DETERMINATION OF FLUORIDE ANIONS BY ION-SELECTIVE ELECTRODE

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1. Theory

1.1. Potentiometry

Potentiometry is an electrochemical method, in which the potential difference (electromotive force, ΔE) of a cell composed of indicator and reference electrode is measured. The potential of the indicator electrode depends on the activity of the analyte present in the sample, while the potential of the reference electrode is constant (and independent of the composition of the measured solution) during the measurement. An electromotive force (ΔE) is measured using a digital voltmeter with high input impedance at practically zero current.[1]

In practical applications, there are two variants of potentiometry:

a) **direct potentiometry** determines the analyte's concentration directly from the measured ΔE). In this case, the determination is carried out using a calibration curve $\Delta E = f(\log c_{\text{analyte}})$.

b) **potentiometric titration** determines the analyte's concentration based on the consumption of a titrant. In this case, the equilibrium electromotive force of the cell is measured as a function of the amount of added titrant, allowing for the determination of the titration endpoint.

1.2. Indicator electrodes: Ion-selective electrodes

In potentiometry, ion-selective membrane electrodes (ISEs) are indicator electrodes and designed for specific ion determination of. A typical representative of ISEs is the calcium electrode (selective for Ca^{2+} ions), cyanide electrode (selective for CN^{-} ions), fluoride electrode (selective for F^{-} ions), and so on. The membrane of the ISE plays crucial role for selective ion determination and the selectivity is influenced by its composition. Ion-selective membranes separate the internal electrode system from the measured solution and can be made from various materials.

The membrane of a Ca-ISE consists of a polyvinyl chloride membrane with a selective ionophore for calcium ions. The membrane of an F-ISE is composed of a single crystal of lanthanum fluoride (LaF_3) with addition of a europium fluoride (EuF_2). The EuF_2 incorporated into the crystal lattice of LaF3 creates vacant sites, which can be filled by neighbouring fluoride anions and thus the membrane exhibits high selectivity for fluoride anions of F-ISE **Fig. 1**).

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[1] There is a negligible current (in the order of magnitude of 10^{-14} A) in the electrochemical cell.

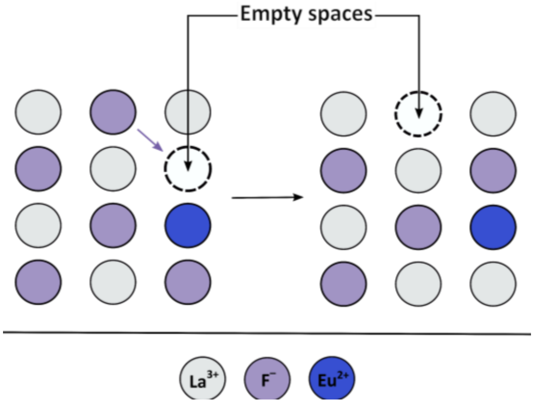

Fig. 1 The mechanism of the potentiometric response of a fluoride ion-selective electrode involves the migration of fluoride anions through the lattice of europium-doped lanthanum fluoride.

In the laboratory, both half cell and combination F-ISEs are employed. In the case of half cell F-ISE, it is necessary to use an external reference electrode. (**Fig. 2A**). In the case of the combination F-ISE, the electrode is equipped with an integrated reference system (**Fig. 2B**).

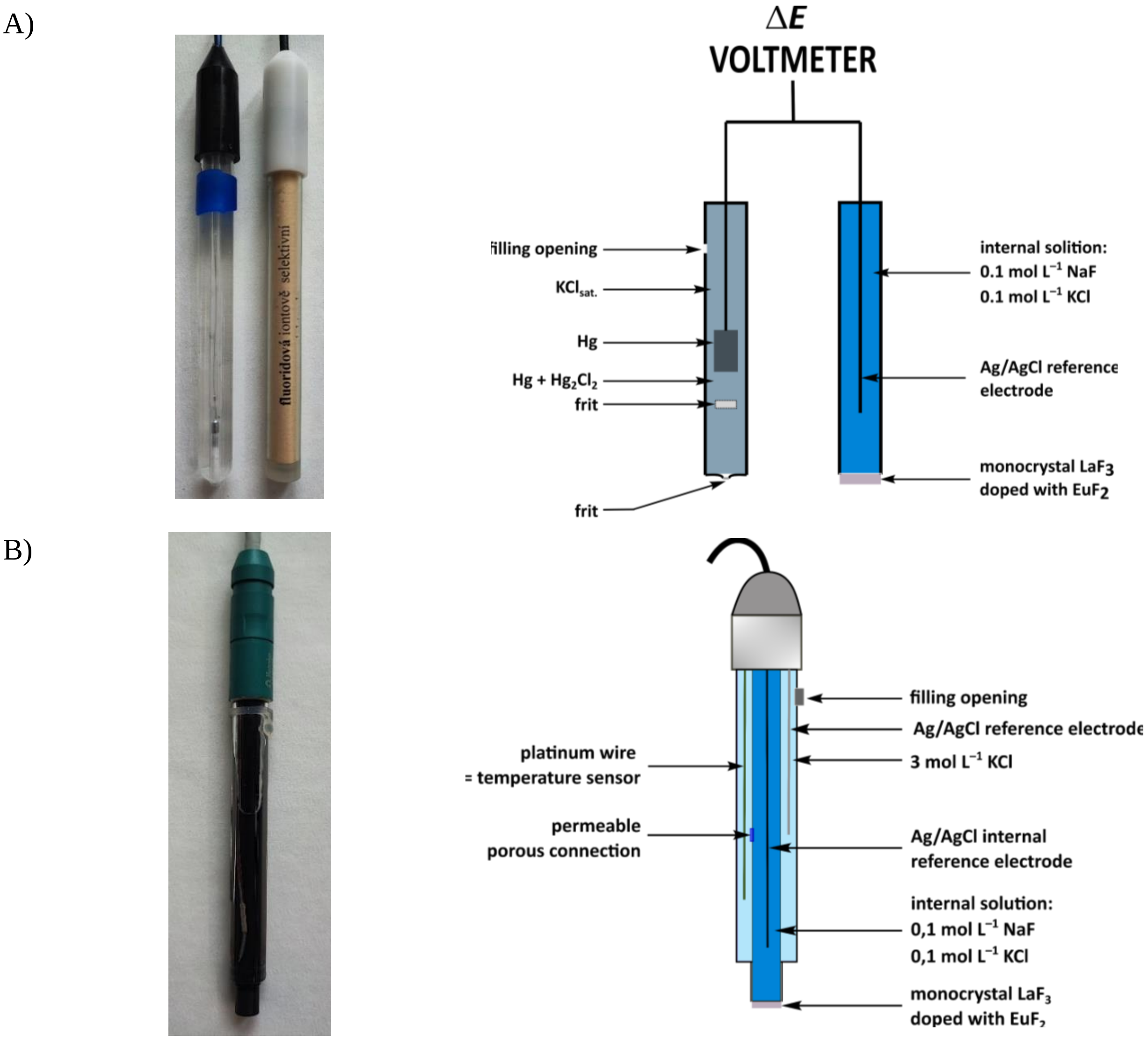

Fig. 2 Photograph and schematic representation of half cell (A) and combination (B) fluoride ion-selective electrodes. The electrode arrangements in the photographs correspond to the schematics.

1.3. Characteristics of ion-selective electrodes

The main characteristic properties of ISEs are sensitivity (mV per decade), concentration range (mol L^{-1}), and practical detection limit ($c_{\min}$, mol L^{-1}) which are determined from the calibration curve (**Scheme 1**). The calibration curve is a result of measurement of the dependence between the electromotive force of the cell and the decimal logarithm of the activity of the specific ion ($\Delta E = f(\log a)$ [2]. Measurements are carried out from the lowest to the highest ion concentration. Prior to measurement, the ISE electrode is activated by overnight immersion in a solution containing the specific ion at a concentration of 10^{-3} mol L^{-1}.

The concentration range is the linear range of the calibration curve ($R^2 = 0.999$) for the specific ion (**Scheme 1**), where Nernstian response applies, and the slope (sensitivity) of experimental ISE is determined. Deviations from linear range (the nonlinear part of the calibration curve) can be caused by: a) high ion concentrations and a problem of maintaining constant ionic strength of the analysed solution; b) specific interactions occurring at the membrane-solution interface (for example, adsorption on the membrane's surface) at the range of the very low ion concentrations. The F-ISE is applicable in the concentration range from 10^{-6} to 10^{-1} mol L^{-1}.

The practical detection limit ($c_{\min}$) is defined by the intersection of two lines, namely the extrapolated portion of the Nernstian linear response with the line parallel to the x-axis corresponding to zero concentration of fluoride ions (TISAB solution without fluoride ions). (**Scheme 1**).

The slope (sensitivity) of an ISE ($S = 2{,}303\,\frac{RT}{zF}$) is the change in electromotive force of the cell when the concentration changes by one order of magnitude in the linear range of the calibration curve (i.e., within the concentration range). The slope (theoretical Nernstian response) for monovalent ions ($z = \pm1$) has a theoretical value of ±59.2 mV per decade (±59.2 mV dec^{-1}), and for divalent ions ($z = \pm2$), it is ±29.6 mV per decade (±29.6 mV dec^{-1}) (**Scheme 2**). The positive sign of the slope (sensitivity) corresponds to the potentiometric cationic response. It means that an increase in the cation concentration leads to a higher value of ΔE. Conversely, the negative sign of the slope (sensitivity) corresponds to the anionic potentiometric response. It means that an increase in the anionic concentration leads to decreasing of ΔE.

The calibration dependence $\Delta E = f(\log[F^-])$ is obtained using linear regression in MS Excel (in the form $y = ax + b$) (where 'y' is the measured electromotive force of the cell (ΔE), 'a' is the experimental slope of the ISE (S), 'x' is the logarithm of ion concentrations in the measured solution ($\log [F^-]$).

Selectivity is most commonly expressed using **the decimal logarithm of the selectivity coefficient** ($\log K^{pot}_{F^-,J}$), where F^- is the primary ion and J is the interfering ion. The value of $\log K^{pot}_{F^-,J}$ can be either negative or positive. The negative value of $\log K^{pot}_{F^-,J}$ means that the interfering ion has a lesser effect on the potentiometric determination of the primary ion.

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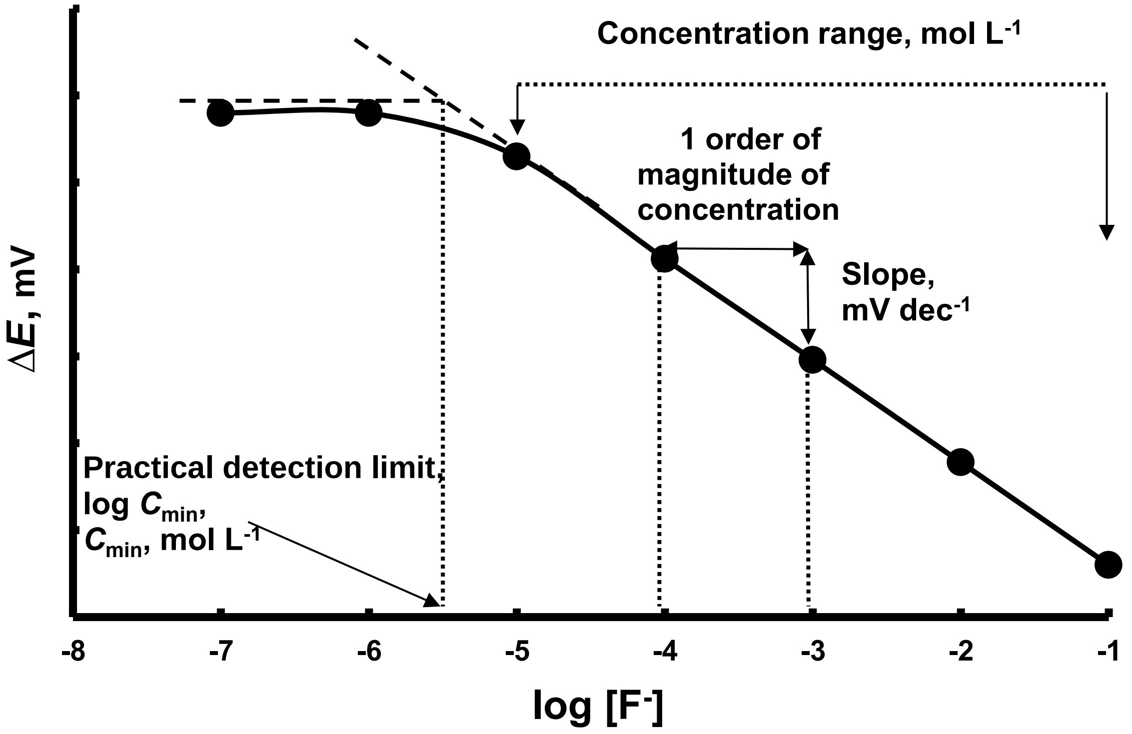
[2] a represents the activity (effective concentration) of the monitored ion. Activity is expressed as the product of the relative equilibrium concentration [X] and the activity coefficient $\gamma(X)$: $a(X) = \gamma(X)\cdot[X]$. In diluted solutions, where we assume that activity coefficients are close to unity, we can, therefore, replace activity with concentration.

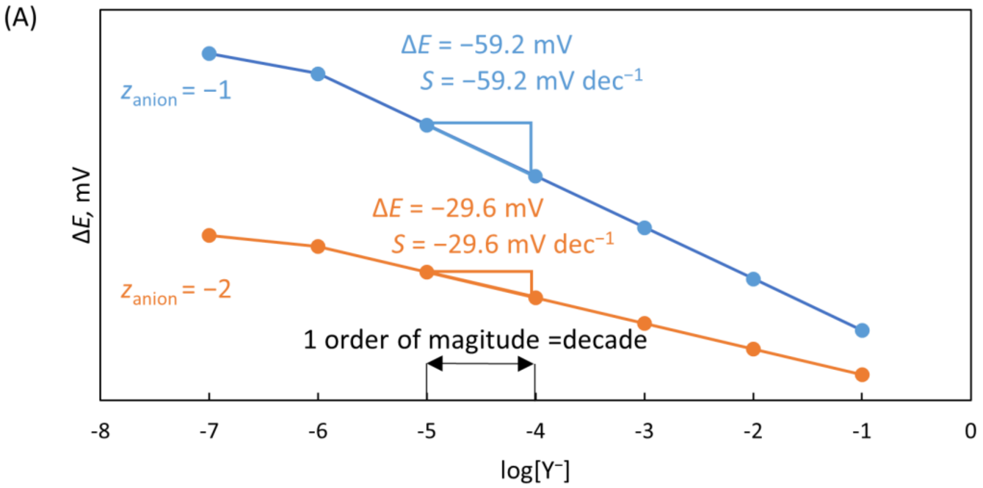
The more positive value of $\log K_{\mathrm{F^-,J}}^{pot}$ means that the interfering ion has a higher effect on the potentiometric determination of the primary ion. The values of $\log K_{\mathrm{F^-,J}}^{pot}$ are determined experimentally. Knowledge of selectivity coefficients is crucial for the practical use of ISE.

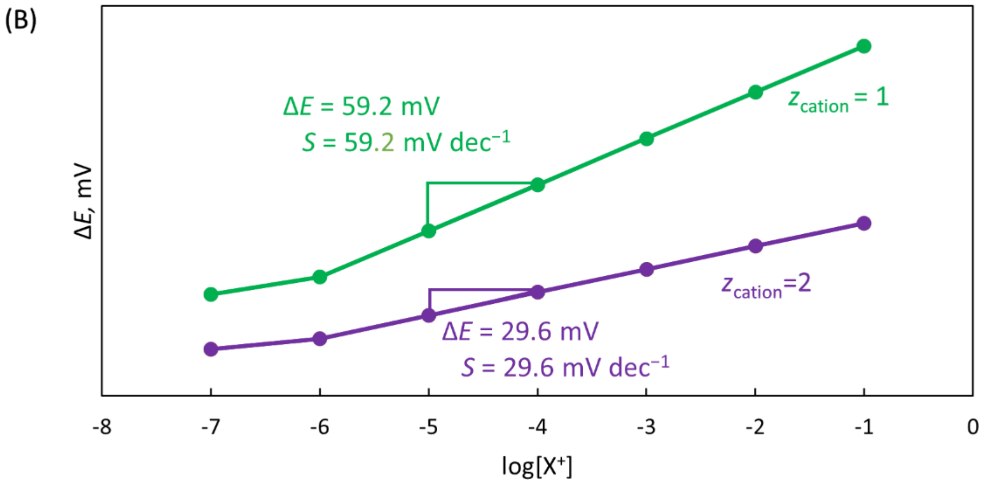
For F-ISE, interfering anions are OH^- ions, and interfering cations are cations that form complexes with fluorides (Fe^{3+}, Al^{3+}, and others). Therefore, the potentiometric determination of fluorides is carried out in the 'Total Ionic Strength Adjustment Buffer' (TISAB) solution, which maintains a pH range of 5 to 6 and thus eliminates interference of OH^- ions.

The hysteresis (so-called the memory effect) of ISE is related to the adsorption and desorption processes. This phenomenon can be observed when transitioning from more concentrated solutions to more diluted ones (for example, the transition from 10^{-3} to 10^{-4} mol L^{-1}) during measurements of real samples.



Scheme 1 Determination of the characteristic properties of anion-selective ISE from the calibration curve.





Scheme 2 Calibration curves corresponding to anionic (A) and cationic (B) potentiometric responses of ion-selective electrode.

2. Measurement with ion-selective electrodes

2.1. Regeneration

To obtain reproducible potentiometric signal, ISEs should be regenerated before potentiometric measurements. Regeneration is typically accomplished by immersing the electrodes into a regenerating solution that has the composition (pH, ionic strength, and the presence of interferents) similar to calibration solutions. Regeneration of F-ISEs involves immersing the electrodes into a stirred solution of a 0.01 mol L^{-1} TISAB.

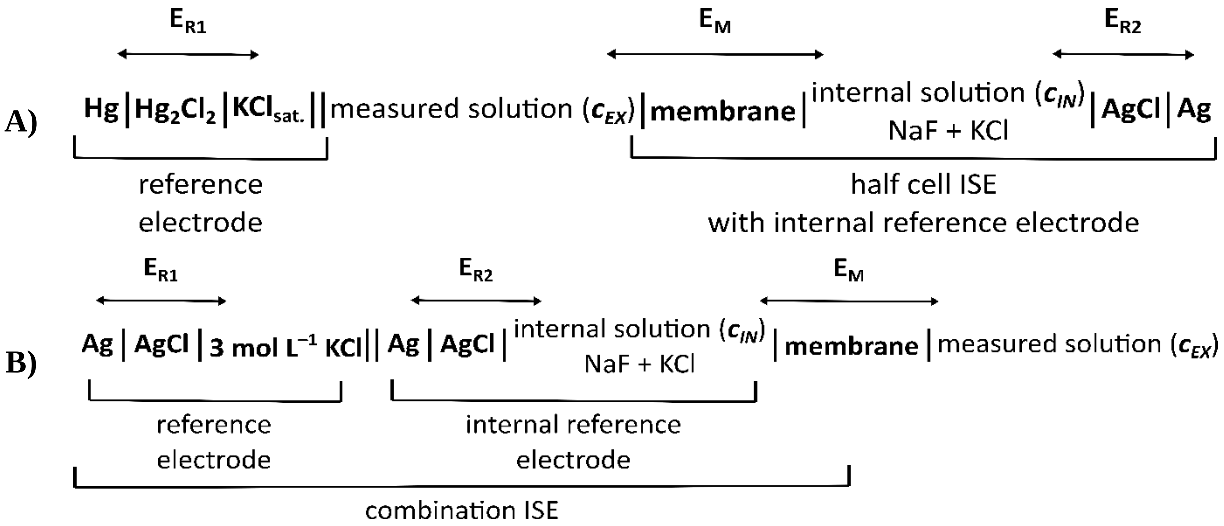
Regeneration of the ISE is recommended to be perform before measurement of each calibration and sample measurement. **Fresh regenerating solution is required for each regeneration**. The duration of regeneration is related to the memory effect of the individual ion-selective membrane.

2.2. Stirring

The response time (the time required to reach a stable ΔE value) of the electrode is determined by the thickness of the hydrodynamic layer on the electrode surface. Therefore it is important to carry out the measurements in stirred solutions. Stirring reduces the thickness of the hydrodynamic layer at the membrane surface, shortening the response time of the ISE and improving the reproducibility of results. It's important that **the rate of solution stirring and the geometry of the working space should remain constant**.

2.3. Potentiometric signal

In potentiometry, the electromotive force (ΔE) of the cell is the difference in potentials between the ISE and the reference electrode. The cells for both half cell and combination F-ISEs can be described by **Scheme 3**.



Scheme 3 Electrochemical cell describing measurements with half cell (A) and combination (B) ion-selective electrode. E_{R1} represents the potential of an external (half cell) calomel reference electrode or the internal reference silver chloride electrode, E_M is the membrane potential at the interface between the measured solution (EX) and the internal solution (IN), E_{R2} is the potential of the internal reference silver chloride electrode.

The electromotive **force** (ΔE) of the cell is:

$$\Delta E = E_{R2} + E_M - E_{R1} \tag{1}$$

$$E_{ISE} = E_{R2} + E_M \tag{2}$$

$$E_M = \frac{RT}{zF} ln \frac{a(\mathrm{F^-})_{\mathrm{EX}}}{a(\mathrm{F^-})_{\mathrm{IN}}} = 2{,}303 \frac{RT}{zF} log \frac{\gamma(\mathrm{F^-})_{\mathrm{EX}} \cdot [\mathrm{F^-}]_{\mathrm{EX}}}{\gamma(\mathrm{F^-})_{\mathrm{IN}} \cdot [\mathrm{F^-}]_{\mathrm{IN}}} \tag{3}$$

where $[\mathrm{F^-}]_{\mathrm{EX}}$ is the unknown concentration. At a constant ionic strength of the solution (as further discussed), the activity coefficient $\gamma(\mathrm{F^-})$ can also be considered constant and can be incorporated into the constant K. For the potential of the F-ISE at 25 °C (298.15 K), the following equation obeys:

$$E_{F-ISE} = K - 0{,}0592 \cdot \log[\mathrm{F^-}]. \tag{4}$$

The potential of an F-ISE in the presence of interfering ions, is described by the Nikolsky-Eisenmann equation:

$$E_{F-ISE} = K - S \cdot \log\left([\mathrm{F}^-] + \sum_{\mathrm{J}} K_{\mathrm{F}^-,\mathrm{J}}^{pot} \cdot c[\mathrm{J}]^{z_\mathrm{F}/z_\mathrm{J}} \right) \qquad (5)$$

where S is the slope (sensitivity, experimentally determined), $[\mathrm{F}^-]$ and [J] are the respective concentrations of fluorides and interfering ions, z_F and z_J are the charges of fluorides and interferents, and $K_{\mathrm{F}^-,\mathrm{J}}^{pot}$ is the selectivity coefficient (commonly expressed in logarithmic form for practical purposes). For F-ISE, the main interferents are OH^-, Al^{3+}, and Fe^{3+} ions.

2.4. Potentiometric selectivity

The selectivity of the ISE to the ion against various interferents is described by the potentiometric selectivity coefficient ($\log K_{\mathrm{F}^-,\mathrm{J}}^{pot}$) (see ' Characteristics of Ion-Selective Electrodes ' [1]). There are three methods for determining potentiometric selectivity coefficients:

- The Fixed Interference Method (FIM),
- The Separate Solution Method (SSM),
- The Matched Potential Method (MPM).

Appendix 1 schematically illustrates the methods for determining potentiometric selectivity coefficients. The most commonly used methods are the Separate Solution Method (SSM) and the FIM.

3. Measurement techniques

3.1. Calibration curve method

This method is generally suitable for determination ion content in a simple matrix (e.g., drinking water or mineral water). The composition of samples and standard solutions must be as similar as possible, especially in terms of pH, ionic strength, and the presence of interferents, for the determination to be done with acceptable accuracy. The precision of the determination is not generally very high. With a precision of potential measurement (±1 mV) at laboratory temperature, the relative error of determination is ±4 % for monovalent ions and ±8 % for bivalent ions.

It is desirable for the concentration of the target ion in the samples to fall within the linear range of the calibration curve (concentration range). The concentration of the target ion is calculated directly from the modified Nernst equation evaluated from the experimentally calibration curve.

In the case of F-ISE, the equation obeys:

$$\Delta E_x = K' - S \cdot \log[\mathrm{F}^-] \tag{6}$$

ΔE_x	is the electromotive force of the potentiometric cell measured in the sample solution,
K'	is an additive constant determined from the experimental equation (6) after calibrating the ISE electrode,
S	is the experimental value of the slope determined from the experimental equation (6) after calibrating the ISE electrode,
$[\mathrm{F}^-]$	is the unknown concentration of fluoride anions being determined in the sample.

3.2. Standard addition method

This method is more suitable for determining ion concentrations in a complex matrix (such as blood serum or blood). The main advantage is that the entire measurement is performed in the presence of the sample matrix, which allows to attain better precision and accuracy. The basis of this method is the measurement of the cell electromotive force in the sample without the addition (ΔE_x, Equation (6)) and with addition (ΔE_1, ΔE_2, ΔE_3, …ΔE_n) of the standard solution (c_s) with a volume of V_S to the sample with a volume of V_x:

$$\Delta E_1 = K' - S \cdot \log \frac{c_x V_x + c_s V_{s1}}{V_x + V_{s1}} \tag{7}$$[3]

$$\Delta E_\mathrm{n} = K' - S \cdot \log \frac{c_x V_x + c_s V_{sn}}{V_x + V_{sn}} \tag{8}$$

$$c_x = \frac{c_s V_{sn}}{(V_x + V_{sn}) \cdot 10^{\frac{\Delta E}{S}} - V_x} \tag{9}$$

ΔE_x	is the electromotive force of the cell in the sample without the addition of the standard,
ΔE_1…ΔE_n	are the electromotive force of the cell in the sample with the addition of the standard,
ΔE	is the difference in electromotive force of the cell with and without the addition of the standard solution,
c_x and c_s	are the unknown c and the known concentration of fluorides in sample and the added standard, respectively,

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[3] The argument of the logarithm should be dimensionless (we should use relative equilibrium concentrations).

V_x and V_{sn}	are the volumes of the unknown sample prepared for measurement and the added standard, respectively,
$Vs_1 \ldots Vs_n$	are the volumes of the standard solution added to the unknown sample,
K'	is the additive constant, which depends on the construction of the ISE electrode,
S	is the experimental slope value, which is determined during the electrode calibration process.

4. Fluoride presence in real samples

Fluorides are present in mineral waters. Mattoni contains 0.55–1.80 mg L^{-1} (currently unreported), Ondrášovka contains 1.08 mg L^{-1}, Dobrá voda contains 0.46 mg L^{-1}, and Vincentka contains 2.54 mg L^{-1}. Higher fluoride content is found in tea (green tea: 71–180 mg kg^{-1}; black tea: 30–441 mg kg^{-1}), Coca-Cola (0.82–0.98 mg L^{-1}), and grapefruit juice (6.80 mg L^{-1}). It is well known that fluoride intake is particularly beneficial for the development of healthy teeth. Therefore, some toothpaste intentionally contain elevated levels of fluoride compounds such as sodium fluoride, aminofluorides, and fluorophosphates. The concentration of fluoride varies among different types of toothpaste, with the highest levels found in so-called therapeutic toothpaste.

For adults, an acceptable concentration is reported to be in the range of 1,000 to 1,500 mg kg^{-1}, while for children up to 4–5 years of age, the content is lower, around 250–400 mg kg^{-1}. This is due to the repeated observation that young children occasionally swallow toothpaste. The task at hand involves determining the fluoride content in various samples of toothpaste.

Laboratory manual

DETERMINATION OF FLUORIDE ANIONS IN A TOOTHPASTE

Tasks:

1. Preparation of solutions and samples
2. Determination of properties of F-ISE:
   - Slope (S, mV dec^{-1})
   - Concentration range (mol L^{-1})
3. Determination of fluoride anion content in toothpaste using the methods of:
   - Calibration curve
   - Standard addition
4. The effect of pH on potentiometric determination of fluoride anions by F-ISE

Required solutions and equipment:

- 2 mol L^{-1} stock solution of TISAB
- Laboratory standard of fluorides (ρ_{std}, g L^{-1}, concentration is indicated on the label)
- Portable 913 pH meter Lab (Metrohm, Czech Republic)
- Magnetic stirrer
- Electrode holder
- Combined F-ISE (Metrohm, Czech Republic) (fluoride ISE type 600500600, price 35,360 CZK)
- ROW-automatic micropipette 100–1000 µL (5,499 CZK) with tips
- "Kartell" rubber bulb
- Manuals
- Notebook (shared by 3 students, price 8,290 CZK)

Technical equipment: 913 pH meter

The laboratory instrument 913 pH Meter allows to measure direct current electromotive force, pH, and temperature. The device is powered by a built-in battery (3.7 V) or a network adapter. Technical specifications are provided in **Table 1**. The instrument is equipped with an LCD monitor and a control panel. Individual connectors and control elements are described in **Fig. 3**.

Table 1 Technical Specifications of the Device 913 pH Meter

Measured quantity	Electromotive force
Range	From –1,200 to +1,200 mV
Resolution	0.1 mV
Accuracy	±0.2 mV

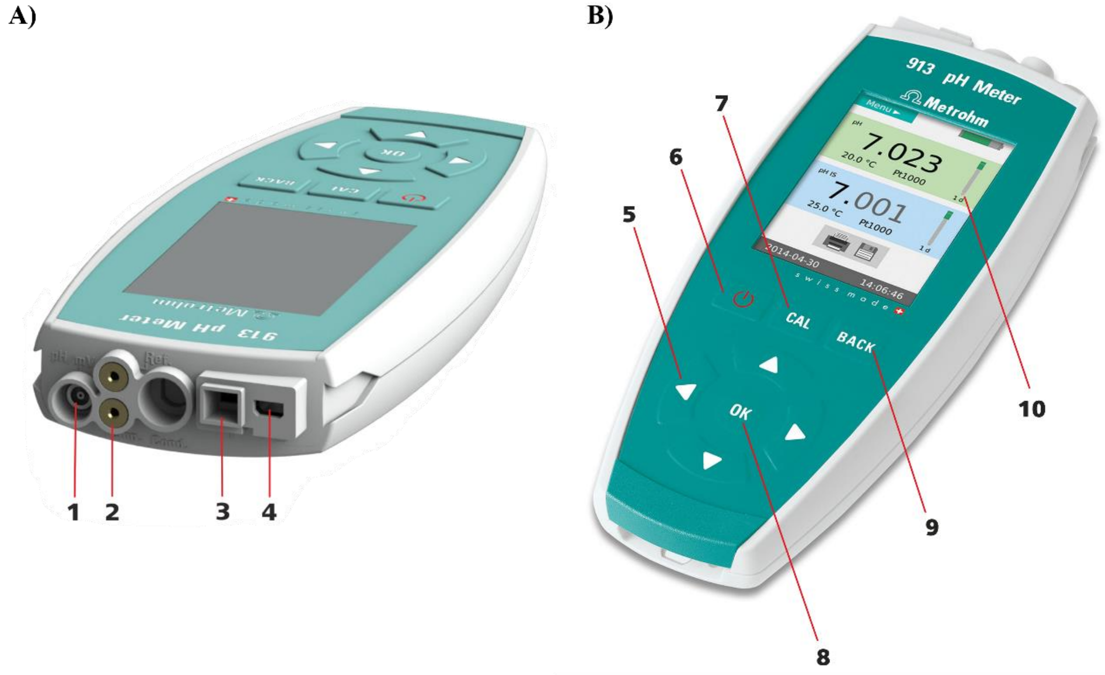

Fig. 3 The device 913 pH meter:

A) Connectors: 1 – connection socket for analogue measuring electrode 2 – connection for temperature sensor/reference electrode (up – blue, down – red), 3 – connection socket for special chip (not available in the laboratory), 4 – connection socket for energy supply/data transmission
B) Front panel: 5 – arrow keys 6 – power on/off button, 7 – button for recording calibration points (not used), 8 – confirmation button, 9 – back button, 10 – LCD monitor.

Operation

1) When the device is powered from the mains, it is always in "Standby" mode. To turn it on, press button 6 (**Fig. 3B**). The home screen will appear (**Fig. 4A**). If the electromotive force (ΔE) value is stabilizing, the individual digits on the screen are displayed in gray. After the signal stabilizes, the individual digits turn black.
2) First, it is necessary to enter the user's name without diacritics into the device. To enter the name into the device, use the arrow buttons (5) and OK (8) as follows: Menu → User → User (**Fig. 4A–C**, red frames), where you can enter the name using the on-screen keyboard (**Fig. 4D**). To return to the home screen, use the "back" button (9).

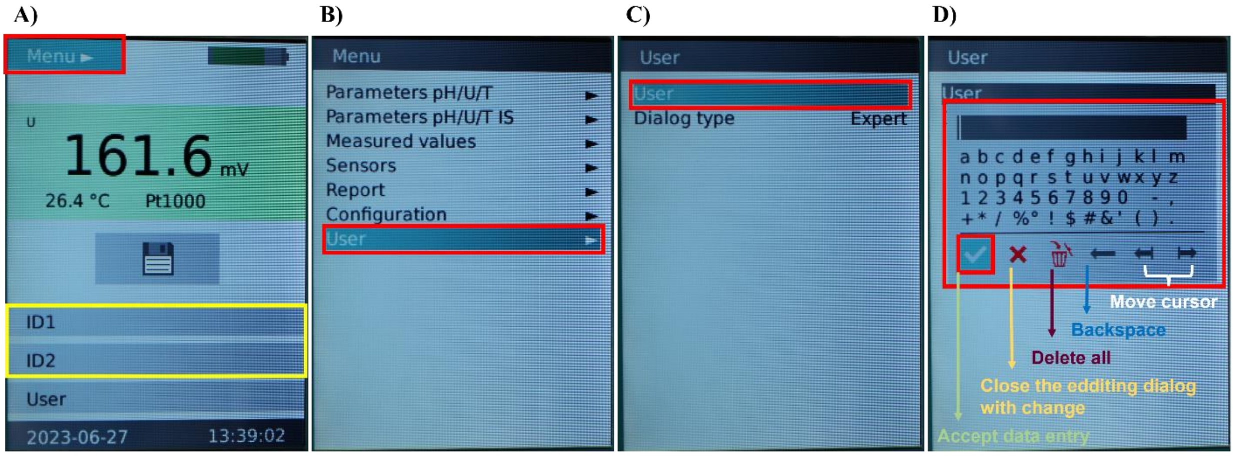

Fig. 4 Home Screen (A) and the process of entering a name into the device (B-D).

3) When measuring individual solutions, you can enter information about the solution to be measured (e.g., the calibration solution or standard addition) into the device. You can enter this information on the home screen under ID1 and ID2 (**Fig. 4A**, yellow box). Under ID1, enter the following for each measurement:

   a. Calibration: CAL 1 to 3

   b. Determination of fluorides in paste: STD

You won't change ID1 within one measurement. You will change ID2 before each addition. In this column, simply record the addition number. Before each addition, change ID2, add the respective addition, and start the timer for 1 minute. After one minute, save the electromotive force value (see point 4).

4) Save the measured Δ*E* values in the device's memory by pressing the floppy disk icon (**Fig. 5A**, purple box) on the home screen. Saved values can be viewed at any time by going to: Menu → Measured values → Values → view (**Fig. 5A–D**, red boxes). The last saved Δ*E* value and all the associated information are automatically displayed. You can navigate between the stored values using the up/down and left/right arrows (5). This way, you can save up to 10,000 values.

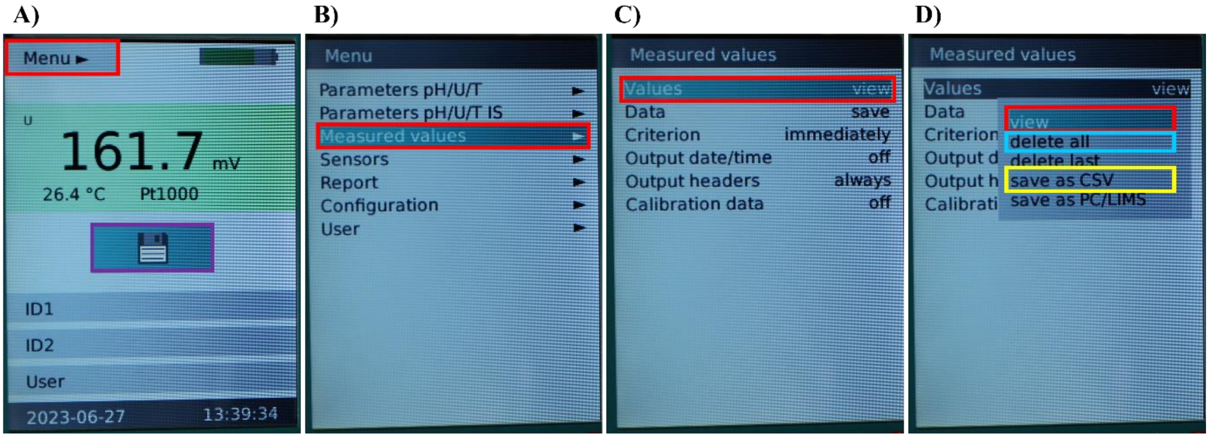

Fig. 5 Procedure for saving measured values, their subsequent display (red boxes), data export to a computer (yellow box), and data deletion at the end of the task (turquoise box).

5) Export the measured and saved Δ*E* values from the device to your computer in CSV format. Enter the export command as follows: Menu → Measured values → Values → save as CSV (Figure 5D, yellow box). Than connect the device to the computer using a USB cable. The connection is similar to a flash drive. The measured Δ*E* values are in the MEASREPORT.csv file.
6) Copy the MEASREPORT.csv file to the computer desktop. Open the MEASREPORT.csv file in MS Excel program. Your measured Δ*E* values are presented in the fifth columns. Copy values corresponding your measurement to the appropriate tables in file **'Template_LastName'**.
7) At the end of the laboratory day, delete all measured Δ*E* values from the device as follows: Menu → Measured values → Values → delete all (**Fig. 5D**, turquoise box).

1. Preparation of solutions and samples

1.1. Preparation of working solution of TISAB (c = 0.01 mol L^{-1})

TISAB is a buffer composed of NaCl, CH_3COONa, CH_3COOH, and *trans*-1,2-diaminocyclohexane-*N*,*N*,*N'*,*N'*-tetraacetic acid. The high concentration of NaCl ensures a constant ionic strength of the solution. The mixture of acetic acid and its sodium salt (acetic acid pH buffer) guarantees pH adjustment to the range of 5–6. The chelating agent (*trans*-1,2-diaminocyclohexane-*N*,*N*,*N'*,*N'*-tetraacetic acid) forms stable complexes with multivalent cations (Fe^{3+}, Al^{3+}), preventing their complexation with fluorides.

1. Transfer 5 mL of the TISAB stock solution (c = 2.0 mol L^{-1}) into a 1000 mL volumetric flask using a pipette.
2. Fill with distilled water up to the mark and mix thoroughly.

1.2. Preparation of toothpaste sample

- Weigh the sample with toothpaste on an analytical balance with a precision of 0.1 mg.
- Transfer **1.5–2.0 g of the sample** from the weigh boat ***using a dry glass rod into a dry beaker with a volume of 400 mL.*** Perform this transfer quickly due to the volatile nature of toothpaste samples. Seal the weigh boat after each transfer. The difference in weight before and after transferring the sample will provide precise information about the exact amount of toothpaste sample being analyzed. Record the precise weight of the toothpaste in your notebook. ***Leave the glass rod in the beaker, and do not wipe it under any circumstances.***
- Add approximately 100 mL of distilled water and a boiling chip (glass marble) to the 400 mL beaker containing the toothpaste sample. **The resulting toothpaste sample should be a finely mixed suspension without foam.** Cover the beaker with a watch glass and place it on a heated hot plate with a stirring rod inserted.
- Heat the prepared toothpaste sample for about 5 minutes. In case the sample starts foaming and there is a risk of overflowing from the beaker, remove the beaker from the hot plate, cool it with tap water, and return it to the hot plate after the foam subsides.

Caution! Do not leave the suspension in the beaker unattended - there is a risk of boiling over and sudden boiling of the heated solution, which can lead to the loss of part of the sample. **In this case, the solution should be discarded, and a new sample should be prepared.**

- Cool the beaker with the toothpaste suspension in a water bath located in the fume hood.
- Rinse the watch glass and glass rod with a small amount of distilled water into the beaker.
- Quantitatively transfer the suspension to a 250 mL volumetric flask, cool to room temperature.
- Add **1.5 mL of stock TISAB solution (c = 2 mol L^{-1})** to the 250 mL volumetric flask. Choose the correct pipette for taking 1.5 mL of liquid (pipette the entire volume at once).
- Fill with distilled water up to the mark and mix thoroughly.

Caution! Some toothpaste solutions can produce a lot of foam. To achieve good results, be patient and follow the assistant's instructions.

2. Determining the key properties of F-ISE

2.1. Regeneration of F-ISE

1. Add 100 mL of the working solution of TISAB (c = 0.01 mol L^{-1}) into a 150 mL beaker.
2. Place the 150 mL beaker with the TISAB solution (c = 0.01 mol L^{-1}) in the centre of the magnetic stirrer.
3. Submerge the F-ISE electrode 1 cm below the surface, **near the wall of the beaker (follow the assistant's instructions)** into the TISAB solution. Ensure that the surface of the magnetic stirrer and the bottom of the beaker are dry.
4. Start the stirring carefully. **CAUTION!** The stirring bar may damage the electrodes, so do not let them touch!
5. Regenerate the electrode for 10 minutes.
6. Turn off the stirring, remove the electrode from the solution, rinse it with distilled water, dry the electrode's surface with cellulose wadding, and proceed with the assigned tasks according to the assistant's instructions.

2.2. Calibration of F-ISE

1. Pipette 50 mL of the working solution TISAB (c = 0.01 mol L^{-1}) into a 100 mL beaker.
2. Place the 100 mL beaker with the prepared solution in the centre of the stirrer. Submerge the F-ISE electrode 1 cm below the surface, close to the beaker's wall. Ensure that both the surface of the stirrer and the bottom of the beaker are dry.
3. Submerge the F-ISE electrode into 50 mL of 0.01 mol L^{-1} TISAB. Start the stirrer. **CAUTION!** Do not touch the electrodes as the stirrer may damage them!
4. Add 100 µl of the laboratory standard fluoride solution (using an automatic pipette) and record the electromotive force after one minute for solution 1 (c_1). The concentration of the laboratory standard fluoride solution is indicated on the label (ρ_{std}, g L^{-1}).
5. Add 200 µl of standard fluoride solution (ρ_{std}, g L^{-1}), start the timer, and record the electromotive force after one minute for solution 2 (c_2).
6. Add 300 µl of standard fluoride solution (ρ_{std}, g L^{-1}), start the timer, and record the electromotive force after one minute for solution 3 (c_3).
7. Add 400 µl of standard fluoride solution (ρ_{std}, g L^{-1}), start the timer, and record the electromotive force after one minute for solution 4 (c_4).
8. Add 800 µl of standard fluoride solution (ρ_{std}, g L^{-1}), start the timer, and record the electromotive force after one minute for solution 5 (c_5).
9. Add 1000 µl of standard fluoride solution (ρ_{std}, g L^{-1}), start the timer, and record the electromotive force after one minute for solution 6 (c_6).
10. Turn off the stirrer, remove the electrode from the solution, rinse it with distilled water, dry the electrode's surface with cellulose wadding, and replace the solution.
11. Replace the measured solution with 50 mL of working solution TISAB (c = 0.01 mol L^{-1}). Regenerate the electrode for 10 minutes.
12. Repeat the calibration three times.
13. Complete Table 2.
14. Calculate the concentration of fluoride anions (c_1, c_2, c_3, c_4, c_5, c_6) (mol L^{-1}).

15. Construct the dependence of the electromotive force of the cell (ΔE) on the logarithm of fluoride ion concentration in the prepared calibration solutions (log $[F^-]$) ($R^2 = 0.999$).
16. Evaluate the experimental calibration equation using linear regression in MS Excel: $y = ax + b$) (where 'y' is the measured electromotive force of the cell (ΔE), 'a' is the experimental slope of the ISE (S), 'x' is the logarithm of ion concentrations in the measured solution (log $[F^-]$).
17. **Discuss the results with the assistant.**
18. Determine the basic properties from the experimental calibration curve.
19. Calculate the average slope value (sensitivity).

Table 2 Parameters used and obtained during the calibration of the fluoride ion-selective electrode ($M_F = 18.9984$ g mol^{-1})

Added standard fluoride solution, μL	100	200	300	400	800	1000
Total volume of added standard fluoride solution, μL	100	300				
Volume 0,01 mol L^{-1} TISAB, mL	50	50	50	50	50	50
Total volume, mL						
$[F^-]$, mol L^{-1}						
ΔE, mV (1st measurement)						
ΔE, mV (2nd measurement)						
ΔE, mV (3rd measurement)						

3. Determination of fluoride anion content in toothpaste sample: method of calibration curve and multiple standard addition

1. Regenerate the electrode in fresh 0.01 mol L^{-1} TISAB solution (10 minutes).
2. Mix the toothpaste sample in a volumetric flask and transfer a portion of the mixed sample into a 150 mL beaker.
3. Pipette 50 mL of the toothpaste sample into a 100 mL beaker.
4. Measure the electromotive force ΔE_0 after 1 minute for the toothpaste sample ($\boldsymbol{c_x}$).
5. Add laboratory standard fluoride solution: 100 µl → 200 µl → 400 µl → 800 µl → 1000 µl. Record the electromotive force after 1 minute for each addition: $\Delta E_1 \rightarrow \Delta E_2 \rightarrow \Delta E_3 \rightarrow \Delta E_4 \rightarrow \Delta E_5$. Fill in table 3.

Table 3 Parameters Used and Obtained During the Analysis of Toothpaste Sample Using the Standard Addition Method

Added standard fluoride solution, µl	0	100	200	400	800	1000
Total volume of added standard fluoride solution, µL	0	100	300			
Volume of the toothpaste sample, mL	50	50	50	50	50	50
Total volume, mL						
ΔE_n, mV						
$[F^-]_n$, mol L^{-1}						
%(m/m)						

3.1. Calibration curve method: Input the measured ΔE (see, point 4) into your experimental calibration equation and determine the fluoride concentration (c_x, mol L^{-1}) in the toothpaste sample. Recalculate the obtained concentration to mass percentage of fluorides % (m/m) F^- in the toothpaste sample.

3.2. Standard addition method: Determine fluoride concentration (c_x, mol L^{-1}) in the toothpaste sample for each addition using experimental data from Table 3 (see, '**Template_LastName**'). Recalculate the obtained concentrations to mass percentage of fluorides % (m/m) F^- in the toothpaste sample (see **Appendix 2**).

Compare the results of toothpaste analysis (%, m/m, F^-) obtained using the calibration curve method and the standard addition method. Interpret any differences if present.

4. Influence of pH on potentiometric determination of fluoride anions

The potentiometric selectivity coefficients for F-ISE are:

$K^{\mathrm{pot}}_{\mathrm{F^-,OH^-}} = 1{,}0 \times 10^{-1}$, $K^{\mathrm{pot}}_{\mathrm{F^-,Cl^-}} = 6{,}3 \times 10^{-5}$, $K^{\mathrm{pot}}_{\mathrm{F^-,Br^-}} = 5{,}0 \times 10^{-4}$, $K^{\mathrm{pot}}_{\mathrm{F^-,I^-}} = 7{,}9 \times 10^{-5}$.

a. Alkaline pH

Hydroxide ion interferes at measurement with F-ISE. Therefore, the response of F-ISE in the presence of hydroxide ion is given by Nikolsky-Eisenmann equation:

$$E_{pH} = K - S \cdot \log\left([\mathrm{F^-}] + \sum_{\mathrm{J}} K^{pot}_{\mathrm{F^-},OH^-} \cdot c[OH^-]^{z_{\mathrm{F}}/z_{\mathrm{J}}} \right) \tag{10}$$

Using Nikolsky-Eisenmann equation (5) calculate the electromotive force ΔE_{pH}value for F-ISE that might be obtained at pH = 12 if concentration of [F$^-$] is 9.01 x 10^{-4} mol L^{-1}. What is the percent error introduced if the hydroxide interference is ignored? The percent error is calculated using the following equation:

$$\%\ (\mathrm{error}) = \frac{\Delta E_{\mathrm{pH}} - \Delta E_{\mathrm{calibration}}}{\Delta E_{\mathrm{calibration}}} \cdot 100\ \% \tag{N1}$$

ΔE_{pH}	is the electromotive force obtained from the Nikolsky-Eisenmann equation (5),
$\Delta E_{\mathrm{calibration}}$	is the electromotive force obtained from the experimental calibration equation (6).

b. Acidic pH

The F-ISE does not respond to HF. What is the minimum pH at which 99% of fluoride is present as F$^-$ and only 1% is present as HF. Calculate the pH value at which the measured solution contains 70% F$^-$ and 30% HF. Use the definition of the dissociation constant (pK_a (HF)= 3.14).

$$K_a = \frac{[\mathrm{H^+}] \cdot [\mathrm{F^-}]}{[\mathrm{HF}]} \cdot 100\ \% \tag{N2}$$

5. Laboratory report

Fill in the prepared template '**Template_LastName**'.

6. Workstations

1. Check the laboratory equipment according to the attached list.
2. After finishing the work:
   - Regenerate the electrode in fresh 0.01 mol L^{-1} TISAB solution (for 10 minutes).
   - Return the F-ISE to its storage solution.
   - Wash the used glassware.
   - Return the functional flask, automatic pipette.
   - Erase stored values in the 913 pH Meter device.

References

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2. J. Koryta, K. Štulík: Iontově-selektivní elektrody, Academia, Praha 1984.
3. F. Opekar, I. Jelinek, P. Rychlovský, Z. Plzák: Základní analytická chemie, UK, Karolinum, Praha 2002.
4. E. Bakker, Ph. Bühlmann, E. Pretsch: Chem. Rev. 97 (1997) 3083.
5. International Union of Pure and Applied Chemistry : Compendium of Terminology in Analytical Chemistry (https://books.rsc.org/books/edited-volume/2059/Compendium-of-Terminology-in-Analytical-Chemistry).

Control questions

1. Describe the principle of direct potentiometry.
2. List factors (at least 3) that influence the accuracy of potentiometric fluoride determination. How do these factors contribute to the accuracy of potentiometric fluoride determination?
3. Define the role of NaCl, CH_3COOH, CH_3COONa in potentiometric fluoride determination.
4. Draw the potentiometric calibration curve for systems (label the axes):

   a. Indicator F-ISE in solutions of 10^{-6} to 10^{-1} mol L^{-1} NaF,

   b. Indicator Na-ISE in solutions of 10^{-6} to 10^{-1} mol L^{-1} NaF,

   c. Indicator F-ISE in solutions of 10^{-6} to 10^{-1} mol L^{-1} NaOH.
5. Which equation is applied at determination of the fluoride content using the calibration curve in the absence and presence of interfering ions?
6. Which of the listed cations interfere at potentiometric fluoride determination: a) Na^+, b) Fe^{3+}, c) K^+? How is eliminated their interfering effect?
7. What phenomenon will you observe when transitioning from concentrated to diluted solutions? How can this phenomenon be suppressed during potentiometric measurements?
8. What is the measured variable (i.e., dependent variable) in measurements with F-ISE? What are its units?
9. List and characterize the basic properties of F-ISE.
10. What is the chemical composition of the membrane in F-ISE? What is the significance of EuF_2 in the F-ISE membrane?
11. Draw a schematic electrochemical cell diagram for the determination of fluorides using half cell and combined F-ISE.
12. What is the relationship between the electromotive force (ΔE) of the cell with F-ISE and the concentration of F^- in the solution? Write the equation. Is this relationship linear?
13. Write the equation obtained during the calibration of pH combined glass ISE, CN-ISE, Na-ISE.
14. What anions and cations interfere when working with F-ISE? How can this phenomenon be eliminated?
15. What is the potentiometric selectivity coefficient? In what units is the potentiometric selectivity coefficient expressed? In what range of values are selectivity coefficients found?
16. In which cases is used the method of calibration curves and standard addition method?
17. Write equations for calculating the unknown concentration of fluoride ions using the calibration curve method.
18. Describe the procedure and write equations for calculating the unknown concentration of fluoride ions using the standard addition method.

19. What will be the substance concentration of fluoride when:

    a) You add 100 μL of fluoride solution ($[F^-] = 10^{-3}$ mol L^{-1}) to 50 mL of water,

    b) You mix 100 μL ($\rho_{\text{fluorides}} = 8.5451$ g L^{-1}) and 50 μL ($\rho_{\text{fluorides}} = 8.5451$ g L^{-1}) with 50 mL of 0.01 mol L^{-1} TISAB ($M_F = 18.9984$ g mol^{-1}, $M_{Cl} = 35.453$ g mol^{-1}),

    c) You add 400 μl of fluoride solution ($\rho_F = 8.5451$ g L^{-1}) to 50 mL of 0.01 mol L^{-1} TISAB? ($M_F = 18.9984$ g mol^{-1})

20. Write equations for reactions that may occur in acidic solutions during fluoride determination.

21. Write the equation obtained during the calibration of Na-ISE, Ca-ISE, CN-ISE.

22. F-ISE regeneration can be performed in:

    a) 0.01 mol L^{-1} TISAB solution

    b) Solutions of 10^{-6} mol L^{-1} NaF

    c) Solutions of 10^{-1} mol L^{-1} NaF.

23. The calibration dependence for F-ISE at 25°C corresponds to the equation:

    $$\Delta E = 0{,}2420 - 0{,}0591 \log[\mathrm{F}^-]$$

    For a given solution, an electromotive force of 0.4462 V was measured. What is the concentration of fluorides in the solution?

24. Hydroxide ions interfere when working with F-ISE. The response of F-ISE is:

    $$\Delta E = 0{,}2420 - \frac{0{,}0591}{z} \log([\mathrm{F}^-] + K^{\mathrm{pot}}_{\mathrm{F}^-,\mathrm{OH}^-}\,[\mathrm{OH}^-])\ ,$$

    where the potentiometric selectivity coefficient is $\boldsymbol{K^{pot}_{F^-,OH^-}} = 1{,}0 \times 10^{-1}$. What will be the fluoride concentration in a solution where the electromotive force (ΔE) change corresponds to 0.4462 V and pH = 9.00?

25. At low pH, F^- is predominantly converted to HF. F-ISE does not respond to HF. What is the minimum pH at which 99% of fluorides are present as F^- and only 1% as HF? (pK_a(HF) = 3.14).

26. What is the sensitivity of ISE? In what units is the sensitivity of F-ISE expressed? What sensitivity does ISE exhibit towards divalent anions and cations?

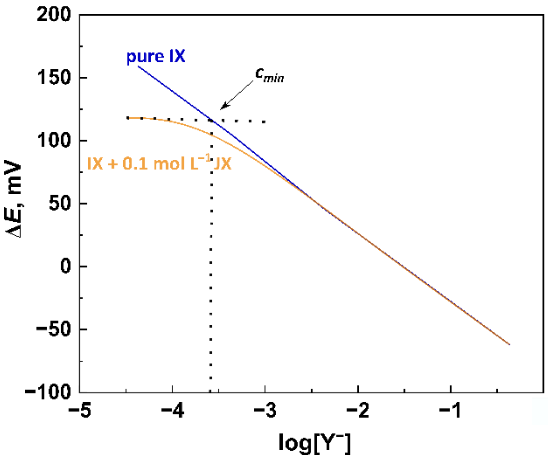
27. What is $\log K^{pot}_{\mathrm{F}^-,\mathrm{J}}$? What do the symbols F^- and J represent? In what range of values do they vary? What does it mean if the value of $\log K^{pot}_{\mathrm{F}^-,\mathrm{J}}$ is negative?

Appendix

Appendix 1

Methods for determining potentiometric selectivity coefficients for anionic ion-selective electrodes.

A)



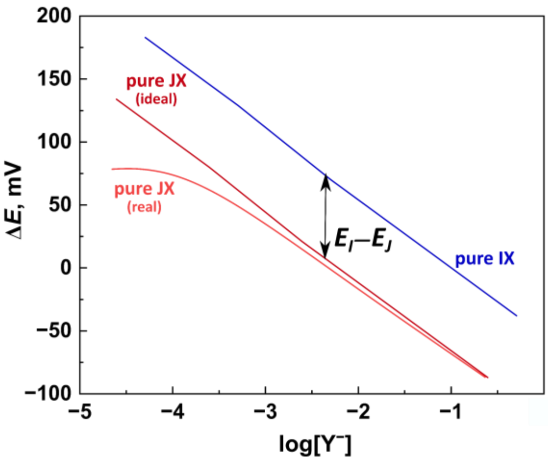
FIM method

$$\log K^{pot}_{\mathrm{I,J}} = \log\left(\frac{c_{min_{\mathrm{I}}}}{c_{\mathrm{J}}^{z_{\mathrm{I}}/z_{\mathrm{J}}}}\right)$$

$c_{min_{\mathrm{I}}}$ is the detection limit for the primary ion, which was determined during the calibration curve measurement in the presence of interferent *J*.

c_{J} is the concentration of interfering ion.

B)

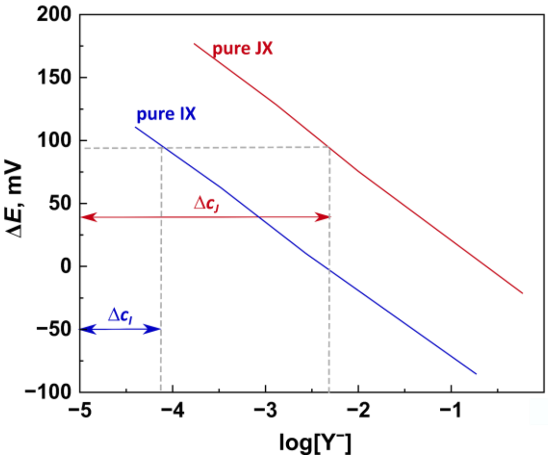


SSM method

$$\log K^{pot}_{\mathrm{I,J}} = \frac{(\Delta E_{\mathrm{I}} - \Delta E_{\mathrm{J}})}{S} + \log\left(\frac{c_{\mathrm{I}}}{c_{\mathrm{J}}^{z_{\mathrm{I}}/z_{\mathrm{J}}}}\right)$$

S is the electrode sensitivity,
ΔE_{I} and ΔE_{J} are the values of electromotive force (EMF) at the same concentration of the primary ion (c_{I}) and interfering ion (c_{J}).

C)



MPM method

$$k^{MPM}_{\mathrm{I,J}} = \frac{\Delta c_{\mathrm{I}}}{\Delta c_{\mathrm{J}}}$$

Δc_{I} represents the change in concentration of the primary ion that causes a change in electromotive force,
Δc_{J} represents the change in concentration of the interfering ion that causes the same change in electromotive force as Δc_{I}.

Appendix 2

Based on the calculated mass percentage of fluorides % (m/m) F^- in the toothpaste sample, determine a confidence interval at the 95% confidence level. The upper and lower bounds of the interval (confidence limits) are obtained from the equation:

$$L_{1,2} = \bar{x} \pm t_{n-1} \cdot \frac{s_{n-1}}{\sqrt{n}}, \qquad (2\text{-}1)$$

L_1 a L_2	are the lower and upper bounds of the confidence interval,
$\bar{x}$	is the average weight percentage of fluorides in the toothpaste % (*m*/*m*),
t_{n-1}	is the critical value of the Student's t-distribution for n−1 degrees of freedom (n is the number of determinations),
s_{n-1}	is the sample standard deviation.

In MS Excel, the function =TINV(0.05;*n*-1)[4] is used to calculate t_{n-1} and the function =SMODCH.VÝBĚR (or STDEV) is used for s_{n-1}.

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[4] The value 0.05 corresponds to a significance level of 5%, which means a confidence level of 95%.