmethyl]-2-dodecyl-2-methyl malonate. Electrode slopes were near-Nernstian, with detection limits of less than 10-5 M.

Schindler et al. [42] developed a High-ion selective sensor by incorporating cryptand derivative into the PVC membrane. The selectivity of sodium ion was found to be > $5.5×10−6$ M. Lukyanenko et al. [43] developed a sodium-selective electrodes based on PVC membranes containing bis(10-crown-3)-hexamethylenebis(3,6,10-trioxa cycloundecane).The selectivity of this sensor is $1×10−5–1$ M. Shuk et al. [44] prepared a sodium ion sensitive electrode based on a molybdenum oxide bronze. This sensor responded to Na+ concentration in the range of $1–10−4$ M. Suzuki et al. [45] designed and synthesized a Sodium Ion-Selective Ionophores which was based on 16-Crown-5 derivative with two decalino subunits (DD16C5) for an Ion-Selective Electrode. This electrode exhibited a Na+ selectivity > 10-4 M.

Wygl et al. [46] designed a miniaturized backside contact sensors with polymeric Na+ selective membranes based on ionophore 4-tert-butylcalix[4]arene-tetraacetic acid tetraethyl ester. The LOD was found to be $1.3×10−5–2.3×10−1$ M. Marques et al. [47] prepared sodium-selective potentiometric microelectrodes with a conducting polymer (polypyrrole doped with cobaltabis(dicarbollide) ions ([3,3′-Co(1,2-C2B9H11)2]−) as solid contact layer between the polymeric sensitive membrane and the platinum substrate. The p-tert-butylcalix[4]arene ethyl ester was used as ionophore for sodium recognition. The lower detection limit of Na+ was $1.45 × 10−6$ M. Tohamy et al. [48] constructed sodium ion selective electrodes by incorporation tungstosilicic acid in PVC membrane. The LOD was observed to be $1.3×10−6$ M. Ioannidis et al. [49] reported an aza-15-crown-5 derivative as a selective ionophore for sodium ion, this ionophore is suitable for detection of Na+ ion. Lin et al. [50] worked on anodized indiumtin oxide electrode for detection of sodium ion. This electrode shows good sensitivity in the range of $10−4 - 1$ M.

Takami et al. [51] used sub-micropepette probe by incorporating ionophore bis(14-crown-4) into a PVC matrix. The LOD of this electrode was found to be $1.3x10^{-6}$ M for Na+. Hübl et al. [52] have evaluated the effect of hemolysis, icteric discoloration, lipemia, paraproteinemia, and uremia on enzymatic methods for determining sodium, potassium, and chloride, according to the National Committee for Clinical Laboratory Standards EP7-P proposals for testing interference from endogenous substances. The sodium determination was done employing beta-galactosidase. The detection range was 2.9-1.2mM/L. Cadogan et al. [53] prepared a sodium-selective electrodes with polymeric membranes containing ester and ketone derivatives of *p-tert*-butyl calix[4]arene. The electrodes were prepared with 2-nitrophenyl octyl ether as the solvent mediator and potassium tetrakis(*p*-chlorophenyl)borate as the ion-exchanger in a poly(vinyl chloride) matrix. Several of the ligands examined produced electrodes with near-Nernstian slopes, detection limits was $10^{−5}$ M for sodium. Diaz et al. [54] prepared an ion-selective electrode based on methyl *p*-t-butylcalix[4]aryl acetate have been prepared that are responsive to sodium ions using a PVC membrane. Examination of the general

performance of the electrodes revealed excellent characteristics in terms of Nernstian response, selectivity, stability, reproducibility and response time.

Chandra et al. [55] used ionophore 1-methyl-1-vinyl-14-crown-5 with potassium tetrakis(*p*-chlorophenyl)borate to prepare Na^+-selective electrode. The response of the electrode was linear with a Nernstian slope of 55.0 mV/decade. The selectivity range was 3.16×10^{-6} to 1.0×10^{-1} M and LOD was 2.81×10^{-6} M. Machini et al. [56] developed a new voltammetric sensor which was based on nanostructured ausmannite-type manganese oxide for the detection of sodium ions.

Lee et al. [57] prepared a self-plasticised acrylic membrane recipe for Na^+ and K^+ ion selective electrodes. Ammann et al. [58] prepared a new, synthetic, and electrically neutral ligand in a membrane solvent incorporated in a PVC-matrix . In this sensor system, two different membrane solvents are compared in respect to selectivity, pH-dependence, lifetime, working range and dynamic response. Both electrodes show a linear response to sodium ion activities in the range of 10^{-1} M to about 10^{-5} M in unbuffered systems, with a selectivity over potassium, calcium and magnesium which permits measurements in blood serum. Analytical characteristics and sensing mechanism of sodium ion-selective electrodes based on $NaCl$-Ga_2S_3-GeS_2 glasses have been investigated by Vlasov et al. [59]. Chalcogenide glass electrodes containing 10% NaCl in the membrane showed near-Nernstian response in the concentration range from 10^{-3} to 1M. These sensors were superior to the conventional pNa oxide glass electrodes in selectivity in the presence of hydrogen ions and in Na^+ ion sensitivity in fluoride media. A new sodium ion image sensor containing a CCD-type semiconductor and a plasticized PVC sodium ion selective membrane was developed by Hattori et al. [60]. The output potential slope was linear for sodium ion concentrations from 10^{-5} to 10^{-1} M. The optimum membrane possessed a near Nernstian response and high selectivity to sodium ions. Sauvage et al. [61] developed a potentiometric ion sensor employing $Na_{0.44}$ MnO_2 powder. Nernstian response (55 mV/dec) was obtained for concentrations ranging from 1to 2×10^{-4} M. The sodium ion sensor developed by Liu et al. [62] has an outer electrolyte which is insensitive to water and has a high transport activity for sodium ions and an inner electrolyte bound by a thin membrane having very high sodium ion selectivity. The sodium ion sensor having such an electrolyte is sensitive only to the transport of sodium ions and may be operated in aqueous solutions without buffering and in the presence of other alkali ions and alkaline earth metal ions. Tavakkoli [63] prepared a sodium ion- selective electrode based on ionophore dibenzopyridino-18-crown-6. The electrode exhibits a Nernstian response for Na^+ ions within the concentration range of 10^{-4} to 10^{-1}M with a slope of 58.5 mV/decade and the LOD was 9.0×10^{-5}M.

Electrochemical Sensors

Electrochemistry is branch of chemistry concern with the effect of electrical potential on chemical reaction. It is named electrochemistry because it's originated from the study of the movement of electrons in an oxidation–reduction reaction. Electrochemical methods are analytical techniques that use a measurement of potential, charge, or current to determine an analytes concentration or to characterize an analytes chemical reactivity. It is a qualitative and quantitative methods of analysis based on electrochemical phenomena occurring within a medium or at the phase boundary and related to changes in the structure, chemical composition, or concentration of the compound being analyzed. By the defination ISEs are also a type of electrochemical sensors based on potentiometry whereas so called electrochemical sensors are based on voltammetry or amperometry.

Flink et al. [64] have reported an electrochemical sensor which was based on self- assembled monolayer (SAM) of 2-[(6-mercaptohexyl)oxy]methyl-12-crown-4 onto the gold surface for selective sensing of sodium ion. The detection limit of this method is 1×10^{-3} M. Wujcik et al. [65] developed an electrochemical sodium ion sensor, composed of a multiwall carbon nanotube (MWNT) functionalized with ionophore cyclo-oligomeric calixarene on nylon-6 matrix. Range of detection is 5 to 60×10^{-3} M. Moore et al. [66] developed an electrochemical sensor based on cation-sensitive redox-active molecules (TTF-crown derivatives with R = $C(O)O(CH_2)nSH$ or CH_2SH) immobilized on a metal surface. Diba et al. [67] have successfully developed

amperometric sensor for sodium, calcium and potassium ion concentrations in biological fluids. The detection was based on measuring current changes associated with the transfer of each cation across a microhole supported water/polyvinylchloride-2-nitrophenyl octylether gel interface. Dibenzo-18-crown-6 was used as an ionophore for sodium ion detection in biological sample. Assisted transfer reactions of each ion from the aqueous to the organic gel layer by the corresponding ionophores were first characterized using cyclic voltammetry and then further analyzed using differential pulse stripping voltammetry. A linear dynamic range from 5×10^{-6} to $100 \times 10^{-6} M$ was observed. Schazmann et al. [68] developed a new method for the real-time quantitative analysis of sodium in human sweat. This temporal data opens up new possibilities in the study of human physiology, broadly applicable from assessing high performance athletes to monitoring Cystic Fibrosis (CF) sufferers. This compact Sodium Sensor Belt (SSB) consists of a sodium selective Ion Selective Electrode (ISE) integrated into a platform that can be interfaced with the human body during exercise. This method has confirmed the accuracy of the new continuous monitoring approach. Zhang et al. [69] , developed sodium ion sensing voatammetric technique using sensing electrode containing sodium ionophore Bis[(12-crown-4)methyl]dodecyl methylmalonate, and 4-tert-Butyl[4]arene-teraacetic acid tetraethylester.

A novel electrochemical approach using simple ionophores for the detection of alkali metal ion using redox probe as mediator ion has been reported by Kumbhat and Singh [70,71]. For sodium ion sensing 4-aminobenzo-15-crown-5 covalently bonded to thioic acid selfassembled monolayer functionalized gold electrode has been used. The sensor is highly selective for sodium ion over potassium, lithium and ammonium ions and is suitable for clinical application.

Ion Selective Field Effect Transistor (ISFET)

The concept of the ion-sensitive field-effect transistor (ISFET) was proposed by Bergveld in 1970s [72], wherein an ionophore is introduced in construction of field-effect transistor. Field-effect transistor (FET) is basically a type of transistor commonly used for weak-signal amplification for example, wireless signals. The device can amplify analog or digital signals. It can also switch DC or function as an oscillator. In the FET, current flows along a semiconductor path called the channel. At one end of the channel, there is an electrode called the source. At the other end of the channel, there is an electrode called the drain. The physical diameter of the channel is fixed, but its effective electrical diameter can be varied by the application of a voltage to a control electrode called the gate. The conductivity of the FET depends, at any given instant in time, on the electrical diameter of the channel [73]. A small change in gate voltage can cause a large variation in the current from the source to the drain.

A variety FETs with possible sensor applications such as pH, chemical and alkali metal ion sensing [74-78] and label-free biosensing [79-82] have been demonstrated using silicon nanowire FETs (Si NWFETs). Further kinetic studies on receptor binding and even intracellular recordings of action potentials could be realized by downscaling of the devices. The sensing principle is based on adsorption of charged species on the sensor surface, leading to a change in surface potential and hence a change in current in the FET channel. Thereby, the high-impedance input signal is transformed into a low-impedance output signal, which is an advantage against classic ion selective electrodes. The possibility of downscaling and integration [83] for the simultaneous detection of multiple parameters make Si NWFETs a promising platform to meet the demand for cheap, multifunctional, and scalable sensors.

Wipf et al. [78] a developed a FET based sodium ion (Na^+) sensor by applying a self-assembled monolayer (SAM) of dithiol onto the gold surface through which 4-aminobenzo-15-crown-5 was attached with a covalent bond, the detection range of this sensor was 10^{-3} to 1 M.

Calix[4]arene derivatives are highly selective for sodium ion, these neutral carriers have been designed especially for sodium ion-sensitive field-effect transistors (Na$^+$ ISFETs) [84-85]. Kimura et al. have used Calix[4]arene neutral carriers incorporating unsymmetrical structures and/or oligosiloxane moieties, in silicone rubber

and have realized high performance of silicone rubber-based sodium-ion sensors, with high sensitivity, selectivity, and durability [86]. The Na$^+$ ISFETs based on silicone rubber membranes of the modified calixarene neutral carriers have proved to be reliable for sodium assay in human body fluids. Brunink et al. [87] developed an ion-sensitive field-effect transistor for sodium ions using Calix[4]arene derivatives incorporated in a poly(vinyl chloride)-based membrane provide the selectivity. A poly(2-hydroxyethyl methacrylate) interlayer between the silicon dioxide gate and the sensing membrane was necessary to obtain a Na$^+$-sensitive ISFET with Nernstian behaviour. Chou et al. [88] have employed the extended gate field effect transistor (EGFET) to fabricate the sodium ion sensor and have studied the effect of interference ions on sodium ion. For this they used entrapment method to prepare the sodium ion membrane, and that the polyurethane incorporates the sodium ion ionophores (B12C4) to form on the window of EGFET. The present results indicate that the good sensitivity, linear regression, rapid response time, the temperature effect, low hysteresis voltage, long working lifetime, interference selectivity coefficients and working range as 1 M to 10^{-5} M of the sodium ion. Hsu et al. [89] have reported sodium and potassium ion sensors based on separated extended gate field effect transistors. Kimura et al. [90] have reported a high-performance sodium ion-sensitive field-effect transistors based on an unsymmetrical calix[4]arene ionophore/silicone rubber composite membrane. Caneiro et al. [91], used sodium super ionic conductor for detection of sodium ion by sol-gel route method. Parker et al. [92] proposed a highly selectivity and sensitivity sensor employing calix(4)crown based ionophore which acts as a receptor and offers a great affinity towards sodium over the simple crown ether receptor. On combining it with a switchable dye, the chromoionophore will selectively amplify the refractive index change upon binding sodium over other cations. Ho et al. [93] developed an ISFET based sensor by treating HfO$_2$ sensing films with carbon tetrafluoride. The detection range of Na$^+$ was 1 to100 x10^{-3} M.

Surface plasmon resonance based sensors

Surface Plasmon resonance (SPR) is a surface-sensitive analytical method for chemical and biochemical sensing that is based on measuring changes in the refractive index (RI) on the noble metal surface. It is a powerful tool for the in situ real-time characterization of a solid/liquid interface and to study interactions between larger molecules [94-99]. Kurihara et al. [100] have reported a SPR based sensor for sodium ion using an ion selective optode membrane film incorporating sodium ionophore (DD16C5). This method was able to detect sodium ion in the range of 10^{-6} to 10^{-1} M. They proposed a new concept which was based on absorption that basically detects changes in the refractive index of complex due to the optical absorption. Benounis et al. [101] have used self-assembled monolayer of calix[4]arene-derivative immobilized on cysteamine modified gold disc of SPR . The LOD of proposed sensor 10^{-10} M and the range detection was 10^{-6} to 10^{-14}M.

CONCLUSION

Alkali metal ions are plays quite significant role in proper functioning of nerves and the contraction of muscles. Sodium ions predominate in the extracellular fluid of body whereas potassium is found mainly in the inside of the cells, the intracellular fluid. Selective detection of these ions has been quite challenging due to similar chemical properties. Need to monitor sodium ion concentration in clinical samples have led to development of various categories of sensors. Present review summarizes different categories of sensors and variety of ionophores used for the development of sodium ion sensor.

CONFLICTS OF INTEREST

Author declares that there is no conflict of interests regarding the publication of this paper.

REFERENCE

1. Faller LD. Mechanistic studies of sodium pump. Arch Biochem Biophys 2008; 476(1): 12-21.
2. Maxwell MH, Kleeman CR. Clinical

disorders of fluid and electrolyte metabolism. New York, Toronto, London: McGraw-Hill Book Company, Inc.; 1962.

3. Bagrov AY, Shapiro JI, Fedrova OV. Endogenous cardiotonic steroids: physiology, pharmacology, and novel therapeutic targets. Pharmacol Rev 2009; 61(1): 39-38.

4. Ng RH, Sparks KM, Statland BE. Colorimetric determination of potassium in plasma and serum by reflectance photometry with a dry-chemistry reagent. Clin Chem 1992; 389 (7): 1371-1372.

5. Prassas I, Diamandis EP. Novel therapeutic applications of cardiac glycosides. Nat Rev Drug Discov. 2008; 7(11): 926-935.

6. Tietz NW. In Fundamentals of Clinical Chemistry. Philadelphia: Saunders; 1970, p 616.

7. Robert P, Heaney MD. Role of Dietary Sodium in Osteoporosis. J Am College Nutri 2006; 25: 271-276.

8. Fuisz RE. Hyponatremia. Medicine 1963; 42: 149-170.

9. Waugh WH. Utility of expressing serum sodium per unit water in addressing hypoanatreamia. Metabolism 1969; 18: 706-712.

10. Chalas J, Francoual J, Lindenbaum A. Evaluation of methods for sodium, potassium and chloride determination in relation to the analytical quality goals. Ann Biol Clin 1994; 52: 783-784.

11. Worth HGJ, A comparison of the measurement of sodium and potassium by flame photometry and ion-selective electrode, Ann Clin Biochem 1985; 22: 343-350.

12. Chalas J, Francoual J, Lindenbaum A. Enzymatic determination of sodium, potassium and chloride in plasma. Ann Biol Clin 1994; 52: 333-339.

13. Nemutlu E, Ozaltin N. Determination of magnesium, calcium, sodium, and potassium in blood plasma samples by capillary zone electrophoresis. Anal Bioanal Chem 2005; 383: 833-838.

14. Wolfbeis OS. Analytical chemistry with optical sensors. Fresenius Z Anal Chem 1986; 325: 387-392.

15. Zhujun Z, Mullin JL, Seitz WR. Optical sensor for sodium based on ion-pair extraction and fluorescence. Anal Chim Acta 1986; 184: 251-258.

16. Schaffar BPH, Wolfbeis OS. A sodium-selective optrode. Microchim Acta 1989; 99: 109-116.

17. Jin T, Ichikawa K, Koyama T. A fluorescent calix[4]arene as an intramolecular excimer-forming Na^+ sensor in nonaqueous solution. Chem Commun 1992; 499-501.

18. Buchholz F, Buschmann N, Cammann K. A fibre-optical sensor for the determination of sodium with a reversible response. Sens Actuators B Chem 1992; 9(1): 41-47.

19. Lai RY, Chiba M, Kitamura N, Bard AJ. Electrogenerated chemiluminescence detection of sodium ion with a ruthenium(II) complex with crown ether moiety at the 3,3'-positions on the 2,2'-bipyridine ligand. Anal Chem 2002; 74(3): 551-553.

20. Benco JS, Grant W, Mc Gimpsey. A sodium ion sensor based on a covalently-linked aminorhodamine B–calix[4]arene chromoionophore. Sens Actuators B Chem 2002; 85(1-2): 126-130.

21. Ramachandran G, Simon G, Cheng Y, Smith TA, Dai L. The dependence of benzo-15-crown-5 ether-containing oligo paraphenylene vinylene (CE-OPV) emission upon complexation with metal ions in solution. J Fluorescence 2003;13: 427-436.

22. Poronik YM, Clermont G, Desce MB, Gryko DT. Nonlinear optical chemosensor for sodium ion based on rhodol chromophore. J Org Chem 2013; 78 (23): 11721-11732.

23. Leray I, Valeur B, Reilly FO, Jiwan JLH, Soumillion JP, Valeur B. A new calix[4]arene-based fluorescent sensor for sodium ion. Chem Commun 1999; 795-796.

24. X, Qina Y, Meyerhoff ME. Paper-based plasticizer-free sodium ion-selective sensor with camera phone as a detector. Chem Commun 2015; 51: 15176-15179.

25. Shortreed M, Bakker E, Kopelman R. Miniature sodium-selective ion-exchange optode with fluorescent ph chromoionophores and tunable dynamic range. Anal Chem 1996; 68(15): 2656-2662.

26. Hisamoto H, Satoh S, Satoh K, Tsubuku

M, Siswanta D, Shichi Y, Koike Y, Suzuki K. Theory and practice of rapid flow-through analysis based on ion-selective optode detection and its application to sodium ion determination. Anal Chim Acta 1999; 396: 131-141.

27. Zha F, Li M, Guo W, Chen J, Wang P. Sodium ion channel optical model: Depolarization spatial distribution and local potential dynamic spatiotemporal processes. Neurocomputing 2013; 99: 261-269.

28. Ekmekci G, Somer G. Preparation and properties of solid state selenite ion selective electrodes and their application. Talanta 1999; 49: 91-98.

29. Mohan MS, Rechnitz GA. Preparation and properties of the sulfate ion selective membrane electrode. Anal Chem 1973; 45:1323-1326.

30. Ekmekci G, Kalayc, Somer G. A solid-state hydroxide ion selective electrode for the measurement of high pH values. Sensor Actuat B Chem 2004; 101: 260-264.

31. Somer G, Kalayc, Ekmekci G. Preparation and application of iodide–mercury selective membrane electrode based on ion exchangers. Sensor Actuat B Chem 2001; 81: 122-127.

32. Kalayc, Somer G, Ekmekci G. Preparation and application of a new glucose sensor based on iodide ion selective electrode. Talanta 2005; 65: 87-91.

33. Bard AJ, Faulkner L. Electrochemical Methods: Fundamentals and Applications. New York: Wiley; 2000.

34. Eisenman G, Rudin DO, Casby JU. Glass electrode for measuring sodium ion. Science 1957; 126 (3278): 831-834.

35. Zelmat MS. Direct and indirect ion selective electrodes methods: the differences specified through a case of Waldenström's macroglobulinemia. Ann Biol Clin 2015; 73: 345-352.

36. Moore EW, Wilson DW. The determination of sodium in body fluids by the glass electrode. J Clin Invest 1963; 42 (3): 293-304.

37. Levy GB. Determination of sodium ion with ion-selective electrode. Clin Chem 1981; 27(8): 1437-1438.

38. Zhou X, Luo Y, Wu C, Zou Z, Hu Q. Sodium ion-selective membrane electrode based on a new crown ether. Anal Chim Acta 1988; 212: 325-329.

39. Landenson JH. Direct potentiometric measurement of sodium and potassium in whole blood. Clin Chem 1977; 23(10): 1912-1916.

40. Diamond D, Svehla G, Seward EM, McKervey MA. A sodium ion-selective electrodebased on methyl p-t-butylcalix[4]aryl acetate as the ionophore. Anal Chim Acta 1988; 204: 223-231.

41. Moody GH, Saad BB, Thomas JD. Studies on bis(crown ether)-based ion-selective electrodes for the potentiometric determination of sodium and potassium in serum. Analyst 1989; 114(1): 15-20.

42. Schindler JG, Schindler MM, Herna K. High-ion selective sodium-sensor. Fresenius J Anal Chem 1991; 340(11): 696.

43. Lukyanenko G, Titova NY, Karpinchik OS, Melnik OT. Sodium-selective electrodes based on PVC membranes containing bis [(3n+1)-crown-n] ether Derivatives. Anal Chim Acta 1992; 259(1):145-148.

44. Shuk P, Greenblatt M, Ramanujachary KV. Sodium ion sensitive electrode based on a molybdenum oxide bronze. Solid State Ionics 1996; 91(3–4): 233-238.

45. Suzuki K, Sato K, Hisamoto H, Siswanta D, Hayashi K, Kasahara N, Watanabe K, Yamamoto N, Sasakura H. Synthesis of Sodium Ion-Selective Ionophores Based on 16-Crown-5 Derivatives for an Ion-Selective Electrode. Anal Chem 1996; 68 (1): 208-215.

46. Wygl K, Durnas M, Parzuchowski P, Brzózka Z, Malinowska E. Miniaturized sodium-selective sensors based on silicon back-side contact structure with novel self-plasticizing ion-selective membranes. Sensors and Actuators 2003; 95(1–3): 366-372.

47. Marques de Oliveira IA, Risco D and Vocanson F, Crespo E, Teixidor F, Zine N, Bausells J, Samitier J, Errachid A. Sodium ion sensitive microelectrode based on a p-tert-butylcalix[4]arene ethyl ester. Sens Actuators B Chem 2008; 130(1): 295-299.

48. Tohamy ME, Razeq S, Maamly ME, Shalaby A. Construction of different types of ion-selective electrodes and validation of direct potentiometric determination of

phenytoin sodium. Cent European J Chem 2010; 8(4): 937-945.

49. Ioannidis M, Gentleman AS, Ho L, Lincoln SF, Sumby CJ. Complexation and structural studies of a sulfonamide aza-15-crown-5 derivative. Inorg Chem Comm 2010; 13(5): 593-598.

50. Lin JL, Hsu HY. Study of sodium ion selective electrodes and differential structures with anodized indium tin oxide. Sensors 2010; 10:1798-1809.

51. Takami T, Son JW, Lee JK, Park BH, Kawai T. Separate Detection of sodium and potassium ions with sub-micropipette probe. Japanese J Appl Phys 2011; 50(8): 1-4.

52. Hübl W, Wejbora R, Keramat IS, Haider A, Hajdusich P, Bayer PM. Enzymatic determination of sodium, potassium, and chloride in abnormal (hemolyzed, icteric, lipemic, paraproteinemic, or uremic) serum samples compared with indirect determination with ion-selective electrodes. Clin Chem 1994; 40(8): 1528-1531.

53. Cadogan AM, Diamond D, Smyth MR, Deasy M, McKervey MA, Harris SJ. Sodium-selective polymeric membrane electrodes based on calix[4]arene ionophores. Analyst 1989; 114: 1551-1554.

54. Diaz MT, Regan F, Diamond D, Smyth MR. Comparison of a calixarene-based ion-selective electrode with two automated analyzers for the clinical determination of sodium in blood plasma, J Pharm Biomed Anal 1990; 8: 695-700.

55. Chandra S, Lang H. A new sodium ion selective electrode based on a novel silacrown ether. Sens Actuat B Chem 2006; 114: 849-854.

56. Machini WBS, Martin CS, Martinez MT, Teixeira SR, Gomes HM, Teixeira MFS. Sens Actuators B Chem 2013; 181: 674.

57. Lee YH, Elizabeth AH. Hall assessing a photocured self-plasticised acrylic membrane recipe for Na^+ and K^+ ion selective electrodes. Anal Chim Acta 2001; 433: 25-40.

58. Ammann D, Pretsch E, Simon W. A Sodium ion-selective electrode based on a neutral carrier. Anal Lett 1974; 7: 23-32.

59. Vlasov, Yu G, Bychkov EA. Sodium ion-selective chalcogenide glass electrodes. Anal Lett 1989; 22: 1125-1144.

60. Hattori T, Yoshitomo M, Mori S, Miyamoto D, Kato R, Sawada K. CCD-type sodium ion image sensor: dynamic observation of ion-exchange reactions of a single Na-type cation-exchange resin bead. Electroanal 2012; 24:114-120.

61. Sauvage F, Baudrin E, Tarascon JM. Study of the potentiometric response towards sodium ions of $Na_{0.44-x}MnO_2$ for the development of selective sodium ion sensors. Sens Actuators B Chem 2007;120: 638-644.

62. Liu M, Joshi AV. Sodium ion sensor. Patent: US 5120422 A; 1992.

63. Tavakkoli N. Sodium ion-selective membrane electrode based on dibenzopyridino-18-crown-6. Bull Korean Chem Soc 2004; 25(10): 1474-1476.

64. Flink S, Boukamp BA, van den Berg A, van Veggel FCJM, Reinhoudt DN. Electrochemical detection of electrochemically inactive cations by self-assembled monolayers of crown ethers. J Am Chem Soc 1998; 120:4652-4657.

65. Wujcik EK, Blasdel NJ, Trowbridge D, Monty CN. Ion sensor for the quantification of sodium in sweat samples. IEEE Sens J 2013; 13(9): 3430-3436.

66. Moore AJ, Goldenberg LM, Bryce MR, Petty MC, Monkman AP, Marenco C, Yarwood J, Joyce MJ, Port SN. Cation recognition by self-assembled layers of novel crown-annelated tetrathiafulvalenes. Adv Mater 1998; 10:395-398.

67. Diba FS, Lee HJ. Amperometric sensing of sodium, calcium and potassium in biological fluids using a microhole supported liquid/gel interface. J Electroanal Chem 2016; 769: 5-10.

68. Schazmann B, Morris D, Slater C, Beirne S, Fay C, Reuveny R, Moyna N, Diamond D. A wearable electrochemical sensor for the real-time measurement of sweat sodium concentration. Anal Methods 2010; 2: 342-348.

69. Zhang J, Bond AM, Harris AR. Voltammetric ion sensor. Patent No. US 2008/0011606 A1.

70. Kumbhat S, Singh U. A potassium-selective electrochemical sensor based on crown-ether functionalized self assembled monolayer. J Electroanal Chem 2018; 809: 31-35.

71. Singh U, Kumbhat S. Functionalized surface for electrochemical sensing of electrochemically inactive alkali metal ion. Indian J Chem A 2017; 56A: 934-938.

72. Bergveld P. Development of an ion-sensitive solid-state device for neurophysiological measurements. IEEE Trans Biomed Eng 1970; BME-17: 70-71.

73. Millman J. Electronic devices and circuits. US: McGraw-Hill International; 1985, p 397.

74. Sudhölter E, van der Wal P, Skowronska-Ptasinska M, van den Berg A, Reinhoudt D. Ion-sensing using chemically-modified ISFETs. Sens. Actuators 1989; 17: 189-194.

75. Reinhoudt DN, Engbersen JFJ, Brzozka Z, van der Vlekkert HH, Honig GWN, Holterman HAJ, Verkerk UH. Development of durable K+-selective chemically modified field effect transistors with functionalized polysiloxane membranes. Anal Chem 1994; 66: 3618-3623.

76. Park L, Hur Y, Sohn B. Effect of membrane structure on the performance of field-effect transistor potassium-sensitive sensor. Sens. Actuators A Chem 1996; 57: 239-243.

77. Knopfmacher O, Tarasov A, Fu W, Wipf M, Niesen B, Calame M, Schönenberger C. Nernst limit in dual-gated Si-nanowire FET sensors. Nano Lett 2010; 10: 2268-2274.

78. Wipf M, Stoop RL, Tarasov A, Bedner K, Fu W, Wright IA, Martin CJ, Constable EC, Calame M, Schönenberger C. Selective sodium sensing with gold-coated silicon nanowire field-effect transistors in a differential setup. ACS Nano 2013; 7(7):5978-5983.

79. Cui Y, Wei Q, Park H, Lieber CM. Nanowire nanosensors for highly sensitive and selective detection of biological and chemical species. Science 2001; 293:1289-1292.

80. Gao A, Lu N, Wang Y, Dai P, Li T, Gao X, Wang Y, Fan C. Enhanced sensing of nucleic acids with silicon nanowire field effect transistor biosensors. Nano Lett 2012; 12:5262-5268.

81. Zheng G, Patolsky F, Cui Y, Wang WU, Lieber CM. Multiplexed electrical detection of cancer markers with nanowire sensor arrays. Nat Biotechnol 2005; 23: 1294-1301.

82. Stern E, Vacic A, Rajan NK, Criscione JM, Park J, Ilic BR, Mooney DJ, Reed MA, Fahmy TM. Label-Free biomarker detection from whole blood. Nat Nanotechnol 2010; 5: 138-142.

83. Rothberg JM, Hinz W, Rearick TM, Schultz J, Mileski W, Davey M, Leamon JH, Johnson K, Milgrew MJ, Edwards M. An integrated semiconductor device enabling non-optical genome sequencing. Nature 2011; 475: 348-352.

84. Chang SK, Cho I. New metal cation-selective ionophores derived from calixarenes: their syntheses and ion-binding properties. J Chem Soc Perkin Trans 1986; 211-214.

85. Arduini A, Pochini A, Reverberi S, Ungaro R, Andreetti G D, Ugozzoli F. The preparation and properties of a new lipophilic sodium selective ether ester ligand derived from p-t-butylcalyx[4]arene. Tetrahedron 1986; 42: 2089.

86. Kimura K, Tsujimura Y, Yokoyama M. Silicone-rubber membrane sodium-ion sensors based on calix[4]arene neutral carriers. Pure Appl Chem 1995; 67(7):1085-1089.

87. Brunink JAJ, Haak J R and Bomer JG, Reinhoudt D N. Chemically modified field-effect transistors; a sodium ion selective sensor based on calix[4]arene receptor molecules. Anal Chim Acta 1991; 254: 75-80.

88. Chou JC, Huang YP. Fabrication and stability analysis for sodium ion sensor. Sens Lett 2008; 6: 920-923.

89. Hsu HY, Wu CY, Lee HC, Lin JL, Chin YL, Sun TP. Sodium and potassium sensors base on separated extended gate field effect transistors. Biomed Eng Appl Basis Commun 2009; 21: 441-444.

90. Kimura K, Matsuba T, Tsujimura Y, Yokoyama M. Unsymmetrical calix[4]arene ionophore/silicone rubber composite membranes for high-performance sodium ion-sensitive field-effect transistors. Anal Chem 1992; 64(21): 2508-2511.

91. Caneiro A, Fabry P, Khireddine H, Siebert E. Performance characteristics

of sodium super ionic conductor prepared by the sol-gel route for sodium ion sensors. Anal Chem 1991; 63: 2550-2557.

92. Parker RM, Gates JC, Grossel MC, Smith PGR. Optofluidic integrated Bragg grating chemical sensor utilizing a sodium-selective receptor surface to enhance detection. Lasers and Electro-Optics Europe: 12th European Quantum Electronics Conference; 2011.

93. Ho KI, Lu TF, Chang CP, Lai CS. Sodium and potassium ion sensing properties of EIS and ISFET structures with fluorinated hafnium oxide sensing film, IEEE Sensors 2009; p 1128.

94. Samble JR, Bradbery GW, Yang F. Optical excitation of surface plasmons: An introduction. Contemp Phys 1991; 32:173-183.

95. Kurihara K, Suzuki K. Theoretical understanding of an absorption-based surface plasmon resonance sensor based on Kretchmann's Theory. Anal Chem 2002; 74: 696-701.

96. Homola J, Yee S, Gauglitz G. Surface plasmon resonance sensors: review. Sens Actuators B Chem 1999; 54: 3-15.

97. Chah S, Yi J, Zare RN. Surface plasmon resonance analysis of aqueous mercuric ions. Sens Actuators B Chem 2004; 99: 216-222.

98. Boussaad S, Pean J, Tao NJ. High-Resolution multiwavelength surface Plasmon resonance spectroscopy for probing conformational and electronic changes in redox proteins. Anal Chem 2000; 72: 222-226.

99. Zacher T, Wischerhoff E. Real-time two-wavelength surface plasmon resonance as a tool for the vertical resolution of binding processes in biosensing hydrogels. Langmuir 2002; 18: 1748-1759.

100. Kurihara K, Nakamura K, Hirayama E, Suzuki K. An absorption-based surface plasmon resonance sensor applied to sodium ion sensing based on an ion-selective optode membrane. Anal Chem 2002; 74: 6323-6333.

101. Benounis M, Jaffrezic N, Bonnamour I, Messai N. Detection of sodium ions by SPR sensor using modified self assembled calix[4]arene derivative monolayer. Appl Mech Mat 2015; 799-800: 915-918.