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Handling of Ion-Selective Field-Effect Transistors (ISFETs) on Automatic Measurements in Agricultural Applications Under Real-Field Conditions

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Abstract: The use of ion-selective field-effect transistors (ISFETs) facilitates real-time nutrient analysis in agricultural applications, including soil analysis and hydroponics. The rapid digital availability of analysis results allows for the implementation of ion-specific fertilisation control. The success, accuracy, and robustness of measurements using ISFET technology strongly depend on the handling of the process. This article presents a detailed overview of the sub-process steps required for the implementation of a stable automated application-specific ISFET-based measurement. This article provides experience-based recommendations for handling the conditioning, full calibration, and single-point calibration of the ISFET sensors. The hypotheses were empirically tested under authentic conditions and subsequently integrated into an overall process optimisation strategy. A comprehensive investigation has been conducted with the objective of gaining a deeper understanding of the ISFET baseline drift and implementing corrective measures. The results show that the baseline drift can be quantified and taken into account in the evaluation of the ISFET measurements. The efficacy of these measures was validated using standard laboratory analyses.

Keywords: ion-selective sensor; ISFET; agricultural sensor technology; real-time nutrient analysis; soil nutrients analysis; hydroponics; nutrients control; handling; calibration; offset correction

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1. Introduction

The employment of ion-selective field-effect transistors (ISFET) offers options to construct highly accurate measuring sensor systems for ion-selective, real-time express analysis [1,2]. However, when handling and using ISFET technology, it is important to be aware of the external influences and to avoid them during a measurement. This is essential for the successful and accurate use of ISFET technology. The implementation of an ISFET-based measurement system in agricultural applications can be compared with the implementation of electromagnetic compatibility (EMC)-compliant design of a system. In such a system, three essential points are followed to ensure stability and functionality: (1) preliminary measures to avoid interference; (2) avoidance of propagation from the source of interference; and (3) avoidance of the effects of interference [3]. The handling of a system or its individual components in this context exerts a decisive influence on the degree to which these three points may be achieved. This publication describes procedures for the correct handling of ISFET-based measurement systems. These procedures already have an influence on the robustness of the measurement. The usage of ISFET measuring technology provides the capability to analyse the concentration of nutrients in liquid solutions in real time, with the resulting data presented in a digital format for subsequent processing. This provides a foundation for the development of novel applications in the agricultural sector. To illustrate, the mobile field laboratory (soil2data) enables the collection of soil samples in the field, the subsequent wet chemical processing, and direct analysis in the field itself [4,5]. The results of the analysis are transmitted directly from the mobile field laboratory to the cloud, where they are available for subsequent sub-process steps in an automated fertiliser calculation. Similarly, in hydroponic systems, the control and optimisation of nutrient management can be conducted on an ion-specific basis through the utilisation of ISFET measurement technology [6,7]. The optimal dosing of nutrients is a necessary requirement for the full exploitation of the yield and yield quality potential of hydroponic systems. Moreover, it results in a reduction in water consumption.

Nevertheless, the successful implementation of ISFET measurement technology in practical applications requires the development of an application-specific system concept [8,9]. The utilisation of ISFET measurement technology is contingent upon the fulfilment of specific operational and application conditions. It is essential to establish the requisite conditions within the system. It is of the utmost importance to identify and minimise or eliminate any potential disturbances that could influence the results of the measurements. Such disturbances may include changes in the temperature of the measurement solutions or ambient light conditions [8].

In addition to external factors that can influence the measurement results when using ISFET measurement technology, it is essential to consider the factors and steps involved in preparing the measuring solution or the ISFET sensors themselves as a key component for ensuring accurate and reproducible measurement outcomes. For instance, when analysing soil samples directly in the field with the objective of expeditiously obtaining the analysis results, the extraction method should be adapted to align with the requisite rapid availability of the analysis results [10]. For use with ISFET sensors, the express soil extraction method, designated as the ‘soil2data method’, allows a soil sample to be prepared and nutrients extracted in a two-stage preparation process [4,10]. The total preparation time is 20 min, and the soil sample is extracted for 10 min per preparation stage. In the first stage, 0.0125 molar $CaCl_2$ is employed as the extraction solution, with the objective of extracting H+ and NO_3- ions from the soil sample. In the second stage, a concentrated extraction solvent (calcium acetate lactate (CAL)) is used to extract potassium (K^+) and dihydrogen phosphate (H_2PO_4) ions. However, in addition to the fact that an ‘express processing method’ must be comparable to the standard soil processing method [10,11], it is also extremely important in this case to identify the differences in the behaviour of the ISFET sensor compared to the application of a conventional aqueous solution and to take these into account in the evaluation of the measurement results.

ISFET measurement technology is already being employed in a number of experimental or research contexts within the fields of agriculture and the environment [9]. In particular, experimental applications are being conducted in the analysis of soil in the field [10,11], as well as in hydroponic systems [8].

As a consequence, in order to achieve accurate and reproducible measurement results, the ISFET sensor itself, as the key component in the entire analysis process, requires special handling steps before, during, and after the measurement. In this context, the quality of the raw data is relevant for further algorithms and data interpretation. Hanson Stall et al. [12] emphasise the need for more robust, high-quality raw data to fuel the AI boom and prevent a bust. The implementation of preventive measures at the hardware level [8] and the adoption of special handling procedures for ISFET sensors at all stages of the measurement process can significantly enhance the quality of the raw data. These handling procedures include the conditioning, the calibration, the determination of the ISFET sensor time drift and the storage of the ISFET sensor between and after the measurements.

Conditioning of the ISFET sensors: Prior to the initial utilisation of an ISFET sensor, it is requisite that the sensor be conditioned with an aqueous ion-specific solution to obtain the equilibrium of ions between membrane end measurement solutions. This is particularly relevant in the case of ion-selective ISFET sensors with ion-specific membranes. Lazo Fraga et al. [13] describe the activation of the membrane during the conditioning process. De Marco et al. [14] have found that the electrical membrane resistance undergoes a change during the conditioning period. It has been demonstrated that this process is dependent on time. During the initial three-hour period, the electrical membrane resistance of a polymer membrane exhibits a pronounced increase, followed by a subsequent decline. Following a conditioning period of approximately 20 h, the membrane resistance reaches a state of equilibrium [14]. The requisite conditioning time is contingent upon the specific membrane in question. For example, Marstalerz [15] indicates that a PVC membrane requires a conditioning time of 1 ½ to 2 h, while a polysiloxane membrane requires 4 to 5 h to achieve a stable electrode potential. Mohammed Esa et al. [16] demonstrate that a 3-h conditioning period, rather than a 1-h conditioning period, results in a decrease in measurement sensitivity when measuring with an ISFET sensor to detect histamine. It is of great importance for the user to be fully informed of the conditions under which the ISFET sensors are conditioned prior to their initial utilisation. This encompasses the composition of the requisite conditioning solution, its concentration, and the necessary conditioning time.

Calibration of ISFET sensors: The subsequent most crucial sub-process stage for the establishment of a stable and robust application-specific ISFET-based measurement is calibration. Given that the ISFET sensors provide the voltage solely as the output signal for the measurement of ion concentration in the measurement solution, calibration of the ISFET sensor with the calibration solutions with the known concentrations of the measured ion is essential. The objective is to calculate a calibration curve for the ISFET sensor, which is used to convert the output signal of the ISFET sensor—usually given in A or V—into the concentration of the measured ions in the measurement solution. The strategy employed is of paramount importance during the planning phase, particularly with regard to the selection of calibration solutions and the choice of an appropriate data-processing model. The preparation of mixed calibration solutions is typically constrained by quantitative limitations by using sensor arrays [17]. Consequently, the incorporation of an additional single component or concentration level results in a considerable rise in the number of requisite calibration solutions. To reduce the number of required calibration solutions, the experimental design can be optimised. The reduction in the number of calibration solutions required for a four-component system with four concentration levels through the implementation of optimised procedures has been demonstrated by Ni et al. [18]. In order to develop an experimental plan, fractional factorial designs are often employed in lieu of full factorials [19]. In fractional designs, interaction effects are disregarded, yet the calculation of main effects remains feasible. As a result of this simplification in the case of ISFET multi-sensory array, the developed designs require a significantly lower number of calibration solutions and are more reasonable from the point of view of workload and time required [20].

The ISFET measurement process is of significant importance for the quality and robustness of the complete system. The objective of the development and implementation of this measurement process is to create optimal measurement conditions for the use of the ISFET measurement technology in order to obtain a stable and reproducible output signal from the ISFET sensor. In the context of employing ISFET measurement technologies in agricultural applications under authentic field conditions, it is essential to recognise that the samples to be analysed are consistently an unidentified mixture of multiple ion species at varying concentrations. This is particularly relevant in scenarios such as soil nutrient analysis in the field, the determination of nutrient levels in hydroponic cultures, or the monitoring of environmental contamination in agricultural waters. The term ‘cross sensitivity’, which describes the ability of the ISFET sensor to respond to ions other than the target ion it is designed to measure in a mixed liquid, plays a crucial role in this context and should be taken into account [20] as part of the development and implementation of this measurement process, as well as the evaluation of measurement results.

Drift of ISFET sensors: The subsequent crucial phase in the ISFET measurement sub-process is the phenomenon of drift in the ISFET sensor. The term ‘drift’ by ISFET sensors refers to the alterations in output signals over time (time drift) that occur independently of the actual change in the ion concentration in the measurement solution. Contamination, migration of substances in or out of the sensor surface, and surface hydration can also cause a drift in the ISFET sensor [21]. A number of compensation techniques, both on- and off-chip, have been proposed as potential solutions to this problem. Most on-chip approaches focus on optimising the hardware with the objective of reducing time drifts and temperature effects. The drift of ISFET sensors can be addressed through correlated double sampling [22], while temperature effects can be managed through direct temperature control or the cancellation of the sensor thermal coefficient, as outlined in references [23,24] and [25,26], respectively. Moreover, the selection of an appropriate thermodynamic operating point can facilitate the minimisation or elimination of temperature-related effects in the output signal of ISFET sensors [27]. Other methods described in the literature include resetting the gate electrode of the ISFET sensor [28,29] and performing differential measurements with respect to a reference FET for output signal correction [30,31]. Techniques that are not implemented on-chip (i.e., algorithmic techniques or post-processing of measurement data) include analytical methods and those based on machine learning (ML) approaches. Analytical methods entail the differentiation of samples in order to correct for drift [21,32,33] or to compensate for output signal drift effects by dynamically biasing at the thermodynamic point [33].

Storage of ISFET sensors: The final sub-process in the handling of the ISFET is the storage of the ISFET sensor between and after measurements. ISFET sensors are designed for use in liquid solutions. The ISFET sensor must be kept hydrated between measurements. If the membrane dries out, it will shrink, and salt crystals may form on the membrane from the remaining measurement solution [14]. In such cases, the ISFET sensor or membrane must be reconditioned before a new measurement. The manufacturer of the ISFET sensor elements used here recommends a 10 mmol/L storage solution with a specific ion corresponding to the ion sensitivity of the ISFET sensor module. Except for the H_2PO_4- ISFET sensor module, a 10 mmol/L NaCl storage solution is recommended. For prolonged storage of the ISFET sensor elements, the sensor must be thoroughly rinsed with distilled water and allowed to dry. The ISFET element must be reconditioned before use after prolonged storage [34]. Koppenhoefer (2016) points out that if an ISFET or membrane is allowed to dry out, it may be damaged, or its performance may deteriorate. It is, therefore, important to ensure that appropriate handling and storage conditions are maintained before and after use to maintain the functionality of the ISFET or membrane [35].

The findings of this research have been derived from prolonged experimental studies and subsequently implemented in agricultural applications through research projects, where they have been subjected to evaluation under authentic field conditions. The test applications are tailored to two specific agricultural processes: soil nutrient analysis directly in the field and nutrient analysis in hydroponic systems. The used ISFET sensors have been integrated both as multi-sensor modules and as single sensor units to measure plant-available nutrients in aqueous solution. The sensors selected are commercially available and have been chosen for their suitability for the intended future range of measurements.

2. Materials and Methods

Commercially available ISFET sensors from MICROSENS (Lausanne, Switzerland) were employed in the experiments [36]. The sensors exhibit selectivity for potassium (K^+), nitrate ($NO_3{}^-$), ammonia ($NH_4{}^+$), and dihydrogen phosphate ($H_2PO_4{}^-$). Their selective membrane is based on polyvinyl chloride (PVC). The sensors were selected for use in specific agricultural applications based on their measuring range.

2.1. ISFET Multi-Sensor Module NUTRISTAT

In order to meet the customer's specific requirements for ISFET-based soil nutrient analysis, the manufacturer assembled individual ISFET sensors into a multi-sensor module, designated NUTRISTAT [37], for the soil nutrient measurement application (Figure 1). The design of the multi-sensor module comprised a closed, opaque LTCC (Low-Temperature

Cofired Ceramics) housing, which served to enhance its durability and reliability. The measurement chamber had a total volume of approximately 2 mL and was integrated into the LTCC housing. In addition, two additional tubes were integrated into the housing of the multi-sensor module: an inlet tube and an outlet tube. This configuration allowed the prepared soil sample suspension to enter and exit in a liquid state, facilitating the feeding of the multi-sensor module and the performance of the measurements. The multi-sensor module comprises the measuring chamber with four individual ISFET sensors integrated into one housing, each designed for the determination of a specific ion concentration: pH, K^+; $NO_3{}^-$; and $H_2PO_4{}^-$. The measuring liquid is passed simultaneously past all sensors. The configuration of independent control electronics determines whether the ISFET sensors are operated in parallel or sequential, one-after-the-other manner during measurement. These four sensors share a common solid-state Ag/AgCl reference electrode, which is mounted into the deck of the measurement chamber. Additionally, the muti-sensor module includes sensors for the determination of temperature and the electrical conductivity (EC) value of the measuring solution.

(**a**) (**b**)

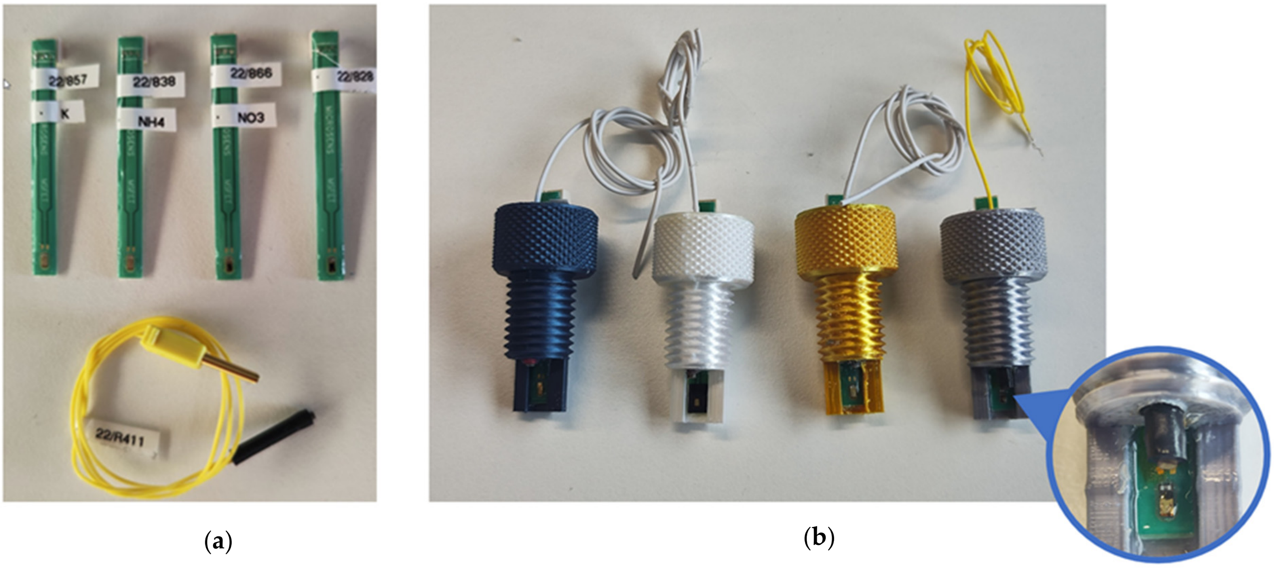
Figure 1. Multi-sensor module NUTRISTAT for soil application. (**a**) Closed housing with inlet and outlet tubes for the measuring liquid; (**b**) the open housing of the multi-sensor ISFET in individual integrated ISFET sensors [8].

2.2. Single-ISFET Sensors

Single-ISFET sensors with analogous characteristics to those integrated into the ISFET multi-sensor module designed for soil nutrient analysis were procured from MICROSENS SA and employed in the second agricultural application, namely, real-time capable nutrient measurement in hydroponic crops. Each ISFET sensor (for measurement K^+, $NO_3{}^-$, $NH_4{}^+$, and pH) was combined with its own reference electrode and mounted in a threaded sensor housing (see Figure 2). For measurement in hydroponic cultures, the sensor housing was screwed into a newly developed measuring chamber, which was filled with measurement solution.

2.3. Readout Electronic

New readout control electronics were developed, tested, and implemented for the control and readout of the output signal of the ISFET sensors, both as a multi-sensor module and individual ISFET sensors. The numerous adaptations made in relation to planned agricultural applications during the development phase have resulted in the newly developed electronics providing a stable output signal from the ISFET sensors with a noise level of approximately 3 mV. The output signal was amplified, and an analogue-to-digital converter was employed to digitise the analogue signal. Interface adaptations were implemented, including connection to a bus interface for further signal processing (Figure 3). All these adaptations were subjected to comprehensive laboratory testing and validations to ensure that the control and readout electronics of the ISFET multi-sensor module fully meet the specified application-specific requirements [38]. The operating point of the ISFET was recommended by the manufacturer and adopted for the measurements, with a voltage of 0.5 V and a current of 100 µA. The data sampling frequency was set to 1 Hz.



(**a**) (**b**)

Figure 2. (**a**) Single-ISFET sensors for measuring K^+, NH_4^+, NO_3^-, and pH and one reference electrode. (**b**) The ISFET sensors were integrated with a reference electrode in a self-printed housing, and the housings were colour-coded to reliably identify the correct ISFET sensor during operation [8].

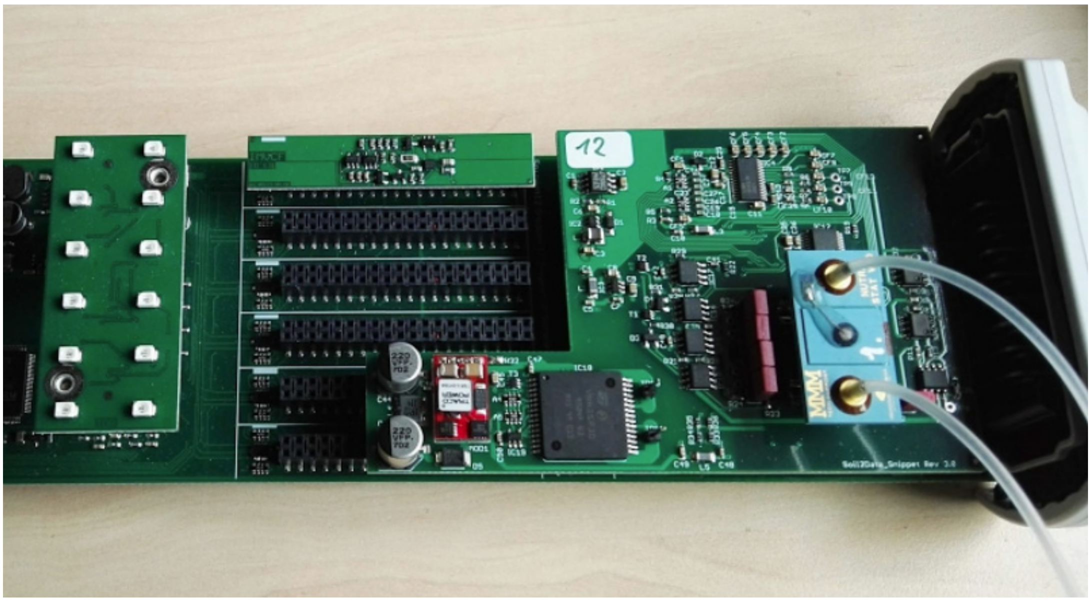


Figure 3. Development and realisation of the control and readout electronics for an ISFET multi-sensor module, including inlet and outlet pipes for the injection of the measuring liquid [8].

2.4. Chemicals

As part of these experiments, various calibration and measurement solutions of different ion compositions and concentrations were prepared, details of which can be found in Section 3. A stock solution of 500 or 1000 mmol/L was prepared for the preparation of calibration (0.1 mmol/L, 0.5 mmol/L, 1 mmol/L, 5 mmol/L, 10 mmol/L) and measurement solutions. Merck salts (a product of the EMSURE line) were employed in the preparation of nutrient calibration solutions and the creation of test measurement solutions. Technical pH buffer solutions (e.g., from PanReac AppliChem or Merck) were employed in the preparation of pH calibration solutions (pH 4.01, pH 6, pH 7, pH 8, pH 12) and the creation of test measurement solutions. The prepared nutrient calibration solutions used for calibration and measurement evaluation were analysed in the laboratory using the standard LUFA method [39] to verify the concentrations of the ions present.

3. Experiments and Results

The structure of this section is designed to facilitate the reader's clarity and is divided into the following subsections. Section 3.1 presents a detailed description of the experiments carried out and the results obtained by conditioning the ISFET sensors. Section 3.2 describes the calibration procedure of ISFET sensors, which is the next step in their use. Section 3.3 discusses the procedure of temporary storage between measurements, which affects the drift of the ISFET output signal in subsequent measurements. Section 3.4 analyses the drift of the output signal and describes the method for automatic drift correction.

3.1. Conditioning of the ISFET Sensors

ISFET sensor conditioning is a critical aspect of the nutrient analysis process. Prior to use, ISFET sensors must be immersed in a nutrient solution similar to the expected sample nutrient matrix to stabilise their response to the target ion. The ISFET sensor requires the presence of water molecules in the membrane to achieve its full and optimum functionality. This involves a swelling of the membrane, which increases both the external and internal surface areas. This results in greater absorption of the measuring solution due to the increased surface area and complete wetting of the ion-sensitive membrane itself. Conversely, chemical processes occur within the membrane and on the membrane surface, leading to the dissolution of unwanted crystallites, which occurred during the manufacturing process or their reduction. An additional purpose of conditioning is to remove any interfering particles or roughness from the membrane. This is to improve the low detection limit of measurement, help to minimise drift and ensure a consistent baseline in response to changes in the measured ion concentration [14,16]. Additionally, the electrical and chemical properties of the membrane are altered as a consequence of the conditioning process.

The conditioning process of the ISFET sensor is contingent upon the specific characteristics of the membrane in question, which must be taken into account in order to ensure optimal performance. Such characteristics include, but are not limited to, the material and composition of the membrane, its thickness, and its dimensions [14–16]. Due to the fact that the conditioning process is sensor-specific, it is not possible to make generalisations with regard to conditioning times and the composition of the conditioning solution that is required for conditioning or the concentration of said solution. Furthermore, the manufacturer (MICROSENS SA, Lousanne, Switzerland) has also modified the recommendations for conditioning over time. In this context, the authors elected to ascertain the optimal conditioning conditions via an experimental approach.

In order to identify the optimal conditions for the conditioning of the ISFET sensors selected for agricultural applications, a series of experiments under laboratory conditions were conducted to exclude the influence of external interference factors [8]. Four individual ISFET sensors were selected from each batch supplied (4xK^+ ISFETs, 4xNO_3^- ISFETs, 4xNH_4^+ ISFETs and 4xH_2PO_4-ISFETs) and subjected to conditioning with the appropriate conditioning solution. The conditioning solutions comprised potassium chloride (KCl), sodium nitrate ($NaNO_3$), ammonium nitrate (NH_4NO_3), and sodium chloride (NaCl). The four concentrations employed were 0.1 mmol/L, 1 mmol/L, 10 mmol/L, and 20 mmol/L, and the conditioning process was conducted over a 24-h period.

The output signal of each ISFET sensor was recorded in order to ascertain the point at which the output signal stabilised under constant measurement conditions (temperature, light conditions, concentration of the measurement solution) remained unchanged, and the sensor was ready for operational use. Figure 4 provides an illustrative example of the outcomes of the conditioning measurement series for the four NO_3^- ISFET sensors.

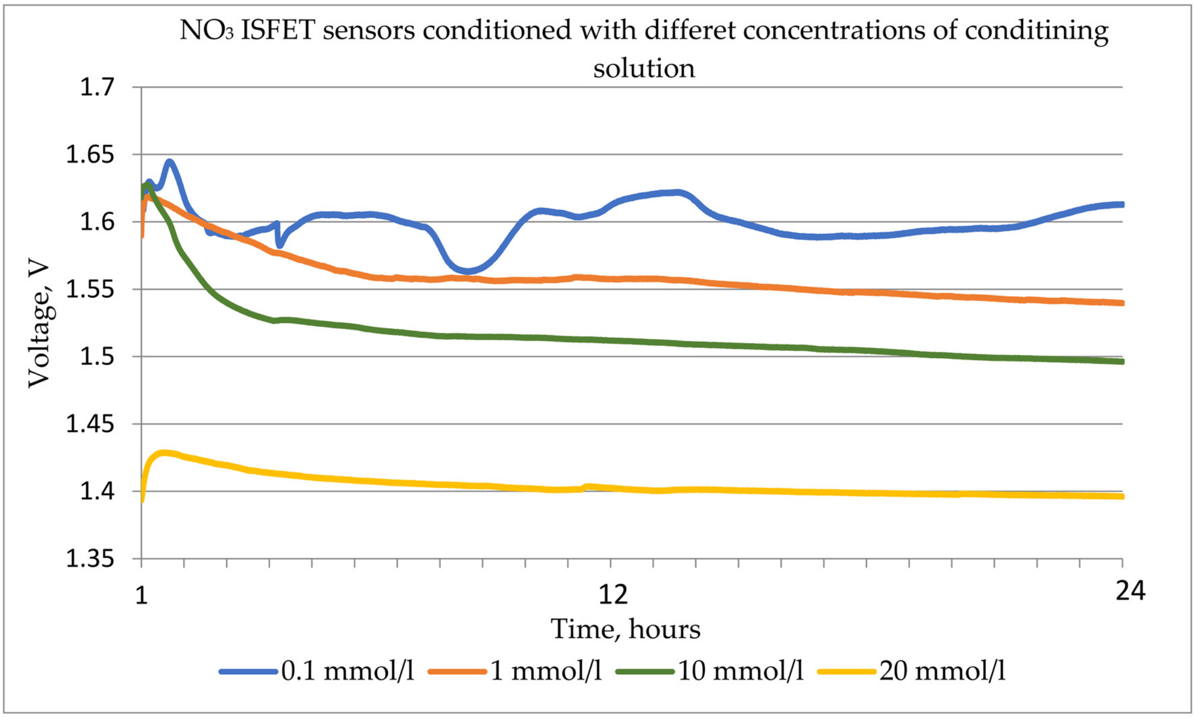


Figure 4. Experimental measurements with four individual NO_3 ISFET sensors and an NH_4NO_3 conditioning solution to identify the optimal conditioning parameters for the conditioning process for an ISFET-based measurement system. It is shown that the concentration of 0.1 mmol/L is not sufficient for complete conditioning of ISFET sensor.

It is evident that the measurement conducted with a solution containing nitrate at a concentration of 0.1 mmol/L results in an unstable output signal, even after a 24-h measurement period. Conversely, at concentrations of 1 mmol/L, 10 mmol/L, and 20 mmol/L, the measurement signal of the ISFET sensor stabilises after approximately 10 h. The output signal at concentrations of 1 mmol/L then exhibits a sustained decline after approximately 14 h. In contrast, the output signal at concentrations of 10 mmol/L declines after approximately 10 h. In this case, we observe a drift effect of the ISFET sensor, whereby the sensor's output signal undergoes a change over time despite the chemical composition and operation point at the input remaining fixed (see Section 3.4—Drift of ISFET sensor). It is worth noting that the output signal remains relatively constant for a concentration of 20 mmol/L for the entirety of the observation period. It should be noted that the 20 mmol/L solution concentration over the expected measurement range in the context of intended agricultural applications can result in adverse effects when using the ISFET sensors directly following the conditioning process (see Section 3.3—Storage of ISFET sensors). In consideration of the anticipated nutrient concentrations range—up to max. 12 mmol/L—in our planned agricultural applications involving the use of ISFET sensors and the experimental findings on the intermediate storage of the ISFET sensors used and taking into account the manufacturer's recommendations, we opted for a multi-conditioning solution comprising KNO_3 and NaCl at a concentration of 1 mmol/L. The above solution allows for the conditioning of individual ISFET sensors as well as the simultaneous conditioning of all ISFET sensors integrated into the NUTRISTAT multi-sensor module, which is exposed to identical conditioning conditions. In order to minimise the influence of undesirable effects, such as drift, saturation, or destruction of the ion-selective membrane on subsequent measurements, the total conditioning time of the ISFET sensors used was limited to 10 h based on experimental measurement data.

3.2. Calibration of ISFET Sensors

Calibration represents the most crucial phase of multi-component analysis using ISFET sensor arrays, as it is the foundation upon which the entire process is built. The strategy employed is of paramount importance at the planning stage, specifically in the selection of calibration solutions and also during data processing, where the choice of an appropriate model is crucial. In the classical calibration procedure, the measured values of all possible combinations of the nutrients to be quantified are obtained at selected concentration levels. This is to account for the response of the ISFET sensor to be calibrated to changes in the composition of the ions in the measuring solution, thereby ensuring a more precise calibration. The preparation of mixed calibration solutions, in this case, is typically constrained by considerations of quantity. The total number of solutions required can be calculated using the following equation:

$$\boldsymbol{N = S^{c}} \tag{1}$$

In this context, N represents the total amount of required calibration solutions; C denotes the number of concentration levels, and S denotes the number of ions in the solution [17]. To illustrate, a complete factorial experiment for a solution comprising four nutrients (S) and three levels (C) of concentration necessitates the preparation of 64 mixed solutions (N). Consequently, the incorporation of a single component or concentration level will markedly augment the number of requisite calibration solutions. In order to reduce the number of required calibration solutions, the experimental design can be optimised.

In order to calibrate the ISFET multi-sensor, a multivariate calibration method was employed. The objective of multivariate calibration in classical electrochemistry is to ascertain the concentration of one or more pertinent analytes from a substantial number of measurements. This typically entails determining the concentration of analytes from voltametric data or multiple amperometric electrodes. In the case of ISFET-based analytical methods, the concentration of one or more analytes is also determined in a measurement solution that can be described as a combination of several analytes with unknown composition and concentration of individual analytes. When a measurement solution consisting of several analytes with an unknown composition undergoes voltammetry, the resulting voltammogram is a combination of the individual analyte voltammograms. In such cases, the peaks of the combined voltammogram may overlap or otherwise interfere with each other, obscuring the identity of the analytes [40,41]. Multivariate calibration, in this case, is necessary to resolve the peaks and quantify the analytes. Two approaches can be taken to address this issue. The first involves deconvoluting the voltammogram to determine the contributions from each analyte, which can then be calibrated using a simple method, such as peak area. The second approach treats the voltammogram as a unified entity without explicitly dividing it into its constituent components [42]. In selecting the second method for use in an ISFET-based analysis procedure, it is essential to consider the selectivity of the ISFET sensor. The selectivity of ISFET sensors is a significant parameter that indicates the sensor's ability to distinguish between different ions or molecules. This ability is quantified by a selectivity coefficient, which is of paramount importance for the accuracy and reliability of measurements in applications such as pH measurement or the monitoring of specific ions in liquid solutions [43]. The selectivity coefficient is a numerical measure characterizing the ability of an ISFET sensor to distinguish between an interfering ion and a target ion and is calculated with the simplified Nikolsky–Eisenman equation as follows:

$$\boldsymbol{E = E_0 + RT/(Z_A F)\ln\left[a_A + \sum\nolimits_B K_{A,B}^{pot}\,(a_B)\right]^{Z_A/Z_B}} \tag{2}$$

where E is the measured potential; $E0$ is a constant that includes the standard potential of the electrode, the reference electrode potential, and the junction potential; Z_A and Z_B are charge numbers of the primary ion A and the interfering ion B; $\boldsymbol{a_A}$ and $\boldsymbol{a_B}$ are the activities of the primary ion A and the interfering ion B, and $\boldsymbol{K_{A,B}^{Pot}}$ is the potentiometric selectivity coefficient for the primary ion A against the interfering ion B. *R* is the gas constant; **T** is the absolute temperature, and *F* is the Faraday constant [44,45]. The selectivity coefficient $\boldsymbol{K_{A,B}^{Pot}}$ is often referred to as the Nikolsky coefficient and is often determined by the so-called separate solution method by comparing two solutions each containing only salt from the primary and interfering ions [46]. The smaller the $\boldsymbol{K_{A,B}^{Pot}}$, the less sensitive the ISFET sensor is to the interfering ion. In the scientific literature, a variety of representations of the selectivity coefficient as a logarithmic function can be found. This is because the sensitivity of ISFET sensors to interfering ions is often based on an exponential relationship, whereby the logarithmic representation enables more straightforward analysis and interpretation of the data.

The ISFET sensors, initially deployed in experiments and subsequently in agricultural applications, were supplied by the manufacturer, MICROSENS SA, with the requisite information on selectivity coefficients for known interfering ions (Table 1). This information can then be employed to devise an appropriate strategy for the calibration of ISFET-based multi-sensor systems, considering the planned calibration method and the selected components.

Table 1. Selectivity coefficients of used ISFET sensors indicated by the manufacturer [34].

Target Ion	Sensitivity	Interfering Ions	Selectivity Coefficient Log $K_{A,B}^{Pot}$	Measument Range
H^+	55 mV/pH	K^+, Na^+, Ca^+		3–12 pH
K^+	50 (±5) mV/decade	Na^+, $NH_4{}^+$	vs. Na+: −3.8/vs. $NH_4{}^+$: −2.0	5×10^{-4}–0.1 M
$NH_4{}^+$	50 (±5) mV/decade	K^+, Na^+	vs. K^+ −0.8/vs. Na^+: −2.9	5×10^{-4}–0.1 M
NO_3^-	48 (±5) mV/decade	Cl^-	vs. Cl^-: −2.0	5×10^{-4}–0.1 M
H_2PO_4	42 (±5) mV/decade	NO_3^-, Cl^-	vs. Cl^-: −1.8	10^{-3}–0.1 M

It is obvious that the interfering ions must be present in the measuring solution at concentrations many times higher (by a factor of 100 or 1000) than the target ion in order to significantly affect the measurement of the target ion. Nevertheless, the presence of interfering ions in the measurement solution must be taken into account in the calibration and interpretation of the measurement data of any ISFET sensor by assuming that the concentration of interfering ions in the calibration solution is much lower than the concentration of target ions. This means that the influence of the interfering ions in such cases is very small or zero.

The manufacturer (MICROSENS) has indicated that it might also be possible to carry out calibration with a mixed calibration solution. This information served as a starting point for the calibration concept of this work, which was subsequently subjected to experimental validation in accordance with the relevant standards and measurement conditions in planned agricultural applications. Based on the favourable selectivity coefficients and the expected low concentration of ions, both target and interfering ions, in future agricultural applications, several series of measurements were carried out to validate the calibration concept. For this purpose, each ISFET sensor was first assessed with a calibration series consisting of solutions containing only the target ions in different concentrations depending on the measuring range and then tested with the possible interfering ions that are also present as message ions in other selected ISFET sensors (e.g., KCl and KNO_3, $NO_3NH_4{}^-$ and KCl^-, NaH_2PO_4 and $NH_4NO_3{}^-$).

Figure 5 illustrates the output signal curve during the validation of the calibration procedure for the NUTRISTAT multi-sensor module. The objective of this experiment is to ascertain the response of the integrated ISFETs to the multi-nutrient liquids to be measured. To this end, a series of tests were conducted in order to evaluate the cross-sensitivity of the utilised ISFET sensors. The multi-nutrient solution, comprising nitrate, ammonium, and potassium chloride, was employed at varying concentrations (0.5 mmol/L, 1 mmol/L, 5 mmol/L, and 10 mmol/L). The duration of each measurement was limited to five minutes. As illustrated in the diagram, there was minimal change in the output signal of the test liquid produced by the H_2PO_4-ISFET sensor and the pH–ISFET sensor. Furthermore, both sensors exhibited no significant response to the alteration in the concentration of the measured liquid over the course of the experiment.

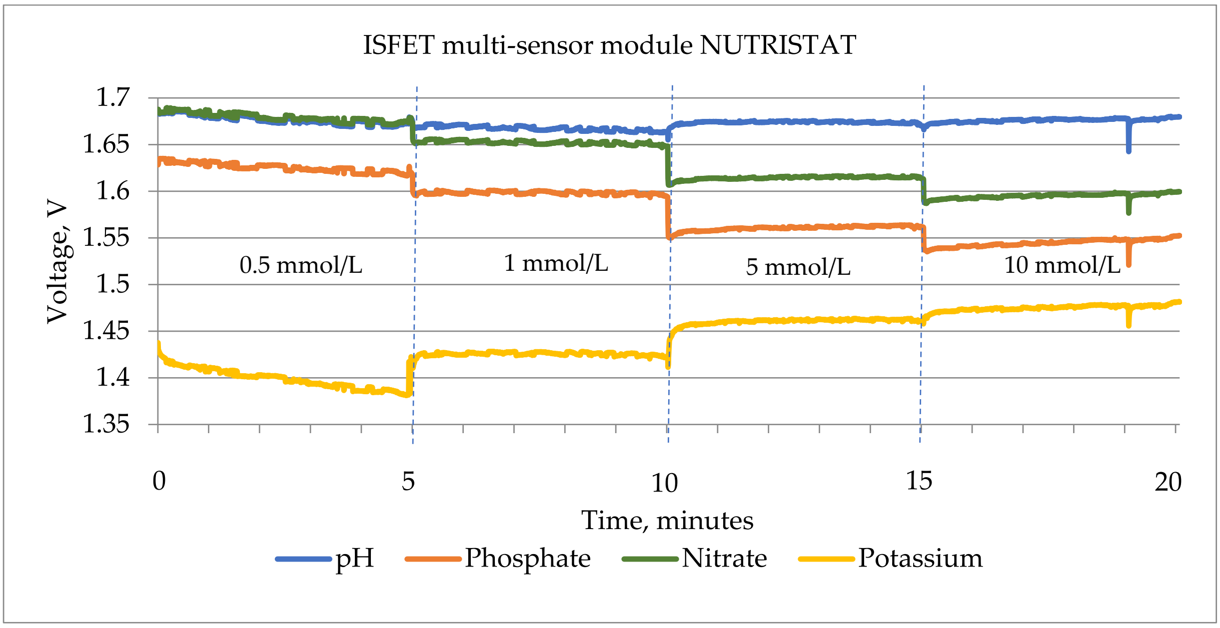


Figure 5. Calibration of ISFET multi-sensor module NUTRISTAT with NH_4NO_3 KH_2PO_4 calibration solution at concentrations of 0.5 mmol/L, 1 mmol/L, 5 mmol/L, and 10 mmol/L, the calibration solutions were filled into the ISFET multi-sensor module one after the other, and the concentration levels were retained in the sensor for 5 min.

Furthermore, experiments conducted with the K^+ ISFET sensor have no significant influence of interfering ions on measurement signals with respect to cross-sensitivity to interfering ions in a multi-nutrient solution (Figure 6). The used K^+ ISFET sensor demonstrated no interference from interfering ions (Na^+, NH_4^+) within the anticipated measurement range of agricultural applications, as long as the concentrations of the target and interfering ions remained within the optimal ratio. The optimal ratio is defined as a condition whereby the selectivity coefficients indicated in Table 1 are not exceeded. Both Na^+ and NH_4^+ are interfering ions for K^+ in the test sample. However, the concentration ratios of these ions with respect to K^+ are 1:1. It can, therefore, be concluded that no interference from Na^+ or NH_4^+ is to be expected when measuring with the K^+-ISFET sensor. The blue curve illustrates the anticipated rise in the measured value with rising K^+ concentration in the absence of interfering ions. One of the test samples—measured solution with KNO_3 and NaH_2PO_4—contains Na^+ as an interfering ion. The recorded data curve for the measurement conducted with this test sample (Figure 6, orange curve) demonstrates a proportional increase in comparison to that observed for KCl (Figure 6, blue curve). NH_4NO_3 with the interfering ion NH_4^+ was used as another measuring solution (Figure 6, green curve). The K^+-ISFET sensor is not affected by the NH_4^+ ion, provided that the selectivity coefficient given in Table 1 is not exceeded.

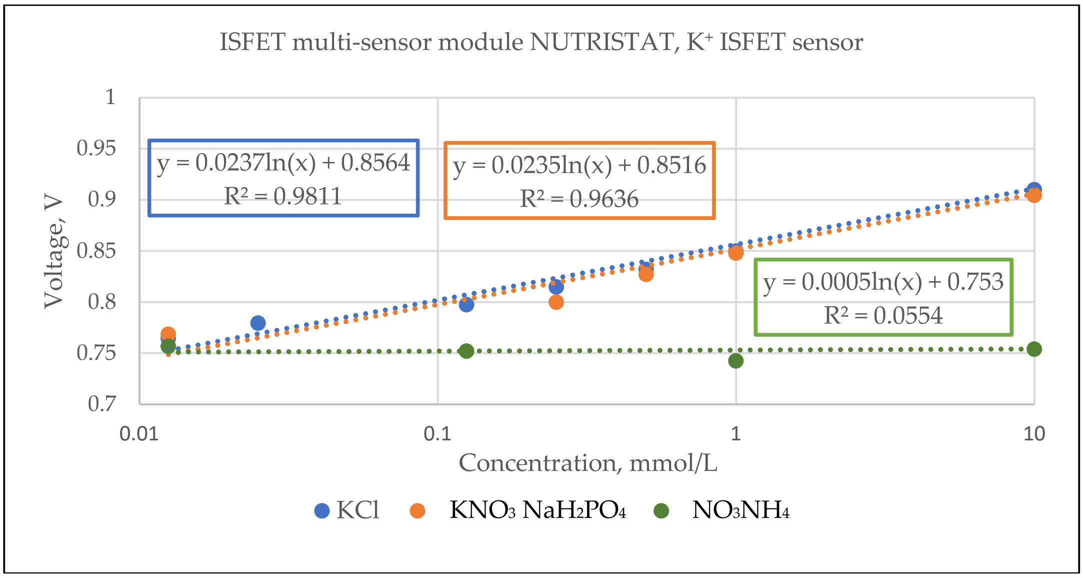


Figure 6. Calibration tests of K^+ ISFET sensor with different calibration solution compositions and concentrations to verify the influence of interfering ion.

During the calibration test, it was observed that the ISFET sensor exhibited a reaction to the interfering ions present in the multi-ion solution. The ISFET sensor begins to respond to the interfering ions when a specific concentration of interfering ions is reached in the solution under measurement. This can be attributed to the absence or low concentration of target ions in the solution, which, according to Nikolsky–Eisenman, prompts the ISFET to react to the interfering ions in accordance with the selectivity coefficient. This observed phenomenon is illustrated in Figure 7 using NO_3-ISFET calibration data as an example. The blue curve in Figure 7 shows the calibration curve for the NO_3^- ISFET sensor. NO_3^- is an anion, and it is typical for the curve for an anion to slope down as the concentration increases. In contrast, the curve for a cation rises with increasing concentration. The NO_3-ISFET was also filled and measured with KCl measuring solution (Figure 7, orange curve) or NaH_2PO_4 measuring solution (Figure 7, green curve). The measurement results for the KCl and NaH_2PO_4 solutions show a reaction at the NO_3-ISFET sensor. As expected, the NO_3-ISFET sensor reacts to the interfering ion Cl^-. From a concentration of 1 mmol/L, a drop in the curve can be seen. This can be explained by the cross-sensitivity of Cl^- to NO_3^- (see Table 1, line NO_3). The NO_3-ISFET sensor is also sensitive to the anion $H_2PO_4^-$. The measured value for NO_3^- decreases from a concentration of 1 mmol/L. Compared to the KCl curve, the NaH_2PO_4 curve drops more sharply. The hypothesis is that the anion $H_2PO_4^-$ has a stronger influence on the NO_3-ISFET sensor than the anion Cl. No selectivity coefficient was given by the manufacturer for $H_2PO_4^-$.

The findings indicate that there is no notable discrepancy in the response of ISFET sensors to calibration solutions comprising solely the target ion and those containing the interfering ions at the anticipated concentration levels in the intended agricultural applications. Consequently, the calibration process can be conducted using a multi-solution comprising all ions pertinent to the calibration of four ISFET sensors (K^+, NO_3^-, NH_4^+, and $H_2PO_4^-$) in their corresponding concentrations. The implementation of this calibration method has the effect of reducing the number of calibration solutions that are required in this particular case. Furthermore, it provides a significant reduction in the time that is required for the preparation procedure to be carried out prior to the measurement.

The experimental results illustrate the necessity of considering the presence of interfering ions during the calibration process. In certain instances, the ISFET sensor displayed no discernible response to the presence of interfering ions or the absence of target ions. Conversely, in other cases, it was of great importance to include target ions in combination with interfering ions (as a background value) in the calibration solution. Given the lack of prior knowledge regarding the concentrations of target and interfering ions and their ratio to each other in the test solution, particularly in the context of planned agricultural applications, it was decided to employ the multi-nutrient calibration method. For this purpose, four concentrations were defined in relation to the expected nutrient concentrations in the intended agricultural applications: 0.5 mmol/L; 1 mmol/L; 5 mmol/L; and 10 mmol/L. Additionally, a mixed calibration solution was created with the target ions and possible interfering ions in equal concentration ratios to one another. This approach was deemed necessary to enhance the precision of nutrient analysis with ISFET sensors, given the potential impact of interfering ions in the measuring solution. The calibration measurements were conducted in a controlled setting, with external factors such as light and temperature held constant, in order to minimise the influence of potential external interfering factors.

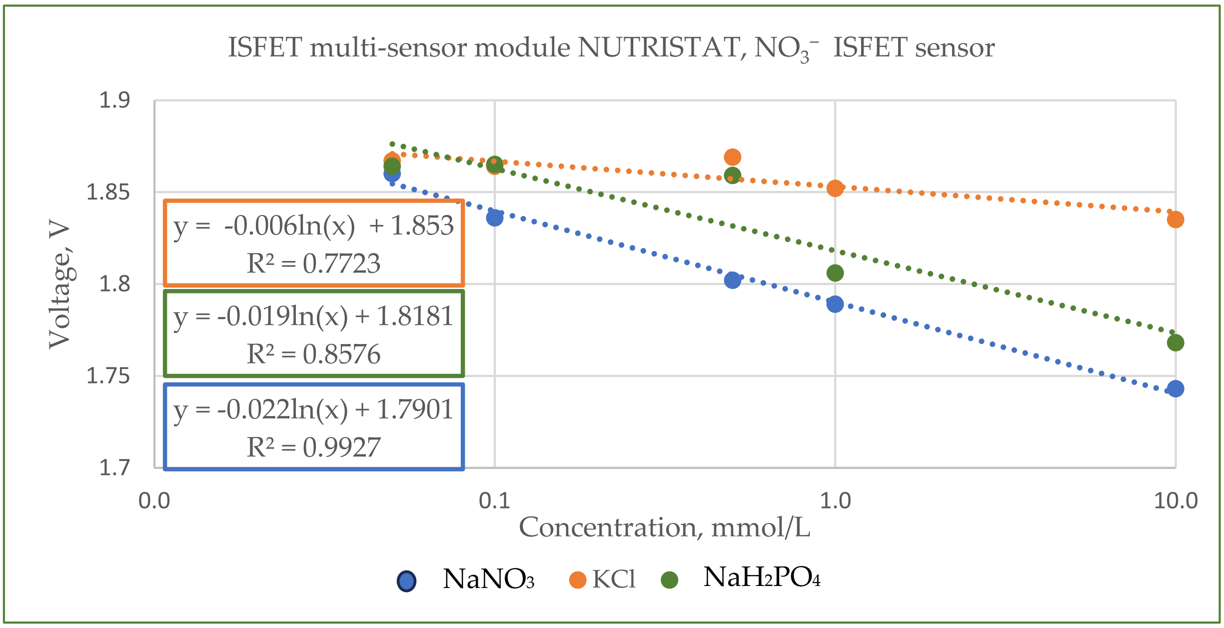


Figure 7. Calibration tests of NO_3^- ISFET sensor with different calibration solution compositions and concentrations to verify the influence of interfering ions.

In the case of an ISFET-based measurement in hydroponic cultures, the multi-nutrient calibration method, which has been developed and tested, can be employed without further adjustment. Nevertheless, when ISFET sensors are employed for soil nutrient analysis in conjunction with an ISFET-based multi-sensor NUTRISTAT, it is essential that the calibration procedure undergoes further modification to facilitate adaptation to the recently developed 'soil2data extraction method', which was specifically designed for this purpose [10]. The extraction method is standardised in the design for the LUFA extraction method [39] and is comprised of two distinct phases. This indicates that the ions are extracted from the soil sample in two steps with the assistance of two standardised extraction agents. In the first stage of the extraction process, the H^+ and NO_3^- ions are extracted using the extraction agent $CaCl_2$ at a concentration of 12.5 mmol/L. In the second stage of this process, a conc Ca acetate lactate (CAL) solution is employed for the extraction of potassium (K^+) and phosphorus (P) ions from the soil sample. This is an indication that the measurement solution contains alternative liquids rather than distilled water, which is the basis of the ISFET sensor multi-nutrient calibration method described and illustrated above. In addition, the extraction solutions used in the soil2data extraction method also contain the interfering ions (see Table 1) that influence the accuracy of ISFET-based nutrient measurements. The benefit of this approach is that the concentration of the extraction agents, and, thus, the concentration of interfering ions employed to extract the nutrients in this extraction method is known and maintained at a constant level. This suggests that the impact of interfering ions from extraction agents can be reduced by analysing the ISFET measurement data using the same extraction agent that was employed to extract the target ions as the basis for the calibration solutions. A series of calibrations were developed and carried out to prove the influence of the extraction agent as an additional component in the measuring solution using the ISFET-based nutrient analysis:

- For the pH–ISFET sensor, the calibration series comprised pH 4, pH 6, and pH 8, with a $CaCl_2$ extraction solution utilised as the base. This approach was adopted with the recognition that Ca^+ is an interfering ion for pH–ISFET sensors;
- For the NO_3-ISFET sensor, the calibration series comprised 0.5 mmol/L, 1 mmol/L, 5 mmol/L, and 10 mmol/L, with the $CaCl_2$ extraction solution serving as the basis;
- The calibration series employed for the K^+ ISFET and $H_2PO_4^-$ ISFET sensors was as follows: the 0.5 mmol/L; 1 mmol/L; 5 mmol/L; and 10 mmol/L solutions with $CaCl_2$ and CAL extraction solutions that were quantified in proportion using the 'soil2data extraction method' as a basis.

Figure 8 shows the measurement results of a calibration curve for NO_3^- from an H_2O-based measurement solution and a measurement solution mixed with the extractant $CaCl_2$. The $CaCl_2$ extractant solution shows higher voltages than the water-based solution. It is assumed that the chloride from the extractant—as an interfering ion for NO_3^-—influences the activity on the membrane or ionophore—due to the same charge of NO_3^- and Cl^- ions, which corresponds to the same size of those anions—and, thus, increases the measured value. The extraction agent CAL has a similar effect on the measurement of K^+ or $H_2PO_4^-$. When measuring K^+, the measuring solution with the CAL extractant has a lower measuring voltage than the water-based measuring solution (Figure 9). If the measurement results of the water-based $H_2PO_4^-$-measuring solution are compared with those using the CAL extraction agent, an influence on the measurement voltage is also evident here. The $H_2PO_4^-$ measurement solution with CAL is significantly higher than the water-based measurement solution (Figure 10). The measurement results of the technical pH buffer solution show a smaller change in the measurement voltage between the pure pH buffer solution and the pH buffer solution mixed with the extraction solution $CaCl_2$ (Figure 11).

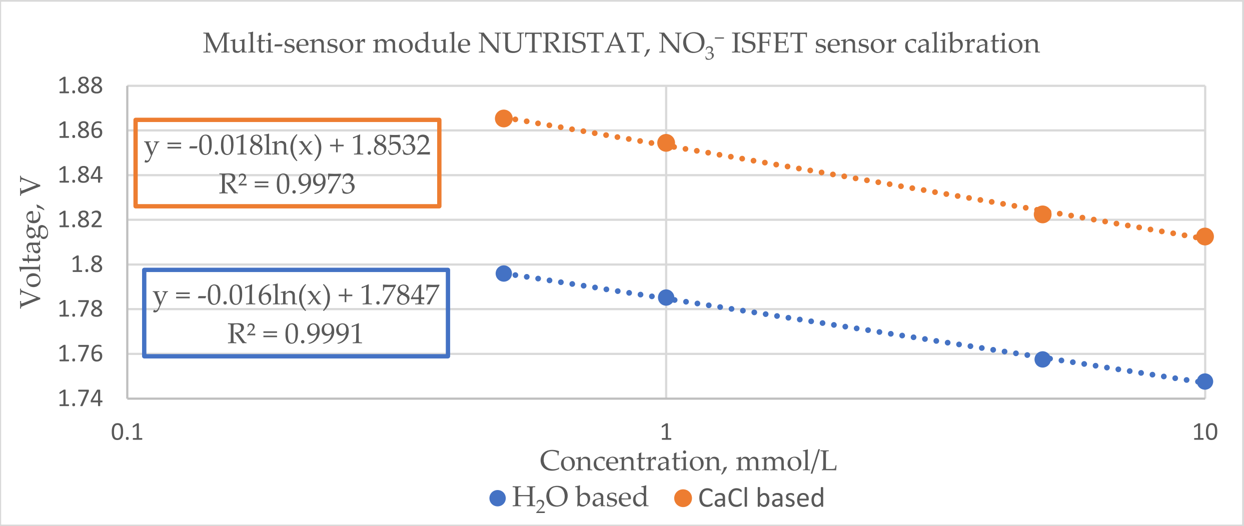


Figure 8. Comparison of measurement results of NO_3^- calibration series with calibration solutions based on two extraction agents to determine the influence of the extraction agent on the measurement result.

The measurement results show significant differences depending on whether a water-based measurement solution or a measurement solution with an added extractant was used (Figures 8–10). This observation highlights the necessity of ensuring that the extraction agents used to extract ions from soil samples are also employed in the preparation of calibration solutions for ISFET sensors. This approach enables the consideration of the impact of interfering ions on ISFET measurement data, thereby ensuring the accuracy and reliability of the ISFET-based analytical process.

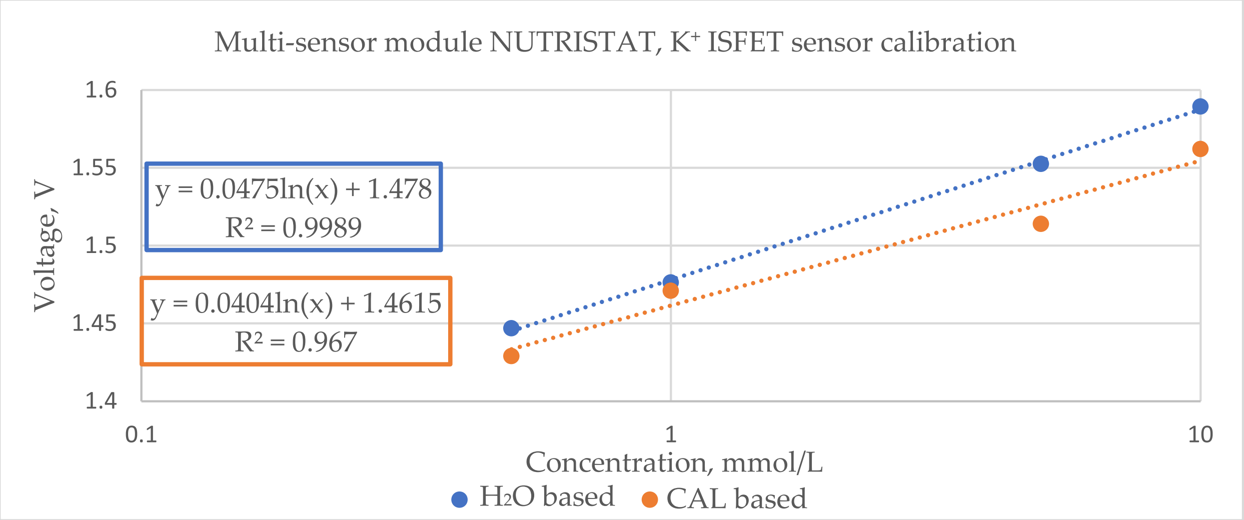


Figure 9. Comparison of measurement results of K^+ calibration series with calibration solutions based on two extraction agents to determine the influence of the extraction agent on the measurement result.

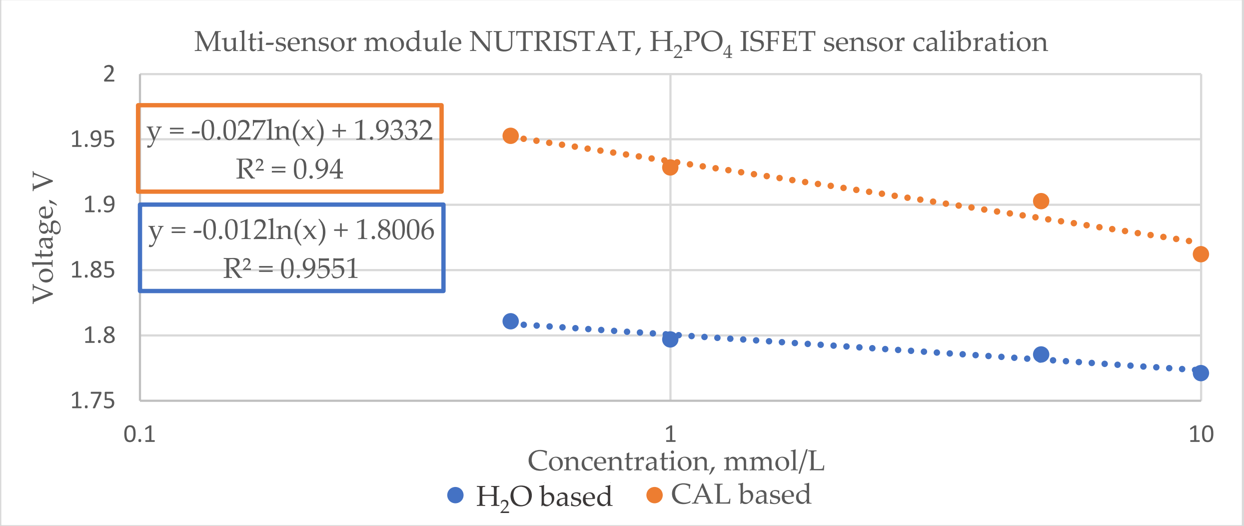


Figure 10. Comparison of measurement results of $H_2PO_4^-$ calibration series with calibration solutions based on two extraction agents to determine the influence of the extraction agent on the measurement result.

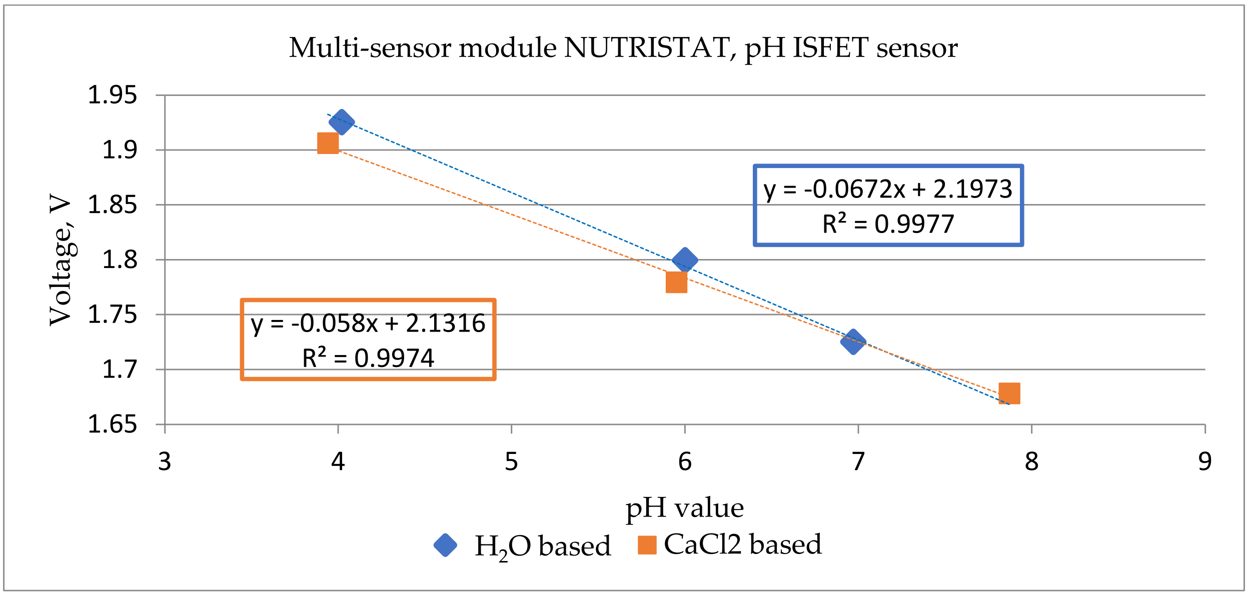


Figure 11. Comparison of measurement results of pH calibration series with calibration solutions based on two extraction agents to determine the influence of the extraction agent on the measurement result.

3.3. *Storage of the ISFET Sensor*

As mentioned in the introduction, in order to maintain optimal sensing performance, the ISFET sensors, which feature an ion-sensitive membrane, should be kept in a hydrated stage between measurements and for short-term storage. In regard to the **individual ISFET sensors**, the manufacturer has recommended the usage of a storage solution with the target ion in question and a concentration of 10 mmol/L. For example, it is stated that a storage solution containing potassium (e.g., potassium chloride (KCl)) is used for the K^+ ISFET sensor; a storage solution containing ammonium is used for the NH_4^+ ISFET sensor, and a storage solution containing nitrate (e.g., ammonium nitrate (NH_4NO_3)) is used for the NO_3^- ISFET sensor. The $H_2PO_4^-$ ISFET sensor is an exception; the manufacturer recommends that the $H_2PO_4^-$ ISFET sensor should not be permanently filled with a storage or conditioning solution containing dihydrogen phosphate in order to protect the ion-sensitive membrane. Instead of a dihydrogen phosphate storage solution, a chloride storage solution is recommended. A 10 mmol/L KNO_3NaCl storage solution is used for the **NUTRISTAT ISFET multisensor module**. An ion-specific storage solution with a concentration of 10 mmol/L, depending on the ion sensitivity of the ISFET sensor, is used for the individual ISFET sensors. For example, a storage solution containing ammonium nitrate with a concentration of 10 mmol/L is used for the NH_4^+ and NO_3^- ISFET sensors.

The manufacturer's recommendations were duly implemented and subsequently verified. It was observed that when ISFET sensors were stored in the storage liquid with a concentration of 10 mmol/L for an extended period (exceeding 10 h) and subsequently employed to ascertain the concentration of the measuring solution, the initial measurement outcome exhibited a persistent discrepancy in voltage value when compared to the subsequent repetitions (see Figure 12). The first measurement was conducted with a measuring solution containing 1 mmol/L potassium (Figure 12, blue line). The second measurement was conducted with a solution containing 1 mmol/L potassium after 20 min of the previous measurement. The two measured curves are completely different and show a different voltage at the same concentration level at the first repetition.

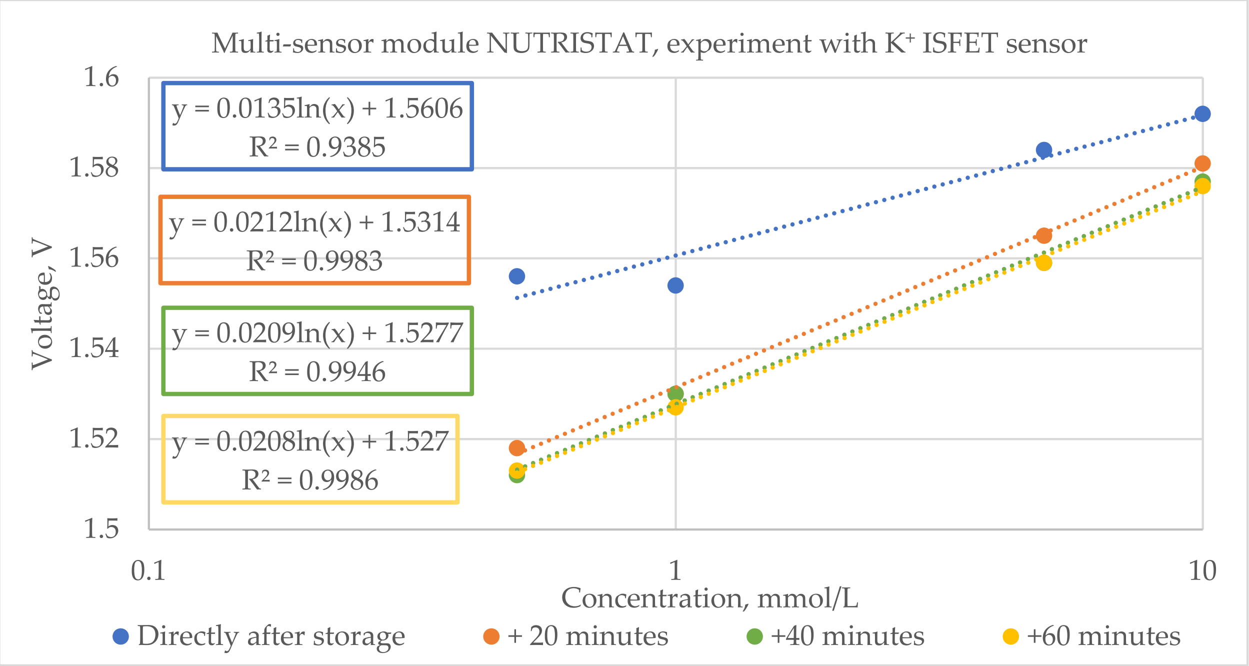


Figure 12. In experiments on the reproducibility of the output signal of K^+ ISFET sensors after storage of the ISFET sensor in storage solution (concentration = 10 mmo/L) and further measurement repetition with measuring solution (concentration = 1 mmo/L), the measurement directly after storage indicates a deviating measured value in comparison to the following measurements with the measuring solution.

The third and fourth repetitions of the measurement—40 and 60 min after the first measurement—show that these three curves are highly correlated with each other and differ significantly in the measured voltage from the first curve (Figure 12, orange, green, and yellow lines).

Based on the experimental data collected, it was hypothesised that during storage of the ISFET sensors in a storage solution with an ion concentration of 10 mmol/L, the ISFET membrane or ionophores store the target ions and enter a saturated state. Therefore, a measurement of the test measurement solution (in our case, a calibration solution) with a significantly lower ion concentration than that of the storage solution (in our case, 0.5 mmol/L versus 10 mmol/L) leads to incorrect measurement results. Bühlmann et al. [47] explain that the potential drifts occur as a result of the slow equilibration of the corresponding surface layers with the bulk of the solution and/or membrane when the sample concentration changes. Based on our experiments, we can confirm this statement. As part of the present analysis, it was found that the manufacturer's recommendation for short-term storage must be optimised in order to ensure the stability of the output signal when the ISFET sensors are stored for an extended period of time. To this end, the concentration of the storage solution was adjusted to the expected concentrations in selected agricultural applications and changed to 1 mmol/L. The composition of the storage solution has remained constant and contained all the target ions. The selected concentration is not at the limit of the measuring range of the ISFET sensors and is consistent with the expected concentration of the measuring solution in hydroponic systems and in ISFET-based soil nutrient analysis.

3.4. Drift of the ISFET Sensor

In the context of ISFET sensors, the term 'drift' is used to describe the changes in output signals under constant measurement conditions like temperature, light conditions, etc., over time (time drift) that occur independently of the actual change in ion concentration in the measured solution. While the causes of ISFET sensor drift can be minimised, they cannot be completely eliminated. The numerous techniques described in Section 1—Introduction—that have been developed and tested to compensate for drift cannot be used in agricultural applications in the majority of cases. Some of such compensation techniques are too complex to use and require additional equipment, while others require ideal measurement conditions for ISFET-based measurement (in terms of temperature, humidity, light conditions, etc.), which would hardly be possible in agricultural applications.

It is of the utmost importance to initially comprehend the extent to which ISFET sensor drift affects the outcome of the ISFET-based nutrient analysis. A series of experiments were executed in order to achieve this goal. The present experiment was carried out in an active hydroponic system with constant environmental conditions (light, temperature, humidity) with the aim of identifying instances of drift in ISFET sensors. It is important to note that constant room temperature and humidity were maintained in order to minimise the influence of external factors and, thus, ensure the comparability of the results. In the present study, the ISFET sensors to measure pH, NO_3^-, NH_4^+, and K^+ were integrated into individual light-impermeable measuring chambers on a hydroponic system. The temperature of the measurement solution during experiments was maintained at a constant level throughout the entirety of the experimental period. The measurements were conducted over a period of three weeks. In the present study, the ISFET sensors were calibrated three times during the aforementioned period: initially, after one week and then after two weeks (Figures 12–14). It can be observed that as a result of the drift, the measuring voltage for the measuring curves of NH_4^+ (Figure 13) and K^+ (Figure 15) increases, while that for NO_3^- (Figure 14) decreases. However, it can also be observed that the gradient of the respective ion-specific calibration curves remains constant from the measurement of the first week to the second week and the third week. In contrast, the offset voltage value undergoes a change from the calibration curve of the first week to the second week and the third week.

On the day of measurement, three samples were obtained for ISFET-based analysis: one in the morning; one at noon; and one in the evening. Each sample was subjected to three rounds of analysis with ISFET sensors, with the objective of demonstrating the reproducibility of the ISFET measurement. This resulted in a total of nine measurements per ISFET sensor and day. The average standard deviation for repeated measurements is 0.003 mV for the NH_4^+ ISFET sensor, 0.002 mV for the NO_3^- ISFET sensor, and 0.005 mV for the K^+ ISFET sensor during the measurement period. The following concentration standard deviation is expressed in percentage terms: 0.96% for the NH_4^+ ISFET sensor; 0.96% for the NO_3^- ISFET sensor, and 2.54% for the K^+ ISFET sensor. As these characteristics are ISFET-sensor-specific, there is no way to determine the spread of these values between sensors in a batch, and they must be determined individually for each ISFET sensor.

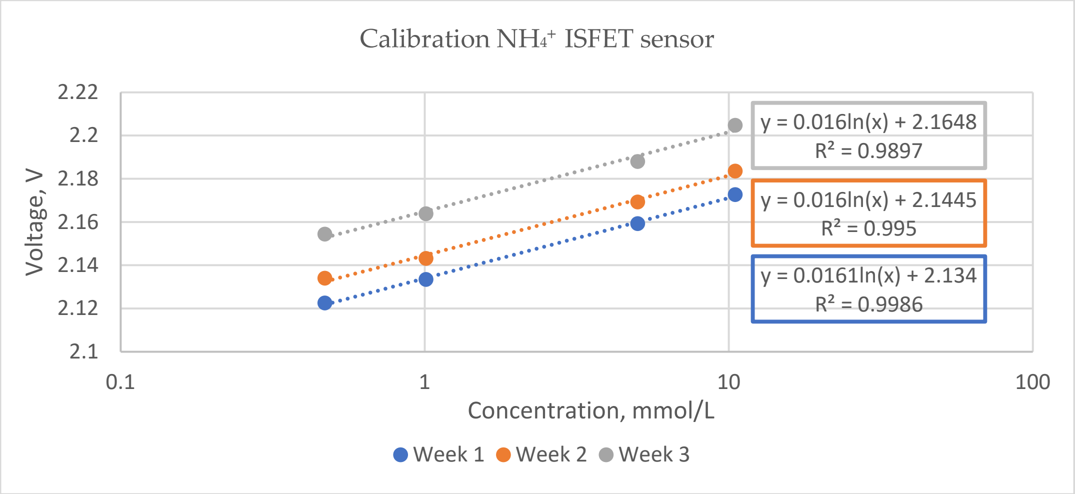


Figure 13. Time drift experiments on a single NH_4^+ ISFET sensor showing a parallel shift in the measurement curve with a change in the zero-offset value.

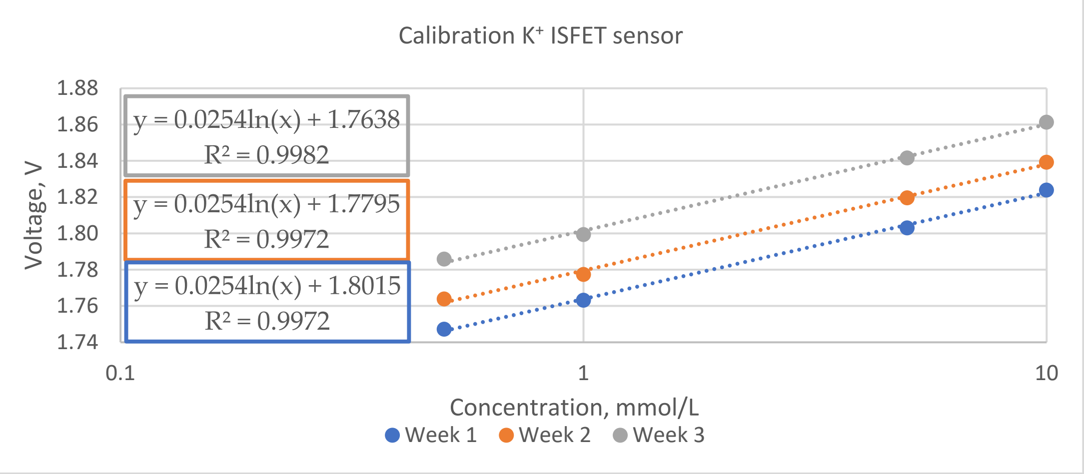


Figure 14. Time drift experiments on a single K^+ ISFET sensor showing a parallel shift in the measurement curve with a change in the zero-offset value.

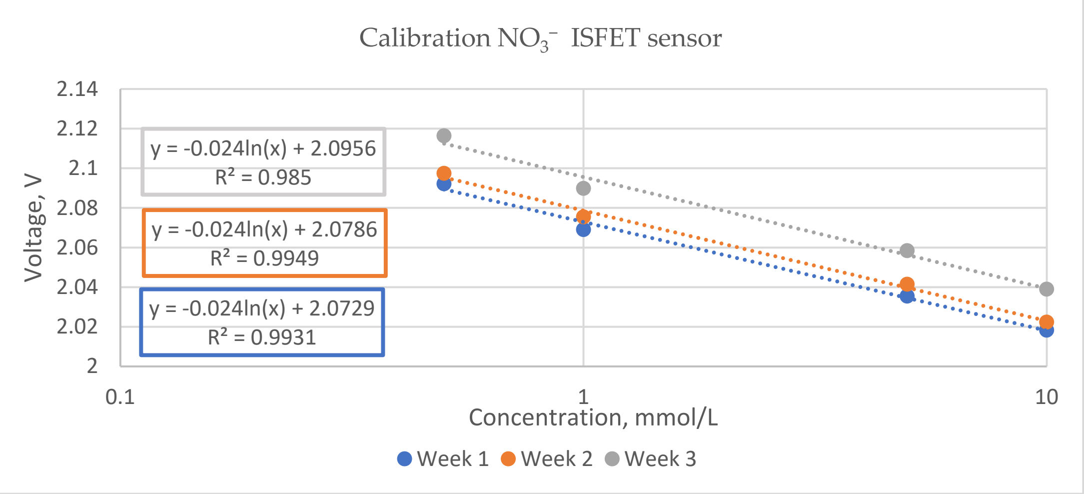


Figure 15. Time drift experiments on a single $NO_3{}^-$ ISFET sensor showing a parallel shift in the measurement curve with a change in the zero-offset value.

Furthermore, an aliquot was taken from each sample, analysed using ISFET sensors, and analysed as a reference sample in a laboratory using conventional analytical techniques. The laboratory results were used to validate the results of the ISFET-based analysis.

Figure 16 shows an example of a comparative analysis of the NO_3 ISFET sensor measurements with the corresponding laboratory results. The results of the sample taken at the scheduled sampling time are presented in the following section. The initial calibration was performed with the first sample on the first day. It can be seen that the drift on the calibration day is very small over the course of the measurement day, as can be seen from the example of three samples taken (morning, midday, evening). From the second day, a significant drift of the $NO_3{}^-$ ISFET sensor can be observed, with the drift increasing with each subsequent day. On the sixth day, the sensor was recalibrated, and the newly generated calibration curve was used to calculate the concentration of the measured solution. It can be observed that on the day of calibration, the discrepancies between the ISFET-measured values and the results of the laboratory reference measurements are minimal. However, over time, one day after calibration and subsequently, the ISFET-measured values deviate from the results of the laboratory reference measurements until the ISFET sensor is recalibrated. Further calibrations were carried out on day 13.

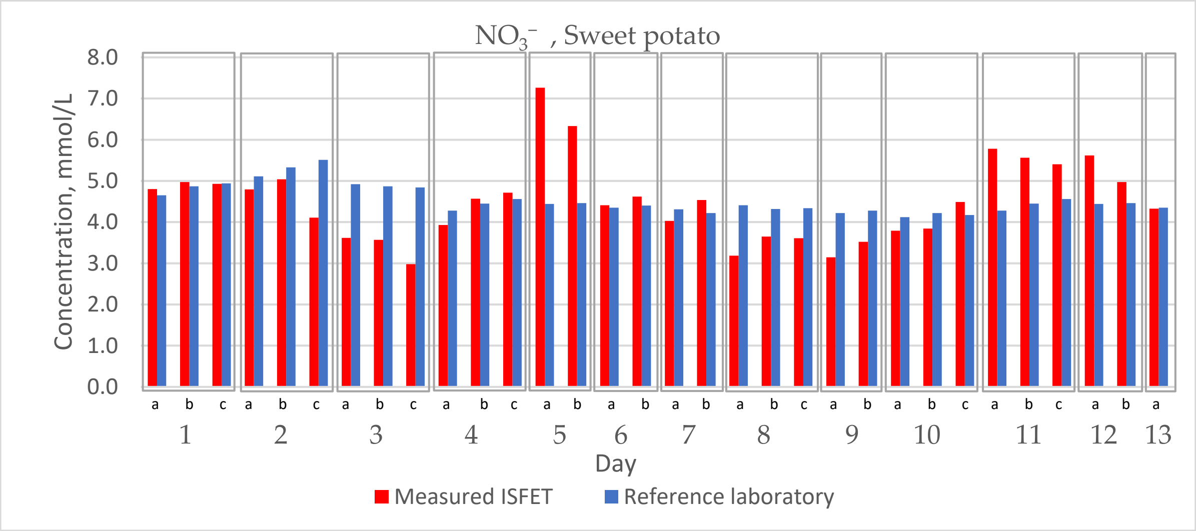
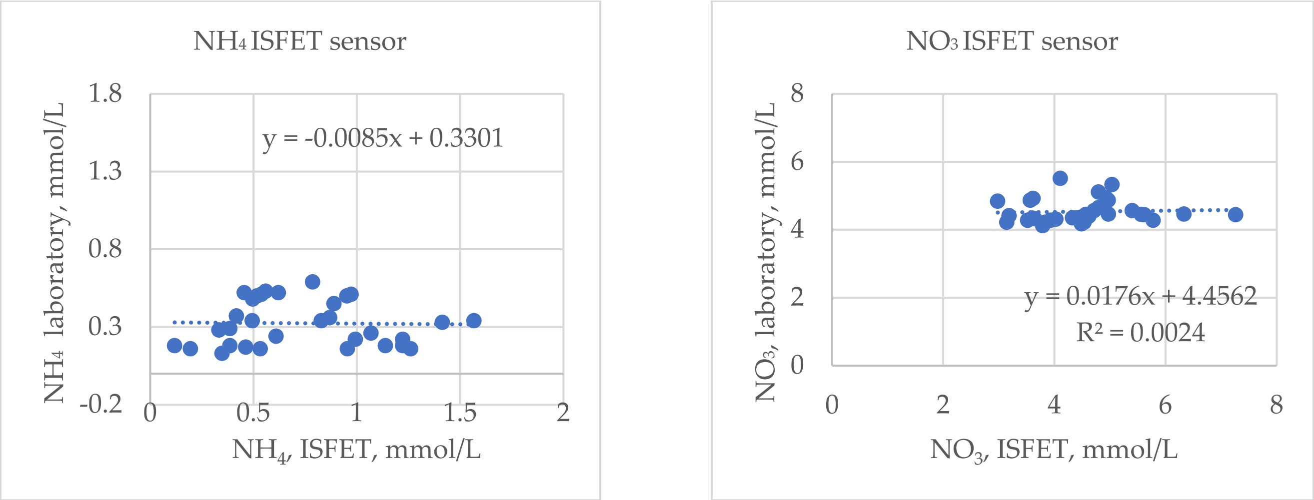


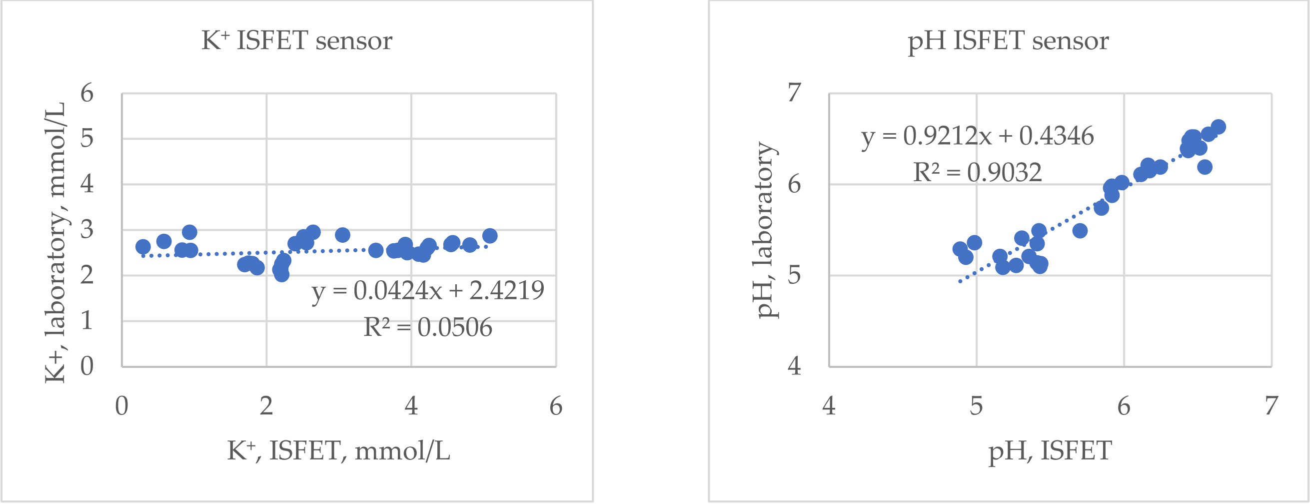
Figure 16. ISFET-based measurement without corrections (red bars) under real field conditions in a hydroponic system compared to laboratory nutrient analysis results (blue bars) of reference sample; the number shows the measurement day, and the small letter indicates the measurement repetition on the measurement day.

Due to the drift, the correlation between the laboratory results and the measurement results of the ISFET sensors deteriorates, especially for nutrient measurement. The correlation, indicated as the coefficient of determination, is very low (Figures 17a and 18a,b). In comparison to ISFET sensors with ion-sensitive membranes, such as those utilised for the measurement of NO_3^-, NH_4^-, K^+, and HPO_4^-, the pH–ISFET sensor demonstrates a significantly slower rate of time drift. The primary source of this drift in pH–ISFET sensors results from the oxidation processes occurring directly on the surface of the sensor. The correlation between the laboratory result and the ISFET measurement can be described as high based on the coefficient of determination (Figure 18b). This provides confirmation of the technical functionality of the measurement system.



(**a**) (**b**)

Figure 17. ISFET-based measurement without corrections in a hydroponic system compared to laboratory nutrient analysis results of reference samples (**a**) for NH_4^+ ISFET sensor, (**b**) for NO_3^- ISFET sensor.



(**a**) (**b**)

Figure 18. ISFET-based measurement without corrections in a hydroponic system compared to laboratory nutrient analysis results of reference samples (**a**) for K^+ ISFET sensor, (**b**) for pH ISFET sensor.

The measurement voltage of the ISFET sensor changes due to sensor drift, regardless of the prevailing measurement conditions, which were kept constant during the experiments (temperature, light, humidity, etc.). The drift can be attributed to chemical and physical processes leading to a change in the membrane or ionophore. Deviations between laboratory reference samples and ISFET readings on the day of calibration—day 1, day 5, and day 13—are very small (approx. 3%). The extent of the deviation on the subsequent measurement days is contingent upon the temporal interval that has elapsed between the last calibration and the present moment. This suggests that a near-daily recalibration of the measurement system is required to ensure the accuracy of ISFET-based nutrient analysis. However, a full multi-point calibration is very time-consuming. A simple solution was, therefore, sought, and a concept for a method known as single-point calibration was developed. This is achieved by using the storage solution with a known nutrient concentration (see Section 3.3—Storage of ISFET sensors) and should be employed by the implementation for an automated daily calculation of the correction coefficients in ISFET-based measurement.

Automated Drift Correction for ISFET-Based Measurement

The theoretical foundation of the automatic offset correction concept is based on the experimental observation that the calibration curves of the used ISFET sensors are shifted parallel to the previous calibration curve when the sensor exhibits a drift (see Section 3.4 Drift of the ISFET sensor, Figures 13–15). Moreover, the ion concentration in the storage solution is known and remains constant as the storage liquid is introduced into the ISFET-based measuring system from a separate container. This suggests the possibility of calculating a correction coefficient through the measurement of a single known ion concentration rather than a comprehensive new calibration series. This approach allows for the description of the shift in the calibration curve of the ISFET sensor in drift, thereby facilitating a more precise evaluation of the measurement results of ISFET-based measurement. (Figure 19).

The automatic offset correction concept was validated under real measurement conditions in hydroponic cultures. To this end, measurements were conducted over a 25-day period using ISFET sensors to determine the pH value, K^+, NO_3^-, and NH_4^+ nutrient levels. As part of the validation process, calibration was performed on six occasions to ascertain any shifts in the calibration curve of used ISFET sensors. On a daily basis, after the ISFET-based measurement of the nutrient solution in the hydroponic system, the individual measuring chambers with integrated ISFET sensors (for nitrate, ammonium, potassium, and pH) were filled with a storage solution (KNO_3NH_4 with a concentration of 1 mmol/L) in an automated process. The data obtained from the ISFET sensors' measurement of the storage solution were recorded and employed for the automated calculation of the correction coefficient and the automatic adjustment of the calibration curve to account for the specific ISFET sensors utilised. The measured values (voltage as the output value of the corresponding ISFET sensor) of the measured nutrient solution of the hydroponic system stored on the day of measurement were evaluated with the incorporation of a correction coefficient utilising an adjusted calibration curve and subsequently converted into the concentration of the nutrient in question (mmol/L).

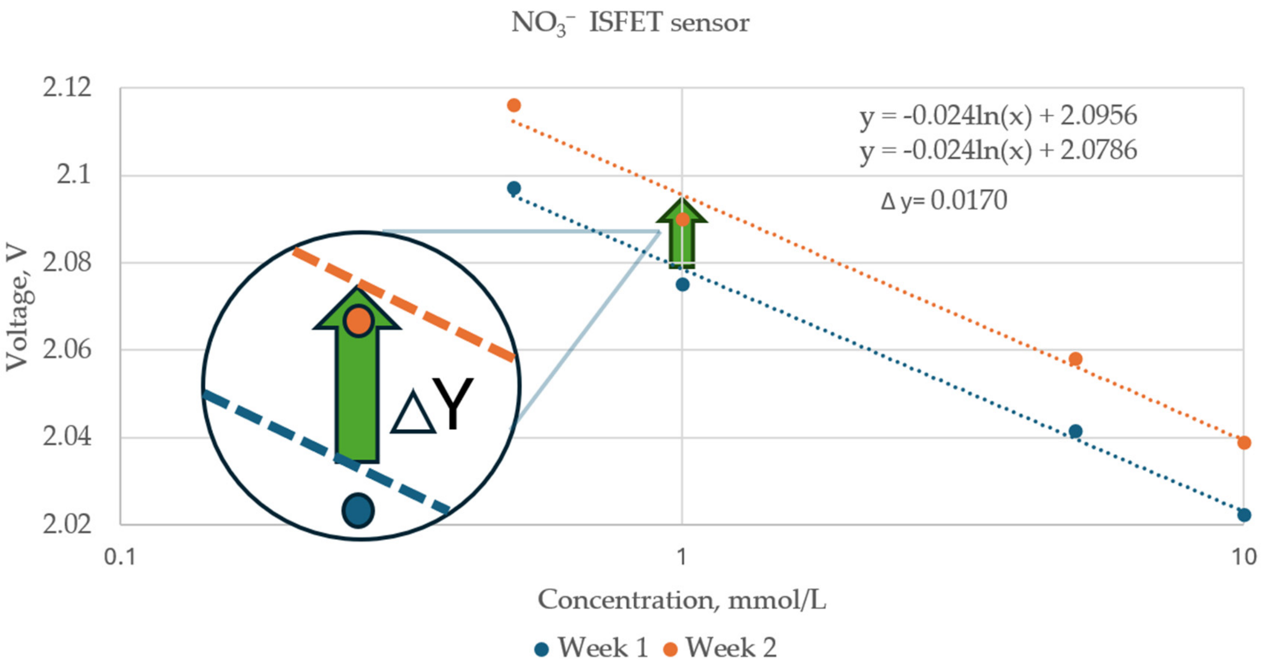


Figure 19. Concept of the automatic offset corrections with the example of the calibration curves of the NO_3^- ISFET sensor.

The results of the laboratory analysis of the reference samples, which had previously been taken from the measured samples (blue bars), are presented in Figure 20 alongside the evaluated ISFET measurement data as an illustrative example for a NO_3-ISFET sensor.

The ISFET sensors were calibrated on days 2, 7, 12, 17, 22, and 25. The evaluation of the ISFET measurements, displayed in green, was conducted using correction coefficients calculated through automatic offset correction. In contrast, no correction coefficients were employed in the assessment of the ISFET measurement data represented in red.

It is evident that the implementation of a single-point calibration procedure effectively eliminates the drift observed in the measurement outcomes. Furthermore, a notable correlation is evident between the laboratory results obtained from analysing the reference samples and the ISFET measurement outcomes for the ISFET sensors employed.

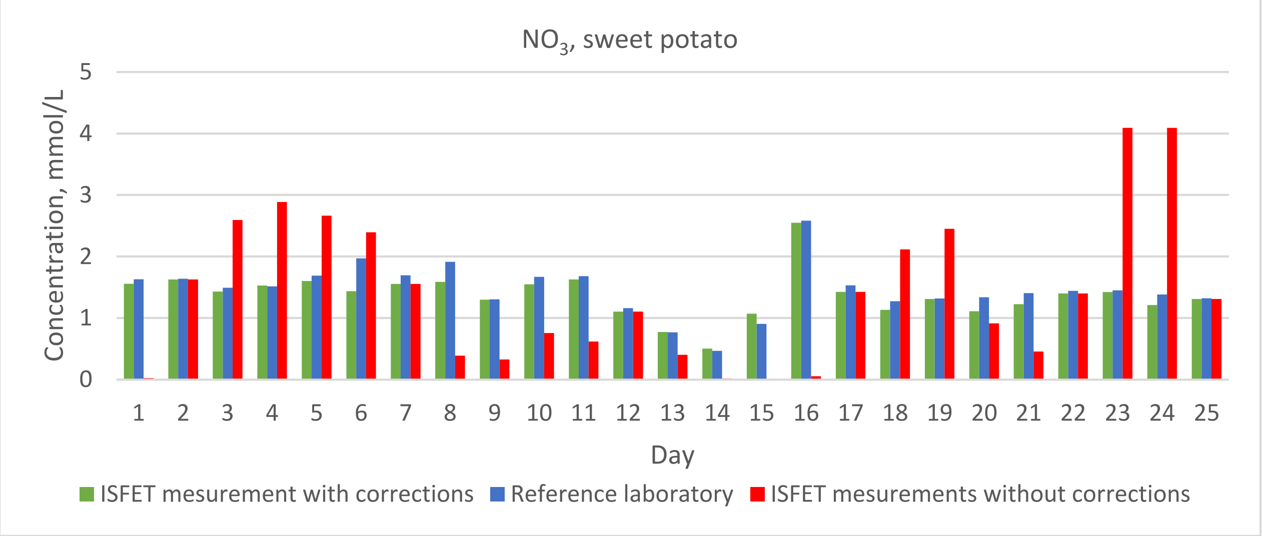


Figure 20. ISFET-based measurement without corrections (red bars) under real field conditions in a hydroponic system compared to ISFET-based measurement with automatic offset corrections (green bars) and laboratory nutrient analysis results (blue bars) of reference samples.

4. Discussion

Despite the long history of ISFET measurement technology, its practical application remains constrained by a number of challenges. Nevertheless, the majority of these obstacles can be overcome or eliminated through the implementation of an appropriate handling process. The impact of external factors, such as light and temperature, can be diminished or eliminated through modifications to the hardware structure. Furthermore, the manner in which the ISFET measurement technology is handled can also exert an influence. The conditioning of an ISFET sensor has been described in detail in the existing literature. The existing literature reports a range of recommended conditioning times, with varying lengths of time being suggested [13–16]. It is also important to note that the structure of the ISFET itself exerts an influence on the conditioning time. A review of the literature indicates that the optimal conditions for conditioning, including the concentration and composition of the conditioning solution and the requisite conditioning time, vary depending on the specific sensor and membrane in question. A review of the literature revealed no information regarding the concentration level. The results obtained from our own experiments demonstrated that the requisite conditioning times differed contingent on the concentration of the conditioning solution and the target ion. In the event that the concentration is insufficient, it is not possible to obtain a stable measurement signal (see Figure 4). A stable signal was obtained at a concentration of 20 mmol/L after 10 h. However, conditioning must also be considered in relation to subsequent measurements. In the event that the concentration of the conditioning solution is significantly higher than that of the subsequent samples, it may be necessary to adjust the concentration of the conditioning solution (see Section 3.1).

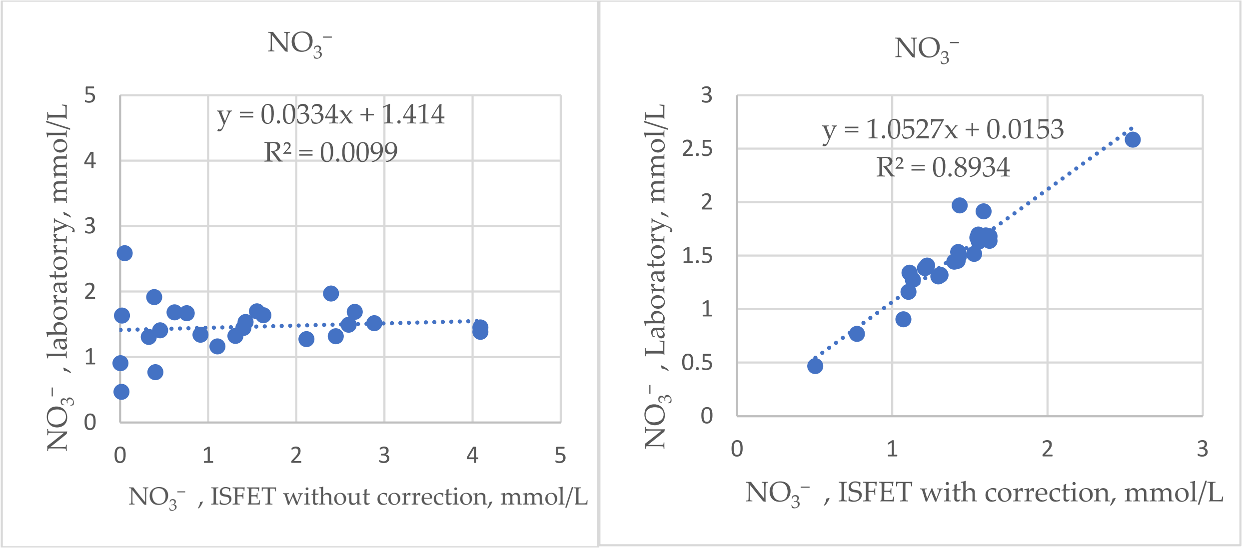
The objective of calibration is to transform the raw ISFET signal, expressed in volts, into a concentration value (in mmol/L) for the target ions. In an optimal scenario, multiple calibration points are conducted with a calibration concentration within the anticipated concentration range and comprising the target ion. In the case of individual ISFET sensors, the employed ISFET is target ion-specific, and a calibration solution containing the specific target ion is used accordingly. The NURISTAT ISFET multi-sensor module comprises four ion-specific ISFETs, enabling the measurement of nitrate, potassium, hydrogen phosphate, and pH. In order to minimise the number of calibration measurements required for the ion-specific ISFET elements to four (see Figure 5) and for pH to three, a separate calibration method has been developed. The objective of the proposed calibration method is to significantly reduce the number of required calibration solutions and, consequently, the number of calibration measurements, thereby saving labour time. The instructions provided by the manufacturer for the calibration procedure were expanded, and the ISFET sensors were calibrated using a multi-ion calibration solution. The objective was to ascertain whether the interfering ions present in the calibration solution exert an influence on the calibration of the target-ion-specific ISFET elements, potentially acting as interfering ions. The mutual influence of target and interfering ions was observed and subjected to experimental investigation. It was observed that in the presence of interfering ions at a concentration equivalent to that of the target ion, no effect on the measurement results was expected (see Figure 6), as the selectivity coefficient (see Table 1) was below the threshold for such an effect. Figure 6 also demonstrates that the interfering ion NH_4^+ has no effect on the K^+ ISFET sensor despite the selectivity coefficient mentioned in Table 1 being exceeded. Figure 7 illustrates the impact of the interfering ions chloride (Cl^-) and hydrogen phosphate anion ($H_2PO_4^-$) on the nitrate ISFET sensor. Furthermore, the NO_3-ISFET sensor displays sensitivity to the interfering ion Cl^- (see Table 1). Nevertheless, the impact of the interfering ion H_2PO_4 is considerably more pronounced in comparison. However, the manufacturer does not provide any information regarding the selectivity coefficient for the interfering ion H_2PO_4 (see Table 1). It is evident that H_2PO_4 has a considerably more pronounced impact on the NO_3-ISFET than Cl^-, as evidenced by the markedly stronger gradient. Based on the aforementioned information and our own experience of the measurement behaviour of the interfering ions, calibration series were developed and carried out with the target ions using the appropriate extraction agents. The aforementioned results were then compared with those obtained from the H_2O-based calibration series, as illustrated in Figures 8–11. It can be observed that the utilisation of an extraction agent has an impact on the results when compared to a calibration series based on H_2O. The ISFET sensors exhibit an offset, and the slope of the curve undergoes a change. Furthermore, the impact of the extraction agent on the pH–ISFET measurement was also determined (see Figure 11). In comparison to an H_2O-based pH calibration series, a pH calibration series utilising the corresponding extraction agent, $CaCl_2$ (0.0125 M), exhibits a shift in the curve and a change in the slope. In their publication, Hajji et al. [46] also highlight such an influence when measuring pH with ISFET sensors and elucidate this phenomenon through the accumulation of Ca^+ and other cations from the measuring solution on the surface of the ISFET sensor.

The phenomenon of interference from other ions by ISFET sensors has been well documented in prior research, and our own findings corroborate this. This also applies to the pH–ISFET measurement. The impact of the extraction agent, which serves as the basis for measurement solutions, on the ISFET measurement output was corroborated by the data obtained. It is recommended that the calibration be performed with a background value of the ions and the extraction agent, if applicable, that are expected to be present in the measured samples. In this manner, the impact of the interfering ions and the extraction agent is incorporated into the calibration process as a background value (Section 3.2—Calibration of ISFET sensors).

It is of the utmost importance to maintain the hydration of ISFET sensors between measurements. This is essential to prevent the membrane from drying out and guarantee the sustained optimal functionality of the sensor. In order to achieve this, the manufacturer recommends the use of a storage solution containing the corresponding target ion for the ISFET element at a concentration of 10 mmol/L. However, the results demonstrate that when a solution with a low concentration is subsequently measured, the recorded values indicate an output signal that is incongruent with the actual concentration present (see Figure 12). To address this issue, the concentration of the storage solution has been reduced to 1 mmol/L. The initial measurements with a test solution whose concentration is now comparable to that of the storage solution indicate no elevated readings.

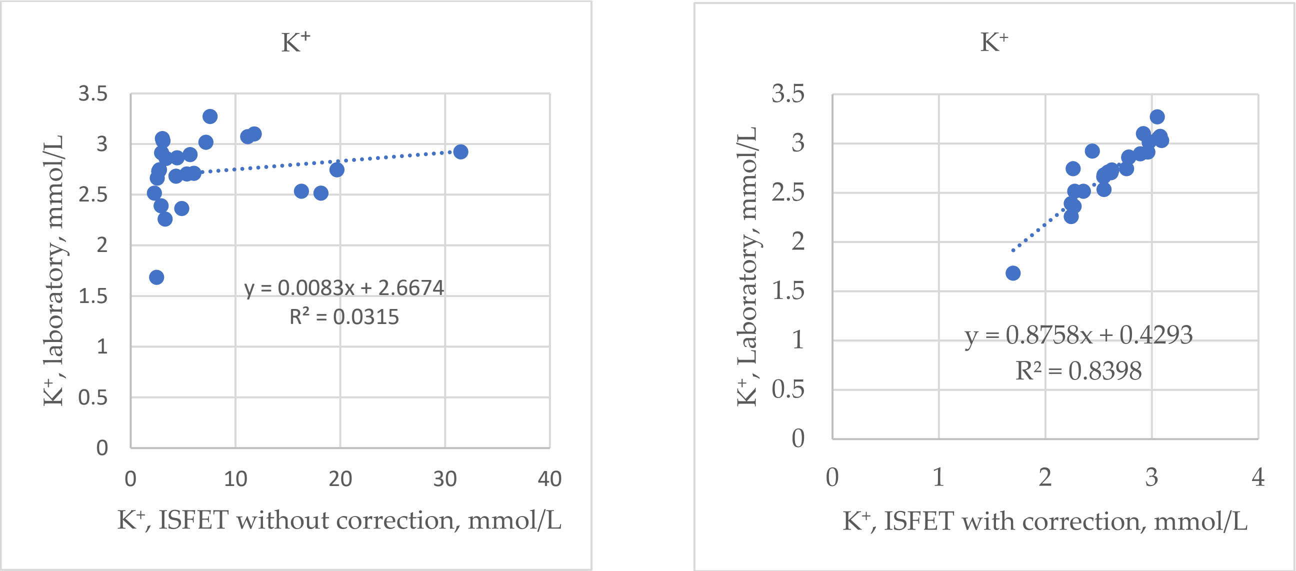
In this context, drift control refers to the drift of the measured value due to the ageing of the membrane with the ionophore, which is a topic of investigation in the literature [21,34]. Over time, a series of ongoing changes occur in the hydrated membrane and the ionophore.

Such alterations impact the sensitivity and measurement properties of the ion-sensitive membrane [34]. The consequence is a gradual yet persistent alteration in the output voltage at a fixed concentration of the measuring solution. Consequently, the discrepancy between the ISFET-measured value and the laboratory value derived from a reference sample increases gradually over time, as illustrated in Figure 16. This also indicates that the correlations between the ISFET-measured value and the laboratory value are either absent or exhibit only minimal correlation (see Figures 17a and 18a). The drift is particularly evident in ion-selective ISFET sensors, which possess an ion-selective membrane. No drift behaviour is observed in the pH ISFET sensors. Furthermore, the correlation between the ISFET pH value and the laboratory pH value demonstrates a high degree of correlation over an extended period (here, 13 days) (see Figure 18a). This drift can be attributed to the ageing process of the ion-selective membrane and is best described as an offset in the calibration curve. Over time, the measurement calibration curve shifts parallel to the previous measurement calibration curves, maintaining the same gradient. The drift alters the zero offset of the curve (see Figures 13–15). It is imperative to ensure the accurate recording of the difference in zero offsets between the measurement calibration curve a and the measurement calibration curve b (see Figure 19) over the course of a measurement period. To guarantee precision, a known measuring solution with a known constant concentration should be employed for the calculation of the offset correction. The storage solution fulfils this function and is utilised accordingly for the newly developed offset correction procedure, which automatically calculates the offset correction. The automatic offset correction procedure serves two purposes. Primarily, it rectifies the offset observed in the ISFET measurement. Secondly, it addresses the daily fluctuations in the concentrations of the ions in question. Further details on this can be found in Figure 20. The correlations are accordingly enhanced and may be characterised as high (see Figures 21 and 22). Figure 23 illustrates the ISFET-measured values for NH_4^+ and the corresponding laboratory values. It can be observed that no correlation is evident, as the measured values are not normally distributed. The presence of extremely low concentrations of NH_4^+ in the nutrient solution, which fell below the measuring range of the ISFET sensor, resulted in unreliable detection. In general, the drift of the ISFET measurement technology can be reliably corrected through the newly developed and validated automatic offset correction method.



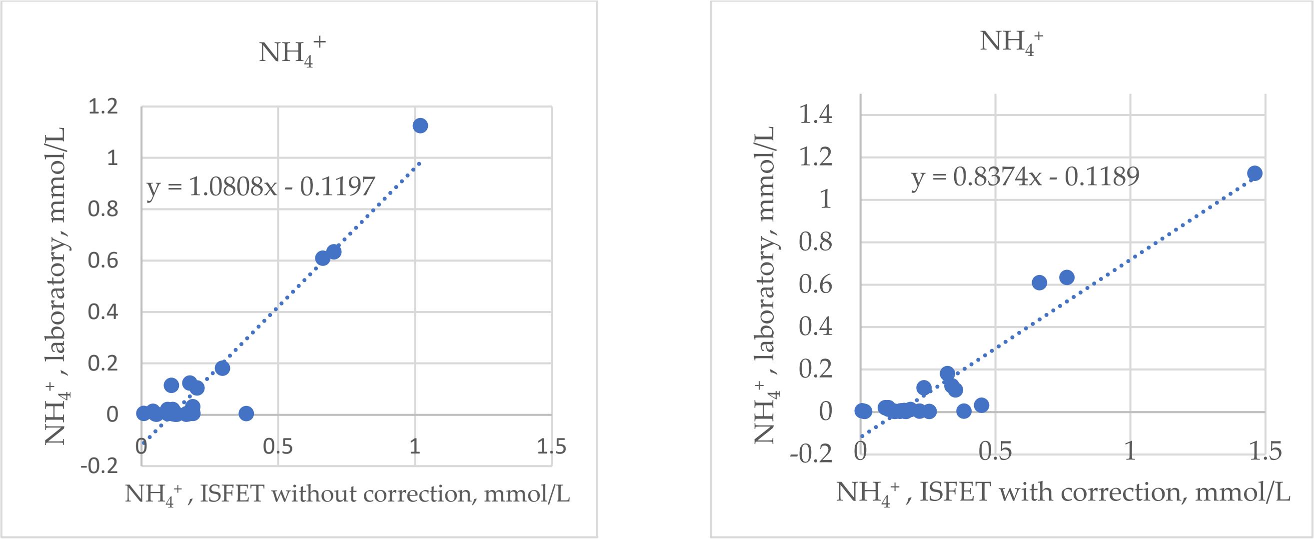
(**a**) (**b**)

Figure 21. ISFET-based measurement in a hydroponic system compared to laboratory nutrient analysis results of reference samples for NO_3^- ISFET sensor (**a**) without corrections (**b**) with automatic offset corrections.



(**a**) (**b**)

Figure 22. ISFET-based measurement in a hydroponic system compared to laboratory nutrient analysis results of reference samples for K^+ ISFET sensor (**a**) without corrections (**b**) with automatic offset corrections.



(**a**) (**b**)

Figure 23. ISFET-based measurement in a hydroponic system compared to laboratory nutrient analysis results of reference samples for NH_4^+ ISFET sensor (**a**) without corrections (**b**) with automatic offset corrections. The coefficient of determination was not provided as the series of figures did not exhibit a normal distribution.

5. Conclusions

The innovative ISFET-based measurement systems allow for the continuous and automated determination of the nutrient concentrations of nitrate (NO_3^-), ammonium (NH_4^+), potassium (K^+), hydrogen phosphate ($H_2PO_4^-$), and pH in selected agricultural applications, including soil nutrient analysis in the field and nutrient determination in hydroponic cultures. The use of ISFET-based analysis of soil samples in a field-based approach provides a novel opportunity to use measurement data as a basis for demand-based fertilisation. The user is immediately provided with information about the current status of soil nutrient status, which can then be applied in subsequent processes [48]. The integration of ISFET sensors into the automated continuous-flow analyzer in the second application, namely, in hydroponic cultures, enables the real-time online acquisition of data pertaining to nutrient levels. The ion-specific analysis is the prerequisite for timely ion-specific dosing of the fertiliser unit of the nutrient solution in hydroponic systems.

ISFET sensors, renowned for their high sensitivity and rapid response, enhance the precision and efficacy of real-time nutrient detection. It is, nevertheless, imperative to take a number of factors into account when employing ISFET measurement technology in order to guarantee the acquisition of stable, precise, and interference-free measurements. In the utilisation of ISFET technology, it is of paramount importance to consider the impact of external factors, such as ambient light, temperature, and humidity, on the output signal of the measuring system. Riedel et al. (2024) conducted an analysis of this and other factors based on a series of experiments [8]. The impact of these external factors needs to be mitigated through appropriate countermeasures. However, it is not only these environmental conditions that affect the measurement signal of the ISFET sensor. Preparatory measures and steps taken before, during, and after the ISFET-based nutrient measurement also play a role in determining the stability, reproducibility, and reliability of the measurement results.

The aim of this study was to develop the methodology and optimise the use of ISFET sensors in agricultural applications to achieve the accuracy and stability of real-time nutrient measurement using ISFET instrumentation technology with minimal interference. The selectivity and sensitivity of the ISFET sensor were investigated in relation to its practical utilisation. A comprehensive investigation and optimisation of pivotal parameters was conducted through the utilisation of ISFET measurement technology.

The handling processes, including conditioning, calibration, and storage, were modified to ensure optimal implementation in planned agricultural applications. This included an examination of the concentration and composition of the conditioning solution and the determination of the optimal time for complete conditioning of the ISFET sensors as a single electrode and an ISFET multi-sensor module. A crucial aspect of the investigative process was the identification of the optimal composition of the calibration solutions and the determination of the requisite number of calibration solutions required to optimise the full calibration process, with due consideration for the intended agricultural applications. It is essential to select the composition and concentration of the storage solution in a manner that minimises its influence on the measurement results of the ISFET sensor when it is resumed. Following a series of comprehensive investigations, the necessity for the development of drift detection and subsequent drift correction procedure was established. Consequently, an automated offset correction procedure was developed, evaluated under real measurement conditions, and integrated into a running hydroponic system, thereby enhancing the measurement accuracy (see Figure 20) of the ISFET-based nutrient analysis. The resulting optimal conditions were pivotal for the enhanced precision and stability of the ISFET-based measurement method.

The appropriate methodology for handling ISFET measurement technology is complex but of paramount importance for the attainment of stable and precise measurement results. The identification and removal of potential external or internal influences on the measurement process serve to enhance the reliability of the ISFET-based measurement procedure. In this context, the handling of ISFET sensors is a prerequisite for increasing the robustness of the measurement system, thereby providing the potential for the deployment of real-time ISFET-based measurement systems in highly automated processes and robotics in agriculture.

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