Electrochemical analysis in liquid solutions is concerned with the measurement of electrical quantities, such as potential, current, and charge, to gain information about the composition of the solution and the reaction kinetics of its components. The main techniques are based on the quantitative determination of reagents needed to complete a reaction or the reaction products themselves. Four traditional methods of electrochemistry are described here (Figure 55.1): potentiometry, voltammetry, coulometry, and conductometry. Potentiometry implies the measurement of an electrode potential in a system in which the electrode and the solution are in electrochemical equilibrium. Voltammetry is a technique in which the potential is controlled according to some prescribed function while the current is measured. Coulometry involves the measurement of charge needed to completely convert an analyte, and conductometry determines the electrical conductivity of the investigated test solution. The practical applications of these measurement techniques for analytical purposes range from industrial process control and environmental monitoring to food analysis and biomedical diagnostics. The analytical methods and their instrumentation as well as recent trends, such as electrochemical sensors, are discussed.
55.1 Basic Concepts and Definitions

55.1.1 Electrodes and the Electrical Double Layer

In electrochemistry, electrodes are devices for the detection of charge transfer and charge separation at phase boundaries or for the generation and variation of the charge transfer and separation with an impressed current across the phase boundary. One important feature of electrodes is a potential difference across the electrode/electrolyte phase boundary. At this interface, the conduction mechanism changes since electrode materials conduct the current via electrons, whereas electrolytes conduct via ions. To understand the processes that lead to the formation of the potential difference, it is helpful to consider first an atomistic model, which was given by Helmholtz. It leads to the idea of an electrical double layer.

If an electrode is immersed in an electrolyte solution, the bulk regions of the two homogeneous phases—the electrode material and the electrolyte—are in equilibrium. Thus means that far away from the phase boundary (>1 μm), the sum of the forces on the particles is zero and charges are distributed homogeneously. Since the cohesion forces that bind the individual particles together in the bulk are significantly reduced at the surface of the electrode, particles in this region will have less neighbors or neighbors from the other phase. Thus, close to the phase boundary, the equilibrium conditions are drastically different from the equilibrium conditions in the bulk of the electrolyte. Thus change in the equilibrium of forces on particles at the interface can lead to an interfacial tension. In addition, the surface of a condensed phase usually has different electrical properties than the bulk phase, for example, due to the accumulation of free charge on the surface of an electrically charged solid. Besides, the orientation of dipoles in the surface region and adsorption of ions and dipoles from the electrolyte can lead to a change in the electrical properties. Thus excess charge from ions, electrons, and dipoles produces an electric field that is accompanied by a potential difference across the phase boundary. The region in which these charges are present is termed the electrical double layer (Hamann et al. 2007). The formation of an electrical double layer at interfaces is a general phenomenon but only the electrode/electrolyte interface will be considered here in more detail.

According to the hypothesis of Helmholtz, the electrical double layer has the character of a plate capacitor, whose plates consist of a homogeneously distributed charge in the metal electrode and ions of opposite charge lying in a parallel plane in the solution at a minimal distance from the surface of the electrode (Rieger 1987). Modern conceptions are based on the assumption that the electron cloud in the metal extends to a certain degree into a thin layer of solvent molecules in the immediate vicinity of the electrode surface. In this layer, the dipoles of the solvent molecules (e.g., H₂O) are oriented to various degrees toward the electrode surface. Ions can accumulate in it due to electrostatic forces or be adsorbed specifically on the electrode through van der Waals and chemical forces. These substances are called surface-active substances or surfactants. The sum of oriented solvent molecules and surfactants...
in the immediate vicinity of the electrode is considered as one layer. The plane through the centers of these molecules and ions parallel to the electrode surface is termed inner Helmholtz plane (Figure 55.2). If only electrostatic attraction is taken into account, ions from the solution can approach the surface to a distance given by their primary solvation sheaths. This means that at least a monomolecular solvent layer remains between the electrode and the solvated ion. The plane through the centers of these ions is called outer Helmholtz plane, and the solution region between the electrode surface and this outer Helmholtz plane is called Helmholtz or compact layer. In reality, electrostatic forces cannot retain ions at a minimal distance from the electrode surface. Due to thermal motion, the excess charge is smeared out in the direction of the electrolyte bulk to form a diffuse layer, also termed the Gouy-Chapman layer. It describes the region between the outer Helmholtz plane and the bulk of the solution. In concentrated electrolyte solutions (approx. 1 mol L⁻¹), the diffuse layer is as thin as the inner Helmholtz plane and may be considered as rigid. In highly dilute solutions, its thickness can be as large as 100 nm. As in the early model of Helmholtz, the double layer acts as a capacitor (Wang 2006). Here, two different dielectric layers with permittivities \( \varepsilon_1 \) and \( \varepsilon_2 \) represent the region between the electrode surface and the inner Helmholtz plane and the region between the inner and the outer Helmholtz plane, respectively (Figure 55.2).

In addition to these ideal electrostatic processes that lead to the formation of the electrical double layer, one has also to consider the transition of charge, ions, and/or electrons from the electrode phase into the electrolyte phase or vice versa. In the equivalent circuit representation, such a charge transport through the double layer is symbolized as a transfer resistance \( R_t \) connected in parallel with the capacitor. If any charge transport through the double layer is excluded, the transfer resistance is nearly infinite. According to Ohm's law, any current impressed across the electrode surface leads to a high polarization.
voltage determining the electrode as *ideally polarizable*. One example of a polarizable electrode is the dropping mercury electrode (DME), which is frequently used in polarography. In the opposite case with a nearly vanishing transfer resistance, the electrode is termed *ideally unpolarizable*. In the equivalent circuit representation, this corresponds to short circuit of the capacitor. The current flow then does not influence the voltage drop across the phase boundary. *Reference electrodes*, whose voltage has to be constant when immersed in an electrolyte, are nearly unpolarizable electrodes. Since every voltage measurement is accompanied by a small current flow, the difference between polarizable and unpolarizable electrodes is very important in measurement technique.

### 55.1.2 Nernst Equation

If the electrode phase and the electrolyte phase contain a common ion, the potential difference across the phase boundary is determined by the effective concentration (activity) of this ion in the solution. This fact is described quantitatively by the *Nernst equation* and will be derived in the following. If one mole of ions of a species $i$ has to be transferred from a given reference state outside into the bulk of an electrically charged phase, work must be expended to overcome the chemical bonding forces and the electric forces. This work is given by the electrochemical potential $\mu_i$. Since the chemical interactions of a species with its environment always possess electric components, generally the electrochemical potential cannot be separated into chemical and electrical parts. Nonetheless, the electrochemical potential is frequently given formally as a sum of the chemical potential $\mu_i$ and an electrostatic work $zF\phi$:

$$\mu_i = \bar{\mu}_i + zF\phi$$  \hspace{1cm} (55.1)

The chemical potential $\mu_i$ of an uncharged component of a system is the amount of Gibbs energy $G$ inherent in 1 mol of that component (Koryta and Stulik 2009):

$$\mu_i = \left(\frac{\partial G}{\partial n_i}\right)_{p,T}$$  \hspace{1cm} (55.2)

Here, $n_i$ is the number of moles of the given component. In the case of a dilute solution, the chemical potential of a component $i$ is

$$\mu_i = \mu_i^0 + RT \ln c_i$$  \hspace{1cm} (55.3)

where

- $\bar{\mu}_i^0$ denotes the standard chemical potential
- $c_i$ denotes the concentration of the species $i$
- $R$ is the gas constant
- $T$ is the absolute temperature

The values of standard chemical potentials can be found in standard textbooks of thermodynamics and in tables of physicochemical constants under the name standard molar Gibbs energies. $\mu_i^0$ is independent of the concentration $c_i$. In concentrated electrolytes, the concentration $c_i$ has to be replaced by the respective activity $a_i$. The activity $a_i$ is given by the relationship $a_i = \gamma c_i$, where $\gamma$ is the activity coefficient that is a correction factor for nonideal behavior. In the second term of Equation 55.1, $z$ denotes the charge number of the ion $i$, $F$ is the Faraday constant, and $\phi$ is the *inner electric potential*, which is, in general, the electric work necessary for the transfer of a unit charge; for example, 1 C, from infinity to a given site.

The inner electric potential may consist of two components: an *outer electric potential* $\psi$ and a *surface electric potential* $\chi$. Whereas the outer electric potential of a phase is produced by excess electric charge...
supplied from outside, the surface electric potential is an effect of electric forces at the interface that leads to the electrical double layer introduced earlier. The difference of the outer potentials of the electrode (e) and the solution (s)

\[ \psi_e - \psi_s = \Delta \psi \]

(55.4)

is termed Volta potential difference and is the only measurable quantity. Neither the difference of the surface potentials of the appropriate phases \( \Delta \psi \) nor the difference of the inner electric potentials

\[ \Delta \phi = \Delta \psi + \Delta \chi \]

(55.5)

defined as the Galvani potential difference can be measured directly. Strictly speaking, even the Volta potential difference between the solution and the electrode is not a measurable quantity since only the Volta potential difference between two electrodes can be measured. To determine the potential of the solution phase, one has to dip an electrode in the solution. This, however, creates a new electrode/solution interphase, and consequently, one measures the sum of two potential differences. This is the reason for the lack of absolute potentials in electrochemistry. Therefore, one uses a reference electrode that has a known potential relative to a standard electrode.

In thermodynamic equilibrium, the electrochemical potentials of the considered species are equal in both phases. For a charged particle \( i \) that may cross the phase boundary solution/electrode, this means

\[ \mu_i^0 + RT \ln a_{i,s} + z_i F \phi_s = \mu_i^0 + RT \ln a_{i,e} + z_i F \phi_e \]

(55.6)

and therefore, in equilibrium the Galvani potential difference is given by

\[ \Delta \phi = \phi_e - \phi_s = \frac{\mu_i^0 - \mu_i^0}{z_i F} + \frac{RT}{z_i F} \ln \frac{a_{i,s}}{a_{i,e}} \]

(55.7)

Since the chemical standard potentials of the respective phases are constants, the first term in Equation 55.7 can be expressed as a standard Galvani potential difference \( \Delta \phi^0 \):

\[ \Delta \phi = \Delta \phi^0 + \frac{RT}{z_i F} \ln \frac{a_{i,s}}{a_{i,e}} \]

(55.8)

For metal electrodes, the activity of the metal atoms \( M \) and that of the electrons in the electrode phase equals unity per definition. Thus, for an electrode reaction of type

\[ M^{z+} + ze^- \leftrightarrow M \]

(55.9)

Equation 55.8 becomes the Nernst equation

\[ \Delta \phi = \Delta \phi^0 + \frac{RT}{zF} \ln a_i \]

(55.10)

which gives the relation between the activity of the potential determining ion \( a_i \) and the Galvani potential difference \( \Delta \phi \). Using base 10 logarithms, the Nernst equation is given as

\[ \Delta \phi = \Delta \phi^0 + \frac{RT \cdot 2.3}{zF} \log a_i = \Delta \phi^0 + k \cdot \log a_i \]

(55.11)

where \( k \) is called the Nernst constant.
FIGURE 55.3 Schematic of an electrochemical cell with a working electrode and a reference electrode immersed in the test solution (electrolyte).

The classical form of the Nernst equation (Equation 55.10) can be formulated more generally for a redox reaction. If $a_{\text{ox}}$ and $a_{\text{red}}$ are the activities of the oxidized and reduced form of the considered ion, the Galvani potential difference is given as

$$
\Delta \phi = \Delta \phi^0 + \frac{RT}{zF} \ln \frac{a_{\text{ox}}}{a_{\text{red}}}
$$

In potentiometry, the activity of a certain ion can be determined directly by the measurement of the equilibrium Galvani potential difference of a suitable electrode (direct potentiometry). On the other hand, changes of the activity of the detected ion and equivalence points (EPs) can be detected in titration reactions (potentiometric endpoint titration).

After this rather theoretical definition of the Galvani potential difference, the question arises on how to measure this potential difference between the bulk of the electrode and the solution. Since a potential difference cannot be measured with only one electrode, a second one must be immersed in the solution. Both are connected to a voltmeter, to complete the electrochemical cell (Figure 55.3). An electrochemical cell generally consists of two (or more) electrodes immersed in an analyte. Thus, in some of the old literature, a single electrode is often referred to as a half-cell and its potential is called half-cell potential. In modern electrochemistry, usually the term electrode potential is used. An electrochemical cell is in a current-free state during potentiometric measurements (e.g., with an ion-selective electrode [ISE]), but may also supply electric energy (a galvanic cell) or accept electric energy from an external source (an electrolytic cell). Since a second electrode potential arises at the phase boundary second electrode/electrolyte, only the sum of at least two Galvani potential differences can be measured. A separation into the two individual parts is impossible. Hence, the function of the second electrode, namely reference electrode, is to act as an electrode of constant potential against which variations in the potential of the measuring electrode in various samples can be measured. In the Nernst equation, the Galvani potential $\phi$ is then replaced by $E$, the symbol for measurable voltages.

55.1.3 Classification of Electrodes

Electrodes are termed reversible electrodes if they transfer electrons and ions with negligible impedance. Therefore, under current, the electrochemical potential of electrons, ions, and neutral species does not change across the different interfaces that may exist in an electrode. Otherwise, the electrode is not suitable to measure thermodynamic (equilibrium) quantities such as ion activity. Since distribution
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The equilibrium of charged species is considered here, the electrode and the solution phase must have at least one charged species in common. Depending on the number of equilibria being involved in the forming of the electrode potential, reversible electrodes can be divided into different groups:

1. **Electrodes of the first kind.** These may be cationic or anionic electrodes at which equilibrium is established between the atoms or molecules in the electrode material and the respective cations or anions in the solution. According to the Nernst equation, the equilibrium Galvani potential difference is here determined by the activity of the considered ion in the solution. Examples for electrodes of the first kind are ISEs including metal and amalgam electrodes and the hydrogen electrode.

2. **Electrodes of the second kind.** These electrodes consist of three phases. A metal wire is covered by a layer of its sparingly soluble salt that usually has the character of a solid electrolyte (e.g., Ag and AgCl). The wire is immersed in a solution containing a soluble salt of the anions of this solid electrolyte (e.g., KCl). Here, the equilibrium between the Ag atoms in the metal and the anions in the solution is established through two equilibria: the first one is given between the metal and the cation in its sparingly soluble salt, for example,

   \[ \text{Ag} \leftrightarrow \text{Ag}^+ + e^- \]  

   (55.13)

   and the second one between the anion in the sparingly soluble salt and the anion in the solution, for example,

   \[ \text{AgCl} \leftrightarrow \text{Ag}^+ + \text{Cl}^- \]  

   (55.14)

   The electrode potential of electrodes of the second kind is rather insensitive to small current flows. Thus, they are often used as reference electrodes.

3. **Electrodes of the third kind.** In this electrode, the sparingly soluble salt contains a second cation that also forms a sparingly soluble compound with the common anion but with a higher solubility product than the electrode metal compound (e.g., Ag$_2$S and PbS). Here, the electrode potential depends on the activity of this cation in the solution.

4. **Oxidation-reduction (redox) electrodes.** These consist of an inert metal such as Pt, Au, or Hg that is immersed in a solution of two soluble oxidation forms of a single substance (e.g., Fe$^{3+}$ and Fe$^{2+}$). Thus, for the electrode reaction

   \[ \text{Fe}^{3+} + e^- \leftrightarrow \text{Fe}^{2+} \]  

   (55.15)

   the Nernst equation is

   \[ E_{\text{Fe}^{3+}/\text{Fe}^{2+}} = E^0_{\text{Fe}^{3+}/\text{Fe}^{2+}} + \frac{RT}{F} \ln \frac{a_{\text{Fe}^{3+}}}{a_{\text{Fe}^{2+}}} \]  

   (55.16)

   according to Equation 55.10. Here, $E$ is termed the electrode potential and $E^0$ is designated the standard electrode (or redox) potential of the electrode reaction if it is measured versus the standard hydrogen electrode (SHE). The subscripts of $E$ and $E^0$ denote the redox couple of the considered electrode reaction. The standard redox potential is a measure of the reducing or oxidizing ability of a substance. If one considers, for example, two systems 1 and 2 with their respective standard redox potentials $E_1^0$ and $E_2^0$, system 1 is a stronger oxidant than system 2 if $E_1^0 > E_2^0$. This means that in a mixture of the solutions of these two systems where originally the activities of the reduced forms equal that of the oxidized forms ($a_{\text{red}}^{1} = a_{\text{ox}}^{1}$ and $a_{\text{red}}^{2} = a_{\text{ox}}^{2}$), an equilibrium will be
established with $a_{\text{act}}^i > a_{\text{ref}}^i$ and $a_{\text{red}}^i > a_{\text{ox}}^i$. The experimentally determined standard potentials of well-known redox systems are listed in (Haynes 2011). Table 55.1 gives some examples. In redox electrodes, the metal acts as a medium for the electron transfer between the two forms. In contrast to electrodes of the first kind, the solution should not contain ions of the electrode metal in order to avoid an additional Galvani potential difference at the electrode determined by the activity of the electrode metal ions in the solution. The disturbing ion activity is negligible if the standard potential of the electrode metal is a few 100 mV higher than the redox potential to be measured. Thus, mainly platinum electrodes ($E_{\text{Pt}}^{\text{II}}/\text{Pt} = 1.20$ V) and gold electrodes ($E_{\text{Au}}^{\text{III}}/\text{Au} = 1.42$ V) are used as redox electrodes.

### Table 55.1 Some Standard Electrode Potentials and Redox Potentials

<table>
<thead>
<tr>
<th>Electrode or Half-Cell Reaction</th>
<th>$E^\circ$ (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Li}^+ + e^- \rightleftharpoons \text{Li}$</td>
<td>-3.0403</td>
</tr>
<tr>
<td>$\text{K}^+ + e^- \rightleftharpoons \text{K}$</td>
<td>-2.931</td>
</tr>
<tr>
<td>$\text{Ca}^{2+} + 2e^- \rightleftharpoons \text{Ca}$</td>
<td>-2.868</td>
</tr>
<tr>
<td>$\text{Mg}^{2+} + 2e^- \rightleftharpoons \text{Mg}$</td>
<td>-2.372</td>
</tr>
<tr>
<td>$\text{Al}^{3+} + 3e^- \rightleftharpoons \text{Al}$</td>
<td>-1.662</td>
</tr>
<tr>
<td>$\text{Zn}^{2+} + 2e^- \rightleftharpoons \text{Zn}$</td>
<td>-0.762</td>
</tr>
<tr>
<td>$\text{Fe}^{2+} + 2e^- \rightleftharpoons \text{Fe}$</td>
<td>-0.447</td>
</tr>
<tr>
<td>$\text{Pb}^{2+} + 2e^- \rightleftharpoons \text{Pb}$</td>
<td>-0.1264</td>
</tr>
<tr>
<td>$\text{AgCl} + e^- \rightleftharpoons \text{Ag} + \text{Cl}^-$</td>
<td>0.22216</td>
</tr>
<tr>
<td>$\text{Hg}_2\text{Cl}_2 + 2e^- \rightleftharpoons 2\text{Hg} + 2\text{Cl}^-$</td>
<td>0.26791</td>
</tr>
<tr>
<td>$\text{Cu}^{2+} + 2e^- \rightleftharpoons \text{Cu}$</td>
<td>0.3417</td>
</tr>
<tr>
<td>$\text{I}_2 + 2e^- \rightleftharpoons 2\text{I}^-$</td>
<td>0.5353</td>
</tr>
<tr>
<td>$\text{Fe}^{3+} + e^- \rightleftharpoons \text{Fe}^{2+}$</td>
<td>0.771</td>
</tr>
<tr>
<td>$\text{Ag}^+ + e^- \rightleftharpoons \text{Ag}$</td>
<td>0.7994</td>
</tr>
<tr>
<td>$\text{Tl}^{3+} + 2e^- \rightleftharpoons \text{Tl}^+$</td>
<td>1.2152</td>
</tr>
<tr>
<td>$2\text{Cl}^- \rightleftharpoons \text{Cl}_2 + 2e^-$</td>
<td>1.35793</td>
</tr>
<tr>
<td>$\text{Ce}^{4+} + e^- \rightleftharpoons \text{Ce}^{3+}$</td>
<td>1.610</td>
</tr>
</tbody>
</table>

### 55.1.4 Reference Electrodes

The potential of an ISE is always measured with respect to a reference electrode. Ideally, the reference electrode should not cause chemical changes in the sample solution, or vice versa. It should maintain a constant potential relative to the sample solution, regardless of its composition. In practice, any changes of its potential with composition should be at least as small as possible and reproducible. Reference electrodes with liquid junctions, strictly speaking reference electrode assemblies, consist of a reference element immersed in a filling solution (often called bridge solution) contained within the electrode. The reference element should possess a fixed activity of the ion defining the potential of the element with respect to the filling solution. The electric contact between the electrode and the sample solution is made by the liquid junction consisting of a porous plug or a flow restriction that permits the filling solution to flow very slowly into the sample.

At the junction between the two electrolyte solutions, ions from both solutions diffuse into each other. Since different ions have different mobilities, they will diffuse at different rates. Thus, a charge separation will occur related in size to the difference in mobilities of the anions and cations in the two solutions. This charge separation produces a potential difference across the junction called the liquid junction potential (Morf 1981). In reference electrodes, usually the bridge solution is given a slightly higher pressure than the sample so that the solution, of concentrated potassium chloride, flows out.
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relatively rapidly into the sample and diffusion of the sample back into the salt bridge is impeded. If the bridge solution is concentrated enough, it is assumed that variations in the liquid junction potential due to the varying composition of the sample are suppressed. This is the basis on which the reference electrode assembly is used. Since the potential of the whole assembly \( E_{\text{ref}} \) is the sum of the potential of the reference element \( E_i \) in the bridge solution and the liquid junction potential \( E_j \)

\[
E_{\text{ref}} = E_i + E_j
\]  

(55.17)

any change in the liquid junction potential appears as a change in the potential of the assembly. An extra liquid junction potential must be included if a double-junction reference electrode is considered. When an analysis using a cell with an IES is carried out, standard solutions are used to calibrate the ISE. A change in the liquid junction potential that occurs when the standard solutions are replaced by the sample is termed the residual liquid junction potential and constitutes an error in the analytical measurement. The needed constancy of the potential can be approached by a suitable choice of standards and/or sample pretreatment and by the use of a proper bridge solution and the best physical form of the liquid junction.

Several types of liquid junctions exist from which the best ones with regard to stability and reproducibility are complicated to realize in practice and the worst ones are easy to use but much less stable and reproducible. Most of the commercial reference electrodes with adequate properties possess restrained diffusion junctions where the most common junctions available are the ceramic plug, the asbestos wick or fiber, two types of ground sleeve junction, and the palladium annulus junction (Figure 55.4). For a very large majority of applications with IESs, a ceramic plug will perform adequately. The flow rate of the bridge solution into the sample solution is sometimes called leak rate and is given in mL per 5 cm head of

![Image](https://example.com/image.png)

**FIGURE 55.4** Different types of liquid junctions: (a) ceramic plug, (b) ground glass sleeve (type 1), (c) ground glass sleeve (type 2), (d) asbestos wick, and (e) palladium annulus.
bridge solution per day. The head of bridge solution is measured as the height of the surface of the bridge solution above the surface of the sample. In order to work satisfactorily, the surface of the bridge solution of all these restricted junction devices has to be at least 1 cm above the sample solution. Otherwise, if the bridge solution falls too low, the junction and the bridge will become contaminated by species dif using from the sample. The bridge solution has then to be replaced. For the same reason, reference electrodes should be stored, when not in use, with the junction immersed in bridge solution.

Whereas the ceramic plug and the asbestos wick and fiber (Figure 55.4a and d) have relatively slow flow rates of about 0.01–0.1 mL per 5 cm head of bridge solution per day, ground sleeve junctions of type (b) have a flow rate of 1–2 mL. On the other hand, the flow rates of different asbestos wick junctions may vary by a factor up to 100, and the liquid junction potential may have a day-to-day (in) stability of ±2 mV under the favorable conditions of a junction between strong potassium chloride solution and an intermediate pH buffer. Under the same conditions, ground glass sleeve junctions of type (b) and the little-used palladium annulus junction show stabilities of ±0.06 and ±0.2 mV, respectively. It is worth mentioning that palladium annulus junctions may partly respond as a redox electrode in strong oxidants (e.g., 0.2 M KMnO₄ in 0.05 M H₂SO₄) and mild or strong reductants (e.g., 0.5 M SnCl₂ in 1 M HCl). In such samples, reference electrodes with palladium or platinum annulus junctions should not be used. Although ground glass sleeve junctions have inconveniently high flow rates and the bridge solution needs to be replenished frequently, these junction types have found particular use in applications where the junction has the tendency to clog, such as measurements in protein solutions. However, the stability of the liquid junction potential appears to be relatively poor in fast-flowing sample solutions and may be very sensitive to sample flow rate. Asbestos wick junctions are particularly liable to blockage and should consequently be used in clear solutions only.

In double-junction reference electrodes, the filling solution in which the reference element is immersed (reference solution) makes contact with another solution, the bridge solution, by means of a liquid junction. A second liquid junction enables contact to be made between the bridge solution and the sample. Such electrodes are useful when it is essential that contamination of the sample by the inner filling solution must be kept at a very low level. The outer bridge solution can be selected to be compatible with the sample. In order to minimize the liquid junction potentials that can drift and cause instability, the bridge solution should be equitranferent; that is, the transport numbers of its anion and cation should be nearly equal. However, the complication of a second liquid junction in the cell should be avoided if possible.

### 55.1.4.1 Standard Hydrogen Electrode

Aqueous solutions are of major concern in electrochemistry because of their hydrogen ion content. Thus, it is advantageous to use a reference electrode where a reaction occurs that involves the participation of hydrogen ions. One of these reactions is

\[ \frac{1}{2}H_2 + H_2O \leftrightarrow H_3O^+ + e^- \]  

(55.18)

Figure 55.5 shows a hydrogen electrode. A hydrogen electrode usually consists of a platinum sheet covered by a thin layer of spongelike structured platinum, so-called platinum black that has a high specific surface area. The electrode is rinsed with pure gaseous hydrogen in order to form a complete layer of adsorbed H₂ molecules at the surface. If this electrode is immersed in an electrolyte, it acts as an electrode consisting of hydrogen at which the gaseous hydrogen is oxidized to hydronium ions or the hydronium ions are reduced to hydrogen, respectively, according to Equation 55.18. The real mechanism of this electrode process is rather complicated because the platinum electrode is in contact with the hydronium ions in the solution as well as with the gaseous hydrogen that is bubbled through it. Thus, the final equilibrium between the gaseous hydrogen, the dissolved hydronium ions, and the electrode phase consists of several successive equilibrium steps that can be found in Koryta (1991).
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FIGURE 55.5 Schematic of a hydrogen electrode.

To calculate the potential of a hydrogen electrode, which is strictly speaking the difference between the potential of the electrode and that of the solution, one has to consider the electrochemical potentials of the respective phases. The chemical potential of gases is usually expressed in terms of the pressure $p$ instead of the molar concentration $c$. Due to the elementary relationship $pV = nRT$ for ideal gases, where $V$ is the volume of the gas and $n$ is the amount of moles the pressure, $p$ is proportional to the molar concentration $c = n/V$. Thus, according to Equation 55.3,

$$\mu_{H_2} = \mu_{H_2}^0 + RT \ln \frac{P_{H_2}}{P_{H_2}^0} \quad (55.19)$$

where $\mu_{H_2}$ and $\mu_{H_2}^0$ are the pressure and standard pressure of hydrogen, respectively. In the case of moderate ion concentrations, the chemical potential of the solvent water is equal to its standard chemical potential. Hence, the potential difference between the electrode and the solution is, according to Equation 55.7,

$$\Delta \phi = \mu_{H_2}^0 - \mu_{H_2} - \mu_{H_2}^0 + \frac{RT}{F} \ln c_{H_2O}^+ - \frac{RT}{2F} \ln \frac{P_{H_2}}{P_{H_2}^0} \quad (55.20)$$

This equation is generally valid for hydrogen electrodes. The electrode is called SHE if the molar concentration is such that the activity of the hydronium ions is unity ($a_{H_2O} = 1$) and the pressure of hydrogen is equal to its standard pressure. Hence, for an SHE, the second and third terms in Equation 55.20 vanish. The combination of standard chemical potentials in the first term of Equation 55.20 is defined as zero. Consequently, the total potential difference across the interface SHE/electrolyte is equal to zero by definition at any temperature. Since SHEs are very difficult to prepare, they are not used as reference electrodes in practice. However, electrode potentials are usually standardized with respect to the SHE, and their values are thus called “on the hydrogen scale.”

55.1.4.2 Calomel Electrode

The calomel electrode is the most common of all reference electrodes. It consists of a pool of mercury that is covered by a layer of mercurous chloride (calomel, Hg$_2$Cl$_2$). The calomel is in contact with a
reference solution that is nearly always a solution of potassium chloride, saturated with mercurous chloride. Thus, the calomel electrode is a typical electrode of the second kind. Figure 55.6 shows a typical arrangement of a commercial calomel electrode assembly where the electrode is inverted, with the mercury uppermost, and packed into a narrow tube. Depending on the strength of the potassium chloride solution used, the electrode is called saturated calomel electrode (SCE), 3.8 or 3.5 M calomel electrode, respectively. Potassium chloride is used as reference solution because it gives rise to a small liquid junction potential at the outer liquid junction of the electrode, that is, the liquid junction with the sample. Hence, potassium chloride is a suitable reference solution as well as a good bridge solution. Furthermore, mercurous chloride has a very low solubility in potassium chloride solutions, regardless of concentration. The electrode reaction of a calomel electrode is

\[
\text{Hg} + \text{Cl}^- \leftrightarrow \frac{1}{2} \text{Hg}_2\text{Cl}_2 + e^- \quad (55.21)
\]

Its standard potential, including the liquid junction, is 0.2444 V versus SHE at 25 °C for the SCE and 0.2501 V for the 3.5 M calomel electrode (Bailey 1980; Koryta et al. 1993).

The components of a calomel electrode are chemically stable except for the mercurous chloride, which significantly disproportionates at temperatures above 70 °C according to the following equation:

\[
\text{Hg}_2\text{Cl}_2 \leftrightarrow \text{Hg} + \text{HgCl}_2 \quad (55.22)
\]

Hence, potential drift occurs and lifetime decreases with increasing working temperature. On the other hand, calomel electrodes can be used at temperatures down to −30 °C if 50% glycerol is added to the potassium chloride solution.

Impurities in the potassium chloride solution, such as bromide and sulfide ions as well as redox agents and complexants, cause a small shift in the electrode potential. Nevertheless, the measurement of potential differences is not affected. However, the most unsatisfactory feature of the performance of the calomel electrode is its thermal hysteresis that occurs if the electrode filling material is not in thermal equilibrium or if the electrode and the sample have different temperatures. Thus, temperature stability
during the storage and measurements is very important. In any cases where the temperature of the reference electrode or the sample has to be varied, it is thus usually better to use a silver/silver chloride electrode instead of a calomel electrode.

55.1.4.3 Silver/Silver Chloride Electrode

The silver/silver chloride electrode consists of a silver wire or plate that is coated with silver chloride. For the same reasons as with the calomel electrode, this phase is in contact with a strong potassium chloride solution, here saturated with silver chloride. Figure 55.7 shows the diagram of a typical Ag/AgCl reference electrode. Since this kind of reference electrode is the simplest and for many applications the most satisfactory one, it is commonly used as internal reference electrode of pH electrodes and other IESs. Besides, Ag/AgCl electrodes can be easily prepared in the laboratory. In contrast to mercury-based electrodes, the Ag/AgCl electrode does not contain toxic chemicals and is therefore recommendable for measurements in food.

The major problem with the Ag/AgCl electrode is the considerably high solubility of AgCl in concentrated potassium chloride solution. Thus, especially for the use at high temperatures, a sufficient excess of solid silver chloride must be present in the reference solution. This can be achieved, for example, through the addition of a few drops of diluted silver nitrate solution. Otherwise, silver chloride will dissolve of the electrode until saturation is reached. As a consequence, the electrode potential will drift and the lifetime of the electrode will be shortened. However, in contrast to the calomel electrode, the Ag/AgCl electrode can be used successfully up to 125 °C. Its electrode potential is very stable in the long term in pure potassium chloride solutions, but is affected by impurities like reduct reagents and species that react with the silver chloride, as with the calomel electrode. Unlike the calomel electrode, in the Ag/AgCl electrode, the concentration of the electrode coating in the bridge solution is rather high. Thus, a greater amount of reaction products (e.g., solid silver sulfide) may arise in the reference solution and block the liquid junction causing drift and instability of the electrode potential. In contrast to the calomel electrode, the silver/silver chloride electrode shows only very small thermal hysteresis effects that are usually negligible. Hence, this kind of electrode is suitable for measurements in samples with varying temperatures. Ag/AgCl electrodes are relatively insensitive to polarization. The standard potentials, including the liquid junction potentials of saturated and 3.5 M silver/silver chloride electrodes, at 25 °C are 0.1989 and 0.2046 V, respectively (Bailey 1980). As with the calomel electrode, the nomenclature of the electrodes is derived from the potassium chloride concentration of the respective reference solution.

![Schematic of a Ag/AgCl reference electrode.](image-url)
55.2 Volumetry

The basic concept of voltammetry is the measurement of the current \( i \) at a redox electrode as a function of the electrode potential \( E \) (Bard and Faulkner 2001). During the experiment, the electrode is immersed in a solution that contains an electroactive species, that is, a species that can undergo an electrode reaction (standard redox potential \( E^0 \)). The electrode potential is changed from a value \( E_1 < E^0 \) to a value \( E_2 > E^0 \) or vice versa in a manner that is predetermined by the operator. Thus, during the measurement, the electrochemical equilibrium shifts from the oxidized (reduced) form of the analyte to the reduced (oxidized) form. The resulting charge transfer across the interface electrode/solution can be observed as a current flow, which is termed faradaic.

55.2.1 Instrumentation

Voltammetric measurements are usually performed with a cell arrangement of three electrodes (Figure 55.8). The redox electrode at which the electrode processes occurs is called working electrode. Its potential is measured against a suitable reference electrode, of en Ag/AgCl or calomel. To adjust the potential difference between the working and the reference electrode to a certain value, a current is forced through the working electrode. Because the current and the electrode potential are related functionally, this current is unique. However, the current through the reference electrode must be kept as small as possible. Therefore, a third electrode called auxiliary electrode or counter electrode is usually employed to close the current circuit. It should be emphasized that there are two circuits: one in which the current flows and which contains the working and the auxiliary electrode and another, a current-free one, in which the potential difference between the working and the reference electrode is measured. Since almost no current flows through the reference electrode, its potential can be regarded as constant and the measured change in potential equals the potential change of the working electrode. The current through the working electrode, and thus its potential, can be adjusted by controlling the voltage between the working and the auxiliary electrode. The task is performed by an instrument called a potentiostat, which basically consists of a voltage source and a high-impedance feedback loop. With a function generator that may be integrated into the potentiostat, the potential time course can be predetermined. Modern potentiostats are controlled by a PC and offer the possibility to program many different potential time courses. Thus, they allow the performance of several voltammetric techniques, as are discussed later. The measured current can be displayed as a function of the electrode potential or of time using a chart strip or xy recorder or a PC.

There are two possibilities to operate an electrochemical cell: in so-called batch cells, the electrolyte solution rests stationary during the measurement, whereas in flow-through cells, it flows across the electrode. Between two measurements with different solutions, the cell must be cleaned in order to remove

![Figure 55.8](https://example.com/figure55.8.png)  
For voltammetric measurements a three-electrode arrangement is usually employed.
residues of the preceding measurement’s solution that could disturb the new measurement. The electrochemical cell is usually built of glass or Teflon because of these materials’ chemical inertness.

The chemical inertness is also important for the choice of the working electrode because the electrode must not change during the measurement. Common materials are gold, platinum, and mercury. Several kinds of carbon electrodes (e.g., glassy carbon) are also used but are often covered with gold or mercury. An advantage of the solid-state electrodes is their easy handling. They can be employed as planar or as wire electrodes. Further, with the noble metal electrodes, substances having a more positive redox potential than mercury can be investigated. However, the use of mercury electrodes has distinct advantages and the voltammetric techniques using mercury electrodes are extremely well developed. These techniques play a major role in electroanalytical methods and are summarized under the term polarography.

In polarography, mercury is used either as a thin mercury film electrode (TMFE) or as a hanging mercury drop electrode (HME). The HME can be a stationary mercury drop electrode (SMDE) or a DME. The drop is produced from a thin capillary with an inner diameter that can range from several tenths to a few hundred micrometers. The size of an SMDE is held constant during the measurement, whereas a DME constantly grows during its lifetime until it falls from the capillary due to its weight.

The main advantages of mercury drop electrodes are their good reproducibility and their high overpotential for the hydrogen evolution, that is, the fact that hydrogen evolution is inhibited and thus occurs at much higher potentials than would be expected from the standard potential. The good reproducibility is achieved because a new drop can easily and rapidly be produced from the capillary for each measurement. Hence, the contamination of the electrode with substances from a preceding measurement and from impurities in the solution is near zero. However, a drawback of HMEs is their relative mechanical instability, which can be a problem in flow-through cells, in field measurements, and if the solution is stirred.

Stirring of the solution is often applied during the measurement if the supply of reactive species at the electrode should be enhanced. However, this forced convection affects the electrode current. Moreover, the electrolyte is often stirred and bubbled with an inert gas like nitrogen or argon before voltammetric measurements are carried out to remove dissolved oxygen. It is usually necessary to reduce background currents from oxygen reduction and to prevent undesirable oxidation or precipitation of solution components. Because the electrode currents, especially in trace and ultratrace analysis, can be quite small, it is common to place the cell in a Faraday cage to shield it from electromagnetic stray fields. Coaxial cables are then used for the electric connections from the cell to the instruments.

55.2.2 Principles of Voltammetry

Actually, the electrode current measured in voltammetry is a sum of two currents that arise due to different processes. Besides the faradaic current \( i_f \), a capacitive current \( i_c \) results from changes in the double-layer charging. Although the faradaic current is a direct measure for the rate of the electrode reaction, several effects usually occur that have to be considered.

55.2.2.1 Diffusion Limitation of the Faradaic Current

The decrease of the analyte concentration at the electrode surface due to an electrode reaction must be balanced by the diffusion of species from the bulk solution. In most measurements, the consumption of reactive species is faster than the supply by diffusion, and the effect of diffusion limitation of the faradaic electrode current is observed. To understand this important point, the time-dependent concentration profile of the analyte has to be calculated using Fick’s laws. The electrode current can then be derived as a function of time. According to Fick’s first law, the flux \( j \) of the analyte at the point \( r \) and at the time \( t \) is proportional to the gradient of the analyte concentration \( c \):

\[
j(r, t) = -D \nabla c(r, t)
\]  

(55.23)
The proportionality factor $D$ is called the diffusion coefficient. At the electrode surface, the flux must be equal to the number of moles $N$ converted per unit of time and surface area by the electrode reaction:

$$ j(0, t) = \frac{dN}{dt} $$  \hspace{1cm} (55.24)

The faradaic current $i_f$ is related to $dN/dt$ according to

$$ i_f = nFAD\frac{dN}{dt} $$  \hspace{1cm} (55.25)

where

- $n$ is the number of electrons involved in the reaction of a single analyte particle
- $F$ is the Faraday constant and
- $A$ is the surface area of the working electrode.

The Nernst diffusion layer model assumes that within a layer of thickness $\delta$, the analyte concentration depends linearly on the distance from the electrode surface until it reaches the bulk concentration $c_0$. For simplicity, the diffusion problem is often considered to be 1D as it is the case for a planar working electrode in a cylindrical cell. The combination of Equations 55.23 through 55.25 then gives

$$ i_f = nFAD\left(\frac{(c_0 - c_e)}{\delta}\right) $$  \hspace{1cm} (55.26)

where $c_e$ is the concentration at the electrode surface. For a sufficiently large difference between the applied potential and the standard potential of the analyte's redox couple, all species reaching the electrode surface by diffusion are immediately converted, and the faradaic current reaches a maximum. In this case, the analyte concentration $c_e$ at the electrode surface can be regarded as zero.

The diffusion profile and thus the dependence of $\delta$ from time can be obtained by solving the differential equation that is known as Fick's second law:

$$ \frac{\partial c(r, t)}{\partial t} = D\nabla^2 c(r, t) $$  \hspace{1cm} (55.27)

where $\nabla^2$ is the Laplacian operator. For linear diffusion—that is, 1D diffusion as it was considered in Equation 55.26—the solution of Equation 55.27 with the appropriate boundary conditions ($c_e(t = 0) = c_0$; $c_e(t > 0) = 0$; $c(x > \delta = c_0)$) yields

$$ \delta = \sqrt{\pi Dr} $$  \hspace{1cm} (55.28)

Combination with Equation 55.26 leads to the Cottrell equation:

$$ i_f(t) = nFAc_0\sqrt{\frac{D}{\pi t}} $$  \hspace{1cm} (55.29)

After reaching a maximum value, the current decreases with $t^{-3/2}$ and is proportional to $c_0$, whereas the diffusion layer thickness increases with $t^{1/2}$ (Figure 55.9).

For a spherical electrode of radius $r_0$, as it is the case for HIMDES, one has to change to spherical coordinates and Fick's second law becomes

$$ \frac{dc(r, t)}{dt} = D \left[ \frac{d^2 c(r, t)}{dr^2} + \frac{1}{r} \frac{dc(r, t)}{dr} \right] $$  \hspace{1cm} (55.30)
Electrochemical Composition Measurement

**FIGURE 55.9** At a planar electrode, the diffusion layer thickness increases with $t^{1/2}$ (a), whereas the diffusion-limited current decreases with $t^{-1/2}$ (b).

where $r > r_0$ is the radial distance from the electrode center. The solution of Equation 55.30 with the appropriate boundary conditions $c(r, 0) = c_0, \lim_{r \to \infty} c(r, t) = c_0, c(r_0, t > 0) = 0$ yields the current–time relation

$$i_z(t) = nFADc_0 \left[ \frac{1}{(\pi Dt)^{1/2}} + \frac{1}{r_0} \right]$$  \hspace{1cm} (55.31)

The first term in brackets equals that for the linear case; the second, constant term reflects the fact that the surface of the spherical diffusion layer grows and thus can draw an increasing number of reactive species.

The situation is even more complicated for DMEs because in addition to the surface of the diffusion layer, the surface and the radius of the drop are growing during the drop's lifetime. At any time, the growing electrode surface forces the depletion layer to stretch over a still larger sphere, which makes the layer thinner than it otherwise would be. A rigorous mathematical approach to this is rather difficult because the relative convective movement between the solution and the electrode during drop growth must be considered (Bard and Faulkner 2001). However, a simplified approach that is valid when the second term in Equation 55.31 is negligible and the diffusion problem can be regarded as linear yields the Ilkovic equation

$$i_z(t) = 708nDcm^{2/3}t^{1/6}$$  \hspace{1cm} (55.32)
At a DME the measurement is performed during a time interval $\Delta t_m$ at the end of the drop’s lifetime when the ratio $i/I_c$ is very large.

where $m$ is the mercury flow rate (mass/time) from the capillary. Consequently, the current increases during the lifetime $t_d$ of the drop (drop time), whereas it decreases with time in the other arrangements that have been described. Figure 55.10 depicts this current–time relation of a DME with the characteristic current plateau at the end of the drop’s lifetime.

In the considerations that have been made previously, analyte transport by convection and migration in the electric field have been neglected. Convection can be regarded as absent if the solution is unstirred and if the working electrode rests motionless. However, in longer-lasting measurements, convective mass transport can play a role due to arising inhomogeneities in the density of the solution. Furthermore, if a DME is employed, the growth of the drop may cause a considerable convection of the solution. When the drop falls off, it stirs the surrounding solution and the depletion effect almost vanishes. Consequently, every drop is born in an almost homogeneous environment. The migration of electrically charged analyte particles due to the electric field in the solution can easily be suppressed using an inert supporting electrolyte with a concentration that is much larger than the analyte concentration. Since all charged species contribute to the migration current, the migration of the analyte species can then be neglected.

### 55.2.2.2 Double-Layer Charging Current

A process that affects all kinds of voltammetric measurements is the flow of capacitive current. The accumulation of charge on one side of the electrode/solution interface causes the necessity of a mirror charge on the other side. Hence, a change of the electrode potential (i.e., in the electrode charging) causes a corresponding flux of charged particles between the double layer and the bulk solution. Therefore, the interface has a certain capacitance that is called the double-layer capacitance. The resulting double-layer charging current $i_d$ is superimposed on the faradaic current and can perturb its measurement. In analytical techniques, one is often concerned with the reduction of the capacitive/faradaic current ratio. However, the actual measurement of the double-layer capacitance is demanding and requires the technique of impedance spectroscopy, as described, for example, in Gileadi (1993) and Bard and Faulkner (2001).

### 55.2.2.3 Irreversible Electrode Processes

Another assumption that has been made implicitly is that the rate of the electrode reaction is very fast in comparison to the supply of analyte by diffusion (reversible electrode process). Under this condition, all analyte species reaching the electrode are immediately converted. However, if the reaction rate is too slow, the consumption of reactive species is compensated by the diffusion of the analyte (irreversible electrode process), and thus, the concentration at the electrode surface never drops to zero. The electrode current is then determined by the reaction rate, and the previous calculations do not hold. In practice,
the situation is sometimes complicated if so-called quasi-reversible electrode processes with intermediate reaction rates occur. Although this concept of electrochemical reversibility is a simplification, it is a suitable working basis and can be summarized in the following statement: in a given electrochemical experiment, an electrode process that follows the Nernst equation at any time is called reversible.

55.2.2.4 Influence of Adsorption, Catalysts, and Chemical Reactions

Besides the diffusion and reaction rate, some other processes can influence the electrode current. Adsorption of the analyte or its reaction product on the electrode changes the double-layer capacitance or can passivate the electrode surface and thus lower the current. Moreover, if a species serves as a catalyst, it may shift the equilibrium potential. In the case that the catalyst returns the product of the electrode reaction back into the initial form of the analyte, the analyte concentration at the electrode surface will always be large and thus increases the limiting current and shifts the equilibrium. All these catalytic currents are subject to analytical studies. Besides adsorption and catalysis, complicated scenarios occur if the electrode reaction is followed by a chemical reaction whose product itself undergoes an electrode reaction within the observed potential range.

55.2.3 Techniques

These several voltammetric (i.e., potential-controlled) techniques differ just in the manner in which the electrode potential is varied with time. The potential can be changed in distinct steps, in a continuous sweep, or it can be pulsed or superimposed with an ac signal. In addition, the rate of potential change can be varied. The characteristics, advantages, and drawbacks of the most important techniques will be discussed in the following sections. Special attention will be given to polarography due to its practical importance in electroanalysis. Besides, the emphasis will be on reversible electrode processes because only they allow the realization of analytical investigations, on which this chapter is focused.

55.2.3.1 Amperometry

If in a potential step experiment the working electrode potential is abruptly changed from a constant value \( E_1 \) where faradaic processes do not occur to another constant value \( E_2 \) where the electrochemical equilibrium is on the side of the oxidized or reduced form of the analyte, then a faradaic current begins to flow (Figure 55.11a). In the case that the difference between the applied potential and the standard potential \( E^0 \) of the analyte's redox couple is sufficiently large, the effect of diffusion limitation sets in and a further increase of the potential difference yields no increase in the electrode current. The current is then called limiting current. The current-time relationship follows the Cottrell equation (Equation 55.29), with the current decreasing while the diffusion layer thickness increases.

If the diffusion layer thickness could be held constant, then from Equation 55.26, it follows that the current would not decrease with time but remain at a constant value. This can be accomplished if the solution is stirred or flows across the electrode in a proper way. According to Equation 55.26 (with \( c_a = 0 \), the current then is proportional to the analyte concentration in the solution.

The described method corresponds to the electroanalytical technique called amperometry (Oehme 1991), with the exception that in this the potential step is omitted and the electrode current is measured at a fixed potential \( E \) at which the analyte undergoes an electrode reaction and the faradaic current is in the limited region. The solution usually crosses the electrode in a laminar flow, keeping the diffusion layer thickness constant.

Because the electrode current is proportional to the concentration of the analyte, only two measurements are needed for calibration. The basic current is measured in an analyte-free solution, and a second measurement is performed at a known analyte concentration. It should be mentioned that amperometry cannot only be used to determine liquid and ionic components of a solution but also to measure the amount of dissolved gas in a liquid. Moreover, with modified electrochemical cells, even gas analysis can be accomplished.
The main disadvantage of amperometry is its poor selectivity. Given a certain analyte and operating at a higher potential than the corresponding standard potential $E^0$, all components of the solution with a standard potential smaller than $E$ also contribute to the faradaic current. Operating at a potential $E < E^0$, the same problem occurs if substances with a standard potential larger than $E$ are present in the solution. For this reason, amperometry is preferably carried out in solutions containing only one electroactive substance or, if possible, at a potential at which only one substance is involved in an electrode reaction. If this is impossible, the selectivity can often be enhanced by covering the working electrode with a membrane that, in comparison to the diffusion rate of the analyte through the membrane, is virtually impermeable for the interfering substances.

In addition to analytical purposes, amperometric methods can also be used to investigate reaction constants of chemical reactions. In reversed potential step techniques, the first potential step is followed by a second one in the opposite direction, of en back to the initial value. The reaction product $B$ of the first step is then reconverted into the original analyte $A$. However, if the first electrode reaction is followed by an additional chemical reaction, a certain part of $B$ is converted into a product $C$ before the reversed step is applied. Therefore, the current during the reversed step is reduced. The ratio of the electrode currents during the forward and reversed steps depends on the reaction constant of the chemical reaction. Because the reconversion of $B$ into $A$ is required, batch arrangements without convection of the electrolyte are used for reversed step methods. Otherwise, a large part of $B$ would be flushed away from the electrode surface and could not be reconverted.

### 55.2.3.2 Amperometric Titration

In amperometric titration techniques (Willard et al. 1988; Settle et al. 2011), a titrant that reacts with the analyte is added to the analyte solution. During the titration, the limiting current is measured
as a function of the volume of titrant added. The titrant has to be chosen such that the reaction product is not reducible or oxidizable at the applied potential and, hence, does not contribute to the current.

If the analyte and the titrant are electroactive at the applied potential, then the current flow will be large at the beginning of the measurement and decreases linearly with the volume of the titrant added, because both, the analyte and the titrant, are consumed by the reaction. The concentration of electroactive species then diminishes until the analyte is totally consumed. Further addition of titrant leads to a linearly increasing current because the titrant is no longer consumed. In the plot of the current versus the volume of titrant added, the point where the slope changes is called endpoint of the titration. From the corresponding amount of titrant added and the stoichiometry of the reaction, the original volume of analyte can be computed. If only the analyte is electroactive, then from the endpoint the current will not increase but remain zero. If only the titrant undergoes an electrode reaction, the current will be zero until all analyte is consumed and then will linearly increase from the endpoint. In practical operation, the slope of the current does not change abruptly due to background currents, and the endpoint has to be determined by extrapolation of the two linear regions.

In contrast to the majority of other electrochemical techniques, amperometric titration offers the advantage that even analytes that are not reducible or oxidizable can be determined using the oxidation-reduction characteristics of the titrant. Moreover, it is possible to analyze systems that have no measurable standard potential but can be electrolyzed.

55.2.3.3 Sampled-Current Voltammetry

Consider a potential step experiment like the one in the section next to the previous one. If the potential difference between \( E_2 \) and \( E^0 \) is too small, the electrode reaction is not so efficient that the analyte concentration at the electrode surface becomes zero (i.e., \( c_e > 0 \) in Equation 55.26). Within this region, the current depends on the applied potential. However, even in this situation, a depletion effect occurs so that the current always decreases with time. Recording the current \( i \) for different values of \( E_2 \) at a fixed time \( t \) after switching the potential (sampled-current voltammetry), a sigmoidal (wave-shaped) curve is obtained (Figure 55.11b).

The shape of this curve can also be calculated by exactly solving the diffusion problem. A wave rising from a baseline to the diffusion-limited current \( i_d \) is obtained. The diffusion coefficients of the analyte and its redox partner are nearly equal to the half-wave potential \( E_{1/2} \), where \( i = i_d/2 \) is almost identical with the standard potential \( E^0 \). Therefore, \( E_{1/2} \) is often used in qualitative analysis to determine the analyte. Quantitative information about the analyte concentration is obtained from the maximum current (Cottrell current), which according to Equation 55.29 is proportional to \( c_0 \).

The influence of the double-layer charging current has been neglected thus far, but is worth considering. It obeys the equation:

\[
i_c = \frac{\Delta E}{R_s} \exp \left( \frac{-t}{(R_s C_{dl})} \right)
\]  (55.33)

where

- \( \Delta E \) is the potential step width
- \( R_s \) the solution resistance
- \( C_{dl} \) is the double-layer capacitance

Although the measurement of \( R_s \) and \( C_{dl} \) is not trivial, one can obtain qualitative information from this formula. Comparison of Equations 55.33 and 55.29 yields that the capacitive current decreases exponentially, while the faradaic current decreases according to \( t^{-1/2} \). Consequently, the electrode current is measured a sufficiently long time after the potential step when the capacitive current has largely decayed,
whereas the faradaic current is still significant. In polarography with DM Es, the growth of the electrode surface alters the temporal decrease of the double-layer charging current according to

\[ i_c \sim m^{2/3} t^{-1/3} \]  

(55.34)

whereas the faradaic current increases according to \( t^{1/6} \) (Equation 55.32). The current is measured shortly before the drop falls of (Figure 55.10).

The lower detection limit (LDL) amounts to \( 10^{-6}-10^{-4} \) mol L \(^{-1} \) for the determination of organic and inorganic analytes. The half-wave potential of different substances should be at least 100 mV apart for a simultaneous determination.

### 55.2.3.4 Linear Sweep and Cyclic Voltammetry

In **linear sweep voltammetry** (LSV), the electrode potential is changed continuously from an initial to a final value at a constant rate \( v = dE/dt \), such that \( E(t) = E_i + vt \). Starting at a potential \( E_i \) where no faradaic process occurs, a current begins to flow when the electrode potential comes into the vicinity of \( E^0 \). The current rises to a maximum and then decreases due to the depletion effect (Figure 55.12). The solution of the diffusion equations, which yields the shape of the \( i-E \) wave, can only be found numerically. For the electrode process to always follow the Nernst equation and thus be reversible, the sweep rate must not be too high (e.g., \( v < 100 \) mV s \(^{-1} \)). The peak potential \( E_p \) can then be calculated to be

\[ E_p = E_{i/2} \pm 1.1 \left( \frac{RT}{nF} \right) = E_{i/2} \pm \left( \frac{28.0}{n} \right) \text{ mV (at 25 °C)} \]  

(55.35)

![Graph showing potential and current over time](image)

**FIGURE 55.12** In LSV the potential varies linearly with time (a). The current-potential relation yields a peak-shaped curve with a half-wave potential \( E_{i/2} = E^0 \) (b). The peak current is proportional to the analyte's bulk concentration \( c_0 \).
The positive sign in Equation 55.35 applies to an anodic sweep (from negative to positive potential with \( \nu > 0 \)) and the negative sign to a cathodic one (from positive to negative potentials with \( \nu < 0 \)). The peak current is given by

\[
i_p = 0.446nFA\left(\frac{nF}{RT}\right)^{1/2}D^{1/2}c_0\nu^{1/2}
\]  

(55.36)

Thus, the peak current is proportional to the bulk concentration \( c_0 \) of the analyte and depends on the sweep rate according to \( \nu^{1/2} \).

Another contribution to the measured current is the capacitive double-layer-charging current \( i_c \), which always flows in LSV due to the continuous change of potential. It can be calculated using the following equation:

\[
i_c = C\left(\frac{dE}{dt}\right) = CV
\]  

(55.37)

which yields a proportionality to \( \nu \) while the faradaic peak current is proportional to \( \nu^{1/2} \). Thus, for the faradaic current to dominate the measurement, the sweep rate should not be chosen too large. A sweep rate of 100 mV s\(^{-1}\) can be regarded as an upper limit. Moreover, the surface area of the working electrode must be taken into consideration. Rough electrodes have a much larger active than geometric surface area and thus a very large capacitance. Therefore, small, very smooth electrodes should be chosen.

A variation of LSV is a technique called cyclic voltammetry (CV). Here, the electrode potential is swept forth and back between two potentials \( E_1 \) and \( E_2 \) (Figure 55.13a). Although the bulk concentration of the reaction product is essentially zero, its concentration at the electrode surface after the first sweep is quite large. In the backward sweep, the reaction product of the analyte is converted into the analyte again. The current flows in the opposite direction and using an \( x-y \) recorder, an \( i-E \) curve is obtained (Figure 55.13b). From Equation 55.35, it follows that for reversible processes, the peak potentials of the forward and backward sweep have a distance of \( (56/n) \) mV at room temperature. Therefore, CV is a favorable method for the investigation of the reversibility of a system. If the electrode current totally decays in the forward sweep, the analyte concentration has dropped to zero and the product concentration at the electrode surface is about \( c_p \). Ideally, the peak current during the reverse scan should be equal (with reversed sign) to the peak current of the forward sweep.

**FIGURE 55.13** In CV, the potential is swept forth and back between two fixed values (a). The current-potential relation yields a peak-shaped curve with a half-wave potential \( E_{1/2} \approx E^0 \) (b). The peak current is proportional to the analyte's bulk concentration \( c_p \). For totally reversible systems, the peak currents of the forward and the backward sweep are equal in magnitude but of opposite sign.
Although the theory of LSV and CV measurements is very promising, the methods have several practical limitations. One is the frequently insufficient stability of the \( i-E \) characteristic during the first cycles in CV. However, after 5–10 cycles, it tends to become highly reproducible. Yet, one must be careful deriving quantitative information from these later cycles because the initial and boundary conditions of the diffusion problem have changed and convective mass transport may already play a role. Thus, the equations developed for LSV cannot be used. Another problem that concerns both LSV and CV is the potential drop that occurs in the solution between the working and the reference electrode and that leads to a distortion of the shape of the \( i-E \) wave. The error increases with increasing current flow. Thus, the rate of change \( v \) of the electrode potential is not really constant, as has been assumed in the boundary conditions for solving the diffusion equations. Furthermore, the quantitative information is usually obtained from the position \( E_p \) and the height \( i_p \) of the current peak where the error is maximum. Finally, the determination of the peak height itself is sometimes problematic due to difficulties in the extrapolation of the baseline. For all these reasons, it may be advisable to verify the results of quantitative analysis with additional methods. Nevertheless, on easy terms, the LDL of LSV and CV in quantitative analysis can amount to \( 10^{-2} \) mol L\(^{-1} \) with a resolution of about 50 mV.

Besides the analysis of faradaic processes, LSV and CV are favorable techniques for the investigation of the adsorption of species on the electrode surface (Bard and Faulkner 2001). In such adsorption processes, the current is called \textit{pseudocapacitive current}. Although it is a charge transfer across the interface, it exhibits many of the properties of a pure capacitive current. The current–potential wave has a very similar shape as for faradaic processes. If \( \Theta \) denotes the coverage \( (0 \leq \Theta \leq 1) \) and \( q_1 \), the charge that is required to form a monolayer of a species, the pseudocapacitive current \( i_a \) can be expressed as

\[
i_a = q_1 \left( \frac{d\Theta}{dt} \right) = q_1 \left( \frac{d\Theta}{dE} \right) \left( \frac{dE}{dt} \right) = C_a \nu
\]

(55.38)

where \( C_a \) is called the \textit{adsorption pseudocapacitance}. The calculation of \( C_a \) yields the pseudocapacitance does not depend on \( v \). Therefore, at any potential the current is proportional to the sweep rate \( (i \sim v) \). The peak potential gives information about the adsorption kinetics. In contrast to faradaic CV, it has the same value for the forward and the backward sweep.

### 55.2.3.5 Pulse Techniques

Voltammetric pulse techniques are derived from potential step experiments to suppress the capacitive currents during the measurement. A potential step that can vary in amplitude and sign is periodically repeated and superimposed with a potential ramp. The current is measured at the end of the step when the double-layer charging current has largely decayed.

**Normal Pulse Voltammetry:** In normal pulse techniques, periodic voltage pulses with an increasing amplitude from pulse to pulse are superimposed on a constant potential. Typical pulse duration is about 50 ms and the current is measured during a time interval \( \Delta t_m \) of about 10–15 ms at the end of each pulse. Between two pulses there is a waiting period of a few seconds (Figure 55.14). In polarography with a DM, each drop is dislodged directly after the pulse and thus used for just one measurement.

Because normal pulse voltammetry equals a series of potential step measurements with increasing step widths, the current obeys to Equation 55.29 and the evaluation of the measured current values can be carried out using the sampled-current method. In comparison with the step technique, the LDL is enhanced for one to two orders of magnitude up to \( 10^{-6} \) and \( 10^{-7} \) mol L\(^{-1} \) (Henze 2008). The peak resolution is about 100 mV.

**Square-Wave Voltammetry:** In square-wave techniques, a periodic rectangular voltage is superimposed on a linearly rising potential ramp. The measuring interval lies at the end of a pulse when the capacitive current can be neglected (Figure 55.15a). Typical pulses have frequencies between 200 and 250 Hz and an amplitude of \( \Delta E_p = 5–30 \) mV (Henze 2008). The capacitive current is suppressed even more effectively if the pulse is tilted to decrease during the pulse period. No pulse tilt is required.
FIGURE 55.14 Normal pulse voltammetry equals a series of potential step measurements with increasing step widths. The current is measured during a time interval $t_m$ near the end of the pulse. In polarography with a DME, the drop is dislodged after each measurement. The drop's lifetime is denoted by $t_d$.

FIGURE 55.15 In square-wave voltammetry, a periodic rectangular voltage pulse is superimposed on (a) a linearly changing potential ramp (dotted line) or (b) on a stepped ramp (dashed curve). The current is measured during a time interval $\Delta t_m$ at the end of each pulse.

If the potential ramp is stepped (staircase ramp) instead of a linear ramp, the voltage pulse is then applied on the plateau of the stepped ramp (Figure 55.15b).

After rectification of the measured current values, one obtains peak-shaped $i-E$ curves. The peak potential corresponds to the half-wave potential of LSV and, thus, to the standard potential of the analyte's redox couple. The peak current $i_p$ depends on the frequency and amplitude $\Delta E$ of the voltage pulses and obeys

$$i_p \sim n^2 D \Delta E c_0$$  \hspace{1cm} (55.39)

where the frequency dependence is included in the proportionality constant. The LDL is in the range of $10^{-8}$ mol L$^{-1}$ and the peak resolution amounts to 40–50 mV.
FIGURE 55.16 In differential pulse voltammetry, periodic rectangular pulses are superimposed on a stepped potential ramp. The difference between the current measured in a time interval $\Delta t_m$ directly before each pulse and during a time interval $\Delta t_m$ at the end of each pulse is plotted against the base potential. In polarography with a DME, the drop is dislodged after each pulse. The drop’s lifetime is denoted by $t_d$.

Shorter analysis times are achieved if very short and relatively large rectangular pulses with a duration $t_p = 5$–10 ms and an amplitude of $\Delta E = 50$ mV are superimposed on a stepped potential ramp with the same duration but smaller potential steps of about 10 mV. The potential can then be scanned at extremely high rates of up to 1200 mV s$^{-1}$. However, the sensitivity decreases because the ratio of faradaic to capacitive currents is lowered by the short pulse times.

Differential Pulse Voltammetry: Differential pulse methods are the most important ones in analytical voltammetry. Periodically repeated rectangular voltage pulses with a constant amplitude $\Delta E$ of several 10 mV are superimposed on a stepped potential ramp (Figure 55.16). The pulse duration $\Delta t_p$ is about 5–100 ms (Henze 2008). Between two pulses, the potential is held constant for a few seconds. The current is measured in a short time interval ($\Delta t_m \approx 1$–20 ms) directly before a pulse is applied and for the same duration near the pulse end. If a DME is used, the drop is knocked off mechanically between two pulses and each drop serves for just one measurement.

For the evaluation, the difference between the two measured current values $\Delta i$ that corresponds to one pulse is recorded as a function of the base potential. A peak-shaped curve is obtained with a maximum very close to the half-wave potential $E_{1/2}$. The peak height is proportional to the analyte concentration in the bulk:

$$\Delta i_p \sim nFA \left( \frac{D}{\pi t_p} \right)^{1/2} c_0$$ (55.40)

With differential pulse measurements, a LDL of $10^{-8}$ mol L$^{-1}$ and a resolution of 50–100 mV can be achieved.

55.2.3.6 Alternating Current Voltammetry

Alternating current techniques are similar to differential pulse methods. A linear potential ramp is modulated with a low-frequency ($f \sim 50$ Hz) sinusoidal alternating voltage of small amplitude ($\Delta E \sim 50$ mV) (Henze 2008). The amplitude of the resulting alternating current is plotted against
the base potential. A peak-shaped curve is obtained with a maximum that is proportional to the bulk concentration of the analyte:

\[ i_p \sim \Delta F j^{1/2} c_0 \]  

(55.41)

The LDL is 10^{-5} mol L^{-1} due to the large capacitive currents. It can be enhanced by phase-selective rectification because the capacitive and the faradaic currents have a phase shift of 90° and 45°, respectively. The peak resolution amounts to 50–100 mV.

### 55.2.3.7 Stripping Voltammetry

**Stripping techniques** can be performed with analytes whose reaction products adsorb on the electrode surface. For accumulation, the electrode potential is held at a value at which the electrochemical equilibrium is on the product’s side. Accumulation times usually amount up to several minutes. During this period, the solution is stirred to prevent the depletion of the analyte at the electrode surface. The accumulation is followed by a rest period of 2–30 s, during which the solution remains unstirred and the current falls to a small residual value. In the subsequent *stripping step*, the electrode potential is shifted to a value at which the adsorbed product is reconverted into the analyte by oxidation or reduction. Depending on whether an oxidation or reduction process occurs, the method is called *anodic stripping voltammetry* (ASV) or *cathodic stripping voltammetry* (CSV), respectively. The stripping step can be performed in various manners (Wang 1998) of which the linear sweep method shall be exemplary discussed here. It yields a peak-shaped \( i-E \) curve with a maximum at

\[ E_p = E_{u/2} - \frac{1.1 RT}{nF} \]  

(55.42)

and a peak height that is proportional to the bulk analyte concentration according to

\[ i_p \sim n^{3/2} v^{1/2} c_0 \]  

(55.43)

Different potentials can be determined in successive experiments with an adequate choice of the accumulation potentials. For the first measurement, the accumulation potential is chosen to allow adsorption of only one species; in the next experiment, the first and one further analyte adsorb, and so on. For the simultaneous determination of two or more substances, their peak potentials should be at least 150 mV apart.

A special case of the stripping techniques is *adsorptive stripping voltammetry* (AdSV). Here, the analyte is deposited in the form of metal chelates or organic molecules. For the formation of metal chelates, a complexing agent is added to the electrolyte or the surface of a solid-state electrode is modified with it. The stripping current is then due to the oxidation or reduction of the central atom or the ligand of the metal chelate complex. With this method, organic and organometallic compounds can be determined in the ultratrace range.

A crucial point in stripping analysis is the reproducibility. All experimental parameters have to be selected very carefully. In particular, the electrode surface must not be changed significantly by the adsorption and dissolution processes. Therefore, HgDEs are frequently employed for stripping analysis. A new drop is produced for each measurement. Another advantage of mercury electrodes is the fact that not only their surface but rather the hole bulk is used for the accumulation of analyte species. Consequently, more material can be collected. This leads to an enhanced lower determination limit that can be below 10^{-8} mol L^{-1}. Comprehensive monographs about stripping techniques are given in Brainina et al. (1993) and Wang (1998).
55.2.4 Applications

Analytical applications of voltammetry concern the determination of (heavy) metal cations, typical anions (halides, pseudohalides), organometallic, and organic compounds in the $10^{-4}$–$10^{-9}$ mol L$^{-1}$ concentration range. Therefore, they are established in several fields like environmental, medical, food, and water analysis. A disadvantage is the usually labor-intensive sample preparation necessary, for example, to disintegrate ions from complexes, to adjust the pH of the solution, or to remove interfering species like oxygen and organic molecules. Principally, the preparation of the electrode (surface) is also crucial. However, commercially available equipment is well developed not only to enhance determination limits, sensitivity, selectivity, and reproducibility but also to reduce the expense for electrode and cell preparation. Moreover, sample and electrode preparation can be automated to a certain degree by devices that perform different solutions for cleaning, conditioning, and analysis through the cell setup. A further improvement of the instrumentation is the use of microelectrodes with dimensions of 1–100 μm. Because their dimensions are small in comparison with the diffusion length of the analyte, even for planar microelectrodes the diffusion is rather hemispherical than linear. Therefore, the depletion effect is less strong and the faradaic current is increased. Moreover, planar microelectrodes can be rotated (rotating disk electrode (RDE)) to intensify convection, and the solution can be stirred with ultrasound. Another advantage of microelectrodes is the possibility to realize several electrodes in a close neighborhood, so-called electrode arrays. They serve as one electrode if they are held at one potential and exhibit an improved signal-to-noise ratio due to the better diffusion conditions. In contrast, if different potentials are applied at different electrodes, the simultaneous determination of different species is possible. These techniques have just become commercially available as electrochemical detectors, for example, for high-performance liquid chromatography (HPLC). In this arrangement, the different species in the solution are separated by the HPLC and flow through the detector cell one after the other. Thus, interference between different analytes is minimized. The selectivity can be further improved by the use of membrane-covered microelectrodes. The well-known Clark oxygen sensor and different biochemical sensors represent promising examples of this application in amperometry. Moreover, it opens up new possibilities for the creation of microelectrode arrays.

Due to the high analytical potential and the relatively low costs of voltammetric methods in comparison with spectroscopic techniques, all aspects of voltammetry are still subject of intense research. Current efforts concern the miniaturization of the whole cell, including microchannels, microvalves, micropumps, and microelectrodes by means of precision mechanics and micromachining techniques (Mastrangelo and Tang 1994). They employ fabrication methods of silicon planar technology and Lithographie, Galvanformung, Abformung (LIGA) technique. In-film techniques, like physical and chemical vapor deposition (PVD, CVD), allow the fabrication of electrodes with a thickness in the submicrometer range and with lateral dimensions from the micrometer to the nanometer range. One goal is the realization of a microsystem with the sensitive components (i.e., the electrodes) and microelectronics integrated on a single chip. Currently, there are several commercially available systems. Two companies dominate the market of microelectrode arrays: Multichannel Systems (Reutlingen, Germany) and Panasonic (Tokyo, Japan). Modern microelectrode systems comprise the microelectrode arrays, electronic circuits, and computer software for signal amplification and processing, respectively (Ryynänen et al. 2011).

55.3 Potentiometry

Potentiometry implies the measurement of an electrode potential in a system in which the electrode and the solution are in electrochemical equilibrium. Thus, the potential becomes the dependent variable, for example, as a function of time. In potentiometry, the current is attempted to be kept as small as possible; ideally, it should be zero. Potentiometry implies known fluxes (i.e., concentration gradients at the electrode surface) and thus information on the composition of the sample. In this section, potentiometry is
related to the measurement of potentials, where the voltage source is a form of a galvanic cell, consisting of a measuring electrode and a reference electrode (in general, electrodes of the second kind). The principles of direct potentiometric measurements as well as potentiometric titrations will be described.

55.3.1 Ion-Selective Electrodes

The equipment required for potentiometric analysis includes a measuring electrode, also called an ISE or indicator electrode, and a reference electrode. In addition to the sensitivity, the most important characteristic of the ISE is given by its selectivity. Depending on the type of membrane, ISEs can be classified into four different groups: glass electrodes, solid-state electrodes, liquid-membrane electrodes, and miscellaneous combined electrodes (Pungor 1998; Koryta and Stulik 2009). For all ISEs, the validity of the Nernst equation could be proved.

55.3.1.1 Glass Electrodes

The most common glass electrode is the pH electrode, widely used for hydrogen ion determination. The pH-glass electrode consists of a thin, pH-sensitive glass membrane sealed to the bottom of an ordinary glass tube. The tube is filled with a solution of hydrochloric acid (e.g., 0.1 M HCl) that is saturated with silver chloride. A silver wire, connected to an external potential-measuring device, is immersed in this solution. Note that the internal HCl concentration is constant and, thus, the internal potential (inner surface of glass membrane) of the pH electrode is fixed. Only the potential that occurs between the outer surface of the glass bulb and the test solution responds to pH changes. To measure the hydrogen ion concentration of the test solution, the glass electrode (indicator electrode) must be combined with an external reference electrode, which is required for all kinds of ISE determination. Often, pH-glass electrodes are available as a combination of the indicator electrode and an internal reference electrode (e.g., Ag/AgCl in saturated KCl solution) as schematically shown in Figure 55.17.

The composition of the glass membrane clearly influences the sensitivity of the pH electrode. Usually, three-component systems of, for example, SiO₂/Na₂O/CaO, are employed (Covington 1979). The pH
dependence can be expressed by the Nernst equation (Equation 55.11). At room temperature \( T = 25^\circ C \), Equation 55.11 can be simplified by

\[
E = E^0 + 59.1 \text{ mV pH}
\]  
(55.44)

where \( E^0 \) is the standard Galvani potential with respect to the SHE. Ususally, the measured potential is a linear function of pH within an extremely wide range (10–14 decades). The selective pH response of the pH ISE is due to the ion exchange process, in particular, due to the replacement of sodium ions in the glass membrane \((m)\) by protons in the solution \((s)\), and vice versa:

\[
H^+_{(s)} + Na^+_{(m)} \leftrightarrow H^+_{(m)} + Na^+_{(s)}
\]  
(55.45)

The sodium ion exchange is also responsible for the alkaline error of pH electrodes in solution with pH greater than 10. In spite of the high resistance of the glass membrane against chemical attack, one has to deal with deviations (alkaline error) from the linear pH dependence. This error (i.e., the sensitivity toward alkali-metal ions) can be greatly reduced if Na\(_2\)O is replaced by Li\(_2\)O. Because pH-glass electrodes can be used in the presence of substances that interfere with other electrodes (e.g., proteins, oxidants, reductants, and viscous media), they have a wide range of applications. Typical fields are the clinical and food analysis, environmental monitoring (e.g., industrial waste, acidity of rain), and process control (e.g., fermentation, boiler water, galvanization, and precipitation).

The employment of glass membranes prepared with different glass compositions allows an electrode response sensitive to cations. For example, sodium-, potassium-, and ammonium-selective glasses consist of a mixture of Na\(_2\)O, Al\(_2\)O\(_3\), and SiO\(_2\) in various proportions (aluminosilicate glasses). Using specific compositions and mixtures of chalcogenides, ion-selective chalcogenide glass electrodes with sensitivities toward monovalent ions (e.g., Ag\(^+\), Tl\(^+\), F\(^-\), Cl\(^-\), Br\(^-\), I\(^-\)) and double-charged species (e.g., Cu\(^{2+}\), Pb\(^{2+}\), Cd\(^{2+}\), Hg\(^{2+}\), S\(^{2-}\)) can be prepared (Vlasov et al. 1994). However, in all cases, some sensitivity to charged species (e.g., H\(^+\) ions) remains. The electrode potential under these conditions is described by the Nikolsky-Eisenman equation:

\[
E = E^0 \pm \frac{RT}{zF} \ln(a_i/K_{ij})
\]  
(55.46)

where

- \( a_i \) and \( a_j \) are the ionic charge and activity of the primary or determined \((i)\) and the interfering \((j)\) ion.
- \( K_{ij} \) is the selectivity coefficient.

It is a measure of the ISE ability to discriminate against the interfering ion. A small value of \( K_{ij} \) indicates an ISE with a poor selectivity.

### 55.3.1.2 Solid-State Electrodes

The glass membrane of an ISE can be replaced by a single or a mixed crystal or a polycrystalline (pressed) pellet (Figure 55.18a). With respect to their membrane composition, solid-state electrodes are divided into homogeneous and heterogeneous membrane electrodes.

A typical single-crystal electrode (homogeneous membrane electrode) is the fluoride-sensitive ISE, which contains a LaF\(_3\) crystal doped with Eu\(^{2+}\). The crystal with a thickness of about 2 mm is sealed into the bottom of a plastic tube. The internal solution (0.1 M of NaF and NaCl) controls the potential at the crystal inner side by means of an Ag/AgCl wire as reference electrode. In contact with the test solution at the crystal outer side, an electrochemical equilibrium is established, proportional to the fluoride ion activity. This is due to an ion exchange process at the phase boundary membrane/electrolyte. In particular, fluoride ions from the membrane are replaced by fluoride ions from the solution and vice versa, where the fluoride ions can migrate from one lattice defect to another inside the crystalline membrane.
Further homogeneous membrane electrodes are silver halide electrodes, where the respective silver halide (AgCl, AgI, AgBr, Ag₂S) is pressed into a pellet, placed in a tube, and contacted via a silver wire. In these substances, silver ions are accordingly able to migrate. Such electrodes have been successfully used for the selective determination of chloride, bromide, iodide, silver, and sulfide ions. Likewise, if the pellets contain Ag₂S together with the silver halides or mixtures of PbS, CdS, and CuS, solid-state electrodes sensitive toward Pb²⁺, Cd²⁺, Cu²⁺, and SCN⁻ can be realized. Moreover, the general problem of light sensitivity and high membrane resistance can be reduced by the additional use of Ag₂S.

Instead of the pressed pellets, the ion-selective material can be incorporated into an organic polymer matrix, like silicon rubber, carbon paste, or paraffin. In heterogeneous membrane electrode preparation, a mixture of the precipitate (e.g., AgI/Ag₂S) and polysiloxane is homogenized, and the polymerization is carried out. The resulting disks are fixed on the end of a tube and the internal solution (e.g., 0.1 M KI) is contacted via a Ag/AgCl wire. Coated-wire electrodes represent another possibility. They can be manufactured by coating an appropriate polymeric membrane onto a conducting wire. Of en, the conductor (Pt, Ag, Cu, or graphite) is dipped in a solution of polymer (e.g., polyvinylbenzylchloride (PVC) or polyacrylic acid) and the active substance. These electrodes allow the determination of K⁺, Na⁺, amino acids, and some drugs (e.g., cocaine). In addition to their simple miniaturization, the preparation is easy and inexpensive. However, further work is necessary to improve their analytical performance with regard to reproducibility and long-term stability.

55.3.1.3 Liquid-Membrane Electrodes

Liquid-membrane electrodes are based on two different membrane-active components: solid ion-exchanger and complex-forming neutral-charged carriers. They permit the determination of several polyvalent cations as well as certain anions. The sensor membrane (10–100 μm thickness) is usually prepared
of a plasticized PVC containing the organic sensor-active component that is insoluble in water; a Ag/AgCl wire is immersed into the internal reference solution. The liquid-membrane electrode differs from the glass electrode only in that the test solution is separated from the solution with the known target ion activity by a hydrophobic membrane, instead of the glass layer (Figure 55.18b). As membrane materials besides PVC, Tef on, sintered glass, filtering textile, or disks can be employed to hold the organic layer.

Liquid-membrane electrodes with ion exchangers have been realized for the determination of, for example, Ca²⁺, K⁺, BF₄⁻, ClO₄⁻, IO₃⁻, SCN⁻, I⁻, Br⁻, Cl⁻, HCO₃⁻, H₂PO₄⁻, and NO₃⁻. On the other hand, the synthesis of compounds containing individual cavities of molecule-sized dimensions results in complex-forming neutral-charged carriers. These ionophores (e.g., crown ethers like cyclic polyether, depsipeptides like valinomycin, and macrotetrolides like nonactin and monactin) are capable of enveloping various target ions reversibly in their pockets. For example, valinomycin membranes show a high K⁺ selectivity. Many cyclic and monocyclic carriers with remarkable ion selectivities have been successfully developed for the determination of Li⁺, Cs⁺, Ca²⁺, Na⁺, NH₄⁺, Mg²⁺, Ag⁺, Hg²⁺, SCN⁻, and H₂PO₄⁻. For all kinds of membranes, a high molecular weight (i.e., a slight overpressure) prevents the quick intrusion of the test solution inside. Hence, the electrode’s lifetime is limited as a consequence of diffusion of the sensor-active component into the analyte (leaching out).

55.3.1.4 Combined Electrodes

Two different types of combined electrodes will be presented here: gas-sensing electrodes and enzyme-based electrodes. Gas-sensing electrodes can be used to determine solutions of gases. They consist of an inner sensing element, normally a suitable ISE with an electrolyte solution (0.1 M), surrounded by a gas-permeable membrane (Figure 55.18c). On immersion of this ISE, the gas-permeable membrane contacts the liquid of the gas that if uses through it, and the resultant internal solution will be examined with the ISE. The partial pressure of the gas attains equilibrium between the test solution/membrane and the membrane/ISE phase boundary. For example, the determination of carbon dioxide, which diffuses through the semipermeable membrane, lowers the pH values of the inner solution:

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{HCO}_3^- + \text{H}^+ 
\]

(55.47)

Such pH changes are detected by the ISE, in this case by a pH-sensitive glass electrode. Semipermeable membrane materials are polytetrafluoroethylene, polypropylene, or silicone rubber. The internal solution contains sodium chloride and an electrolyte with the corresponding ion that is determined. Gas-sensing electrodes have been realized for gases dissolved in solution, such as NH₃, NH₄Cl, CO₂, H₂CO₃, NaHCO₃, NO₂⁻, NaNO₂, SO₂, H₂SO₃, K₂S₂O₇, CN⁻, SCN⁻, Cl₂, Br₂, I₂, and H₂S.

Enzyme electrodes are based on the coupling of an enzymatic membrane with any type of appropriate ISE. The enzyme converts (catalyzes) the analyte (substrate) to be determined extremely selective into an ionic product. The latter can be detected by the known ISE (Figure 55.18d). The coupling of the enzyme can be carried out by several immobilization procedures, such as entrapping in a gauze or gel, adsorptive or covalent binding, and cross-linking. A typical example for the operation of an enzyme electrode is given by the urea electrode. The enzyme urease hydrolyzes urea in order to liberate ammonium ions:

\[
\text{CO(NH}_2)_2 + \text{H}_2\text{O} + 2\text{H}^+ \xrightarrow{\text{urease}} 2\text{NH}_4^+ + \text{CO}_2 
\]

(55.48)

Either the alteration of the pH by a pH ISE or the variation of the NH₄⁺ concentration by an ammonium-sensitive gas electrode can be detected. Likewise, penicillin, glucose, lactate, phenol, creatinine, cholesterol, salicylate, or ethanol will be catalyzed by means of the respective enzyme. Using different biological components (enzymes, cells, tissues, antibodies, receptors, or nucleic acids), a wide variety of analytically important substances for clinical, environmental, and food analysis can be determined. However, disadvantages of this type of electrode are its slow response time (several minutes) and the insufficient stability in the long term.
55.3.2 Instrumentation and Measurement

For potentiometric measurements, one uses an indicator electrode (ISE) versus a reference electrode and a potentiometer, also called pH meter or ion meter. Owing to the high resistance of the ISE membranes (e.g., 5–500 MΩ for the glass membrane), a potentiometer with a high input resistance is required. Modern potentiometers consist of an electronic digital voltmeter with a suitable operational amplifier, scaled directly to pH units or mV, with a resolution of better than ±0.002 pH and ±0.1 mV. They may range from simple handheld instruments for field applications to more convenient laboratory models. Frequently, potentiometers include a bias control that can be adjusted to correspond to the temperature of the test solution (automatic temperature compensation).

Direct Potentiometry: Direct potentiometric measurements can be performed for the determination of ionic species for which an appropriate ISE is available. A schematic measuring setup for direct potentiometry is shown in Figure 55.3. The measuring technique is quite simple: comparing the potential of the ISE in the test solution with its potential in a known standard solution. Thus, before the determination, the ISE must be calibrated in solutions of known concentration of the chosen ionic species. Using, for the ion determination to be made, at least two to three reference solutions are necessary that differ by two to five concentration decades. Typical resulting calibration curves for anions and cations are plotted in Figure 55.19. The curves can be separated into three distinct regions: (1) the straight part corresponding to the Nernstian slope (i.e., the sensitivity of the ISE), (2) the curve portion, and (3) the horizontal part below the LDL, where almost no sensitivity exists. The LDL of the ISE is defined as the concentration at which the extrapolated horizontal portion of the graph intersects the extrapolated Nernstian portion of the graph.

For practical applications, there are two aspects to be dealt with: often a total ionic strength adjuster buffer (TISAB) is added to both the standard solutions and the test solution (same temperature) to achieve comparable ionic strengths. Then, the potential difference can be assigned to the equivalent concentration of the calibration curve. Various methods for calibration calculations are described by, for example, Gran's plot or the standard addition method (Mendham et al. 2000). Because all measurements take place in dilute solutions (≤0.1 M), ion concentrations can be used in the Nernst equation instead of ion activities.

Potentiometric Titration: Potentiometric titration can be applied in the fields of acid–base, precipitation, complex formation, and redox reactions. Therefore, the ISE is used in combination with a reference electrode in order to establish the EP in a titration curve. A typical S-shaped potentiometric titration curve,
where the electrode potential is plotted versus the reagent volume (titrant), is given in Figure 55.20a. The titrant is added to the initial solution that is stirred, and the ISE records the potential value at equilibrium. The EP (endpoint) of the reaction is reached when a sudden change in the potential of the ISE occurs. The midpoint in the curve (i.e., the steeply rising portion) is termed endpoint or inflection point. It can be evaluated by analytical methods, namely, the first- and second-derivative curves (Figure 55.20b and c). The first-derivative curve gives the potential change per unit change in volume of reagent and depicts the endpoint at the maximum of the inflection point. The second-derivative curve is zero where ΔE/ΔV reaches its maximum. The greater the slope at the endpoint, the smaller should be the volume increment in order to reduce titration errors.

For practical applications, modern microprocessor-controlled titrators are commercially available (auto-titrator), coupled to a chart recorder to produce the titration curve directly. Such instruments also allow to evaluate the first- and second-derivative curves and provide Gran’s plot. Acid-base (neutralization) titrations are performed with a glass/calomel electrode system and can be used to titrate a mixture of acids that differ greatly in their strengths (e.g., acetic (ethanoic) and hydrochloric acids). For precipitation titrations, the ISE consists of an electrode (e.g., silver or a platinum wire) that quickly reaches equilibrium with the ions to be precipitated. A typical precipitate reagent represents silver nitrate for the determination of halogens, halogenides, mercaptans, sulfides, arsenates, phosphates, and oxalates. For complex-formation titrations, membrane electrodes can be used that involve the formation of soluble complexes, like ethylenediaminetetraacetic acid (EDTA) or silver cyanide (Ag(CN)₂⁻). Oxidation–reduction titrations are performed by a platinum indicator electrode to any redox couples where the potential depends on the concentration ratio of the reactants. Some experimental details for potentiometric titration are described in M endham et al. (2000).

As an alternative principle, chronopotentiometry is based on the observation of the change in potential of a working electrode as a function of time during electrolysis. Usually, this electrolysis is performed with a constant current, whereas the time is measured that is necessary for the potential to go from one level to another. Since chronopotentiometry is disappointing at concentrations below 10⁻⁴ mol L⁻¹, it is only a powerful tool for studying electrode processes at higher concentrations. Consequently, this method is not very important for practical applications.
55.4 Semiconductor Field-Effect Chemical and Biological Sensors

The integration of thin ion-selective membranes with solid-state devices leads to miniaturized chemically sensitive solid-state devices. Among the variety of concepts and transducers principles proposed for solid-state chemical and biological sensors, the integration of chemically or biologically sensitive materials (recognition elements) with semiconductor field-effect devices based on the electrolyte-insulator-semiconductor (EIS) system is one of the most attractive approaches (Bergveld and Sibbald 1988; Madou and Morrison 1999; Grattarola and Massobrio 1998; Bergveld 2003). Representative examples are chemically sensitive field-effect transistors (ChemFETs), chemically sensitive capacitive EIS sensors, and light-addressable potentiometric sensors (LAPS), which are currently being one of the basic structural elements of various chemical and biological microsensors (Poghosian and Schöning 2006, 2007). Although these three kinds of (bio-)chemical sensors have different device configurations and measurement setups, the transducer principle of using an electric field to create excess charge regions in a semiconductor substrate is common to all of them. These field-effect devices are based on the technology used for manufacturing microelectronic chips and thus offer the possibility of mass production. (Bio-)chemical sensors based on other types of field-effect devices, like silicon-nanowire transistors (Timko et al. 2010), silicon thin-film resistors (Nef et al. 2006), or carbon-nanotube transistors (Lee et al. 2009a), are still in the initial state of research and development.

55.4.1 Chemically Sensitive Field-Effect Transistors

The chemFETs can react sensitive to some ions (ion-sensitive FET [ISFET]), biomolecules (biologically sensitive FET [BioFET]), or gases (gas-sensitive FET [GasFET]) in aqueous media, or they can be insensitive (reference FET [RefET]). They incorporate the sensitive membrane directly on the gate area of a field-effect transistor (FET). A schematic of an n-channel ISFET, mounted in a measuring cell and contacted via a reference electrode (e.g., Ag/AgCl electrode), is given in Figure 55.21a.

It consists of a p-type silicon substrate with two n-doped regions, source (S) and drain (D), separated by a short channel that is covered by the gate insulator (typically, a thin SiO₂ layer) and the ion-sensitive membrane. For operating an ISFET, the gate voltage, \( V_G \), is applied by a reference electrode. When the sensor membrane is placed into contact with the test solution containing the ions or analytes to be detected, an additional potential \( \Delta V \) is generated at the membrane-electrolyte interface. If a sufficiently positive bias potential is applied to the gate (with respect to the bulk silicon substrate), an n-type inversion layer (usually less than 10 nm) is formed in the channel and the current, \( I_D \), starts to flow between source and drain.

The drain current and threshold voltage \( V_T \) (the gate voltage at which a conductive channel is formed between source and drain) of the ISFET can be deduced from that of its electronic analogue metal-oxide-semiconductor FET (MOSFET) by simply adding the potential drops at the additional interfaces (Bergveld and Sibbald 1988; Poghosian and Schöning 2006):

\[
I_D = \frac{C_i \mu_b}{L} \left[ (V_G - V_T) V_D - \frac{V_D^2}{2} \right] \quad (55.49)
\]

for the nonsaturated region \( V_D < V_G - V_T \), and

\[
I_D = \frac{C_i \mu_b}{2L} (V_G - V_T)^2 \quad (55.50)
\]
Chemical Variables

**FIGURE 55.21** ISFET configuration (a), transfer characteristic (b), and schematic circuit of CCM (c). The metallic gate from a MOSFET is replaced by the arrangement sensitive membrane/test solution/reference electrode (V<sub>G</sub>, gate-source voltage; V<sub>D</sub>, drain-source voltage).

For the saturated region (V<sub>D</sub> > V<sub>G</sub> − V<sub>T</sub>), with

\[ V_T = E_{ref} - \Delta V + \chi - \frac{W_S}{q} - \frac{Q_s + Q_{ss}}{C_i} - \frac{Q_{ss}}{C_i} + 2\phi_B \]  

(55.51)

where,
- \( \mu \) is the mobility of the electrons in the channel between source and drain
- \( b \) is the width
- \( L \) is the length of the channel
- \( C_i \) represents the capacitance of the gate insulator per unit area
- \( E_{ref} \) is the potential of the reference electrode
- \( \chi \) is the surface-dipole potential of the solution
- \( W_S \) is the silicon electron work functions
- \( q \) is the elementary charge (1.6 × 10<sup>-19</sup> C)
- \( Q_{ss}, Q_s, \) and \( Q_{ss} \) are the charges per unit area in the space-charge region as well as located in the oxide and the surface/interface states, respectively
- \( \phi_B \) is the potential difference between the Fermi level in the bulk semiconductor and the intrinsic Fermi level

If the applied gate (V<sub>G</sub>) and source-drain (V<sub>D</sub>) voltages are fixed, the only variable term is the analyte concentration-dependent interfacial potential \( \Delta V \). Changes in the chemical composition will
induce changes in the potential drop at the electrolyte-membrane interface that consequently will modulate the drain current of the ISFET. After calibration of the ISFET with standard solutions of known ion activity, the variation of $I_D$ can be used to determine the ion concentration in the test solution (Figure 55.21b). Of en, the ISFET is operated in a feedback loop (e.g., the constant charge mode, Figure 55.21c), and the voltage $V_{in}$ needed to maintain $I_D$ at a fixed value represents the sensor response. The sensor response can be described by the same Nernst and Nikolsky equations that characterize conventional ISEs.

Like with the ISEs, the most attention is gained to pH-sensitive ISFETs, built up of SiO$_2$ and an additional thin f Im (about 30–100 nm) of other oxides and nitrides. The additional layer is necessary because the pH response of SiO$_2$, initially used as pH-sensitive dielectric, is poor (20–40 mV/pH) and the material was indeed found to be unstable and to suffer from considerable drift of the sensor signal. Therefore, different materials, like Si$_3$N$_4$, Al$_2$O$_3$, Ta$_2$O$_5$, IrO$_x$, ZrO$_2$, TiO$_2$, SnO$_2$, WO$_3$, HfO$_2$, AlN, TiN, PtTiO$_3$, barium strontium titanate, diamond-like carbon, and nanocrystalline diamond, have been investigated with respect to their pH sensitivity and stability (see, e.g., Poghossian and Schön 2006). For example, Si$_3$N$_4$ shows a sensitivity of about 45–55 mV/pH. The sensitivity can be improved by using Al$_2$O$_3$ or Ta$_2$O$_5$ with 53–57 and 55–59 mV/pH, respectively. Also, the reported drift values are less than 1 mV h$^{-1}$. The pH sensitivity of these gate-insulating materials can be explained by the site-binding theory, which is exemplary discussed for SiO$_2$ in Madou and M Morrison (1989). Other more exotic materials such as AlN, HfO$_2$, PtTiO$_3$, and WO$_3$ sometimes show nearly Nernstian sensitivity, but have only rarely been studied. Methods that have been used to deposit pH-sensitive materials include electron-beam evaporation, thermal evaporation, CVD, sputtering, thermal oxidation, pulsed laser deposition (PLD), and solgel technique.

Being in its basic structure a pH-sensitive device, the selectivity of an ISFET toward other ions can be achieved by means of a modification of the gate surface or a deposition of subsequent organic or inorganic ion-sensitive membranes on top of the gate insulator. For instance, by implantation of high doses of B, Al, Ga, Sn, Ti, Li, or Na, potassium- and sodium-sensitive ISFETs were achieved. Also, the deposition of thin layers of modified chalcogenide glasses of the determination of heavy-metal ions for biological investigations and industrial applications (Vlasov 1994; Schönning and Klock 2007). By means of vacuum evaporation, ion-sensitive f Im of LaF$_3$, Ag$_2$S, or AgX (X = Cl, Br, I) for the determination of F$^-$, Cl$^-$, Br$^-$, I$^-$, Ag$^+$, and S$^{2-}$ can be prepared. A chemical surface modification of the original gate insulator (e.g., the covalent linking of hydrophilic layers that contain the sensing molecule) leads to organic gate materials for the determination of different ions such as Ca$^{2+}$, NH$_4^+$, K$^+$, Cl$^-$, NO$_3^-$, Na$^+$, and Ag$^+$ (Rheinhoudt 1992). Similar results were obtained for homogeneous polymeric membranes, containing solid ion-exchanger or neutral-charged carriers (see section on ISE). In order to achieve well-defined and highly ordered sensor membranes, the gate can be coated with ultrathin Langmuir–Blodgett f Im (Schönning et al. 1995).

BioFETs are constructed from an ISFET by modifying the gate or coupling it with biological recognition elements. The biomolecules of various complexity (e.g., enzyme, antibody, protein, deoxyribonucleic acid [DNA]) or even living biological systems (e.g., cell, tissue slice, or whole organism) can be used as recognition element. Based on the hierarchy of biological complexity, the BioFETs can be subdivided as follows: enzyme-modified FET (EnFET), DNA-modified FET (DNA-FET), cell-based FET, and beetle/chip FET. A review of basic concepts of different kinds of BioFETs is given in Schönning and Poghossian and Schöning (2006), Lee et al. (2009b), and Poghossian et al. (2009).

EnFETs are usually constructed by immobilizing an enzyme or multienzyme system onto the gate insulator of an ISFET using different immobilization techniques (e.g., physical adsorption, enzyme entrapment within polymeric matrices, covalent binding, cross-linking). The EnFET directly corresponds to the enzyme ISE and detects the potentiometric response to either the concentration change in one of the products or reactants catalyzed by the enzyme. A multitude of EnFETs have been reported for the detection of numerous analytes such as glucose, penicillin, urea, lactose, sucrose, lactate, organophosphorus pesticides, creatinine, and glycoalkaloids (see, e.g., Poghossian and Schönning 2006 and
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references there). Frequently, EnFETs are built up of pH ISFETs, in which hydrogen ions are produced or consumed by the enzymatic reactions. For an exact measurement, an on-chip integrated pH-ISFET/EnFET differential arrangement is often employed, where the pH ISFET contains a blank enzyme-free membrane and serves as a reference device. The demand of compatibility with integrated circuit technology provides enzymatic membranes that can be photolithographically patterned (e.g., photocrosslinkable materials). Intensive researches during the last years were focused on the improvement of EnFET characteristics and to circumvent problems, which actually prevent the successful commercialization of EnFETs (e.g., dependence of the sensor response on buffer capacity, ionic strength, and pH of the test sample; restricted dynamic range and nonlinearity; relatively slow response and recovery times; operating and storage stability; reproducibility; dependence on enzyme immobilization method; the incompatibility of most used enzyme-containing layer deposition and patterning methods with silicon technology).

DNA-FETs: Generally, field-effect devices are surface-charge-measuring devices, and therefore, they are principally able to detect charged biomolecules (including DNA molecules) by their intrinsic molecular charge. Due to their small size and compatibility with advanced micro- and nano-fabrication technologies, these devices could offer a next generation of DNA chips with direct electronic readout for a label-free, fast, simple, and real-time analysis of nucleic acid samples. The core principle behind DNA chips is the hybridization event between two single-stranded DNA (ssDNA), where an unknown target ssDNA is identified by its complementary ssDNA molecule. As a result, a double-stranded DNA (dsDNA) helix structure with the two complementary strands is formed. Since DNA molecules are polyanions with negative charges at their phosphate backbone, the charge associated with the target molecule can effectively alter the charge applied to the gate, resulting in a modulation of the threshold voltage and the drain current of the DNA-FET. A critical review of different types of DNA-FETs is given in Poghosian et al. (2007) and Schöning and Poghosian (2008). The major disadvantage of electrostatic DNA detection by its intrinsic charge is the screening of the DNA charge by mobile ions in the surrounding solution. This can significantly reduce the expected sensor signal, especially in high-ionic-strength solutions, where the screening length (Debye length) is very short (~1 nm for a 0.1 M solution of monovalent 1:1 salt). To enhance the sensor signal, the DNA-FET must be operated in a very low-ionic-strength solution (<1 mM) and/or with a tightly packed probe ssDNA (>10^13 ssDNA cm^-2).

To overcome the described problems, an alternative approach based on the detection of the DNA hybridization-induced redistribution of the ion concentration within the intermolecular spaces and/or the alteration of the ion sensitivity of the field-effect device has been proposed in (Poghosian and Schöning 2006).

Cell-based FETs or cell/transistor hybrids are obtained by direct coupling of single living cells (the smallest self-sustaining biological entity) or cell systems to the gate insulator of FETs (Wang 2005; Poghosian et al. 2009). Cell-based FETs can be used for both the monitoring of cellular metabolism (the extracellular acidification rate, concentration of ions, oxygen consumption, CO2 production, and other metabolic products caused by different external stimuli) and the measurement of action potentials of electrogentic cells such as neuronal and muscle cells. For example, with the commercially available Biosense2500, analyzing system metabolically relevant data, including oxygen consumption, acidification rate, and adhesion (cell impedance) of cells, can be noninvasively measured in parallel and over a long period of time (T. Edinga et al. 2007). Moreover, a cell-monitoring system, which includes both FETs for detecting the action potential and ISFETs coupled with different ion-sensitive membranes for the measurement of concentration of extracellular ions, like Na+, K+, and Ca++, has been realized (Wang et al. 2005). These devices are of great interest for a large variety of applications including the detection of pharmaceutical agents, toxic substances, or pollutants and the monitoring of electrical communication within neuronal networks or transmission paths of ionic channels. Moreover, direct electrical interfacing of semiconductor and nerve cells is the physical basis for the development of hybrid neuroelectronic devices.
ReFETs consist of a sensor surface that is as insensitive as possible to all kinds of substances in the test solution. Thus, a differential pair of an ISFET and a ReFET eliminates disturbances, like influence of temperature or light. Appropriate materials to cover the ISFET surface with an insensitive layer are blocking materials, such as TeO2 or different polymers (e.g., parylene, polyacrylate, PVC). However, not well-defined potential processes as well as some ion exchange will result in nonideal behavior. Alternative concepts use nonblocking polymer membranes with a fixed membrane potential or quasi-ReFETs with a delayed pH response. The most promising approaches are the application of an inert metallic layer or wire in a differential ISFET setup as a quasi-reference electrode and the miniaturization of conventional reference electrodes. For example, by means of PVD methods, Ag/AgCl electrodes were miniaturized on silicon chips inside anisotropically etched cavities (Madou and Morrison 1989).

The basic mechanism of GasFETs is due to the chemical modification of the electron work function of a metal–insulator–semiconductor (MIS) field-effect structure, for example, of a suspended gate FET (SGFET) as schematically shown in Figure 55.22.

The SGFET contains an additional insulator, the "gap" within the gate structure, which consists of a vacuum, a gas, or a nonconducting liquid. As gate metal, usually a platinum layer or mesh is used. The chemically sensitive layer on top of this structure, for example, palladium, exhibits sensitivity toward hydrogen. The hydrogen molecules adsorb and dissociate atoms (H₂) on the metal surface (Pd), depending on their partial pressure, as well as desorb from the metal surface by recombination into H₂ and reacting with oxygen to form water:

\[
H_2 \leftrightarrow 2H_\text{a} \quad \text{and} \quad 4H_\text{a} + O_2 \leftrightarrow 2H_2O \quad (55.52)
\]

The adsorbed atoms diffuse rapidly to the inner surface gap/insulator where they become polarized and form an interface dipole layer, resulting in a potential drop. For example, SGFETs with Pd, operated at 100 °C–140 °C, are sensitive to H₂, CO, and H₂S in the ppm range, whereas an increased operating temperature up to 240 °C allows the detection of alcohols (methanol, ethanol, propanol, butanol). To achieve selectivity, the surface of the suspended gate can be modified by inorganic or organic layers. Ammonia sensitivity can be achieved by catalytic metals such as Pt, Ir, Ru, or Rh. By the deposition of organic layers, like polypyrrole, sensitivities to alcohols and aromatic hydrocarbons are achieved. Several related devices based on SGFETs are explained in Josowicz and Janata (1988).

### 55.4.2 (Bio)Chemically Sensitive Capacitors

Sensors on the basis of capacitive field-effect EIS structures are much simpler to fabricate than ISFETs, and consequently they are favorable for laboratory use. Such structures correspond to MIS capacitors
and their operation principle can be derived from the fundamental MIS devices (Sze and Ng 2007). A schematic buildup of an EIS structure and the measuring principle is given in Figure 55.23a.

The sensor consists of a p- or n-type semiconductor (silicon) covered by a thermally grown SiO₂ insulating layer (<100 nm) and the sensor membrane that is directly exposed to the test solution. For operation, a dc polarization voltage $V_\text{p}$ is applied via the reference electrode to set the working point, and a small superimposed ac voltage (10-50 mV) is applied to the system in order to measure the capacitance of the sensor.

The functioning principle and physical properties of a capacitive EIS sensor can be explained by the charge carrier distribution at the insulator/semiconductor interface, which is controlled by both an external dc voltage ($V_\text{p}$) and an electrochemical interaction between the test solution and the sensor membrane ($\Delta V$) (Poghossian and Schöning 2006). For a p-Si substrate, a negative potential ($V_\text{p} < 0$) on the reference electrode accumulates positively charged mobile carriers (i.e., holes) at the Si/SiO₂ interface (accumulation regime). When $V_\text{p}$ becomes positive ($V_\text{p} > 0$), the holes are displaced from the interface, resulting in a space-charge region depleted of mobile carriers (depletion regime). If the potential

![Diagram of EIS structure](image-url)
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gets more positive \((V_g \gg 0)\), an inversion layer of \(n\)-type Si is created although the substrate is \(p\)-type (inversion regime). The electric behavior is given by the small-signal capacitance of the EIS structure. The whole capacitance \((C)\) can be described as a series connection of the membrane capacitance \((C_M)\), insulator capacitance \((C_i)\), and space-charge capacitance \((C_{sc})\) of the semiconductor:

\[
\frac{1}{C} = \frac{1}{C_M} + \frac{1}{C_i} + \frac{1}{C_{sc}}
\]

(55.53)

with

\[
\frac{1}{C_i} = \frac{\varepsilon_i}{d}
\]

(55.54)

where

- \(A\) is the contact area of the gate with an electrolyte solution
- \(d\) is the thickness
- \(\varepsilon_i\) is the permittivity of the gate insulator

\(C_{sc}\) is, among others, a function of the gate voltage applied to the EIS structure and interfacial potential at the membrane-electrolyte interface. Typical \(C/V\) (capacitance/voltage) curves of a \(p\)-type EIS sensor are exemplary given in Figure 55.23b (left) for different ion concentrations. Due to the electrochemical interaction \((\Delta V)\), a horizontal shift of the \(C/V\) curve is provided, depending on the change of the ion concentration in the test solution. As resulting measuring signal (calibration curve), the potential shift can be evaluated at a fixed capacitance value within the linear region of the \(C/V\) curves (e.g., 60% of the maximum capacitance, Figure 55.23c). Using a feedback circuit, the measured capacitance can be adjusted at a fixed value in the constant capacitance \((\text{ConCap})\) mode (Figure 55.23b, right). Thus, potential shifts can be recorded directly.

Chemical and biological sensing EIS structures with different organic and inorganic sensor membranes have been developed within the last years (see, e.g., Poghosian and Schöning 2006 and references there). They consist of nearly identical sensor membrane materials and compositions as ISFETs, ranging from inorganic pH-sensitive layers (e.g., Si₃N₄, Al₂O₃, Ta₂O₅) or crystalline films (e.g., LaF₃, silver halides) over organic Langmuir–Blodgett films to enzymatic layers (e.g., urease, penicillinase). Much effort has been done in order to improve the limiting long-term stability that is often disclosed by FET devices in permanent contact with the analyte. Novel approaches pursue a further optimization with regard to the preparation (e.g., due to specific immobilization procedures) or the deposition of the sensor membrane in order to raise the sensor performance. For example, an extremely long-term stable pH sensor was developed by the suggestion of the PLD process as the thin-film preparation method. The EIS structure consists of a layer sequence of Al/p-Si/SiO₂/Al₂O₃, where no degradation of the pH sensitivity during a measurement period of 2 years was found (Schöning et al. 1996). In addition, a highly sensitive and corrosion-resistant non-glass unbreakable pH sensor has been developed using a Ta₂O₅ layer as pH-sensitive material (Schöning et al. 2005). The capacitive EIS sensors have been integrated into a flowing-through microfluidic channel (fabricated by combining Si and SU-8 technologies) for pH and penicillin measurements (Poghosian and Schöning 2007). Moreover, EIS sensors have been applied for the detection of charged macromolecules (e.g., polyelectrolytes, DNA, dendrimers) and nano-objects (e.g., gold nanoparticles, carbon nanotubes) (Siqueira et al. 2009; Abozur et al. 2011; Gun et al. 2011). Recently, a highly sensitive DNA hybridization/denaturation sensor has been realized using an array of individually addressable field-effect nanofluid silicon-on-insulator (SOI) capacitors modified with gold nanoparticles (5–8 nm) (Abouzur et al. 2012). Finally, the feasibility of EIS sensors for the creation of molecular “AND” and “OR” logic gates has been demonstrated in Poghosian et al. (2011).

Like GasFETs, MIS capacitors and MIS Schottky diodes are also available as gas-sensitive devices. For the MIS capacitor, a concentration-dependent dipole layer is detected as a shift of the \(C/V\) curve.
To reduce the drift of these devices, additional insulating layers, such as Al₂O₃, Si₃N₄, or Ta₂O₅, can be deposited between the metal layer and the SiO₂ insulator. Experimental results of Pd/Al₂O₃/SiO₂/Si structures show sensitivities of 25 mV ppm⁻¹ around 1 ppm (Armgarth and Nylander 1991). Schottky barrier diodes consist of a thin insulating layer (e.g., 2 nm SiO₂) between the metallic gate (e.g., Pd) and the semiconductor, in order to allow the current to pass through it. By variation of the metallic gate fields, different sensitivities can be achieved, comparable to those of the SFGFETs.

55.4.3 Light-Addressable Potentiometric Sensors

A schematic structure (a), a simplified equivalent circuit (b), and typical photocurrent response (c) of the LAPs are presented in Figure 55.24. The LAP structure is similar to that of an EIS structure. Therefore, in the absence of illumination, the LAP behaves like an EIS capacitor. As in the case of the capacitive EIS sensor, a dc bias voltage (V_{bias}) is applied between the reference electrode and the semiconductor substrate in order to induce a space-charge region at the gate insulator-semiconductor interface. However, to detect the variation of the capacitance, the LAP is, in contrast to EIS-based measurements, illuminated with a intensity-modulated light, which induces an ac photocurrent to be measured as the sensor signal (Wagner and Schöning 2007; Poghosian et al. 2009; Yu et al. 2010). The excitation light can be directed to the semiconductor either from front- or backside of the LAP structure by placing

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**FIGURE 55.24** Schematic structure (a), simplified equivalent circuit (b), and typical photocurrent response by different analyte concentrations (c) of the LAP. I_{ph}, measured photocurrent; I_{p}, generated photocurrent; Z, impedance of a reference electrode and a solution; C_i, gate capacitance; C_{SC}, space-charge capacitance; c_1, c_2, and c_3, analyte concentrations.
one or multiple light pointers (light-emitting diode [LED] or laser beam) just below the semiconductor, as shown in Figure 55.24a. When silicon is illuminated with infrared light, there is a generation of electron–hole pairs in the semiconductor. The electron–hole pairs that have diffused from the bulk semiconductor into the depletion region or that are photogenerated within this region are separated in the electric field. Modulating the intensity of an excitation light will modulate the depletion capacitance in the illuminated region of the semiconductor, thus, generating a photocurrent \( I_{ph} \) in the external circuit. Under the condition of strong depletion, the photocurrent \( I_{ph} \) of the LAPS can be described by the following simplified equation (Grattarola and Massobrio 1998):

\[
I_{ph} = I_p \frac{C_i}{C_i + C_{SC}}
\]

(55.55)

where \( I_p \) is the alternating component of the photogeneration of electron–hole pairs. Because the capacitance of the space-charge region, \( C_{SC} \), depends on the applied dc voltage, the measured photocurrent is a function of the bias voltage applied to the LAPS structure.

Figure 55.24c depicts typical photocurrent–voltage characteristics of a \( p \)-type LAPS. By sweeping the applied voltage, the semiconductor surface potential can be driven from accumulation to inversion condition. The amplitude of photocurrent saturates as the bias voltage is increased toward inversion, and the photocurrent disappears when the device is biased into accumulation, where the depletion region and therefore the electric field no longer exist. The LAPS uses this dependence of the photocurrent on bias voltage to sense the interfacial potential changes at the gate/solution interface. For different ion or analyte concentrations, the photocurrent–voltage curve shifts along the voltage axis (Figure 55.24c). By measuring this shift, the analyte concentration can be quantitatively determined. The photocurrent is most sensitive to changes in the chemical composition of the solution in the depletion range (a sharp transition region between a maximum [in inversion mode] and a virtually zero value [in accumulation mode]). Therefore, the shift of the photocurrent–voltage curve is often quantified by tracking the potential of the inflection point of the curve. For chemical imaging applications (a typical chemical image consists of an enormous number of measured spots or pixels), however, the measurement of the complete current–voltage curve is too time-consuming, and a faster measuring method is required. One possible measuring mode is the constant-voltage mode, which is often used for the LAPS-based chemical imaging sensor (Wagner and Schöning 2007). In this mode, the applied bias voltage is simply fixed at a constant value (usually near the inflection point of the current–voltage curve, where the linearity of the curve is high), and the analyte concentration-dependent variation of the photocurrent is recorded. Another mode of operation is the constant-photocurrent mode, in which a feedback system controls the applied bias voltage so that the photocurrent is maintained at a constant value. This mode is most suitable for applications, where measurement of dynamic changes of the sensor signal is necessary.

Thus, not only the sensor structure but also the measurement principle of the LAPS is very similar to that of the EIS capacitance sensor, in which the current signal is induced by the application of an ac voltage. However, in contrast to the capacitive EIS sensor, where the measured value of the ion or analyte concentration is an average over the whole sensing surface in contact with the analyte, the LAPS measurement is spatially resolved. An attractive feature of the LAPS, compared to the EIS sensor and ISFET, is its light addressability. The measurement spot on the sensing surface is defined by the illumination area, where the ac photocurrent to be measured is generated. The main disadvantages of the LAPS are the light sensitivity and the dependence of the photocurrent on the electrolyte conductivity.

Due to the structural similarity between LAPS, capacitive EIS sensor, and ISFET, many of the sensitive materials, deposition or immobilization techniques, and surface modification strategies, which have already been developed for ISFETs and EIS sensors, are also applicable to LAPS devices. Traditionally, the LAPS is mostly employed for \( pH \) recording (see, e.g., Poghossian and Schöning 2006, Wagner and Schöning 2007, and references there). \( Si_3N_4 \) is the most frequently used \( pH \)-sensitive material in LAPS.
devices, although several alternative materials such as Ta₂O₅ and Al₂O₃ have also been proven as alternative pH-sensitive materials. The first and successfully commercialized system using the pH-sensitive LAPS for the determination of extracellular acidification of living cells is the cytometer microphysiometer system, realized in 1990s by the company Molecular Devices Corporation (United States) (Hafner 2000). More recently, various portable miniaturized LAPS devices (e.g., LAPS-card sensor or a pen-shaped LAPS) with integrated signal processing unit have been realized (Wagner and Schöning 2007).

In contrast to ISFETs or capacitive EIS sensors, ion-sensitive and enzyme-modified LAPS are studied in less detail. For example, the application of LAPS as an ion sensor for the detection of different cations (Li⁺, K⁺, Cs⁺, Ca²⁺, and Mg²⁺) and anions (NO₃⁻ and SO₄²⁻) has been demonstrated. A LAPS for heavy-metal detection using a chalcogenide glass membrane was developed. An enzyme-modified LAPS has been realized for the detection of penicillin, urea, glucose, and butyrylcholine. LAPS devices became popular in many chemical and biological applications such as the detection of bacterial growth, the measurement of cell metabolism, and the study of mechanisms of drug action on cell physiology. For example, with the aim to study the influence of drugs on the metabolism of cells, a microphysiometer, based on the multi-light LAPS concept, has been developed for the simultaneous measurement of several extracellular ion concentrations (H⁺, Na⁺, K⁺, and Ca²⁺) (Yicon et al. 2001). More details about different types of LAPS can be found in Poghosian and Schöning (2007) and Wagner and Schöning (2007).

In order to measure a pH- or ion-concentration distribution along the LAPS sensor surface with a spatial resolution, either the light pointer (e.g., focused laser beam) can be scanned along the surface or multiple light pointers can be used. In this way, a map of a 2D distribution of the pH value or the ion concentration can be visualized (chemical imaging). The detection of the metabolic activity of bacteria immobilized on a LAPS surface and the potentiometric imaging of a solution inside the liquid microchannel are two examples of a possible application of LAPS as chemical imaging sensor. The spatial resolution of the LAPS is the most important parameter for both the multi-sensor application and the chemical imaging application. It limits both the smallest size of structures that can be visualized by the chemical imaging sensor and the density of measuring points on the sensor surface. Because of lateral diffusion of photogenerated carriers, the spatial resolution is limited by the diffusion length of the minority carriers or the thickness of the Si substrate. The best values of lateral resolution reported for bulk silicon have been about 20 μm. The high spatial resolution down to several micrometers or less can be achieved using SOI substrates with ultrathin Si (~0.5 μm) or poly-Si layers as well as a LAPS based on amorphous silicon films.

For a detailed understanding of physicochemical phenomena at semiconductor device/cell interfaces, electrically excitable cells have to be connected individually, that is, each cell has to be interfaced with a separate potential-sensitive device (e.g., with a FET). However, because of the restriction of microelectronic fabrication, the number of FETs and therefore the number of active measuring sites are limited. Instead of placing single cells on the separate gates of the FET arrays, cells grown on a LAPS surface can be individually addressed by scanning the light pointer and illuminating the LAPS surface below the single cell of interest. In this way, it should in principle be possible to record the metabolic or electrical activity of a single cell, although there are many cells cultured on the chip surface. Therefore, several attempts have been made to record action potentials of single cells by means of a LAPS; however, the measured signals were small (about 10 μV). In addition, a hybrid device, a so-called scanning probe potentiometer based on cantilever-type micro-LAPS, capable for the measurement of the pH distribution in microvolume solution with the spatial resolution of 10 μm has been developed (Manalis et al. 2000). It is expected that such a scanning probe potentiometer could be used to image pH gradients produced by individual cells. The main technical problem preventing measurements of extracellular acidification rate of single cells with LAPS devices is the problem of confining the produced protons in a very small and defined volume.

55.4.4 Practical Applications and Limitations

Possible practical applications of field-effect chemical and biological sensors reach from medicine, biotechnology, and environmental monitoring over food and drug industries up to defense
and security purposes (see, e.g., Bergveld and Sibbald 1988, Wang et al. 2005, Poghossian and Schöning 2006, Lee et al. 2009a, and Jimenez-Jorquera et al. 2010). For example, ISFETs have been utilized for pH- and ion-concentration measurements in whole blood, plasma, and urine; in vivo pH monitoring in the stomach; acid-rain monitoring; marine monitoring; soil analysis; monitoring of nutrient solutions in greenhouses; online detection of microorganisms in water; determination of pH in meat and Ca\(^{2+}\) in milk; and online process control of pH, K\(^+\), Ca\(^{2+}\) in wine industry. Moreover, EnFETs were applied for the determination of glucose in blood serum and urine, urea in blood serum and in hemodialysis fluids, and creatinine in hemodialysis solutions and in serum of renal failure patients as well as for transcutaneous blood glucose monitoring of diabetic patients. However, despite the intensive research and practical realization of different field-effect (bio-) chemical devices, generally, it could be concluded that their transfer from scientific laboratories to real life remains rather slow. Only very few of field-effect (bio-)chemical sensors, namely, pH-ISFET electrodes and cell-monitoring systems based on ISFET (Bionas 2500 analyzing system) and LAS (cytometer microphysiometer, Molecular Devices Corporation), have successfully been commercialized so far. Commercially available pH ISFETs are exceptionally stable, fully temperature-compensated, rugged, reliable devices and exhibit performances that are comparable to those of pH-glass electrodes. Resistance to breakage is the most obvious feature of the pH ISFETs compared to the pH-glass electrode. Therefore, nowadays in many in-line process-monitoring systems in biotechnology, food, and drug industries, the breakable pH-glass electrode is gradually replaced by non-glass, unbreakable pH sensors based on ISFETs.

The study of the current state of BioFETs reveals that some BioFETs, like EnFETs or cell-based FETs, are at a well-developed stage, whereas other BioFETs (e.g., DNA-FETs) are still in the experimental stage or starting phase. Although, many improvements have been made in the last few years, there are, however, still a number of fundamental and technological problems that must be overcome before the first reliable BioFET-based bioanalytical microsystem will appear on the market. The same can be stated for biologically sensitive capacitive EIS sensors and LAS.

In general, ChemFETs possess significant advantages over classical ISEs, such as high input impedance, a fast response time, and a small weight. The small sensor area includes the possibility of multiple sensor applications (sensor arrays) on a single chip. Moreover, temperature compensation is possible. However, most of these sensors are exposed to a chemically very reactive environment, and therefore, a highly long-term stable protection (encapsulation) of the electronics from the analyte is required. The instability of the materials used induces a sensor drift. In some cases, attachment and fixation of the sensor membranes must be improved. To take advantage of miniaturized FET devices, there is also the necessity of a small reference electrode. For ChemFETs, there exist two approaches for successful commercialization: dealing with small sample volumes for biomedical use and the high-volume fabrication for a low-price market (e.g., environmental and process monitoring, agriculture and food analysis, leak detectors). The employment of capacitive EIS and MIS sensors besides the easier manufacturing technique distinct advantages concerning the improved mechanical and electrochemical stability and sensor lifetime.

55.5 Conductometry

In addition to potentiometry, conductometric analysis represents the most important nonfaradaic method. Conductometry is based on the measurement of the electrical conductance of an electrolyte solution, which directly depends on the number of positively and negatively charged species in the solution. This analysis method is limited due to its nonselective nature, because all ions in the solution will contribute to the total conductance. Nevertheless, direct conductance measurements play an important role in the analysis of binary water/lyte mixtures, for example, in chemical water monitoring. The technique can also be applied to ascertain the endpoint detection in conductometric titrations for the determination of numerous substances.
55.5.1 Measurement of Conductance and Instrumentation

The conductance \( G \) of a solution is the reciprocal of the electrical resistance \( R \) and has the units of siemens (S) that correspond to ohm\(^{-1}\) (Ω\(^{-1}\)). The conductance of a uniform sample with the length \( l \) and cross-sectional area \( A \) is given by

\[
G = \kappa \frac{A}{l}
\]  
(55.56)

where the proportionality constant \( \kappa = 1/\rho \) (\( \rho \): resistivity) describes the conductivity (specific conductance) of the solution, expressed in units of S cm\(^{-1}\). The equivalent conductivity \( \Lambda \) (molar conductivity) of a solution is defined as the conductivity due to one mole, measured between two electrodes that are spaced 1 cm apart and is

\[
\Lambda = \frac{1000 \kappa}{c}
\]  
(55.57)

where \( c \) corresponds to the concentration of the solution in mol L\(^{-1}\). The units of \( \Lambda \) are S cm\(^{-1}\) mol\(^{-1}\). Equation 55.56 permits the calculation of the molar conductivity for a solution of known concentration by considering the experimental values of \( \kappa \). The molar conductivity \( \Lambda \), that is, the mobility of ions in solution, is mainly influenced by interionic effects for strong electrolytes and the degree of dissociation for weak solutions. For strong electrolytes, the molar conductivity increases as the dilution is increased. By linear graphical extrapolation for diluted solutions of strong electrolytes, a limiting value is defined as molar conductivity at infinite dilution \( \Lambda_0 \). At infinite dilution, the interionic attraction is nil, the ions are independent of each other, and the total conductivity is

\[
\Lambda_0 = \lambda_+^0 + \lambda_-^0
\]  
(55.58)

where \( \lambda_+^0 \) and \( \lambda_-^0 \) are the ionic molar conductivities of the cations and anions, respectively, at infinite dilution. For weak electrolytes, due to the nonlinear relationship between \( \Lambda \) and \( c \), a graphical extrapolation cannot be made. Typical values for the limiting molar conductivities for various species in water are listed in Table 55.2.

### Table 55.2 Molar Conductivity at Infinite Dilution \( \Lambda_0 \) (Ω\(^{-1}\)cm\(^2\) mol\(^{-1}\))

<table>
<thead>
<tr>
<th>Cations ( \lambda_+^0 )</th>
<th>Anions ( \lambda_-^0 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(^+)</td>
<td>349.8</td>
</tr>
<tr>
<td>Na(^+)</td>
<td>50.1</td>
</tr>
<tr>
<td>K(^+)</td>
<td>73.5</td>
</tr>
<tr>
<td>Li(^+)</td>
<td>38.7</td>
</tr>
<tr>
<td>NH(_4)^+</td>
<td>73.4</td>
</tr>
<tr>
<td>Ag(^+)</td>
<td>61.9</td>
</tr>
<tr>
<td>N(CH(_3))(_2)^+</td>
<td>44.9</td>
</tr>
<tr>
<td>Ca(^2+)</td>
<td>119.0</td>
</tr>
<tr>
<td>Mg(^2+)</td>
<td>106.2</td>
</tr>
<tr>
<td>Cu(^2+)</td>
<td>107.2</td>
</tr>
<tr>
<td>Zn(^2+)</td>
<td>105.6</td>
</tr>
<tr>
<td>Ba(^2+)</td>
<td>127.7</td>
</tr>
<tr>
<td>Pb(^2+)</td>
<td>139.0</td>
</tr>
<tr>
<td>Fe(^3+)</td>
<td>204.0</td>
</tr>
<tr>
<td>La(^3+)</td>
<td>208.8</td>
</tr>
</tbody>
</table>
The equipment needed for measuring the conductivity includes an electric power source, a cell containing the solution, and a suitable measuring bridge. The electric power source consists of an alternating current source that produces signals of about 1 kHz in order to eliminate effects of faradaic current. The measurement is performed by a Wheatstone bridge arrangement. Modern conductivity meters supply the alternating current and allow the measurement in a wide range of conductivities (0.001 μS cm\(^{-1}\) to 1300 mS cm\(^{-1}\)). Additional electronics eliminate disturbing capacitance effects and offer automatic range switching. An integrated temperature sensor corrects automatically conductivities to their value at 25°C. The conductivity cell consists of a pair of electrodes placed in a defined geometry to each other. Usually, the electrodes are platinumized to increase their effective surface (high capacitance). Thus, disturbing faradaic currents are minimized. For accurate conductivity determination, the precise area of the electrodes and their distance apart \(d\), the cell constant \(K\), must be known exactly. Therefore, the cell constant \((K = A/d)\) must be evaluated by calibration with a solution of accurately known conductivity (e.g., a standard KCl solution). Details of calibration standards and concepts of conductivity cells are given in Oehme (1991).

55.5.2 Applications of Conductometry

55.5.2.1 Direct Conductometric Measurement

In spite of the insufficient selectivity of direct conductometric measurements, the high sensitivity of this procedure makes it an important analytical tool for certain applications. The specific conductivity of pure water (distilled or deionized) is about 5 × 10\(^{-8}\) S cm\(^{-1}\), and the smallest trace of ionic impurity leads to a large increase in conductivity by an order of magnitude and more. Therefore, conductometric monitoring is employed where a high purity of water is required (e.g., laboratories, semiconductor processing, steam-generating power plants, ion exchanger). Conductometric measurements are widely used to control pollution of rivers and lakes and in oceanography to control the salinity of seawater.

55.5.2.2 Conductometric Titration

In conductometric titration, the reaction is followed by means of conductometry and is used for locating endpoints (i.e., the EP in acid-base titrations [neutralization titration]). To define the titration curve, at least three or four measurements before and after the EP are required. The obtained data of the conductivity are plotted as a function of the titrant volume, and the EP is given as the intersection of the two linear extrapolated fractions. A characteristic titration curve of a strong acid (hydrochloric acid) with a strong base (sodium hydroxide) is depicted in Figure 55.25. The solid line represents the resulting

![Conductometric titration curve](image_url)

**FIGURE 55.25** Conductometric titration of a strong acid (HCl) with a strong base (NaOH). The EP is represented by EP.
titration curve, whereas the broken lines indicate the contribution of the individual species. By adding NaOH to the solution, the hydrogen ions are replaced by the equivalent number of less mobile sodium ions (and $H^+ + OH^- \rightarrow H_2O$). As a result, the conductivity decreases to lower values. The solution exhibits its lowest conductivity at the EP, where the concentrations of hydrogen and hydroxide ions are at the minimum. Further addition of NaOH reverses the slope of the titration curve, since both the sodium ion concentration and hydroxide ion concentration increase.

Due to the high linearity between the conductance and the volume of the added species, this method possesses a high accuracy and can be employed in dilute as well as in more concentrated solutions. In contrast to potentiometric titration methods, the immediate EP region has no strong significance. Thus, very weak acids, such as basic acid and phenol, can be titrated. Moreover, mixtures of hydrochloric acid or another strong acid and acetic (ethanoic) acid or any other weak acid can be titrated with a weak base (e.g., aqueous ammonia, acetate) or with a strong base (e.g., sodium hydroxide). Moreover, precipitation and complex-formation titrations of, for example, sodium chloride with silver nitrate are possible. For practical applications, the volume of the solution should not change appreciably during the titration. Therefore, the titrating reagent may be 20–100 times more concentrated than the solution being titrated, whereas the latter should be as diluted as practicable. For additional examples of analytical procedures and results of conductometric titrations, see Skoog et al. (2007).

55.5.2.3 Oscillometry
In order to investigate electrolyte solutions with high resistivities and dielectric constants, high-frequency titration (oscillometry) can be performed at $10^2$–$10^5$ Hz. For that, a specific measuring cell is required, where the metal electrodes encircle the outside of a glass container. In this arrangement, the electrodes are not in contact with the test solution, which is advantageous for dealing with corrosive materials. Oscillometric measurements can be employed for the determination of binary mixtures of nonionic species, where the dielectric behavior predominates (e.g., ethanol/nitrobenzene, benzene/chlorobenzene, and alcohol/water). Further practical examples are EDTA titrations and the determination of thorium T (IV) with sodium carbonate, beryllium (Be²⁺) with sodium hydroxide, and hydrocarbons (e.g., benzene). However, the instrumentation and the interrelations are more complicated than for the classical conductivity method. Thus, oscillometry gets only significance for specific applications, where the presence of the electrodes interferes.

55.5.2.4 Conductometric Sensors
Depending on the demanded size and geometry, miniaturized cells with two or more electrodes (e.g., a four-electrode conductivity meter) as well as contactless cells are commercially available as conductometric sensors. The contactless methods use capacitive and inductive conductivity cells, which are advantageous to circumvent electrochemically caused electrode reactions. Conductivity cells can be coupled as detectors to ion chromatographic systems for measuring ionic concentration in the eluate. For this, special micro-conductivity cells with a volume of about 1.5 μL have been developed.

Within the last 10 years, two aspects of conductometric applications became important: conductometric gas sensors and the use of conductometric chemiresistors as sensors. In the former, a phase change that transfers the gaseous component into a solution is necessary (e.g., by a bubbler nebulizer). All methods deal with acidic gases such as HCl or SO₂ or with alkaline gases, like NH₃. Also, organic halogens can be detected after their conversion into HCl or HF. By means of integrated circuit technology, thin metal films can be photolithographically patterned as interdigital electrodes onto semiconductor substrates with insulating dielectric layers of SiO₂ or Si₃N₄. Both the thin metal films and additionally deposited organic layers on top of the metallic films can lead to a change of the total resistance by variation of the ionic composition of the reacting solution. For chemiresistors, the organic layer usually consists of an ion-selective polymer layer or a Langmuir–Blodgett membrane; for biosensors enzymatic layers are used (see the ISE section). Such sensors allow the determination of different gaseous components, such as CO, NO₂, H₂S, SO₂, or NH₃, as well as the detection of
biologically relevant species like urea, glucose, penicillin, and choline chlorides. Although several companies of such gas analyzer systems, conductometric sensors and chemiresistors are still in the state of research and development.

55.6 Coulometry

Coulometry represents an electroanalytical method, where the analyte is specifically and completely converted due to direct or indirect electrolysis. The quantity of electricity (in coulombs) consumed by this reaction, the charge, is measured. A fundamental requirement of coulometry is that the species in the solution interact with 100% current efficiency; that is, the reaction corresponds to the Faraday law. According to this condition, there exist two alternatives: the analyte participates in the electrode reaction (primary or direct coulometric analysis) and the analyte reacts with a reagent, generated by an electrode reaction (secondary or indirect coulometric analysis). Two general techniques—controlled-potential coulometry and coulometric titration (controlled-current coulometry)—are used for coulometric analysis.

55.6.1 Controlled-Potential Coulometry

In this method, the potential of the working electrode is held at a constant value compared to a reference electrode. The resulting current is adjusted continuously to maintain the desired potential. The substance being determined reacts without involvement of other components in the sample. The reaction is completed when the current has practically decreased to zero. To measure the charge, a potentiostat, an instrument for measuring the time-dependent current, and a current-time integrating device are used. Modern potentiostats have a built-in electronic coulometer and allow extremely accurate determinations. Otherwise, one can use free-standing coulometers.

Controlled-potential coulometry has been widely employed for the determination of various metal ions, such as Cu, Bi, Cd, Zn, Ni, Co, Pu, and U. To apply this method, current-voltage diagrams must be available for the oxidation-reduction system to be measured as well as for any reaction system at the working electrode. Current-voltage diagrams can be obtained by plotting the measured current versus the cathode-reference electrode potential. To fulfill the requirement of the 100% current efficiency in generation, it is necessary to control the potential of the working electrode. With regard to their determination, the metals are deposited at controlled potentials with a mercury cathode as working electrode and a silver wire or a platinum cylinder as anode. Typical applications are the electrolytic determination and synthesis of organic compounds like acetic acid and picric acid. Further, controlled-potential coulometry is frequently used for monitoring the concentration of constituents in gas or liquid streams, typically small oxygen contents. Here, the reduction of oxygen takes place within the pores of a porous silver cathode:

\[ \text{O}_2(g) + 2\text{H}_2\text{O} + 4e^- \leftrightarrow 4\text{OH}^- \quad (55.59) \]

Using a cadmium sheet \((m)\) as anode, the electrode reaction in solution \((s)\) is

\[ \text{Cd}(m) + 2\text{OH}^- \leftrightarrow \text{Cd(OH)}_2(s) + 2e^- \quad (55.60) \]

The quantity of the electricity (current) is passed through a standard resistor and converted to a voltage signal. Hence, the oxygen concentration is proportional to the recorded potential drop. Controlled-potential coulometry needs relatively long electrolysis times, although it proceeds virtually unattended with automatic coulometers. With a multimeter, changes in the range from 1 ppm to 1% can be dissolved. Thus, controlled-potential coulometry permits analysis with an accuracy of a few tenths of a percent.
55.6.2 Coulometric Titration (Controlled-Current Coulometry)

Controlled-current coulometry maintains a constant current throughout the reaction period. Here, an excess of a redox buffer substance must be added in such a way that the potential does not cause any undesirable reaction. That means the product of the electrolysis of the redox buffer must react quantitatively with the unknown substance to be determined. Coulometric titrations need an electrolytically generated titrant that reacts stoichiometrically with the analyte to be determined. As in controlled-potential coulometry, 100% current efficiency is required. The current is accurately fixed at a constant value and the quantity of electricity can be calculated by the product of the current (in A) and the time (in s) using endpoint detection. In principle, any endpoint detection system that fits chemically can be used, for example, chemical indicators (color change) and potentiometric, amperometric, or conductometric procedures. For coulometric titrations the instrumentation consists of a titrator (constant-current source, integrator) and a cell. As the constant-current source, an electronically controlled amperostat is preferably used. The integrator measures the product of current and time (i.e., the number of coulombs). The electrolysis cell, filled with the solution from which the titrant will be generated electrolytically and the solution to be titrated, is schematically shown in Figure 55.26. The generator electrode, at which the reactant is formed, possesses a large surface area (e.g., a rectangular strip of platinum). The auxiliary electrode (e.g., a platinum wire) is in contact with an appropriate electrolyte of higher concentration than the solution to be titrated. It is isolated from the analyte by a sintered disk or some other porous media. This is required to avoid the interference of additional products generated at the second electrode. To circumvent these limitations of internal generation, an external generator cell is often used.

Typical applications of coulometric titrations are neutralization titrations, precipitation and complex-formation titrations, and oxidation–reduction titrations. Neutralization titrations can be employed for both weak and strong acids and bases. The former can be performed with hydroxide ions generated at a platinum anode by the following reaction:

\[ 2\text{H}_2\text{O} + 2e^- \leftrightarrow 2\text{OH}^- + \text{H}_2(\text{g}) \]  

(55.61)

\[ U = R_2 I \]

\[ U = R_2 I \]

To start a timer

Mercury

Electrolyte

Generator electrode

Auxiliary electrode

Disk

FIGURE 55.26 Coulometric titration cell with working electrode and auxiliary electrode and equivalent circuit diagram (schematically).
the latter one with hydrogen ions by the following reaction:

\[ \text{H}_2\text{O} \rightleftharpoons \frac{1}{2}\text{O}_2(g) + 2\text{H}^+ + 2e^- \] (55.62)

A working (generator) electrode of silver as anode of an array of electrode the determination of \( \text{Cl}^-, \text{Br}^-, \text{I}^-, \) and mercaptans in solution(s). For bromide, the reaction becomes

\[ \text{Ag} + \text{Br}^- (s) \rightleftharpoons \text{AgBr}(s) + e^- \] (55.63)

Similar precipitation and complex-formation titrations as well as oxidation–reduction titrations are described in Skoog et al. (2007).

Coulometric titrations possess some practical advantages: no standard solutions are required and unstable reagents can be handled by means of direct current for analytical applications. High accuracy of the titrations is possible, and the method can be readily adapted to automatic remote control of the titrator, with respect to controlled-potential coulometry, a wider field of practical applications exists. Of en, automatic titrators for multipurpose and single analysis employ potentialometric endpoint detection. Examples are sulfur dioxide monitors and water breathers (Karl Fischer). For more detailed information concerning applications of coulometry, see Dahmen (1986).

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Further Information


