

# Basics of Titration



Titration Theory

## Basics of Titration

METTLER TOLEDO



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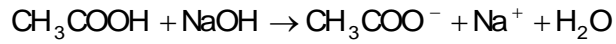
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This booklet is intended as a first introduction to theory and practice of titration. The basic knowledge that is needed to understand titration is given, different kinds of titration types are illustrated and evaluation principles explained. Special attention is given to supply all the necessary information needed to perform titration correctly so as to produce reliable data. Frequent error sources are discussed in detail and also preventive measures are proposed that can be implemented to avoid the generation of faulty results. Finally, a brief introduction to chemistry – relevant to titration – is given.

# 1. Definition of titration

Titration is an analytical technique which allows the quantitative determination of a specific substance (analyte) dissolved in a sample. It is based on a complete chemical reaction between the analyte and a reagent (titrant) of known concentration which is added to the sample. A well-known example is the titration of acetic acid (CH<sub>3</sub>COOH) in vinegar with sodium hydroxide, NaOH:



Analyte          Reagent          Reaction Products

The titrant is added until the reaction is complete. In order to be suitable for a determination the end of the titration reaction has to be easily observable. This means that the reaction has to be monitored (indicated) by appropriate techniques, e.g. potentiometry (potential measurement with a sensor) or with colour indicators.

The measurement of the dispensed titrant volume allows the calculation of the analyte content based on the stoichiometry of the chemical reaction. The reaction involved in a titration must be **fast, complete, unambiguous** and **observable**.

## 2. Historical development

### The classical way

Titration is a classical analytical technique widely used. Originally, it was performed by adding the titrant using a graduated glass cylinder (burette). With a tap the titrant addition was regulated manually. A change in colour indicated the end of the titration reaction (endpoint).

At first, only those titrations showing a significant colour change upon reaching the endpoint were performed. Later titrations were coloured artificially with an indicator dye. The precision achieved depended mainly on the chemist's skills and, in particular, on his ability for perception of different colours.

### The modern way

Titration has experienced a strong development: manual and – later – motor-driven piston burettes allow accurate and repeatable titrant addition. Potentiometric sensors replace the colour indicators, thus achieving higher precision and accuracy of results. The graphical plot of potential versus titrant volume and mathematical evaluation of the resulting titration curve provides a more exact statement about the reaction than the colour change at the endpoint. With microprocessors the titration can be controlled and evaluated automatically. This represents an important step towards complete automation.

### Today

Development is not yet complete. Modern titrators such as the Titration Excellence titrators offer new features that increase the ease of use, efficiency and safety of the instrument as well as the titration process:

- Intuitive user interface on a brilliant touch screen: start your titration with One Click
- Automatic burette recognition and Hot Plug & Play of peripherals
- Plug & Play titration sensors (DGi1xx and DMi1xx): automatic recognition and data storage in the sensor head
- Personal Home Screen and flexible user management
- Modular system that can be tailored exactly to individual needs
- Sample changers and automation accessories for high sample throughput
- Flexible method development to achieve complete analysis sequences based on simple operation functions such as 'Dispense', 'Stir', 'Titration', 'Calculation'
- PC Software LabX<sup>®</sup> titration for titrator control, method development, data archiving and management and full record of all installation, preparation and analysis tasks in the audit trail.



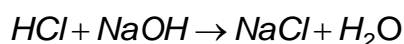
Figure 1: Excellence Titrator T9 with two InMotion™ Autosamplers

### 3. Titration theory

#### 3.1. Types of chemical reactions

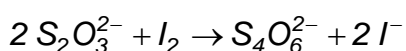
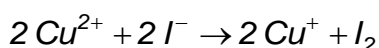
There are several different kinds of chemical reactions that show changes which can be detected and thus utilised for analyses by titration. These categories are given below with an example reaction and some typical applications as well:

##### Acid/Base reactions:



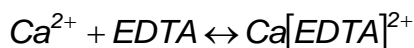
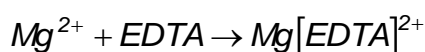
Examples: Acid content in wine, milk, ketchup  
Content of HCl, HNO<sub>3</sub>, H<sub>2</sub>SO<sub>4</sub>.

##### Redox reactions:



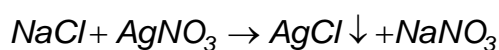
Examples: Copper content  
Chromium and nickel in electroplating baths

##### Complexometric reactions:

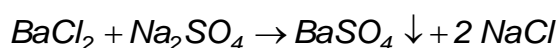


Examples: Total hardness of water (Mg<sup>2+</sup> and Ca<sup>2+</sup>)  
Calcium content in milk and cheese  
Cement analysis

##### Precipitation reactions:

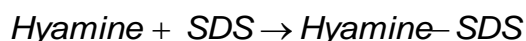


Examples: NaCl (salt) content in crisps, ketchup and food  
Silver content in coins



Examples: Sulphate content in mineral water  
Sulphate content in electroplating baths

##### Colloidal precipitation reaction:



Examples: Anionic surfactant content in detergents, washing powders or shower gels

## 3.2. Titrant addition

### Volumetry

With volumetric titration the titrant is added to the sample by a burette from an external source. The volume of titrant added to the sample is measured during the titration.

### Coulometry

In coulometric titration the titrant is generated electrochemically in the sample within in the titration cell. This means that a precursor of the titrant that reacts with the analyte is already present in the sample before the analysis starts.

Coulometric titration is mainly employed for low water content determination according to the Karl Fischer titration technique. The amounts of water generally determined via coulometric Karl Fischer titration are smaller than 50-100 ppm (0.005-0.01%).

## 3.3. Indication principles

Titration can be classified according to the indication principles and chemical reactions occurring:

Indication	Reaction type/effect	Sensor
<b>Potentiometry:</b> The concentration-dependent potential (mV) of a solution is measured against a reference potential	Aqueous acid/base titrations:	DG(i)111-SC
	• Acidic and basic solutions	DGi101-SC DGi102-Mini
	Aqueous titrations in difficult matrices:	DGi112-Pro
	• Acid mixtures in electrochemical baths	
	Non-aqueous acid/base titrations:	DG(i)113-SC
	• Content determination of pharmaceutical constituents	
	• Acid or base number in oils	
	Acid/base titrations of viscous or protein/sulphide containing samples	DGi114-SC
	Aqueous acid/base titrations of low conductivity or food samples:	DGi115-SC
	• Acid content in fruit/vegetable juices, wine, milk, vinegar	
Non-aqueous acid/base titrations of critical samples:	DGi116-Solvent	
• Acidity/alkalinity of polyols		
Aqueous acid/base titrations, direct pH measurements with simultaneous T-reading:	DGi117-Water	
• pH, acidity, alkalinity of domestic, natural source or rainwater		

	Redox titrations:	DM(i)140-SC
	<ul style="list-style-type: none"> <li>Hydrogen peroxide content with Cerium(IV)sulphate</li> <li>Back titrations with potassium iodide: hypophosphite in plating baths</li> </ul>	DMi101-Mini
	Redox titrations at constant pH:	DMi147-SC
	<ul style="list-style-type: none"> <li>Bromatometric, iodometric or cerimetric determination of pharmaceutical constituents</li> </ul>	
	Precipitation titrations:	DM(i)141-SC
	<ul style="list-style-type: none"> <li>Salt content in ketchup</li> <li>Silver content in alloys</li> <li>Sulphide / mercaptans in oil</li> </ul>	DM(i)102-Mini DM405-SC
	Precipitation titrations:	DMi145-SC
	<ul style="list-style-type: none"> <li>Chloride in crude oil</li> </ul>	
	Precipitation titrations at constant pH:	DMi148-SC
	<ul style="list-style-type: none"> <li>Chloride in physiological solutions</li> </ul>	
	Precipitation surfactant titrations:	DS500
	<ul style="list-style-type: none"> <li>Anionic surfactants in liquid detergents</li> <li>Non-ionic surfactants</li> </ul>	
	Two-Phase precipitation surfactant titrations:	DS800-TwoPhase
	<ul style="list-style-type: none"> <li>Anionic/cationic surfactants in coolants, lubricants or cosmetic products</li> </ul>	
<b>Voltametry:</b>	Karl Fischer:	DM143-SC
The concentration dependent potential of a solution (mV) is measured at a constant electric current	<ul style="list-style-type: none"> <li>Water in butter</li> <li>Water in oil or gasoline</li> </ul> Bromine number or index <ul style="list-style-type: none"> <li>Bromine number or index of gasoline</li> </ul>	
<b>Amperometry:</b>	Amperometric titration:	DM143-SC
The current flowing through a sample solution ( $\mu\text{A}$ ) is measured at a constant potential	<ul style="list-style-type: none"> <li>Iron(II) determination</li> <li>Vitamin C determination</li> </ul>	
<b>Photometry:</b>	Complexometry:	DP5 Phototrode™
The light transmission (mV or % transmission) of a coloured or turbid solution is measured with a photometric sensor	<ul style="list-style-type: none"> <li>Total hardness of water</li> <li>Nickel content in plating baths</li> </ul> Turbidimetry: <ul style="list-style-type: none"> <li>Two-phase surfactant titration according to Epton</li> </ul>	

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**Conductivity:**

The change of conductivity during a titration is measured with a conductivity sensor connected to the conductivity board of an Excellence titrator

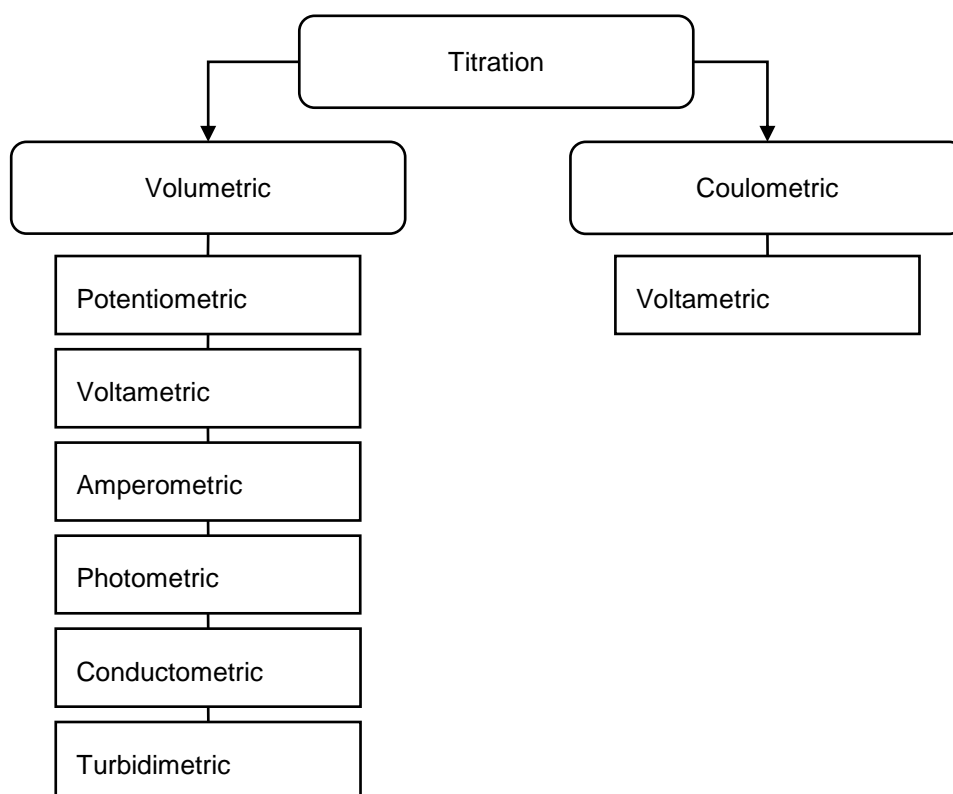
**Conductometric titration:**

- Base number of oils according to IP400
- Sulphate content by precipitation with Barium

InLab<sup>®</sup>717InLab<sup>®</sup>718

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A schematic overview of the different titrant addition and indication techniques is given below:



**Figure 2: Overview of the different titration techniques**

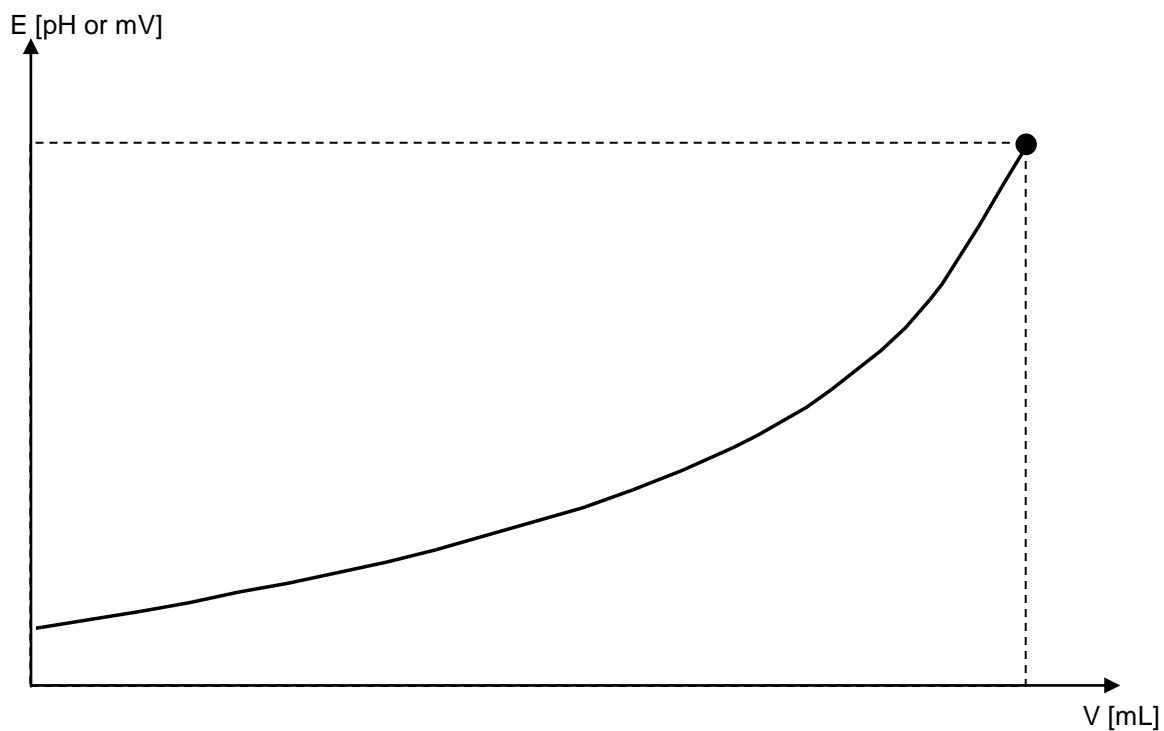
### 3.4. Endpoint titrations - Equivalence point titrations

There are basically two titration modes which can be distinguished: endpoint titrations and equivalence point titrations.

#### Endpoint titration mode (EP)

The endpoint mode represents the classical titration procedure: the titrant is added until the end of the reaction is observed, e.g., by a colour change of an indicator.

With an automatic titrator, the sample is titrated until a predefined measurement value is reached, e.g. pH = 8.2 or E = 100 mV.

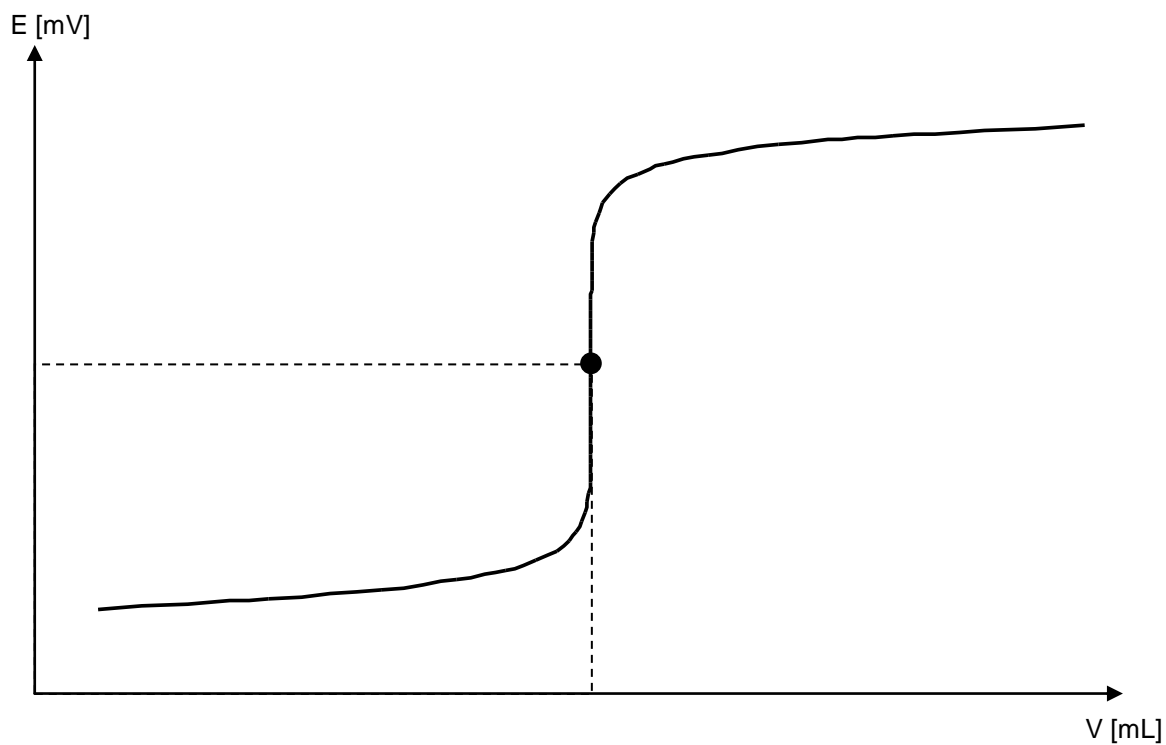


**Figure 3: Endpoint titration curve**

### Equivalence point titration mode (EQP)

In type of titration the point is identified where analyte and reagent are present in equivalent amounts.

In most cases this is virtually identical to the inflection point of the titration curve, for example with titration curves obtained from acid/ base titrations.



**Figure 4: Titration curve of equivalent point titration**

The inflection point of the curve is defined by the corresponding pH, potential (mV), relative transmission (%T), relative Absorbance (A), current (I), temperature (T), etc. and titrant consumption (mL).

From the equivalence point the consumption of a titrant of known concentration is calculated. The product of concentration and the titrant consumption gives the amount of substance which has reacted with the sample.

In the titrator the measured points are evaluated according to specific mathematical procedures which lead to an evaluated titration curve. The equivalence point is then calculated from this evaluated curve.

### 3.5. Fields of use

Titration is a widely applied analytical technique. Some areas where titration is used are given below:

Agriculture	Medicine
Aircraft	Military
Building materials	Mining
Car manufacturing	Oil Industry
Ceramics	Packing materials
Chemical industry	Paints, Pigments
Coal products	Paper & Pulp
Coating	Petroleum
Cosmetics	Pharmaceuticals
Detergents	Photo industry
Drugs	Plastic products
Electronic industry	Printing, Publishing
Electroplating	Rail
Energy	Rubber
Explosives	Soaps
Food	Stone (Clay, Cement)
Glass	Textiles
Government	Tobacco industry
Health	University, School
Leather	Water
Machinery	Zeolites

### **3.6. Advantages of titration**

There are several reasons why titration is used in laboratories worldwide:

- Titration is an established analytical technique
- It is fast
- It is a very accurate and precise technique
- A high degree of automation can be implemented
- Titration offers a good price/performance ratio compared to more sophisticated techniques
- It can be used by low-skilled and low-trained operators
- No need for highly specialised chemical knowledge

## 4. Automated titrators

### 4.1. Definition

A titrator is an instrument which allows the automation of all operations involved in titration: **titrant addition, monitoring of the reaction (signal acquisition), recognition of the endpoint, data storage, calculation and results storage.**

### 4.2. Working principle of automated titrators

Automated titrators follow a defined sequence of operations. This sequence is basically the same for all different models and brands. This sequence is performed and repeated several times until the endpoint or the equivalence point of the titration reaction is reached (titration cycle).

The titration cycle is shown in the figure below and can be divided in roughly 4 parts. Each part has different parameters (e.g. stirring speed) which are defined according to the specific titration application.

More complex applications require more steps, for example dispensing of an additional reagent for back titration, dilution of the sample, adjustment of the initial pH value, etc. These steps and the corresponding parameters are defined in the titration methods used by the titrator.

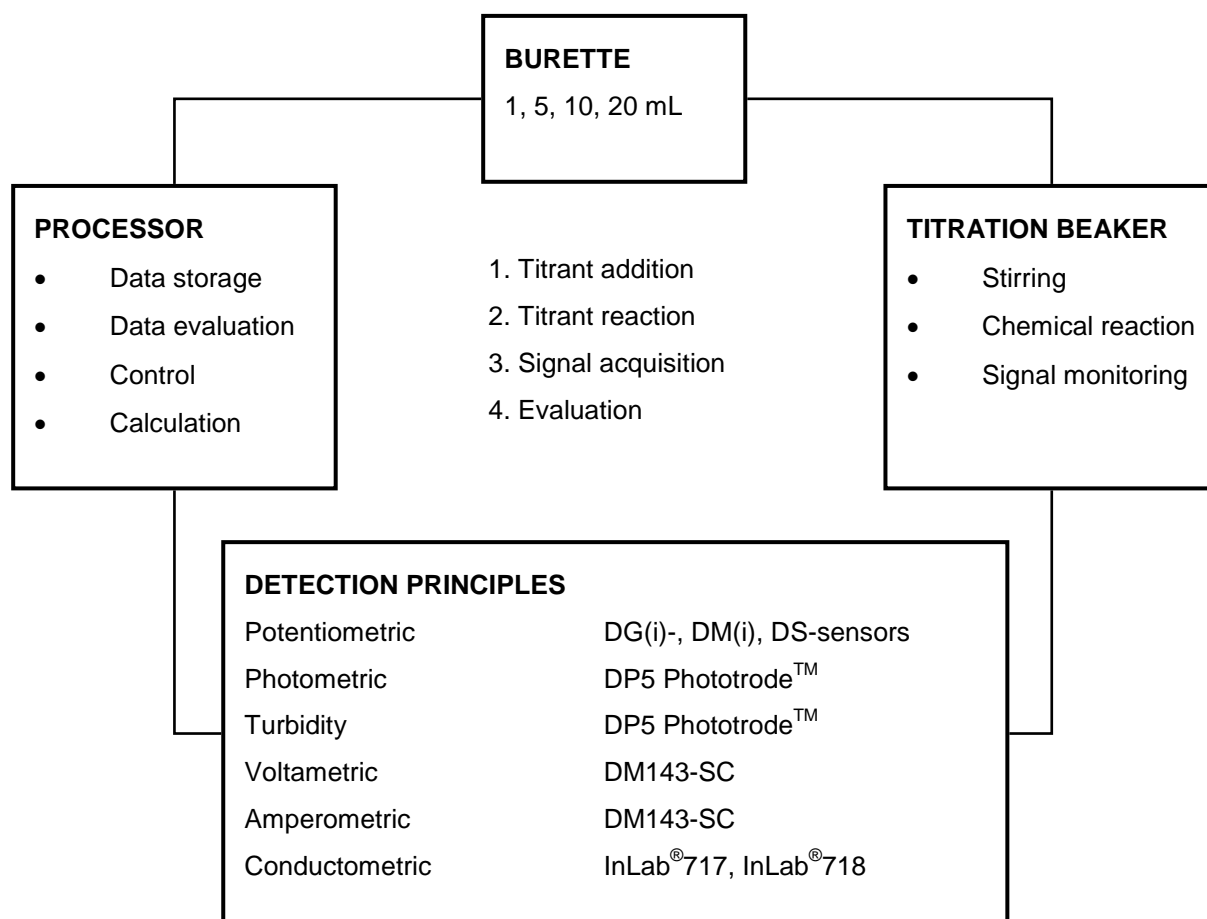


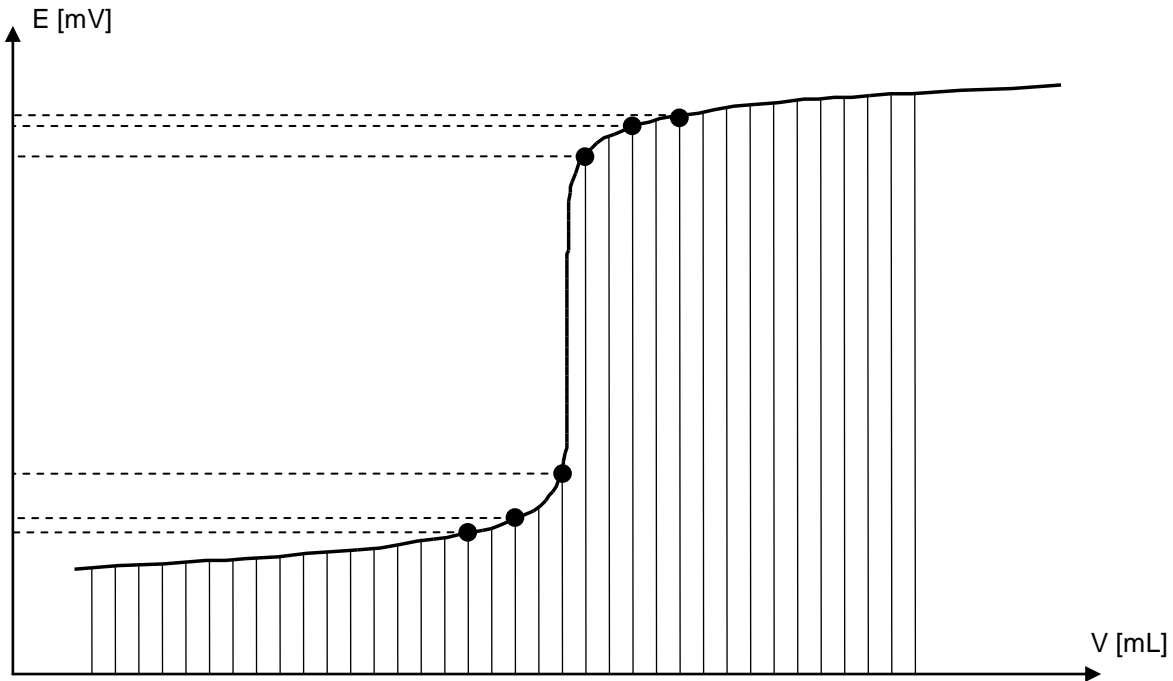
Figure 5: Schematic representation of the different steps in a titrator method

### 4.3. Titrant addition

During a titration titrant is added to the sample and the reaction observed. The titrant can be added to the sample in two different ways. Either fixed amounts of titrant are added for every new measurement point, or the control algorithm in the titrator is free to determine (within limits) how much titrant should be added to the sample for every new measurement point. These two principles are described below.

#### Incremental titrant addition

The titrant is added in constant volume increments  $\Delta V$ :



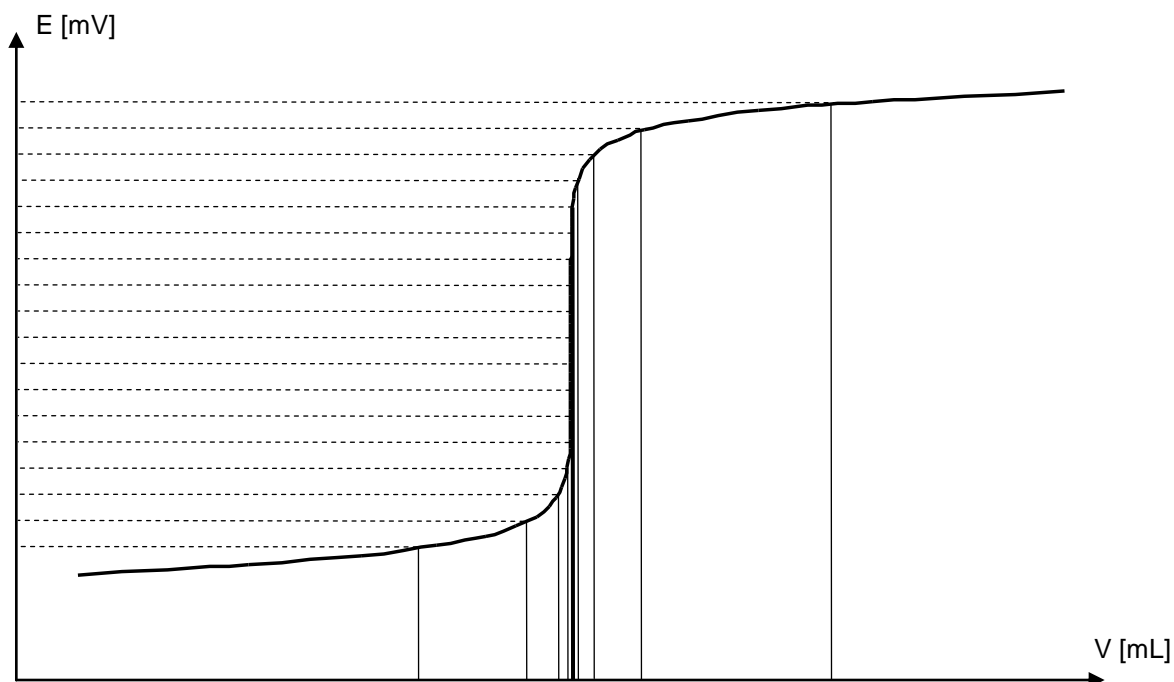
**Figure 6: Incremental addition of titrant**

The incremental titrant addition is used in titrations which are prone to have unstable signals or unexpected equivalence points. Some examples of these reactions are non-aqueous titrations, redox titrations, photometric titrations like total hardness in water or ionic surfactant titrations via turbidimetric detection.

This addition technique may lead to the circumstance that the steepest region of the curve has relatively few measured points, so it might be necessary to make  $\Delta V$  very small.

#### Dynamic titrant addition

With the dynamic titrant addition the control algorithm of the titrator automatically selects the increment per measured point, based on parameters defined by the user. The goal is to achieve a constant measured signal increase of the titration curve that results in a curve with more measured points in the steepest part. This consequently allows a more accurate evaluation in order to find the exact position of the equivalence point.



**Figure 7: Dynamic titrant addition**

An additional benefit of this technique is that the speed of analysis is speeded up significantly by being able to use big increments in the flat regions of the titration curve.

Dynamic titrant addition is used mainly for acid/base titrations, aqueous titrations, precipitation titrations and some redox titrations.

### **Continuous titrant addition**

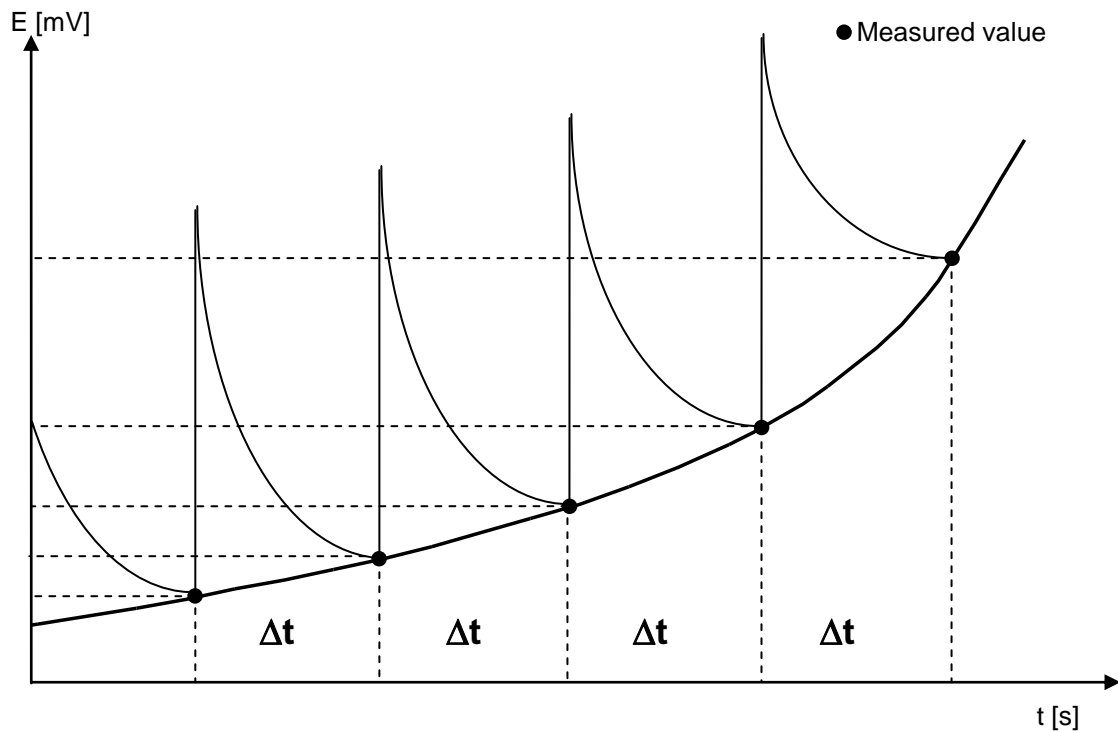
Continuous titrant addition means that titrant is continuously added to the sample until a certain point has been reached. This type of addition is mainly used in endpoint titrations such as KF titrations and is discussed in some further detail in chapter 5.3.

## **4.4. Measured value acquisition**

After incremental or dynamic titrant addition, the measurement of the next data point on the titration curve should be performed only after the previous portion of titrant has completely reacted with the sample. There are two different options to make sure that this is the case. One can either instruct the titrator that a measurement should be taken only after a certain time interval, or, alternatively, one can use the signal stability as an indicator for data acquisition.

### **Timed-increment acquisition**

With timed-increment signal acquisition the detected signal is recorded a fixed waiting time  $\Delta t$  after the last titrant addition.

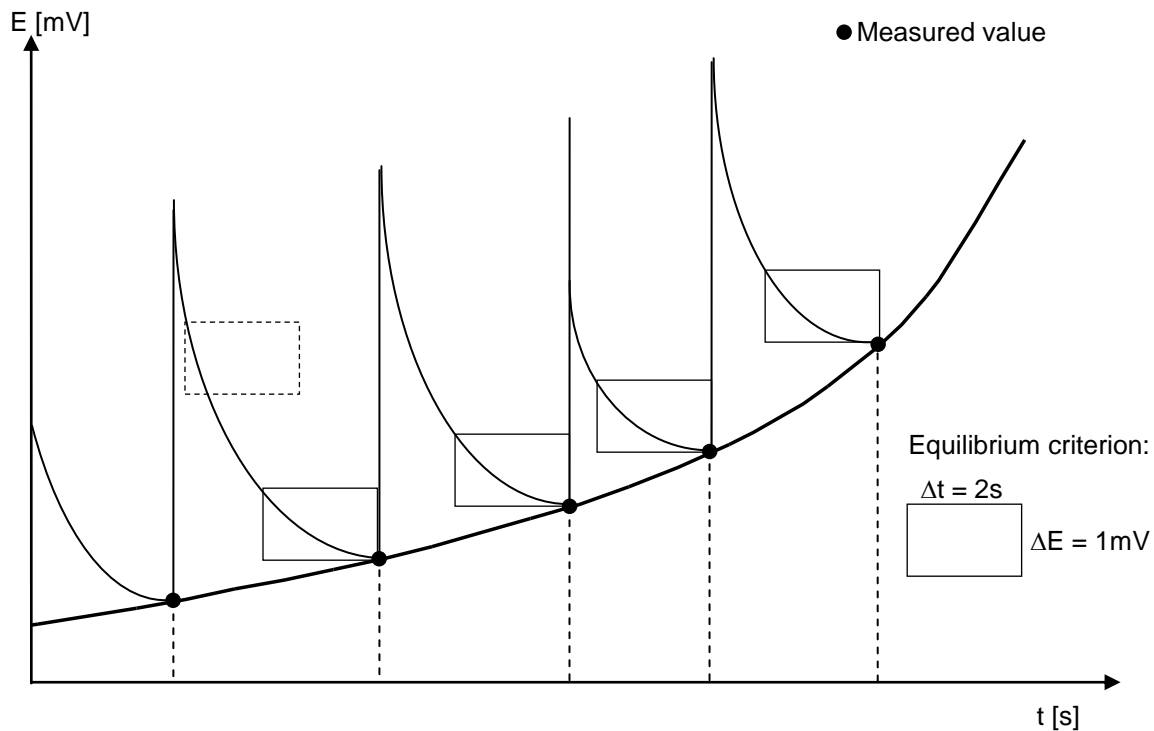


**Figure 8: Fixed time increments on a titration curve**

This mode of data acquisition is favoured when the signal is noisy and finding a stable measurement point can be erratic. In this way also the titration speeds up significantly. In general this data acquisition mode is used in e.g. non-aqueous titrations like base number in oils or titration with  $\text{HClO}_4$  as titrant.

### Equilibrium-controlled acquisition

In equilibrium controlled acquisition the measurement data is only then acquired by the titrator when the pH or potential (mV) of a sample change less than a certain amount ( $\Delta E$ ) within a defined time interval ( $\Delta t$ ). This is a good indicator for the fact that all the titrant has reacted with the sample, so the sample composition will not change any further and thus the observed signal will remain stable.



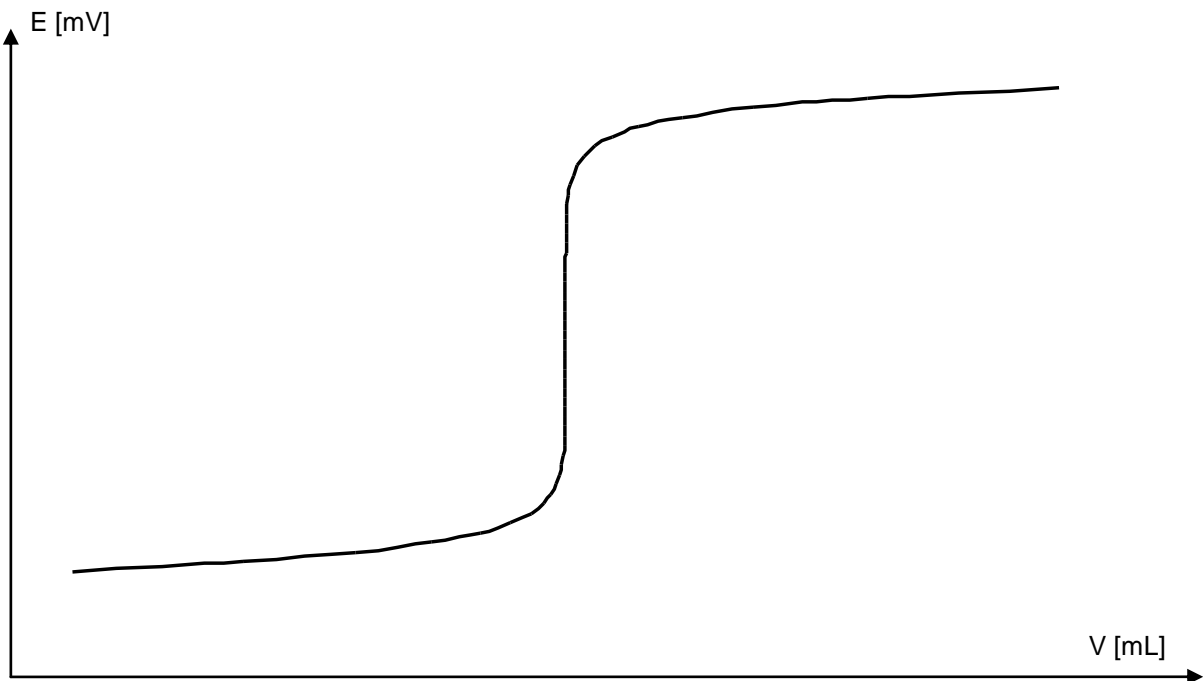
**Figure 9: Equilibrium controlled titration curve**

Here, the user can also define the parameters that shall be used by the titrator algorithm. The algorithm is only allowed to look for equilibrium conditions within time limits of minimum and maximum time ( $t(\min)$  and  $t(\max)$ ), which are defined in the titrator method.

#### 4.5. Evaluation principles

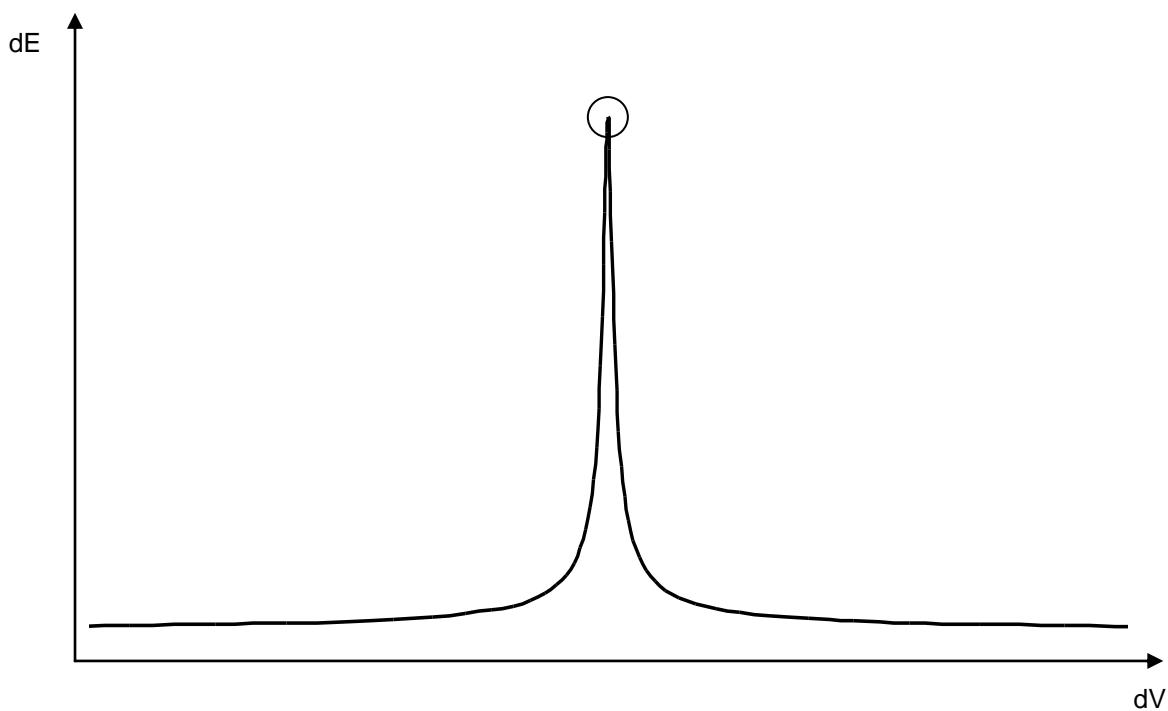
The titration curves made up of the individual data points acquired can take 4 different forms, and should be analysed with the appropriate evaluation algorithms. These four forms are: the **symmetric curve**, **asymmetric curve**, the **minimum/maximum curve**, and the **segmented curve**.

### Symmetric S-shaped curve:



**Figure 10: Symmetric S-shaped curve**

The symmetric titration curve has a symmetric profile and the equivalence point is the inflection point of the curve. Traditionally this curve was evaluated by plotting the first derivative  $dE/dV$  versus titrant consumption  $V$ . The maximum of the derivative is then at the inflection point and indicates the equivalence point. This type of curve is generally produced by acid/base titrations, redox titrations or precipitation titrations.



**Figure 11: First derivative of a titration curve**

In modern titrators the evaluation of these curves is performed in a more sophisticated way via data fitting algorithms to evaluate the equivalence points more accurately than with the simple derivatives method.

**Asymmetric curve:**

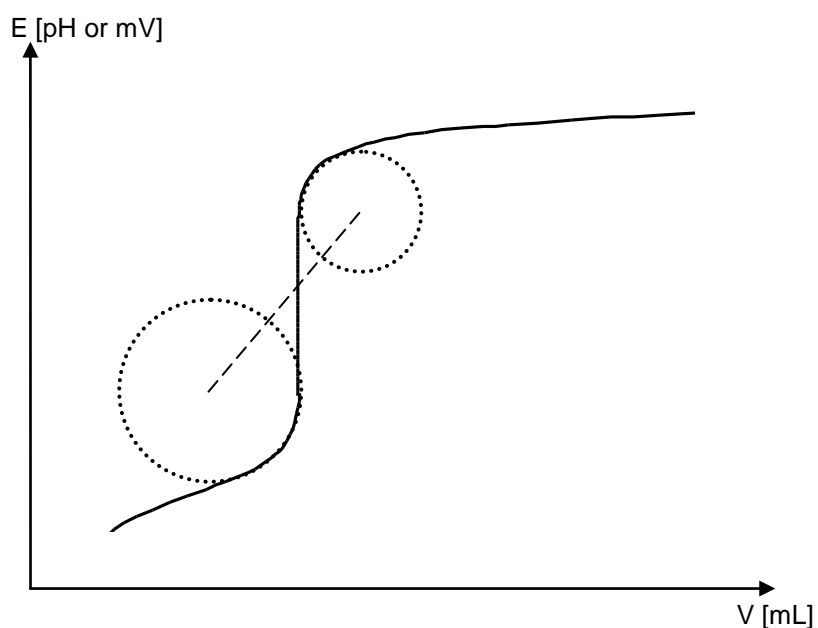
This titration curve shows a different profile than the typical symmetric S-curve, and thus a different evaluation procedure is needed. The asymmetry has to be taken into account for this evaluation since the equivalence point is shifted towards the region with the stronger curvature. In the case depicted towards the region with the stronger curvature, which is located in the upper part of the steepest jump.

This is a typical titration curve for e.g. photometric titrations, redox titrations or turbidimetric titrations.



**Figure 12: Asymmetric titration curve**

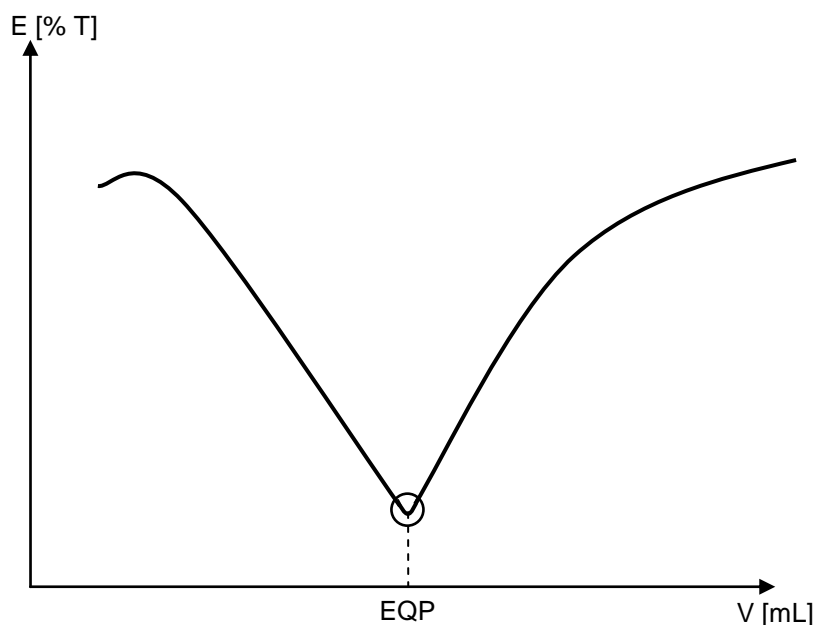
Manually, the evaluation of these types of curves is based on the Tubbs procedure (see "Fundamentals of titration", ME-704153A), where the curve is fitted with two circles, nesting inside the curvature of the titration curve. The intersection point of the line connecting the two circles with the titration curve indicates the equivalence point.



**Figure 13: Evaluation of an asymmetric titration curve**

In the titrator the evaluation algorithm for these types of curves is the one termed 'asymmetric'.

### Minimum (Maximum) curve:



**Figure 14: Minimum/maximum titration curve**

This curve shows the typical profile obtained from turbidimetric titrations, for example, determination of the anionic surfactant content, where a colloidal precipitate is formed by adding the titrant. This precipitate leads to an increased turbidity of the solution. After the EQP the additional titrant added dilutes the sample again, making the solution less opaque. The profile of the curve is therefore characterized by a minimum in the curve, which is the position of the equivalence point EQP.

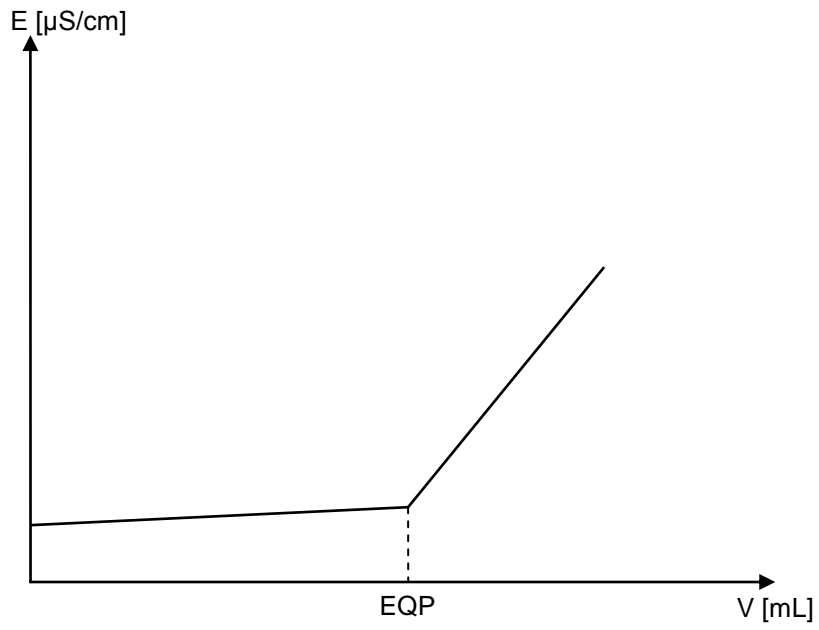
In the titrator the evaluation algorithm to be chosen in this case is **'minimum'**. If a similarly shaped curve is obtained that has a maximum instead of a minimum, the evaluation procedure **'maximum'** should be chosen.

### Segmented curve:

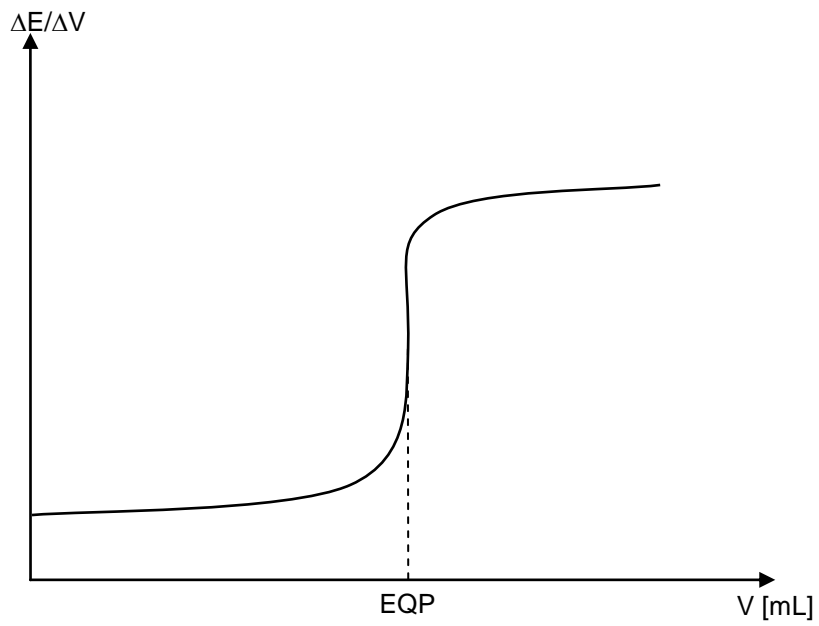
This profile is obtained when conductometric titrations are performed where the signal change in  $\mu\text{S}/\text{cm}$  or  $\text{mS}/\text{cm}$  is recorded as a function of volume. The EQP is defined by an altered change of the conductivity per volume unit, which shows up as a bend in the curve. The curve is evaluated traditionally by determining the maximum of its second derivative.

This type of curve is mainly seen in conductometric titrations, e.g.  $\alpha$ -acids in beer, but is also observed in amperometric Vitamin C content determination.

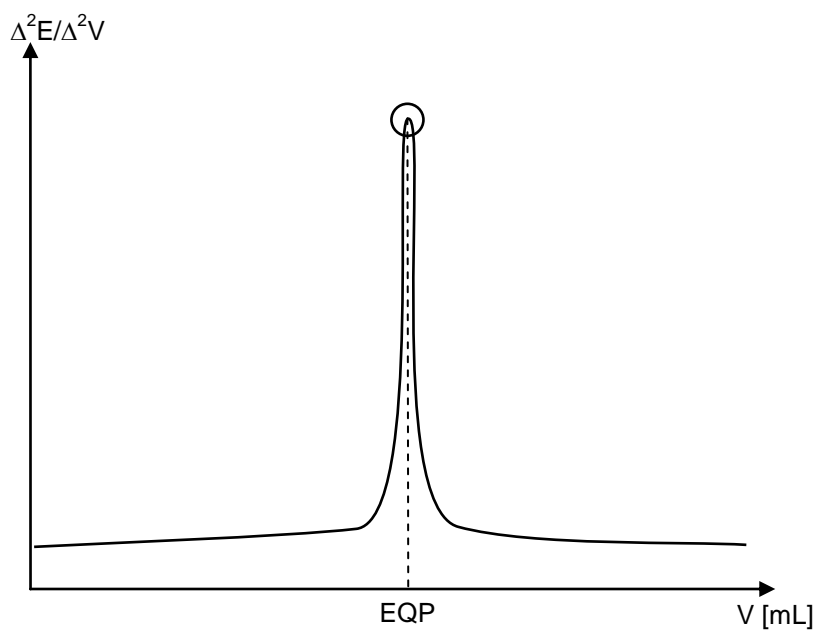
In the titrator this type of curve is evaluation with the procedure **'segmented'**.



**Figure 15: Segmented curve: measured values**



**Figure 16: Segmented curve: first derivative**



**Figure 17: Segmented curve: second derivative**

## 5. How to get the best titration results

The primary goal of any analysis is to get accurate and precise results in as short a time as possible. Often neglecting the smallest thing can have an enormous impact on the reliability and quality of the final result. This chapter discusses some of the critical factors affecting titration results and provides some insight into how to eliminate some of the more common errors.

### Quality management in titration

Quality management has become a relevant topic for the user of analytical instruments. It is mainly based on documentation of the proven technical specifications, the measurements and the analytical methods used. The documentation represents the basics of each quality management system and is requested by the auditors during periodical checks.

### Quality management: why?

- The customer requires correct results with respect to e.g. accuracy, precision, and reproducibility.
- Pharmaceutical companies and government organizations (e.g., FDA, EPA) require traceability of the results and thus qualification of the instruments.

Both can be achieved by a complete documentation of results, compliance to technical specifications and method checks.

The documentation procedure of analytical work in the laboratory is regulated by the applied QM-System (e.g. GLP), the proof of technical specifications is resumed in the certification procedure and specific analytical methods have to be tested in order to get correct results, i.e. the methods have to be validated. Last but not least, the instrument has to be maintained over the whole lifetime to guarantee continuation of correct results.

These individual areas encompass the following:

#### GLP:

Quality of planning, performing, controlling and reporting of laboratory work

#### Certification:

Quality of the instrument and of the measured values obtained by this instrument

#### Validation:

Quality of the analytical method and thus of the achieved results

#### Qualification:

Quality checking over the whole lifetime of the instrument

### GLP

International bodies have elaborated a set of rules concerning the analytical work in the laboratory in order to achieve a standard regulation recognized and accepted in all countries of the world. These rules are commonly known as GLP rules (GLP, Good Laboratory Practice). GLP is a formal framework for testing chemicals and consists of 10 specific rules. The goals of GLP are:

- Quality assurance of test data
- Mutual acceptance of data
- Avoid multiplication of tests

In particular, avoiding the multiplication of tests saves costs and time. For instance, a customer does not have to repeat the same test that the producer performed at the end of the production process of a specific chemical product.

### Certification of an automatic titrator

The certification is a check of the instrument in order to

- Verify if the technical specifications are fulfilled,
- or to verify if the actual specifications meet the required level

Certification is only a part of a list of measures to guarantee correct results. Other points that have to be considered are the system suitability tests, the sensor calibration, the titrant standardization, and method validation which are described in this chapter too.

A complete certification of the titrator can be performed by testing the following hardware:

#### **Sensor input and amplifier:**

- Potential measurement with certified voltmeter
- Temperature sensor input (measurement with certified resistors)

#### **Dosing accuracy:**

- Burette motor drive: Measurement of the piston stroke with a certified micrometer
- Glass burette: Measurement of the deviations from the specified diameter value of the glass cylinder. Different volumes of water are dispensed and their mass is compared to the dispensing of a certified reference burette.

### **Qualification**

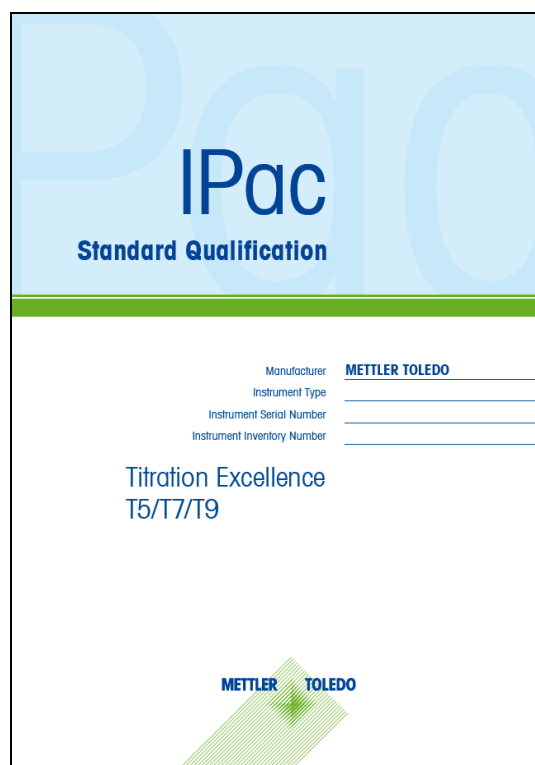
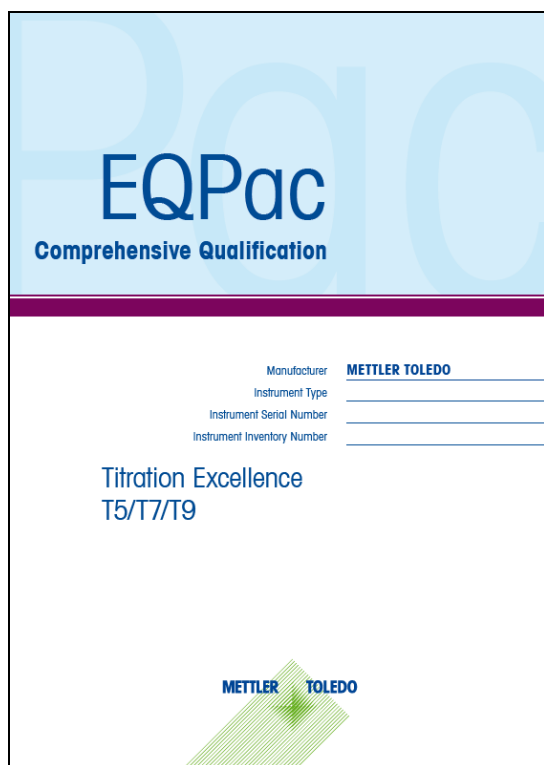
Quality management requires the documentation of the performance over the whole lifetime of the instrument, i.e., from the project phase through manufacturing, installation, operation until disposal of the instrument.

All these steps are resumed in the comprehensive concept of **Qualification**:

- Specification Qualification (**SQ**): Requirements, Functions, Design, HW/SW
- Construction Qualification (**CQ**): Production control for each product
- Design Qualification (**DQ**): Selection of correct instrument for intended use
- Installation Qualification (**IQ**): Evidence of correct installation at customer's facility
- Operational Qualification (**OQ**): Evidence and compliance to specifications, SOPs, initial calibration, user training
- Performance Qualification (**PQ**): Periodical calibration and certification
- Maintenance Qualification (**MQ**): Definition of preventive maintenance and calibration/certification intervals

METTLER TOLEDO titrators are supported with regard to the following:

1. Specially trained MT service engineers that perform the calibration and certification of the titrator hardware with specific calibrated and certified tools (CertiCase, Excellence Test Unit) to ensure traceability to international standards
2. The declaration of System Validation stating that the titrator was developed and manufactured in accordance to a strict quality management system.
3. IPac: service product that offers an initial equipment qualification including installation and operational qualification (IQ/OQ) of the titrator at the installation site and the corresponding qualification documentation
4. EQPac: service product that offers complete qualification including full documentation of the instrument's history.



## Validation of Titration Methods

While the goal of any analysis is to get correct results, very often the 'correct' result is not necessary the 'true' result. As a result our goal is in fact to get the best result possible. This means a result as accurate, precise and true as possible. To do this it is important to critically investigate the factors affecting each of these and minimize the negative influences. Before doing this it is required to define what is meant by the terms accuracy, precision and trueness (the definition used here is according to ISO 5725-1:1994).

### 5.1. Accuracy, precision and trueness

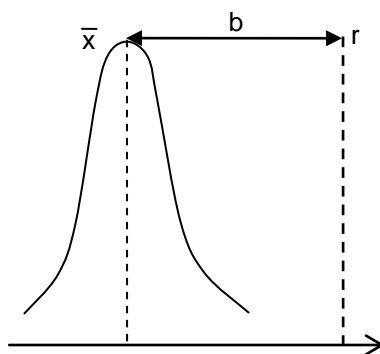
#### Trueness

The trueness of a result is defined as the closeness of the mean value of the results of a measurement series to the 'true' value. But what is the 'true' value? In theory this 'true' value is the result that would be obtained by a perfect measurement. In practice the 'true' value is the universally recognized result or certified value. Synonyms include reference value, best estimate or assigned value.

Mathematically the trueness is given by:

$$b = \bar{x} - r \quad \text{where} \quad r = \text{true value}$$

$$\bar{x} = \frac{\sum x_i}{n} \quad \bar{x} = \text{mean value of a series of } n \text{ measurements}$$



**Figure 18: Trueness of a result**

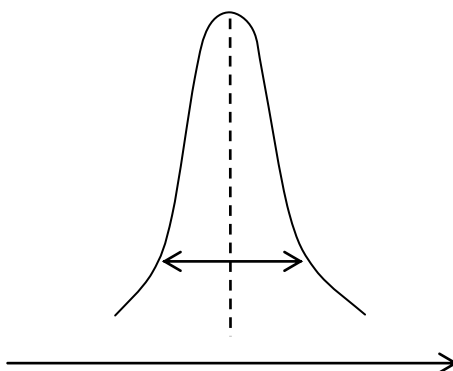
Deviation from the 'true' value is due to systematic errors and can generally be corrected for.

### Precision

The precision of a result is defined as the closeness of the individual results in a series to each other and is given statistically by the standard deviation,  $s$  or relative standard deviation,  $srel$  of a series of measurements.

$$s = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (x_i - \bar{x})^2} \quad \text{and}$$

$$srel = \frac{s}{\bar{x}} \times 100 \quad \text{(also known as \%RSD)}$$



**Figure 19: Precision of a result**

The term precision includes the repeatability of the measurements (measured under identical conditions) as well as the reproducibility of the measurements when conditions are varied e.g. different instrument, different operator, different time of day etc.

Poor precision is generally due to random errors and the source of the imprecision is harder to identify.

## Accuracy

Accuracy is a term used to describe the combination of both the trueness and the precision of the result and is influenced by both systematic and random errors.

### 5.2. Types of errors

An error is defined as any deviation from the true value and can be classified as systematic, random or gross errors.

#### Systematic errors

A systematic error is an error that is constant or drifting slightly and is due to a consistent mistake made during the analysis. Typical systematic errors in titration analyses include:

- Differing or incorrect analytical method compared to that used to determine the 'true' value
- Incorrect calculation formulas
- Sampling errors
- Sample size errors e.g. due to a constant weighing error
- Incorrect titrant concentration
- False or missing blank value
- Incorrect or missing sensor adjustment
- Too high titration speed for the chemical reaction
- Too high titration speed for the electrode response

Once the source of a systematic error is identified it is usually easy to correct for these errors.

#### Random errors

A random error is a component of the overall error that varies in an unpredictable fashion. It is usually difficult to identify these errors. Typical sources of random errors include:

- Poor sample handling
- Inadequate equipment e.g. too low balance resolution, wrong grade of glassware etc.
- Incorrect method parameters e.g. too large increments, insufficient waiting time between increments.
- Bubbles in burette tubes
- Ineffective rinsing between samples
- Lack of operator training
- Inadequate environmental conditions e.g. temperature and humidity fluctuations

If the source of a random error cannot be identified then the only solution is to increase the number of replicates in order to get a more trustworthy mean value. This generally leads to waste of sample, reagents and time.

#### Gross errors

Gross errors are a form of both systematic and random errors caused by blunders or mistakes and are easily identifiable. Another name for gross errors is avoidable mistakes. Typical gross errors include:

- Notation mistakes
- Calculation errors
- Mix up of samples and/or reagents
- Wrong sample sizes

- Misunderstandings in instrument operation
- Transcription errors

Adequate training and care during analysis usually eliminates the sources of gross errors.

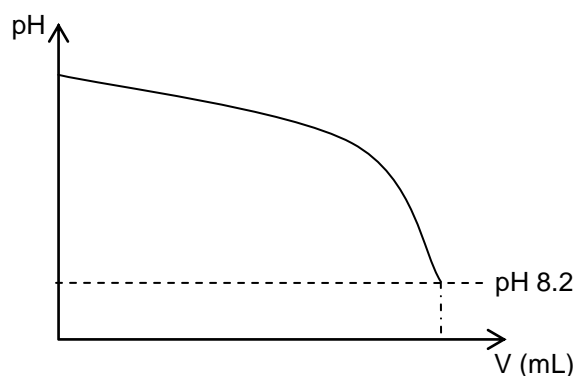
Some of the common sources of errors are discussed below in more detail.

### 5.3. The best method for the job

When performing a titration with a modern automatic titrator there are usually two possibilities when selecting the type of method. These are an endpoint titration to a predefined potential or an equivalence point titration.

#### The endpoint titration

This method of titrating is characterized by setting a predefined end point, usually historically based on the colour change of an indicator or as specified in some standard. The most common form of the endpoint titration is the pH endpoint.



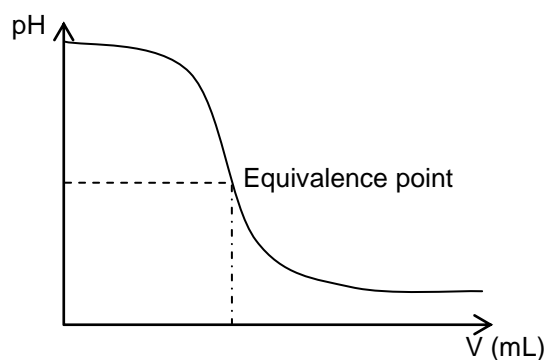
**Figure 20: The endpoint titration**

The endpoint titration has the advantage that it is easy to understand, is usually fairly quick, and closely matches what was done during a manual titration.

The greatest disadvantages of the endpoint titration are that it may not coincide with the 'true' result, it generally requires regular adjustment of the electrode, and often is temperature dependent. The temperature dependence is due to the fact that the measured pH is temperature dependent. As a result it is necessary to measure the sample temperature and compensate for any change if it differs from that measured during electrode adjustment.

#### The equivalence point titration

As the name implies, this method of titration involves determining the point at which the amount of titrant added is exactly equivalent to the amount of analyte originally present in the sample. This point coincides with the chemically 'true' result and is the preferred method. The result is generally accepted as the inflection point in the titration curve.



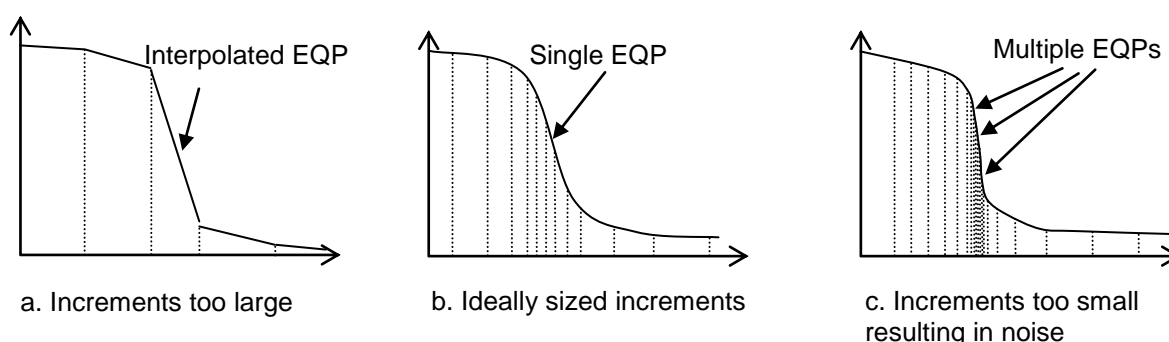
**Figure 21: The equivalence point titration**

This method has the advantages that it is the 'true' result, it does not require sensor calibration and the titration itself is not temperature dependent. The only disadvantages are that it can be slightly slower and only applies when there is a clear inflection point in the curve.

### The correct method parameters

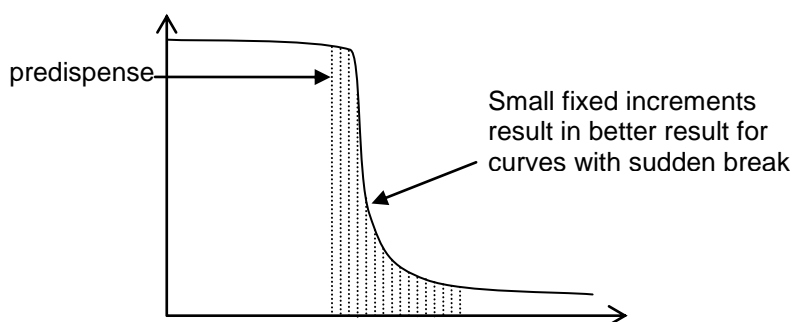
From the above it is clear that the equivalence point method is the preferred method but irrespective of the method chosen, the control and evaluation parameters can critically affect the accuracy and precision of the result. Generally speaking there are three main ways of adding the titrant increments as well as two ways of determining how long to wait between each addition.

With dynamic titrant addition the size of the increment depends on the shape of the titration curve. In flat regions of the curve large increments are added while in the steep region where an equivalence point is expected the titrator adds small increments. This results in a fast but accurate titration but still requires some care in selecting appropriate parameters. If too large increments are added in the steep region of the curve then precision suffers since the instrument has to fit a curve with very few data points. On the other hand, if the minimum increments are too small then noise results and it becomes difficult for the instrument to evaluate an equivalence point.



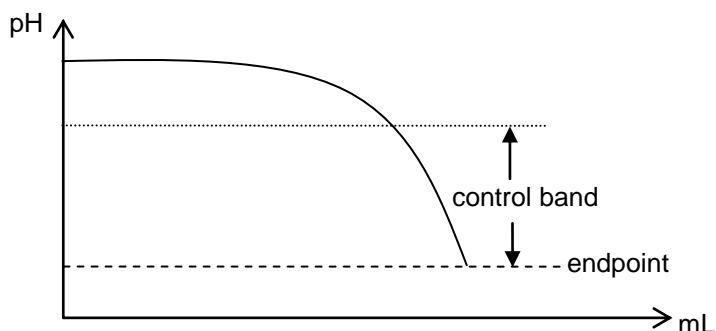
**Figure 22: Increment size and dynamic titrant addition**

For very steep titration curves or curves with a sudden break it is often better to use increment titrant addition or addition using fixed increments rather than dynamic. This is particularly the case with Figure 22: above. Here a large initial increment followed by a succession of small increments would result in a better curve fit and therefore better precision.



**Figure 23: Incremental titrant addition**

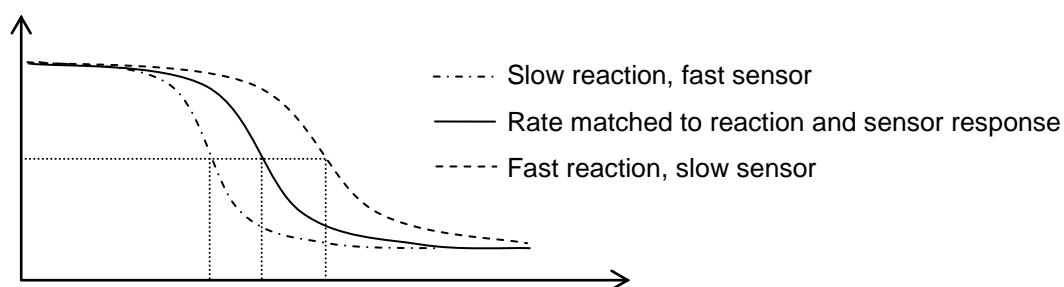
The last method of titrant addition is used exclusively with endpoint titration and is called continuous titrant addition. With this addition the instrument adds titrant continuously at a high rate until a certain distance from the preset endpoint. At this point the rate of addition is reduced until a minimum addition rate or increment size is reached at the endpoint. The distance from the endpoint, sometimes termed the control band, will determine the analysis time as well as the accuracy and precision of the titration. Small control bands result in faster titrations but can result in over titration if the curve is steep. As a rule the steeper the curve the larger the control band must be.



**Figure 24: Continuous titrant addition**

With the time between increments either a fixed time is defined or the equilibrium to be reached is awaited as described in chapter 4.4. In the case of equilibrium both the reaction to be complete and the electrode to respond to any changes is awaited. This is the better method and it is done by defining a maximum drift in the electrode signal before the next increment can be added. If, however, this maximum drift is set to a value that is too high or a fixed time between increments is set that is too short the titrant is added too quickly.

In this case two possible situations can arise. The first is when the titrant is added at a rate faster than the chemical reaction between the titrant and analyte. In this case a build-up of excess titrant, followed by a premature termination of the titration results. This gives results that are consistently too low. In the second case the titrant is added at a rate faster than the electrode response time and this causes a lagging of the electrode signal behind the reaction. Here results that are consistently too high are obtained

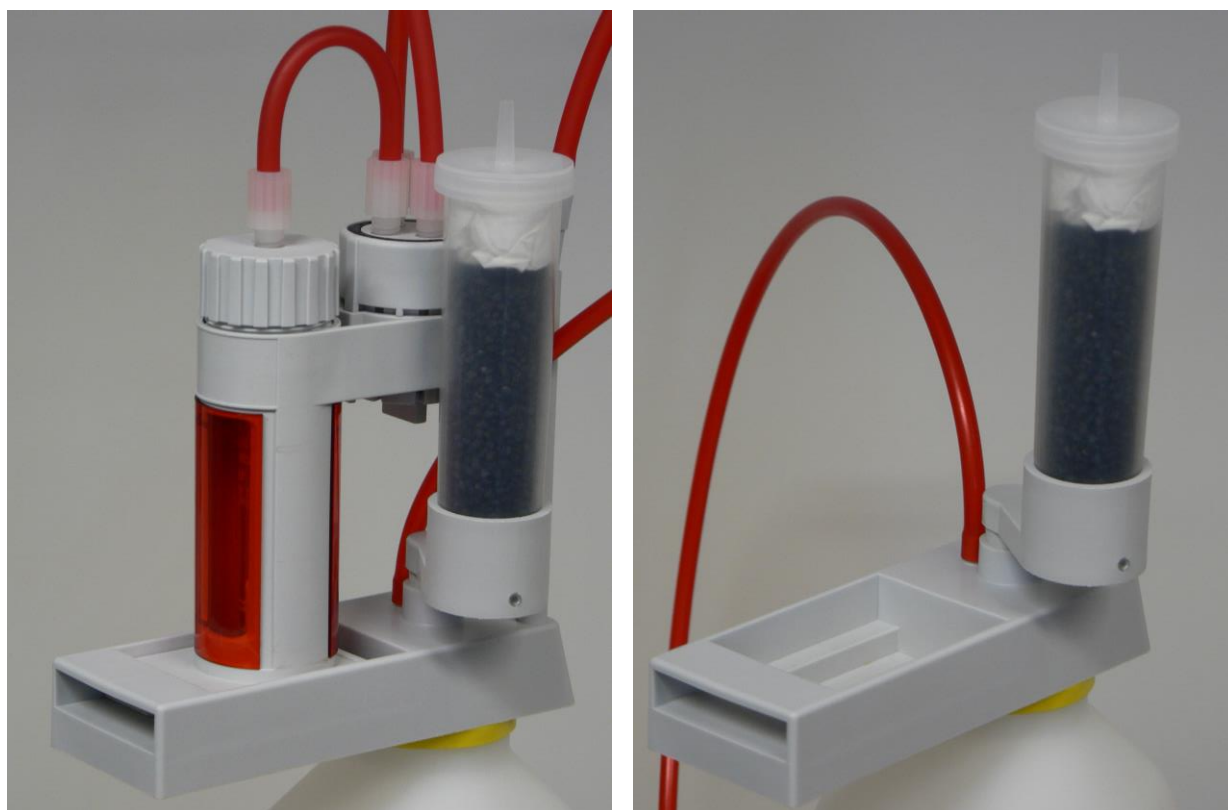


**Figure 25: Waiting time between increments**

## 5.4. Reagent handling

### Preparation and storage of titrants

In order to get accurate and precise results it is imperative that titrants are prepared and stored with care. This is of particular importance with titrants that are not stable over time. In the case of bases e.g. sodium and potassium hydroxide, it is important that the titrants are prepared with carbon dioxide free water or solvent and that they are protected from atmospheric exposure to carbon dioxide. This can be done by attaching a drying tube containing an absorbent (e.g. NaOH on a granular carrier) to the titrant bottle. If not then  $\text{CO}_2$  is absorbed which reacts with the bases to form carbonate. The end result is that the titrant is a mixture of bases and it becomes impossible to get correct results with the titrant.



Many titrants e.g. iodine, permanganate, dichromate, are light sensitive and must be protected by storing short term in brown glass bottles and longer term by storing in the dark. One of the most critical of

titrants when it comes to handling is Karl Fischer reagent used for water determination. This titrant must be protected from light as well as from the ingress of atmospheric humidity. This is done by attaching a drying tube containing silica gel or molecular sieve.

Last but not least, the temperature of titrants should be controlled to prevent expansion and contraction. This results in concentration changes as well as degassing resulting in bubbles in burette tubes.

Irrespective of whether stored and prepared correctly, it is important to regularly determine the titer or true titrant concentration of titrants.

### Titer determination

It should be noted that volumetric titration is not an absolute method since the result is influenced by the titrant concentration or titer. The effective titrant concentration normally differs from the nominal concentration due to either inaccurate preparation, purity of titrant used, or changes due to instability. The effective concentration is determined by means of a titer determination or a titration of a substance of exactly known concentration, usually a primary standard.

It is essential to perform a titer determination on all titrants before used for the first time. This also applies to purchased reagents of certified concentration since the titer determination not only compensates for concentration errors but also any minor burette inaccuracies. This is of particular importance with corrosive bases since they attack the glass walls of the burette resulting in small volume changes.

Depending on the stability of the titrant the titer determination has to be performed more or less frequently. Table 1: lists some common titrants together with recommendations for titer determination.

**Table 1: Common titrants and handling procedures**

Titrant	Standard used	Frequency	Comments
Sodium hydroxide, NaOH	Potassium hydrogen phthalate (KHP)	Weekly	Protect from CO <sub>2</sub> .
Sulphuric acid, H <sub>2</sub> SO <sub>4</sub>	Tris(hydroxymethyl)amino-methane (THAM) or sodium carbonate	Every 14 days	-
2,6-Dichlorophenol Indophenol (DPI)	Ascorbic acid	Daily	Protect from light. Store in a cool and dark place. Replace every 2 days.
Iodine, I <sub>2</sub>	Di-sodium oxalate	Daily	Protect from light and keep cool. Store in the dark.
Potassium permanganate, KMnO <sub>4</sub>	Di-sodium oxalate	Every 14 days	Protect from light. Store in the dark.
Silver nitrate, AgNO <sub>3</sub>	Sodium chloride	Every 14 days	Protect from light.
Karl Fischer Reagent	Disodium tartrate dihydrate	Daily	Protect from humidity and light.

The titer (or factor) of the titrant is defined as the ratio of the actual concentration to the nominal concentration.

## 5.5. Sensor handling and maintenance

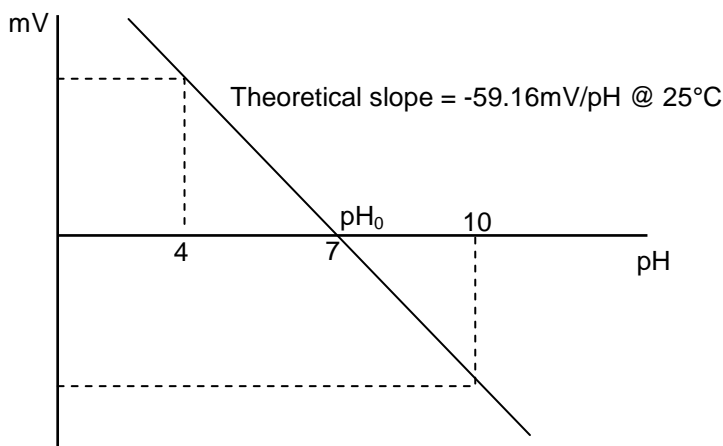
In the case of pH endpoint titration a critical factor affecting result accuracy is the slope and zero point of the electrode. Both of these parameters are used to convert the raw signal from the electrode (in mV) into the pH of the sample solution according to the Nernst equation:

$$pH = pH_0 - \frac{E}{S}, \text{ where}$$

E = measured signal (in mV)

S = electrode slope =  $-2.3 RT/nF$

pH<sub>0</sub> = electrode zero point =  $E_0/S$



**Figure 26: pH calibration curve**

Depending on temperature fluctuations and measurement conditions the sensor calibration (if necessary) should be done at least once per day. In addition to this it is important for all electrodes that the electrolyte is replaced at least once every 3 months and that the electrode is regularly cleaned. Depending on potential contaminants the cleaning agent varies from thiourea for sulphides, pepsin for proteins, acetone for edible fats and oils or toluene or similar for mineral oil or grease.

If glass electrodes are used in non-aqueous applications then it is also important to ensure that the electrode membrane is always hydrated by conditioning the electrode between samples in water or dilute acid. If this is not done then the electrode will become sluggish with time and the accuracy of the results could be affected. Finally when not in use, electrodes should always be stored in electrolyte, never deionised water, and in the majority of cases, not dry. The exception to this is the case of some ion-selective electrodes which can be stored dry.

## 5.6. The effects of temperature on the results

Temperature can have two different effects on a titration. The first becomes apparent when performing an endpoint titration to a predefined pH value. The pH of the sample depends on the degree of dissociation of the acids and bases present, which is temperature dependent. A temperature change therefore gives rise to a real change in the pH of the sample that cannot be corrected for without knowing the sample's exact composition. A further effect concerns the actual measurement process and the slope of the electrode calibration curve. The slope of the calibration curve is temperature dependent so it is important to either perform the analysis at the same temperature as that when the electrode was adjusted or to measure both temperatures and compensate for the change in slope of the calibration curve. Fortunately most modern instruments are able to simultaneously measure the sample temperature and automatically compensate for this error.

The second major effect that temperature has on the titration concerns the density, and therefore the concentration of the titrant. If, for example, the titer of the titrant was determined in the morning with a laboratory temperature of 20°C and samples are titrated in the afternoon at a temperature of 30°C then this 10°C change in temperature can cause a significant reduction in titrant concentration that is not being catered for. This is of particular significance with non-aqueous titrants where the coefficient of thermal expansion is much higher. Below is a table showing typical errors when this is not taken care of.

**Table 2: Error in concentration due to temperature changes**

<b>Titrant</b>	<b>% Error per °C change</b>
0.1 M NaOH	0.027
1 M NaOH	0.036
0.1 M HCl	0.026
1 M HCl	0.029
1 component 5 mg/mL Karl Fischer Reagent	0.092

There are 3 possibilities to minimize this error. The best solution is to maintain constant temperature in the laboratory. If the titer and samples are measured at the same temperature then there is no error. In many cases, however, this is not feasible and an alternative solution must be found. The error can be reduced by re-determining the titer whenever there is a significant change in temperature. The final possibility is to measure the temperature of the titrant and to correct for the change in concentration due to temperature by multiplying by a correction factor. For the case of Karl Fischer reagent listed in the table above, the correction factor is calculated as follows:

$$\text{Factor, } f = 1 + (T_{\text{titer}} - T_{\text{sample}}) \times 0.092/100$$

With a 10°C difference in temperature ( $T_{\text{titer}} - T_{\text{sample}} = -10$ ) this would result in a correction factor of

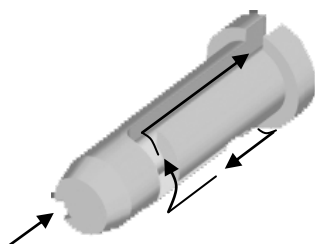
$$\begin{aligned} f &= 1 - 10 \times 0.00092 \\ &= 0.9908 \end{aligned}$$

By multiplying our results by this factor the error is taken care of.

## 5.7. Instrument care and maintenance

### Burette care

Clean and well maintained burettes are crucial to reliable results. It is recommended that burettes are emptied and properly cleaned at least once every 3 months. In particular care should be taken with the burette tips. The majority of burettes for commercially available instruments include what is known as an anti-diffusion tip. This tip serves two purposes. The first is to prevent diffusion of either titrant into the sample or sample into the burette in between actual additions, and the second is to ensure that small drops or a fine stream of titrant is added to the sample. Generally an anti-diffusion tip consists of a restriction in the tube opening and as such can result in tube blockages if regular maintenance is not performed. When tube blockages occur they often result in burette leakage due to pressure build up. These leakages in turn result in problems with result precision. Nevertheless, under no circumstances should the anti-diffusion tips be removed as this will result in far greater precision problems.



**Figure 27: Typical anti-diffusion tip**

During routine use care should be taken to ensure that burette tubes do not contain any bubbles. These bubbles can occur either through degassing of the titrant during the filling of the burette, or due to leaks. To prevent degassing of the titrant it is often possible to reduce the filling speed and hence the amount of vacuum on the titrant during the filling. Any bubbles in the dispensing tube will cause random errors resulting in poor precision.

In addition to cleaning it is also recommended that burettes be calibrated at least once per year to verify the dosing volume accuracy. This is of particular importance with titrants that are corrosive to glass such as strong alkali solutions. This should be done gravimetrically according to ISO8655 part 6. In the case where a burette fails to meet the requirements of the standard the glass cylinder or the entire burette should be replaced.

### **Instrument maintenance**

To ensure accurate and precise results it is recommended that instruments should be routinely serviced at least once per year.

## **5.8. Sample handling**

By far the biggest source of random errors resulting in precision problems is in the sample handling. These errors include inhomogeneity of the sample itself, sample storage problems, incorrect sample size, weighing errors, and careless handling to name but a few. Critical in most cases is the sample size. The sample should be large enough to ensure that it is representative while at the same time it should not be so large that repeated burette fillings are necessary during the titration. The ideal titration should give a titrant consumption of between 30 and 80% of a single burette volume. If inhomogeneity requires the sample to be larger than this, then a more concentrated titrant should be used.

On the other extreme, the sample should also be large enough so that weighing or sample measuring errors are kept to a minimum. Here a suitable balance must be used to ensure that the sample size exceeds the minimum weight of the balance. This minimum weight is defined as the weight which when measured tenfold, results in a repeatability of weighing result of less than a predefined value e.g. United States Pharmacopoeia (USP) states a value of less than 0.1%. If the example of standardization of KF titrant with disodium tartrate dehydrate is considered, a small sample of typically 50 mg due to solubility problems in methanol is required. In this case, in order to ensure a weighing uncertainty of less than 0.1% a balance is needed with a readability of at least 0.01 mg. If pure water is being used to standardize the KF reagent then to ensure a titrant consumption of 30 to 80% of a burette volume a sample size of 7.5 to 20 mg of water must be used. In this case a balance with 0.01 mg readability is insufficient if an uncertainty of 0.1% or better is the target.

In the case of liquid samples the appropriate grade of glassware or volumetric apparatus must be used and care must be taken to avoid handling errors such as parallax.

### **Conclusion**

Achieving both true and precise results is not a trivial task. There are many things that must be taken care of and it is only possible if care is taken from start to finish. Starting with using the correct method,

preparing fresh titrants and standardizing them, calibrating the electrode, and finally with careful handling of the sample. This result in high quality results but consistently superior quality results is only possible if the whole system is routinely maintained.

## 5.9. Summary

Different areas of quality management are concerned with different part of the data acquisition process, as an overview the following can be stated:

<b>GLP</b>	↔	<b>Formal framework, regulations</b>
<b>Certification</b>	↔	<b>Hardware, specifications</b>
<b>Validation</b>	↔	<b>Chemistry, measurement method</b>
<b>Qualification</b>	↔	<b>Lifetime evidence of measuring system</b>

## 6. Chemical background

In the following chapters a brief introduction to chemical parameters which are relevant for the titration analysis is given. More information about chemical reactions can be found in 'Fundamentals of Titration' (ME-704153A).

### 6.1. The mole

In chemical calculations, specific units are used to describe a reaction. This is necessary since the number of atoms, molecules or ions in 1 g of sample can be  $\sim 10^{20}$ . This means that 1 atom weighs approximately  $10^{-20}$  g, a quantity with 20 decimal digits, i.e. a number on the twentieth digit after the comma! Thus, chemical calculations need more convenient units to calculate the amount of reagent and product involved in a reaction.

The base units of chemical calculations are associated with the base quantity 'amount of substance' and its base unit 'mole' of the International System of Units (SI). These concepts are defined by IUPAC (International Union of Pure and Applied Chemistry) as governing body.

Some examples of these definitions are given in Table 3:

**Table 3: Definition of a several of units**

Basic property	Base Unit Name	Symbol
Length	Meter	m
Mass	Kilogram	kg
Time	Second	s
Electric current	Ampere	A
Temperature	Kelvin	K
<b>Amount of substance</b>	<b>Mole</b>	<b>mol</b>
Luminous intensity	Candela	cd

The mole is the amount of substance of a system that contains just as many elementary chemical entities as there are atoms in 12 g of the carbon  $^{12}\text{C}$  isotope. In addition, the exact nature of the entities must be specified, e.g. atoms, molecules, ions, electrons. One mole of a substance contains  $6.025 \times 10^{23}$  elementary entities.

Examples:

$$n(\text{HCl}) = 2 \text{ mol}$$
$$n(\text{Ca}^{2+}) = 0.35 \text{ mmol}$$

The result of a titration is frequently given in a more convenient unit than moles, e.g. in grams or %. Therefore, a conversion factor is necessary to translate the result in grams. In particular, the mass of 1 mole of an elementary entity has to be known. This is the molar mass  $M(\text{X})$  of substance X.

The molar mass of substance X is the mass of  $6.025 \times 10^{23}$  elementary chemical entities (1 mole) of this substance. The unit is g/mol.

For instance, all chemical elements are composed of atoms which are listed in the periodic table of elements. Each element is given with its atomic mass, i.e. the mass of 1 mole of atoms:

Iron (Fe)  $M(\text{Fe}) = 55.85 \text{ g/mol} = 6.025 \times 10^{23} \text{ atoms}$

Sodium (Na)  $M(\text{Na}) = 22.99 \text{ g/mol} = 6.025 \times 10^{23} \text{ atoms}$

The molar mass of 1 mole of molecules (molecular mass) is calculated from the atomic mass of the components according to the molecular formula:

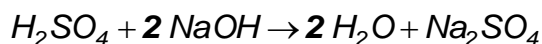
### Sulphuric acid (H<sub>2</sub>SO<sub>4</sub>) :

Atom	Atomic mass	# atoms in molecule	Contribution to molecular mass
H	1.01 g/mol	2 x 1.01 g/mol	= 2.02 g/mol
S	32.06 g/mol	1 x 32.06 g/mol	= 32.06 g/mol
O	16.00 g/mol	4 x 16 g/mol	= 64.00 g/mol
Total molar mass			= 98.08 g/mol

So  $M(\text{H}_2\text{SO}_4) = 98.08 \text{ g/mol}$

## 6.2. Reaction stoichiometry

The reaction stoichiometry gives information on how many molecules or moles of a reagent are needed for a complete reaction with a certain number of molecules or moles of an analyte. The stoichiometry information is always included in any chemical equation:

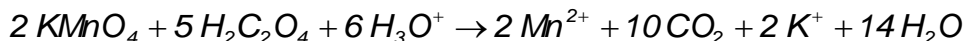


The numbers in the equation above gives the information that 2 moles of sodium hydroxide (NaOH) is required to neutralise 1 mole of sulphuric acid (H<sub>2</sub>SO<sub>4</sub>).

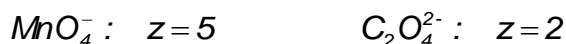
Often, the ratio of reagent and analyte is called the equivalent, equivalent entity (IUPAC) or equivalent number (titrator, abbreviated as 'z').

Since the equivalent entity indicates how many particles of titrant react with the analyte, this number is important in calculations of the amount of analyte present in the sample and has to be defined correctly in the titrator parameters. For the previous example of sulphuric acid and sodium hydroxide the equivalent is 2 since H<sub>2</sub>SO<sub>4</sub> releases 2 protons (H<sup>+</sup>). In the titrator therefore equivalent number has to be set to z=2.

In acid/base titrations the equivalent entity is relatively easy to deduce since the number of H<sup>+</sup> ions to be neutralised is usually easy to assess. The equivalent becomes more difficult to find out in redox reactions where it is not always clear from the numbers in the reaction equations what the equivalent entity is:



In this redox reaction, the analyte oxalate (H<sub>2</sub>C<sub>2</sub>O<sub>4</sub>) donates 2 electrons per molecule and is oxidised. At the same time the titrant permanganate (KMnO<sub>4</sub>) receives 5 electrons per molecule and is thus reduced. This means that the equivalent of MnO<sub>4</sub><sup>-</sup> is 5, while the equivalent entity of C<sub>2</sub>O<sub>4</sub><sup>2-</sup> is 2.



To be able to find out the equivalent numbers of this reaction, one has to know exactly how many electrons are transferred from one ion to the other.

## 6.3. Concentration of a titrant

To be able to calculate with the convenient equivalent entities that are given by the stoichiometric relationships as shown in the previous paragraph it is usual in chemistry to define concentrations not as e.g. g/L or g/kg, but as moles per litre of solvent. This unit is written as mol/L or abbreviated with the letter 'M'. In this way one can write:

$$0.1 \text{ mol/L NaCl} = 0.1 \text{ M NaCl} = 100 \text{ mmol/L NaCl} = 100 \text{ mM NaCl}$$

All of the above are equivalent and mean that the concentration of NaCl is such that 0.1 moles of NaCl are dissolved in 1 litre of water (solvent). The molecular weight of NaCl is 58.44 g/mol and there is 0.1 mole in 1 litre. So, to prepare the solution one has to dissolve  $0.1 \times 58.44 \text{ g}$  in one litre = 5.844 g/L.

When the reaction stoichiometry is such that the ratio of reagent and analyte is not 1:1, so when the equivalent entity for a substance (either reagent or analyte) is not 1, this is often signified in the way how the concentrations of the chemicals are depicted.

Since it is associated in titration the volume of reagent used with the volume of analyte present, the values of the equivalents need to be translated in such a way that the calculation from volume to volume (1:1 ratio) relates correctly to the reaction stoichiometry. For the titrant this is done by defining the concentration in a way that shows the equivalent entity in the representation of the concentration. For the analyte this is done by defining an equivalent number in the titrator (z) which takes care in the titration calculations of the fact that the analyte has a certain equivalent.

If the redox reaction example above of the analyte oxalate with the reagent permanganate is used, the concentration of reagent/titrant needs to be defined in such a way that this shows the equivalent entity.

If, for example the concentration of  $\text{KMnO}_4$  is 0.02 mol/L. Physically there are 0.02 moles of  $\text{KMnO}_4$  in 1 litre of water. But this will react with 5 electrons and thus 5 equivalents. So in number of equivalents the concentration of  $\text{KMnO}_4$  is 5 times as high: 0.1 mol/L. But since this is not the true concentration, one has to modify the notation to signify that equivalents are shown:

$$c(1/5 \text{ KMnO}_4) = 0.1 \text{ mol/L}$$

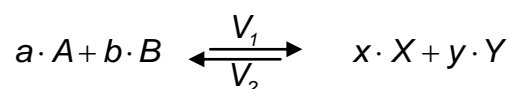
in the titrator therefore the concentration of  $1/5 \text{ KMnO}_4$  as 0.1 mol/L is defined.

## 6.4. Chemistry in titration

In this chapter, more information is given about the chemical reaction occurring during titration of a sample.

### The law of mass action

Every chemical reaction proceeds to an exactly defined equilibrium condition. During the reaction, reagents react to products and products react to reagents until an equilibrium (stable state) between 'forward' and 'backward' reactions is reached. This status is called the chemical equilibrium:



a, b, and x, y are the numbers of moles of substances A, B, and X, Y participating in the reaction in well-defined proportions: the ratios of the substances involved in the chemical reaction are defined by these numbers.

At equilibrium, the rates of forward and backward reactions are equal ( $v_1 = v_2$ ). This is described by the law of mass action:

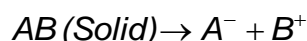
$$K = \frac{[X]^x \cdot [Y]^y}{[A]^a \cdot [B]^b}$$

The constant K is known as the equilibrium constant. [X] and [Y] are the concentrations of X and Y, respectively.

In titration, the reaction has to proceed quantitatively and to completion if one wants to obtain meaningful results. These prerequisites are fulfilled when K is very large so that the equilibrium concentration of sample A (i.e., [A]) is infinitely small compared to its concentration before starting analysis.

### The solubility product of salts

Salts like KCl, NaCl, KBr, etc. dissolve in water and dissociate in their respective ions ( $\text{K}^+$ ,  $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ).



Many salts are only slightly soluble, e.g. barium sulphate (BaSO<sub>4</sub>) or silver chloride (AgCl). If solutions of the corresponding ions are mixed in a glass beaker, precipitates are formed. The solid salt accumulates on the bottom of the glass, even though ions from the salt constantly pass into solution, and ions from the solution are incorporated in the solid salt. A stable state has been established, for which the following constant applies:

$$K = \frac{[A^+] \cdot [B^-]}{[AB]}$$

As long as solid salt AB is present as precipitate, the concentration of AB remains constant and thus it can be included into the equilibrium constant K:

$$K_{sp} = K \cdot [AB] = [A^+] \cdot [B^-]$$

This gives the solubility product K<sub>sp</sub>:

$$K_{sp} = [A^+] \cdot [B^-]$$

The constant K<sub>sp</sub> characterizes the solubility of a salt. If the value K<sub>sp</sub> is small the salt is very insoluble, if the value K<sub>sp</sub> is large the salt is very soluble. The solubility product K<sub>sp</sub> shows a large temperature dependence, since, in general, salts are better soluble at higher temperatures.

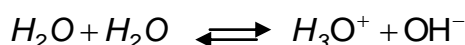
The low solubility of salts like AgCl, BaSO<sub>4</sub>, and PbSO<sub>4</sub> can be used to perform precipitation titrations.

Examples:

- Salt content in food by titration with AgNO<sub>3</sub>
- Sulphate determination by titration with BaCl<sub>2</sub>.

## 6.5. The ionic product of water

When the conductivity of water is examined by very sensitive instruments, even ultrapure distilled water exhibits conductivity. This is due to the autoprotolysis of water: a proton (H<sup>+</sup>) is transferred from one water molecule to another.



This equilibrium is present in all aqueous solutions and can be described according to the law of mass action (paragraph 6.4) In diluted solutions, the concentration of water molecules remains constant for all practical purposes, so the equilibrium constant K can be simplified to:

$$K_w = [H_3O^+] \cdot [OH^-]$$

K<sub>w</sub> is known as the ionic product of water, with a value of 10<sup>-14</sup> mol<sup>2</sup>/L<sup>2</sup> at 25°C. Its value is constant in diluted solutions and is dependent on the temperature. In a neutral solution, where the concentrations [H<sub>3</sub>O<sup>+</sup>] and [OH<sup>-</sup>] are equal, this gives then the following concentrations for both:

$$[H_3O^+] = [OH^-] = 10^{-7} \text{ mol/L}$$

If one of the concentrations is known, the other can be calculated from the ionic product since K<sub>w</sub> is constant (10<sup>-14</sup>). For instance, if [H<sub>3</sub>O<sup>+</sup>] is increased to 10<sup>-2</sup> mol/L by addition of acid, [OH<sup>-</sup>] decreases to 10<sup>-12</sup> mol/L: 10<sup>-2</sup> x 10<sup>-12</sup> = 10<sup>-14</sup>.

The measurement of a certain H<sub>3</sub>O<sup>+</sup> concentration and the calculation of the corresponding pH value from the relationship pH = -log [H<sub>3</sub>O<sup>+</sup>], enables one to determine whether a solution is acidic or basic. In acidic solutions, the pH is less than 7, whereas in basic solutions it is over 7. In a neutral solution the pH is exactly 7, since both [H<sub>3</sub>O<sup>+</sup>] and [OH<sup>-</sup>] are 10<sup>-7</sup> and so pH = -log [10<sup>-7</sup>] = 7.

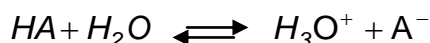
Note that the above presented concept of pH is defined only for aqueous solutions. Thus, it is useless to calibrate an electrode in organic solvents, unless one wants to have measurements only for comparison with reference solutions.

## 6.6. The strength of acids and bases

An acid is a substance which donates  $H^+$ , whereas a base accepts  $H^+$ . Not every acidic solution dissociates its protons completely. Each acid has an individual dissociation strength.

Strong acids that completely dissociate in water are for example  $HClO_4$  (perchloric acid),  $H_2SO_4$  (sulphuric acid) or  $HCl$  (hydrochloric acid). Weak acids are e.g.  $CH_3COOH$  (acetic acid) or  $HF$  (hydrofluoric acid).

The reaction of weak acids (= weak dissociation) with water is described by the equilibrium:



In dilute solutions,  $[H_2O]$  is constant and the equilibrium constant  $K$

$$K = \frac{[H_3O^+] \cdot [A^-]}{[HA] \cdot [H_2O]}$$

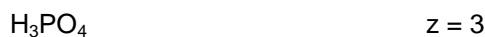
can be simplified to:

$$K_a = \frac{[H_3O^+] \cdot [A^-]}{[HA]}$$

The constant  $K_a$  is known as the acidity constant of acid  $HA$  and characterizes the acid strength. Strong acids have large acidity constants, weak acids a small one. The negative logarithm of  $K_a$  is frequently employed for easier calculation and notation:

$$pK_a = -\log K_a$$

Acids that can dissociate more than one  $H^+$  are called polyprotic acids. E.g. phosphoric acid ( $H_3PO_4$ ) can dissociate 3 protons, and sulphuric acid ( $H_2SO_4$ ) can dissociate 2 protons. This has to be considered when choosing the correct equivalent ( $z$ ) in the titration method:



## 6.7. Acids and bases in non-aqueous solvents

Quite a number of titration reactions are performed in non-aqueous solvents. There can be several reasons to perform non-aqueous titrations, for example the better solubility of samples in solvents other than water, or to avoid side reactions with water.

For acid-base titrations there are further advantages in choosing non-aqueous solvents for the titration, the acid or base can behave as a stronger acid or base in these solvents or acids and bases with very similar dissociation behaviour can be made to act in a less similar way.

### Too weak acid or base

If an acid or base is too weak in water to react with the sample, this can be improved when using a suitable non-aqueous solvent in which the acid or base exhibits more pronounced acidic or basic behaviour.

This property is utilized in titrations of very weak bases with  $HClO_4$  (perchloric acid) in  $CH_3COOH$  (acetic acid) as titrant. In the titrant  $CH_3COOH_2^+$  ions are created as acetic acid is weaker than perchloric acid. These  $CH_3COOH_2^+$  ions are in turn very strong proton donors to normally weak bases and thus the titrant works as an extremely strong acid solution.

With a weak base like e.g. amines this means that the created matrix increases the alkaline properties of the amines. This makes it possible to obtain a more pronounced and observable inflection point would not have been possible in aqueous solutions.

### **Separation of acids/bases with close $pK_a$ values**

When analyzing mixtures of acids or bases in a sample, these can quite often not be separated to show different EQPs in a curve because the acids or bases have similar  $pK_a$  values and therefore these acids/bases have titration curves that are almost identical.

Many non-aqueous solvents show differentiating properties that allow acids and bases with similar  $pK_a$  values in water to be separated in this particular solvent.

An example of this behaviour is the titration of a mixture of HF, HNO<sub>3</sub> and CH<sub>3</sub>COOH found in etching baths. This mixture cannot be separated into 3 discrete EQPs for detection and subsequent calculation in water; if one titrates the sample in a mixture of acetone and 2-propanol though, this separation is possible and 3 distinct equivalence points are observed for the mixture.

## 7. Glossary

<b>Titration</b>	Quantitative chemical analysis The amount of titrant is determined which reacts quantitatively with the sample compound to be analysed. From this volume (titrant consumption) the amount of sample compound is calculated. The calculation is based on the stoichiometry of the assay reaction (Synonyms: volumetry, titrimetry).
<b>Titrant</b>	Solution of a certain chemical reagent. Its concentration is accurately known by standardization.
<b>Primary standard</b>	Certified high purity substance which is used for the accurate determination of the titrant concentration.
<b>Indication</b>	Procedure to follow the reaction and to detect the end of the titration, e.g. potentiometry (electrodes), or use of colour indicators.
<b>End of titration</b>	A titration is terminated when the desired endpoint or the equivalence point is reached. The consumption of titrant to this point is evaluated. Depending on the chemistry, more than 1 equivalence point may occur during the same titration.
<b>Equivalence point</b>	The point at which the number of entities (equivalents) of the added titrant is the same as the number of entities of sample analyte.
<b>Analyte</b>	Specific chemical species of which the content in the sample can be determined by titration.
<b>Standardisation</b>	Determination of the titrant concentration by using a highly pure reference chemical substance (standard).
<b>Stoichiometry</b>	Mole/mass relationships between reagents and products. The reagents always react according to fixed relationships.

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# Basics of Titration

This booklet encompasses a general introduction to the analytical technique of titration. Specifically, it provides an overview about the following topics:

- a) What is titration and how is it being used in various industry segments?
- b) How is titration been performed nowadays?
- c) What has to be considered in order to get the best titration results?
- d) What are the fundamentals of chemistry that are relevant for titration?

Basics of Titration outlines specific aspects in developing and maintaining a good routine operation required for general titration.

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