UserCom

Information for users of
Titration and pH Systems,
Density Meters and Refractometers

6

Basics

Influence of sample viscosity on density measurements with the oscillating tube technique


Peter Wyss

Digital density meters based on the oscillating tube principle are for many reasons superior to traditional methods for density determination (pycnometers, hydrometers): they allow rapid density determinations with low sample volumes, they are easy to use and yield results with excellent repeatability. Sample viscosity can however affect the measurement values obtained from such instruments. The accurate density measurement of viscous samples in some cases requires a so-called viscosity correction.
This article explains why such problems occur, how large the measurement error due to sample viscosity can be and how it is eliminated in modern instruments of this type using automatic viscosity correction.

Origin of the viscosity error

The oscillating tube technique was originally developed to measure the density of low-viscosity samples. The measurement principle of this type of instrument is based on the electromagnetically induced oscillation of a glass U-tube (see Fig. 1). The U-tube is the measuring cell and is filled with a sample of gas or liquid. The resonance frequency of the oscillation is directly related to the density of the gas or the liquid in the U-tube. The instrument calculates the density of the sample from the oscillation frequency and displays the value.

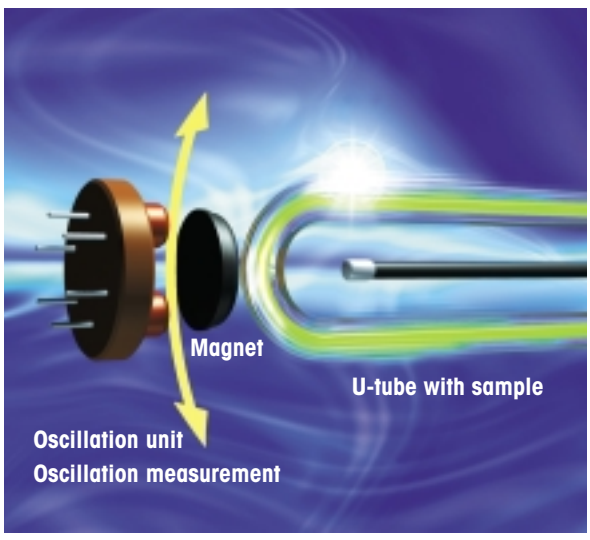


Figure 1: Measuring principle of the oscillating tube

Contents

The method can even be used to determine the density of very viscous samples. The density values obtained are however slightly too high compared with the values obtained with the traditional methods used for low-viscosity samples. The reason for this is that the oscillation of the U-tube is damped due to the shear forces that occur in viscous samples. The oscillation frequency determined in this way is too low and the density value displayed is too high.

Magnitude of the viscosity error

In practice, the error arising from the viscosity of the sample can often be neglected. If, for example, the density of concentrated sulfuric acid (viscosity 25.4 mPas at 20 °C) is determined with an instrument that displays the density with a resolution of 0.0001 g/cm^3, the measurement error of about 0.0001 g/cm^3 due to sample viscosity is less than the resolution of the instrument. The measurement error even for olive oil (viscosity 84.0 mPas at 20 °C) is only about 0.0002 g/cm^3 and can in practice also be neglected. In this case, the instrument would display a density value of 0.9110 g/cm^3 instead of 0.9108 g/cm^3. If, however, the same instrument is used for the determination of the density of glycerin samples, then a correction of the measured value is essential: For pure glycerin (viscosity 1490 mPas at 20 °C) the instrument would in fact display a density value that is at least 0.0007 g/cm^3 too high.

If the viscosity of the sample is known, the measurement error that occurs with this technique due to sample viscosity can be estimated using the curve shown in Figure 2.

Correction for the viscosity error

Previously, in the soft drinks industry, modified calibration and adjustment procedures were used to minimize viscosity errors in the density measurements of viscous samples. Instead of using air and water, the instrument was adjusted with two concentrated sugar solutions whose viscosity was of the same order as that of the viscous syrup samples that were to be measured. Another procedure previously used to correct the viscosity error was to measure the viscosity of the samples and to correct the density values obtained with the instrument using appropriate formulas.

These tedious and time-consuming procedures are rarely used today. For some time now, METTLER TOLEDO offers instruments based on the oscillating tube technique that automatically correct the viscosity error. These instruments are able to determine not only the (density dependent) oscillation frequency of the U-tube but also the damping effect on the oscillation caused by the viscosity of the sample.

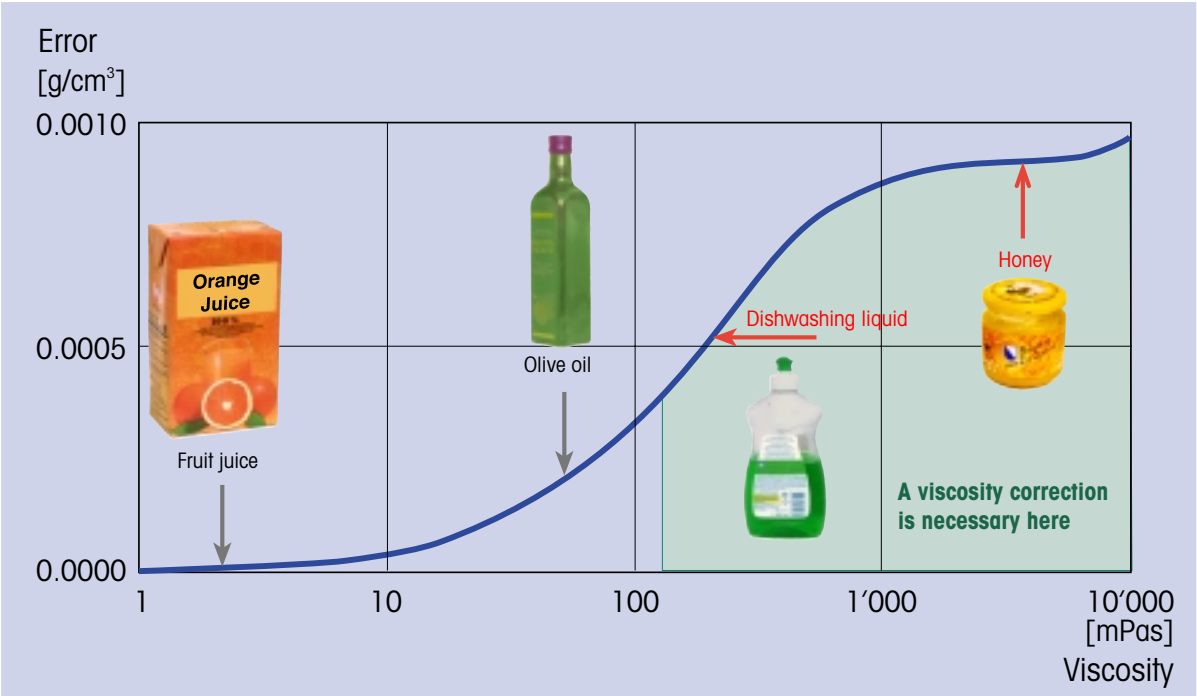


Figure 1: Influence of sample viscosity on density determination with the oscillating tube technique. In the green range a viscosity correction is advisable.

Viscosity [mPas]	Theoretical density [g/cm³] at 20 °C	Measured value DE50	Measured value DE51	Measuring error DE50	Measuring error DE51
1	0.998206	0.998206	0.998206	0.000000	0.000000
500	0.871579	0.872366	0.871557	0.000787	-0.000022
2000	0.880574	0.881490	0.880565	0.000916	-0.000009
63	0.819700	0.819996	0.819725	0.000296	0.000025
160	0.826580	0.827103	0.826539	0.000523	-0.000041
360	0.872550	0.873269	0.872504	0.000719	-0.000046

Table 1: Theoretical and measured density at various viscosities.

The instrument performs three measurements under different conditions, analyses the overtones that occur, and from this information determines the viscosity-dependent damping constant. The instrument then uses the damping constant to calculate the sample viscosity, determines the measurement error due to sample viscosity and finally displays the corrected density value.

Table 1 shows the magnitude of the measurement error that occurs when the density of samples of different viscosity are determined using an oscillating tube instrument with (METTLER TOLEDO DE51) and without (METTLER TOLEDO DE50) viscosity correction.

The viscosity correction of the METTLER TOLEDO instruments operates fully automatically and the viscosity error is properly corrected over the entire viscosity range. The user does not need to know the viscosity of the sample in order to obtain correct results. This is not always the case with other instruments of this type, i.e. the user has to know the viscosity range of the samples and enter this information before performing the measurement.

When is viscosity correction required or unnecessary?

- No correction for the viscosity error is necessary for instruments with a resolution of 3 decimal places (e.g. the METTLER TOLEDO DA-110M and DA-100M).
- For instruments with a resolution of 4 decimal places (resolution 0.0001 g/cm³, e.g. the METTLER TOLEDO DE40), a correction of the viscosity error is usually only necessary for samples that are more viscous than olive oil, i.e. if the viscosity is greater than 85 mPas.
- For instruments with a resolution of 5 decimal places (e.g. the METTLER TOLEDO DE50 and DE51), viscosity correction is necessary even for samples with a viscosity of 7 mPas.

As we have already seen, it is only necessary to correct the viscosity error with instruments with a resolution of 4 decimal places. The 4-place METTLER TOLEDO density meters (DE40) can be easily upgraded with a Memory Card (Order No. 51324003) to automatically correct the viscosity error.

Density determination to an accuracy of 5 decimal places (resolution 1 x 10^{-5} g/cm³) requires a viscosity correction even if relatively low-viscosity samples are measured. For such high resolution density determinations, it is not possible to correct the viscosity error using a purely software viscosity correction with a Memory Card; instruments with resolution of 5 decimal places have to be certified in the factory with special viscosity standards. For this reason, METTLER TOLEDO offers two instrument versions with 5 decimal place resolution: the DE51 with viscosity correction, and the DE50 without automatic viscosity correction.

Tips and tricks for practical daily use

U. Bauer

Every day of the week, METTLER TOLEDO titration specialists receive calls from customers using titrators for their daily routine work in the laboratory. The questions they ask have to do with particular technical points and application problems right through to the optimization of methods.
We know that many of these topics are of interest to other users and want to make this information available to everyone. This article is the first of a new series dealing with tips and tricks for practical daily use. There is however not always a simple answer to some of the questions put to us and a problem can sometimes have several different origins. In this article we would like to describe two typical questions and possible solutions:

Customer: "The result of my titration is wrong. It is only half, or double what I expected. I cannot understand why."

MT: There could be several different reasons for this. The fact that the result is exactly half or double that expected indicates that it is due to a systematic error.
The first thing to do is to check in the installation data whether the **burette volume** given for the titrant used agrees with the burette actually used. The list of titrants contains all the relevant information on titrants including the specified concentration, the burette volume, the burette drive used and the current titer, which is automatically stored after a titer determination.
If a 5 ml burette is specified but you in fact use a 10 ml burette, then the calculated result is only half the expected value or vice versa.
Another reason could be the **concentration of the titrant**. In the calculation of the result, the specified concentration of the titrant is multiplied by the titer, so that an incorrect concentration value can of course also lead to false results. Example: In the list of titrants the concentration of NaOH is given as 0.5 mol/L, but in fact you use a 1.0 mol/L solution. Your result will then be half that expected.
In addition, the **equivalent number z of the reaction** must be correct, i.e. what is the stoichiometric relationship of the reactants? Is it a 1:1 reaction? Incorrect equivalent numbers can of course also lead to results that are half or double that expected.

The standard calculation equation should clarify the factors described above:

$R = Q \cdot C/m$
$C = M/(10 \cdot z)$ [Result in %]
Q = VEQ · c · t: titrant consumption in mmol
VEQ = volume to end-/equivalence point in ml
c = nominal concentration of the titrant in mol/L
t = titer of the titrant
m = sample weight
M = molar mass of the substance being analyzed
z = equivalent number of the reaction

Example:
A titration of H_2SO_4 with 0.1 mol/L NaOH was performed; 5 mL of titrant was consumed up to the equivalence point. The sample weight was 0.5 g. The result was to be calculated in % H_2SO_4. The equivalent number was entered as 1.

VEQ = 5 mL
c = 0.1 mol/L
t = 1
m = 0.5 g
M = 98 g/mol
C = $M/(10 \cdot z) = 98/(10 \cdot 1) = 9.8$
R = $VEQ \cdot c \cdot t \cdot C/m$
$= 5 \cdot 0.1 \cdot 1 \cdot 9.8/0.5 = 9.8\%$

The expected result was however 4.9 %. Where is the mistake?

Answer:
The equivalent number for the reaction of H_2SO_4 as a diprotic acid with sodium hydroxide is '2' and not as given '1'.

The use of the standard equation stored in the titrators greatly simplifies the calculation of titration results. If the variables such as titrant concentration (as equivalent concentration or normality) or molar mass of the substance sought are entered correctly, the titrator calculates the result in any desired unit.

Customer: "The reproducibility of my titration results is poor. What can I do about it?"

MT: In any analysis you should first of all define what requirements with respect to precision are meaningful and necessary. If, after this, you find that some results are still outside the tolerance limits, then you should check the following points:

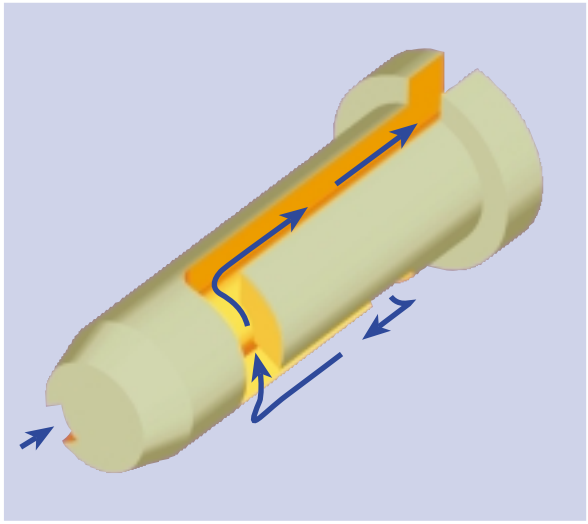
1. Is the sample used for the analysis representative of the sample as a whole? In other words, you should start looking for possible errors right from the beginning when taking the sample. "The result of an analysis can only be as good as the actual sample analyzed." The sample might have been taken from a container that had not been sufficiently mixed or homogenized before the actual analysis samples were taken, or the samples were exposed to different ambient conditions after taking the samples. An example of this is when samples are left for different periods before titration and thereby absorb different quantities of atmospheric CO_2. This should also be taken into consideration when working with vessels that are open to the atmosphere on a sample changer. It is then advisable to seal the vessels first and then use a device for uncovering the vessels (CoverUp™) shortly before the titration, such as that available for the Rondo sample changer.
2. How much sample is used for the analysis? With very small quantities the performance of the balance becomes decisive. A minimum weight test shows whether the balance meets the requirements.

3. With regard to the titrator itself, the following points should be checked:

a) Is there a siphon tip at the end of the dispensing tube and if so does it work properly? The tip prevents undesired diffusion of the titrant into the sample. If it is missing, titrant can pass irreproducibly into the titration cell and react there. It is however not taken into account as consumed volume. This can lead to a larger standard deviation.

b) The burette should be checked for possible leaks. If the fittings have not been properly tightened or if a valve is not working properly, then it is possible for leaks to occur. In this case not all the titrant delivered by the titrator actually reaches the sample. Since such effects are not reproducible, the standard deviation is larger.

c) Gas bubbles may be present in the titrator tubing. This is often caused by dissolved gases such as CO_2, SO_2 or O_2 degassing from the titrant. For this reason, the titrant should be properly degassed before use, e.g. in an ultrasonic bath. The bottle stand available as an accessory for the titrators raises the reservoir bottles to the same level as the burettes. This ensures that no additional reduction in pressure occurs when filling the burettes, which would promote degassing. The reagents used for the Karl Fischer titration are especially sensitive due to the dissolved SO_2. Because of this, the filling speed of the DL31/DL38 Karl Fischer titrators can be reduced.



Titrant flow through the syphon tip

Topics planned for the next edition:

– "My titrator has not performed an evaluation, but I can see that there is an equivalence point on the curve. What can I do?"
– "What is the best way to create a new method for my titrator?"

DL70ES and DL77: Auxiliary values and conditional functions


P. Gilmer

The different possibilities the METTLER TOLEDO DL70ES and DL77 titrators offer for automating titrations are very popular with customers. The Auxiliary Value function is very often used in analysis to calculate values from a blank determination. The conditional function allows the choice of the titrant to be automated (see UserCom 4). An optimum combination of both functions enables even more complex processes to be performed and automated.

The following example shows how this can be put into practice: A laboratory routinely processes 30 samples in **one** series, whereby each sample has to be determined twice. The individual results and the mean values of these duplicate analyses have to be calculated and recorded.
The combination of the Auxiliary Value function with suitable conditions enables these 60 samples to be processed with one method and in one series in such a way that both the individual results and the mean value of the duplicate analyses are recorded. This is done by setting a condition for certain functions in the method, and by using the Auxiliary Value function as a sample counter that ensures that the mean value is calculated each time after two samples.

Auxiliary Value and Auxiliary Value database

The auxiliary value database of the DL70ES and DL77 titrators allows up to twenty auxiliary values to be stored (H1 ... H20). Theses auxiliary values can be results, mean values, raw data and numerical values. To transfer a numerical value or the result of a determination to the auxiliary value database, the Auxiliary Value function is inserted in the method and given the appropriate expression or formula (e.g. H1=0, a numerical value is transferred, or H2=R1, the result of a determination is transferred).

Conditional functions

A condition can be set for most functions in a method. If this condition is satisfied, the corresponding function is executed; if it is not satisfied, then the function is skipped. Comparisons of raw data, results and numerical values that were obtained before the condition e.g. through measurement or calculation, can be used as conditions.

The method

The diagram shows an automated titration method that uses auxiliary values and conditions. The method sequence is always organized sequentially - the titrator processes all the functions of a method one after the other starting at the top.
An auxiliary value function is inserted between the Title and Sample functions (1). This auxiliary value [H1] serves as a counter and is set to (0) before the beginning of each series.
The titrator then processes the Sample function. This function tells it the total number of samples (60 samples). After the Sample function the auxiliary value [H1] is again required (2). The expression [H1=H1 + 1] activates the sample counter and gets the value 1.
The following Stir, Titration and Calculation functions are there to perform the analysis and calculate the results. The result obtained is stored in a buffer memory to use for calculations with the result of the second titration. The Auxiliary Value function is again inserted (3) and the result obtained transferred to the Auxiliary Value database [H2=R1]. A condition is set for this function namely that the result of the titration is only transferred as [H2] to the auxiliary value database if the Auxiliary Value [H1] has accepted the value 1 (this is the case for the first, third, fifth, ... titration). If the counter [H1] has the value 2, the condition is not satisfied and the function is skipped.
The mean value of the results of the first and second titration is calculated by the Calculation function [R2], (4) that follows. A condition is also set for this function, i.e. it is only be performed, if the counter [H1] has the

Expert tips

```
   Title
      Method ID ..................... 1111
      Title ......................... Acid number
      Data/time ..................... 22-Feb-2001 6:48 pm
1  Auxiliary value
      ID text ....................... Counter set to zero
      Formula ....................... H1=0
   Sample
      Number samples ................ 60
      Titration stand ............... ST20 1
      Entry type .................... Fixed volume U
      Volume [mL] ................... 10.0
      ID1 ........................... AN01
      Molar mass M .................. 100.0
      Equivalent number z ........... 1
      Temperature ensor ............. Manual
2  Auxiliary value
      ID text ....................... Counter plus one
      Formula ....................... H1=H1+1
   Stir
      Speed[%] ...................... 50
      Time[s] ....................... 10
   Titration
      Titrant ....................... 1/2 H2SO4
      Conzentration [mol/L] ......... 1.0
      Sensor ........................ DG111-SC
      Unit of meas. ................. As installed
      Titration mode ................ EP
        Titrant addition ............ Dynamic
          dE(set) [mV] .............. 8.0
          dV(min) [mL] .............. 0.02
          dV(max) [mL] .............. 0.1
          dE [mV] ................... 0.5
          dt [s] .................... 0.5
          t(min) [s] ................ 2.0
          t(max) [s] ................ 20.0
          Delay [s] ................. 0
        End point mode .............. EPA
          Potential [mV,pH,...] ..... 7.0
        Tendency ................... Negative
        Maximum volume [mL] ....... 5.0
   Calculation
      Result name ................... Acid number
      Formla ........................ R=VEQ*10
      Constant ......................
      Result unit ................... g/l
      Decimal places ................ 2
3  Auxiliary value
      ID text ....................... Save result
      Formula ....................... H2=R1
      Condition ..................... Yes
        Conditon .................... H1=1
4  Calcutation
      Result name ................... Average
      Formula ....................... R2=(R1+H2)/2
      Constant ......................
      Result unit ................... g/l
      Decimal places ................ 3
      Condition ..................... Yes
        Condition ................... H1=2
5  Auxiliary value
      ID text ....................... Counter set to zero
      Formula ....................... H1=0
      Condition ..................... Yes
        Condition ................... H1=2
   Statistics
      Ri (i=index) .................. R1
      Standard deviation s .......... Yes
      Rel.standard deviation srel ... Yes
   Record
      output unit ................... printer + computer
      All resuts .................... Yes
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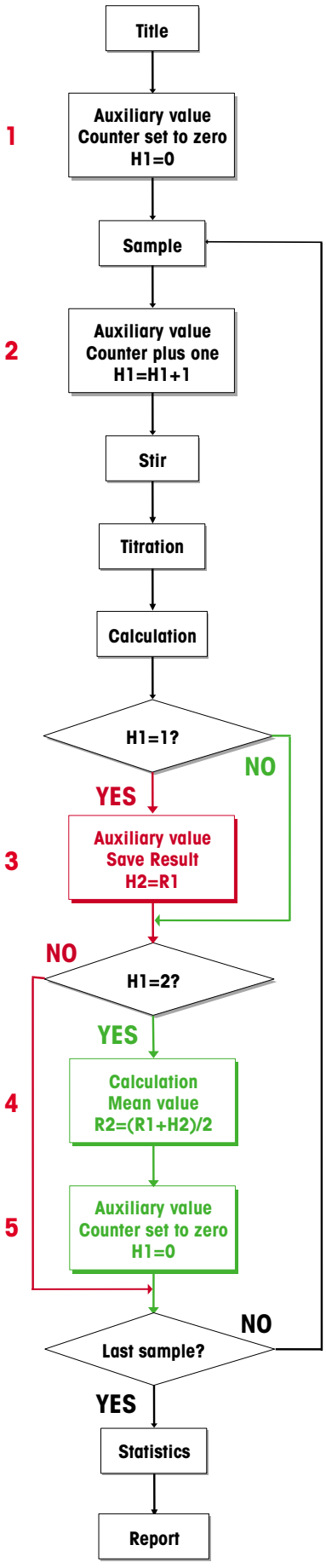


value 2. This condition ensures that the mean value is calculated after every second titration. If the value of the counter [H1] is 1, the calculation is not performed.
A final auxiliary value function (5) follows the calculation of the mean value. The purpose of this is to reset the sample counter [H1] to 0 again. A condition is also set for this function because the counter should only be set to 0 if it currently has the value 2. This condition ensures that the counter value is reset after two titrations. This procedure (1 to 5) is repeated through the loop between the Sample and Statistics functions until all the samples in the series have been processed. The combination of conditional functions and auxiliary values provides an elegant solution for the analytical task. The individual results and the mean value of determination 1 and determination 2 after each second sample are recorded. This eliminates tedious manual calculations, minimizes sources of error and guarantees highly, automated sample throughput.

Instruments

METTLER TOLEDO DL77 or DL70ES titrator
METTLER TOLEDO RONDO 60 sample changer (with sample turntable for 60 samples)
SU24 sampling unit

Instrument configuration discussed in the text

The right electrolyte for every application

K. Sägesser

The characteristics of an electrode are determined largely by the electrolyte. In the following article we will describe the options available to the user and summarize the different factors influencing the choice of the right electrode.

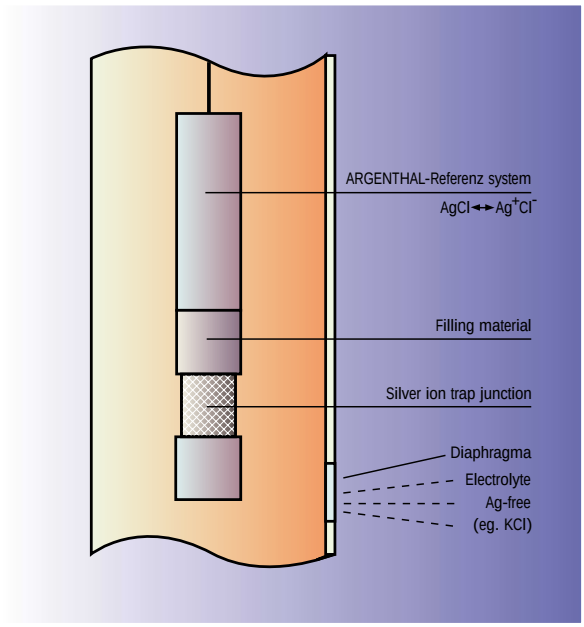
Liquid electrolytes

KCl/water - the universal electrolyte

A 3M solution of potassium chloride (KCl) is nowadays used as electrolyte for almost all electrodes. Why KCl in particular? One reason is that the silver/silver chloride (Ag/AgCl) reference system requires the presence of chloride in the electrolyte. The other reason is that the mobility of the anions and cations in the electrolyte must be comparable in order to prevent the formation of diffusion potentials. KCl provides an optimum solution to these requirements. With samples of low ionic strength, a double chamber-reference electrode and 1M KCl as bridge electrolyte should be used.

When is KCl alone used, and when KCl saturated with AgCl? In principle, a 3M KCl solution (51340049) is only used for electrodes equipped with ARGENTHAL® or Ag/AgCl cartridge reference systems. Examples of such electrodes are most InLab® electrodes. For electrodes with an ARGENTHAL® reference system, the electrolytically deposited AgCl layer is surrounded by silver granules so that the silver reserves are maximized. Since a small amount of silver is constantly consumed, the reference volume is made as large as possible. In addition, the cartridge surrounding the reference element creates a stable micro-environment, which enables a constant reference potential to be maintained. An additional silver ion trap prevents the silver ions entering the electrolyte and thereby coming into contact with the measurement solution.

For electrodes with a conventional Ag/AgCl reference system, a solution of AgCl-saturated 3M KCl must be used. The purpose of the AgCl-saturated electrolyte is to compensate the consumption of silver at the lead-off element. A disadvantage is that the free silver ions can react with sulfides or proteins in the sample.



The Argenthal® principle

LiCl/ethanol or glacial acetic acid – for nonaqueous solutions

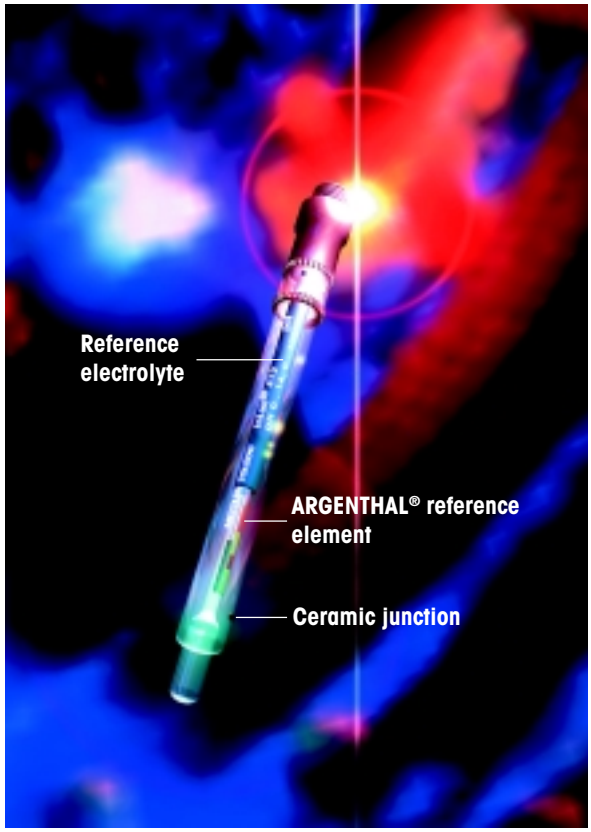
Aqueous electrolytes should not be used for the measurement of nonaqueous solvents or solvent/water mixtures because leakage from the electrode can lead to the formation of two phases. KCl is however only slightly soluble in ethanol and glacial acetic acid. LiCl is therefore normally used instead of KCl. METTLER TOLEDO offers ready-to-use electrolyte solutions of LiCl in ethanol (ME51340052) and LiCl in glacial acetic acid (ME51340051).

Because of the higher diaphragm resistance of LiCl electrolytes, electrodes with ground glass joint diaphragms or multiple diaphragms (e.g. LoT405-60-T-S7/12/9848) are usually recommended. In addition, it is better if the electrodes have an ARGENTHAL® or Ag/AgCl cartridge reference system because LiCl electrolytes are not saturated with AgCl. The calibration of electrodes with LiCl in glacial acetic acid can be hampered by the acetic acid leaking out and exhausting the buffer capacity of the calibration standard or the buffer. The high leakage rate of electrodes with ground glass joint diaphragms can further aggravate the situation. This is above all the case with TAN/TBN titration applications. But even the usual aqueous pH buffers may only be used once for a calibration if LiCl in glacial acetic acid is used.

KNO_3 – for special cases

A solution of 1M potassium nitrate (KNO_3) can be used as the bridge electrolyte if chloride ions present in the electrolyte lead to precipitation in the sample – e.g. in solutions containing Ag^+, Pb^+, Cu^{2+}, Hg^{2+} or proteins.

Potassium nitrate is also used for determinations in which chloride itself is determined. Argentometric titration applications are an example.



A combination pH electrode

Type of sample	Type of electrode	Recommended electrolyte
Aqueous samples that might also contain sulfides or proteins	All electrodes with ARGENTHAL® or Ag/AgCl cartridge	KCl 3M (9823) 51340049
Aqueous samples that do not contain any sulfides or proteins	All electrodes with no ARGENTHAL®or Ag/AgCl cartridge (must not be used in electrodes with ARGENTHAL® or Ag/AgCl cartridge)	KCl 3M, saturated with AgCl (9811) 51340045
Polar, nonaqueous samples	In principle all electrodes, but preferably electrodes with ground glass joint diaphragms or multiple diaphragms and ARGENTHAL® or Ag/AgCl cartridge	LiCl in ethanol 51340052
Nonpolar, lipophilic samples	In principle all electrodes, but preferably electrodes with ground glass joint diaphragms or multiple diaphragms and ARGENTHAL® or Ag/AgCl cartridge	LiCl in glacial acetic acid 51340051
At low temperatures and for media containing proteins and solvents or for nonpolar, lipophilic media	All electrodes with ARGENTHAL® or Ag/AgCl cartridge, Supplied as standard with the InLab® 428	FRISCOLYT-B® (9848) 51340053
Chloride-sensitive samples	As bridge electrolyte in reference electrodes with double chamber reference electrodes	KNO_3 51340047

Table 1: Criteria for the right electrode and electrolyte

FRISCOLYT-B® – for high and low temperatures

FRISCOLYT-B® electrolyte has a particularly wide temperature range from –30 °C to 130 °C. The electrolyte is a 2:1 mixture of glycerine (2 parts) and 3M KCl solution (1 part). The electrical resistance of the electrolyte is high because of the high concentration of glycerine. The measuring range should be limited to pH 2 to 12, or maximum 13 because of the deprotonation of the glycerine. FRISCOLYT-B® has one additional important advantage: the fact that the salt concentration is lower means that proteins present in the sample do not coagulate on the diaphragm. Electrodes containing these electrolytes can therefore also be used for applications in the field of biotechnology and for solvent-containing or nonpolar lipophilic media.

Overview of liquid electrolytes (summary)

Every user wants to know which particular electrolytes he or she can use with an existing electrode. Does a new electrode have to be purchased for a new application or can an electrode that is already available be used? Table 1 summarizes the various electrolytes according to the different types of electrode.

Solid electrolytes

Electrodes with solid electrolytes require less maintenance but have to be replaced if the electrolyte is completely consumed. It is therefore not possible to exchange the electrolyte. There are two types of solid electrodes: those with gel electrolytes and those with polymer electrolytes.

Gel electrolytes

The InLab®406, 407, 417 and LE438 each use a **gel electrolyte**. The gel is composed of KCl, ethylene glycol and cellulose. It is, in addition, saturated with silver nitrate ($AgNO_3$). Since $AgNO_3$ and KCl react to form AgCl, there is sufficient AgCl present in the gel electrolyte to compensate for silver consumption.

Polymer electrolytes

The solid electrolyte **XEROLYT®** is used in electrodes of the type InLab®413 and 418. This solid electrolyte does not require the use of a diaphragm so that there is an open connection between the electrolyte and the sample. This has the great advantage that the electrodes can be used for samples containing proteins, fats and sulfides, i.e. for applications where clogging of the diaphragm can occur when other electrodes are used. XEROLYT® is a cross-linked polyacrylamide. If measurements are performed over a long period of time below pH 2, the polymer undergoes hydrolysis. It can however be used successfully for short periods at pH values down to pH 0. The response times can be longer than for electrodes with ceramic diaphragms because XEROLYT® polymer material tends to swell like a sponge. In addition, large temperature fluctuations should be avoided because otherwise the accompanying temperature-dependent expansion and contraction would cause the diffusion potential to change.

Titration in the pharmaceutical industry

C. A. De Caro

As in many other branches of chemistry, titration has long been one of the standard analytical methods used in the pharmaceutical industry: The analysis (content determination) of active ingredients, drugs and raw materials can be performed easily, quickly, reproducibly and accurately. Titration lends itself in particular to quality control and routine analysis in production facilities. The following article describes the main applications:

1. Purity analysis of pharmaceutically active substances:

Titration is used to determine the content of active ingredients in pharmaceutical products, e.g. acetylsalicylic acid in Aspirin, or vitamin C in multivitamin tablets and for the content determination and purity control of drug additives used for the synthesis of medicinal preparations. Acid-base titrations, i.e. the neutralization reaction between acids and bases, are very frequently performed in the pharmaceutical industry. A good example is the purity control of ephedrine hydrochloride [1]. This drug is often used in cough syrups and in combination preparations for the treatment of bronchial asthma. The content is determined by titrating the drug in an organic solvent consisting of anhydrous acetic acid and mercuric acetate. Perchloric acid is used as titrant:

$$2\ R\text{-}NH_3^+\text{-}Cl^- + Hg(OAc)_2 = 2\ R\text{-}NH_2 + HgCl_2 + 2\ HOAc$$

$$R\text{-}NH_2 + HClO_4 = R\text{-}NH_3^+\text{-}ClO_4^-$$

2. Content analysis by Redox titrations:

Oxidation-reduction titrations (redox) are also used for checking the purity of raw materials, fillers and preservatives. A good example of this is the bromatometric determination of methyl-4-benzoate, a p-hydroxybenzoic acid ester. This compound is used as a preservative in ophthalmic preparations and in ointments for external application. Sodium thiosulfate is used as titrant. The analysis consists of the following steps:

2.1 Saponification (hydrolysis) of the ester with sodium hydroxide

2.2 Oxidation of the hydroxyl group to the ketone

2.3 Electrophilic bromination of the benzene ring

2.4 Excess bromine is reduced by iodide with the formation of iodine

2.5 Iodine is titrated with thiosulfate to iodide: $I_2 + 2\ S_2O_3^{2-} = 2\ I^- + S_4O_6^{2-}$

3. Precipitation titrations:

On account of their structure, some drugs precipitate with a suitable titrant. Examples of this are benzalkonium chloride and clotrimazole. Sodium tetraphenylborate or sodium dodecyl sulfate is used as titrant. The titration can be followed using the METTLER TOLEDO DS500 surfactant sensitive electrode or photometrically with a DP550 phototrode.

4. The pH-stat titration

The so-called pH-stat titration is performed to characterize drugs, to check the purity of enzyme products and to investigate the kinetics of chemical reactions. pH-**stat** means the **stat**ionary pH value, i.e. the pH value is held constant for a certain period of time. This technique is used in particular for the determination of reaction kinetic parameters such as the reactivity of enzymes.

Enzyme reactions that use up or form H^+ ions can be followed with the help of potentiometric pH electrodes. The H^+ ions formed or used are neutralized through the controlled addition of alkali or acid respectively, and the pH value thereby held constant. The rate of titrant addition is proportional to the reaction rate of the sample un-

der investigation (e.g. of an enzyme). The determination of the activity of the lipase enzyme is an example of this.
Another application area of the pH stat technique in the pharmaceutical industry is the determination buffer capacity of antacids [2]. These substances are used as therapeutic agents for neutralizing or counteracting excess acidity in the stomach or intestines caused by gastritis and intestinal disorders. Suitable compounds are for example magnesium hydroxide, oxide, carbonate and silicate, aluminum hydroxide and aluminum phosphate as well as magnesium aluminum silicate [3]. An antacid must be able to keep the pH value of the stomach constant within certain limits during its average residence time of about one hour. This means that it is important to investigate properties such as the reaction rate, acid neutralization capacity and buffer capacity.

5. Karl Fischer water/moisture determination:

The water or moisture content of a pharmaceutical product is a quantity that plays an important role as far as the activity and the storage lifetime of the product are concerned. A water content that is too high or too low impairs the effectiveness of the medicinal preparation: the active ingredient decomposes or does not achieve its maximum effect. On the other hand, water content has a large influence on storage lifetime.
The selective Karl Fischer method for water determination is a long established routine method and is the method of choice [4, 5, 6]. Water is determined through the reaction with iodine in an alcoholic solution.
Water contents of several percent are determined volumetrically with the addition of an iodine containing solution (volumetric Karl Fischer titration, [4]). An example of a volumetric Karl Fischer analysis is the water determination in Aspirin tablets. The tablets are first ground and the powder transferred to the titration cell and titrated directly. The active ingredient, acetyl salicylic acid, affects the Karl Fischer titration because the pH value of the solution is lower after the sample has dissolved. In this case an imidazole buffer solution is added to neutralize the acid and keep the pH value in the optimum range of 6 to 7.
For water contents below 0.5-1%, the quantity of iodine needed for the determination is produced electrochemically in the titration cell (coulometric water determination [5, 6]). An example of a coulometric analysis is the determination of water in lyophilized (freeze-dried) samples. Because of the extremely low water content (in the ppm range), the lyophilized substance is dissolved in anolyte that has been pretitrated to dryness and then titrated directly.
Proper sample preparation is very important in Karl Fischer titrations because only water that is actually free is determined [4]. It is therefore essential that the water present in the sample be completely free before the Karl Fischer determination is begun. This can be achieved for example by stirring the sample for a sufficiently long period of time in the titration cell, by reducing particle size and homogenization, by warming or by external extraction with a solvent, etc.
The use of a drying oven is recommended for insoluble samples or those that undergo side reactions with the Karl Fischer reagent or that release water only slowly. The action of heat liberates the water, which is transferred to the titration vessel as vapor by means of a stream of dry inert gas. If an oven is used, the sample must of course be thermally stable.

To increase efficiency, all the time-consuming steps should be automated:

The titration of several series of samples and the periodic taking of aliquots are both operations that are very costly because the user has to repeatedly perform each individual operation. In addition these operations are very monotonous because the sequence of operations in the standard operating procedures has to be followed exactly. These problems can be overcome if the routine work is properly automated.
The METTLER TOLEDO QUANTO and Rondo 60 sample changers provide the optimum solution for automation. In combination with an automatic titrator, each individual working step is now taken care of by the system as a whole: the titrator controls the analysis of several samples automatically without direct manual intervention. The METTLER TOLEDO DU200 Dispenser, the SU24 Automatic Sampling Unit and the AOE06 Auxiliary Output Expander enhance the flexibility and degree of automation of the system still further.

[1] METTLER TOLEDO Application Brochure No. 25, "Applications in the pharmaceutical industry", ME-51710071, 2001.
[2] METTLER TOLEDO Application M054, "pH-stat of Antacids at pH 3",in Application Brochure 2, ME-724557, 1992.
[3] Römpp Chemie-Lexikon, Heraus. J. Falke und M. Regitz, Vol. 1, 9. Edition, Georg Thieme Verlag, 1989 (in German).
[4] METTLER TOLEDO Application Brochure No. 26, "Fundamentals of the Volumetric Karl Fischer Titration with 10 selected applications", 1998 (ME-51709855).
[5] Hydranal manual, "Eugen Scholz reagents for the Karl Fischer Titration", Riedel-de Haën, 1988.
[6] G. Wieland, "Wasserbestimmung durch Karl-Fischer-Titration: Theorie und Praxis", GIT Verlag, 1985.

Fully automated, continuous and parallel determination of nickel and hypophosphite in chemical nickel baths: the DL77 Titrator makes it possible!

H.-J. Muhr

The title could even be "Nothing is impossible if you have a DL77". The article describes the realization of a highly automated system for a customer concerned with the design and construction of electroplating plants. Discover how you can solve complex applications like this with the new SU24, AOE06 and DU200 automation accessories.

Introduction

Electrolytically deposited films of different metals such as nickel, copper, tin or silver are used for a wide range of different applications. These include decorative coatings for household fittings, corrosion protection and diverse applications in the electronics and electrotechnical industries. The metals are deposited in either electrolytic or current-free, purely chemical processes. Nickel is deposited through the reduction of nickel chloride with sodium hypophosphite. Nickel coatings produced by this chemical process have an extremely uniform distribution of nickel even with complicated or non-conducting parts, are very resistant to corrosion, and are extremely hard due to the incorporation of phosphorus. The continuous determination of the concentration of both active constituents in the chemical nickel bath is of great importance for monitoring the process and making sure that the desired specifications and tolerances for the coating are met.

Analytical requirements

The customer's nickel bath was designed so that samples could be taken for analysis from a bypass setup. The samples then had to be analyzed and the results of the determinations processed using a special software program that the customer himself had created for controlling the baths and also adapted to the titrator. The software also had to control the titrator externally, i.e. to trigger the start of the each analysis. The analytical procedures required for the analysis of the chemical nickel bath had to satisfy the following requirements:

- automatic sampling
- determination of nickel in the concentration range 3-7 g/L
- determination of hypophosphite in the concentration range 8-13 g/L
- nickel had to be determined more frequently (2-3 times an hour) than hypophosphite (3-4 times a day)
- the long reaction time of the hypophosphite determination (approx. 45 min) and the desired higher measurement frequency of the nickel determination meant that the analytical procedures had to be separated to make simultaneous determination possible.
- both determinations should be performed fully automatically (sampling, titration, rinsing).
- possibility of controlling the titrator externally via applications software.
- flexible design with a view to future expansion for the determination of other metals.
- easy to use, rugged and reliable design, low maintenance system.

For such a demanding application like this, only one titrator really fills the bill - the METTLER TOLEDO DL77. This instrument was specially designed for parallel titrations and its flexible method programming concept and conditional functions as well as its capability of controlling external devices make it the ideal solution for realizing such fully automated applications.

The analytical methods

Both constituents can be determined according to standard procedures because the nickel bath contains no metal cations or reducing agents that interfere with the analysis:

- Nickel is determined by a complexometric titration with 0.1M Na_2EDTA in a solution buffered with NH_3/NH_4Cl at pH 10 to a color change (brown-violet of the murexide indicator). Detection was performed photometrically at a wavelength of 550 nm with the DP550 phototrode.
- Hypophosphite is oxidized to phosphate in sulfuric acid solution with an excess of 0.05M iodine solution. The excess iodine is determined by back titration with 0.1M thiosulfate solution. A DM140-SC platinum ring electrode was used for detection.

Design of the fully automatic measurement system

Sampling

Sampling was performed with an SU24 sampling unit. This consists of a sample loop with two DV1000 two-way valves that are simultaneously switched and whose position can be checked via a voltage measurement. Figure 1 shows a schematic diagram of the SU24 sampling unit used in the nickel/hypophosphite application. The position of the valves is checked and the valves, if necessary, switched to the sampling position. In the "E>100mV" sampling position, which is indicated by a green LED, the sample is sucked into the 5 mL sample loop via a 20 mL burette. Afterward the valves are switched to the "E<10mV" transfer position, indicated by a red LED, and the exact volume of sample flushed into the titration beaker with deionized water. The suction and the transfer process can also be performed with SP250 peristaltic pumps. Burettes were used in this application because both operations had to be performed in parallel.

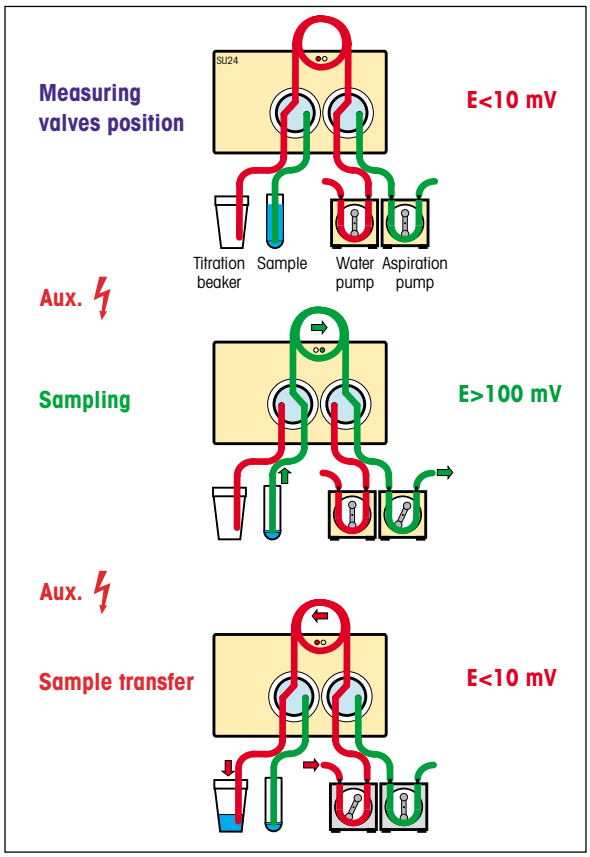


Fig. 1: Sampling with the SU24

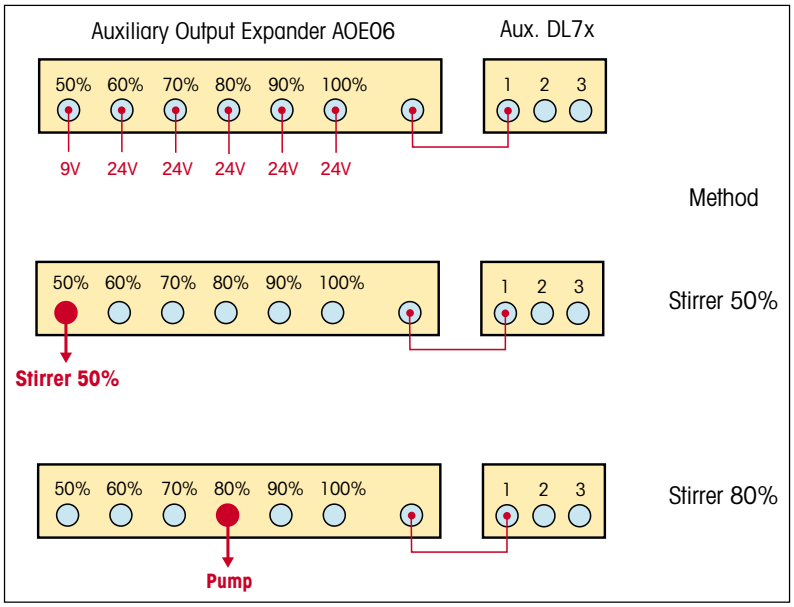


Fig 2: Operating principles of the AOE06

Alternate sample transfer

For the automated parallel operation of both titration methods, samples have to be transferred to both titration stands. This is done using a commercially available 24V two-way valve that is switched via an auxiliary output of the DL77 titrator when the sample is transferred from the sample loop to the corresponding titration stand.

Addition of auxiliary reagents, waste disposal and rinsing

Auxiliary reagents are delivered with SP250 peristaltic pumps, i.e. the NH_3/NH_4Cl buffer and a 1% aqueous solution of the murexide indicator for the nickel determination, and 25% sulfuric acid for the hypophospite determination. The new DU200 dispenser was used to add the standard solution of iodine because the four DL77 burettes are used for the titrations and the sampling. The waste solutions are transferred to the waste container with a peristaltic pump. In the nickel determination the titration beaker is rinsed via the burette used for sample transfer, and in the hypophosphite determination via an additional peristaltic pump.

Control of the peripheral devices with the new AOE06 unit

For the fully automatic parallel operation of both titration methods, two stirrers, six peristaltic pumps, one two-way valve, one DU200 Dispenser and an SU24 Sampling Unit are required, i.e. a total of 11 (!) peripheral devices are controlled via auxiliary outputs of the DL77 Titrator. Since three auxiliary outputs are available as standard, the outputs Aux. 1 and 2 have to be multiplied by means of two of the new AOE06 Auxiliary Output Expanders (Fig. 2). Each AOE06 has six outputs that are activated via stirrer functions with different stirrer speeds of 50 – 100% in intervals of 10%. Output 1, which is triggered with a stirrer speed of 50%, is connected to a 9 V supply, which allows a stirrer to operate at a speed of 50%. Outputs 2-6 are supplied with 24 V, which allows pumps or other pe-

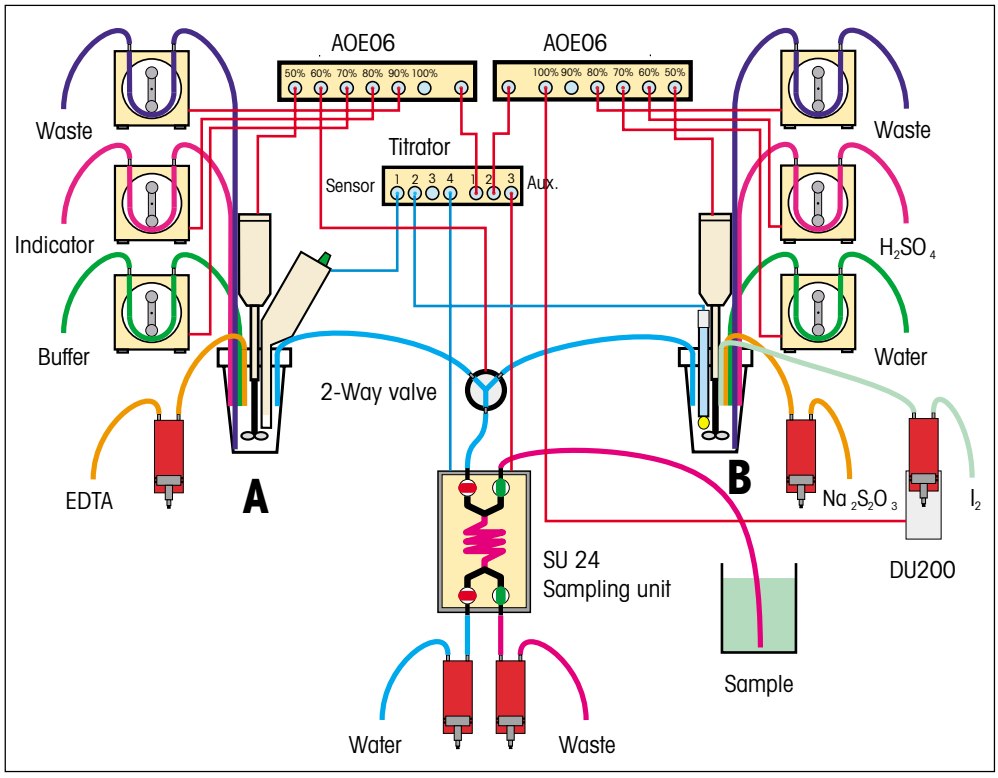


Fig. 3: Design of the system for the parallel determination of nickel and hypophosphite

ripheral devices such as the DU200 Dispenser or the two-way valve to be triggered.

The AOE06 therefore allows five additional peripheral devices to be triggered for each auxiliary output via stirrer functions with the corresponding stirrer speeds.

The system setup

Figure 3 shows the design and connections for the fully automatic parallel analysis of nickel and hypophosphite in a chemical nickel bath.

The auxiliary reagents are transferred to each titration stand via standard burette tubing by means of special triple bored NS14.5 hollow plastic stoppers that are fixed in the holes reserved for electrodes.

Configuration, methods and analysis sequence

In parallel operation, a single sampling method called **dose** is started in the analysis section A, which dispenses the sample to titration stand 2. At the end of the method, an internal synchronization command, *Sync Send*, is sent to analysis section B, whereby, via the command *Sync Send/Wait*, the method called **hpst** for the determination of hypophosphite is started. This method does not have its own sampling routine. In the sample function of the **hpst** method, the Auto stand is defined as titration stand. The method is thereby always automatically ready to run after the cycle or, in other words, the **hpst** method in section B is always switched to standby and is started only by the **dose** method running in analysis section A.

Sampling is integrated in the **nist** method for the determination of nickel. This means that **nist** can be run independently of **hpst** in analysis section A. This is necessary because nickel is determined more frequently than hypophosphite and because the determination of hypophosphite takes much more time (45 min) than the

Analysis section A		Analysis section B	
Method dose			
Title			
Sample (Stand 1 at Aux.1, 60% stir)			
Stir 0%			
Measure SU24			
Aux. Instrument SU24 (Condition E<10)			
Dispense Sample		Method hpst	
Aux. Instrument SU24		Title	
Dispense Water		Sample (Auto stand at Aux.2, 60% stir)	
Sync Send		Sync Send/Wait	
		Stir 60%	H_2SO_4
Method nist		Stir 100%	I_2-Dosing by DU200
Title		Stir 50%	Stirrer
Sample (Stand 1 auf Aux.1, 60% stir)		Titration	
Measure SU24		Calculation	
Aux. Instrument SU24 (Condition E<10)		Record	
Dispense Sample		Stir 80%	Waste
Aux. Instrument SU24		Stir 70%	Water
Dispense Water		Stir 80%	Waste
Stir 70%	Buffer	Statistics	
Stir 80%	Indicator	Record	
Stir 50%	Stirrer		
Titration			
Calculation			
Record			
Stir 90%	Waste		
Stir 60%			
Dispense	Water		
Stir 90%	Waste		
Statistics			
Record			

Fig. 4: The methods

nickel determination (4 min). The **dose** and **nist** methods are processed consecutively in parallel operation by means of the command *List once*.

Summary

This application setup allowed all the customer's requirements regarding the automated titrimetric analysis of the chemical nickel bath to be fulfilled in a very elegant and efficient way. In addition he profited from:

- a minimum engineering outlay – only a two-way valve and four triple bored stoppers had to be provided.
- a very flexible system that can, with very little modification, be used in the same configuration for other determinations (e.g. zinc, palladium, or copper) or for automated solutions (e.g. with two SU24 sampling units).
- a system that is very easy to disassemble and reinstall in spite of its complexity.
- the very popular straightforward METTLER TOLEDO DL77 method programming and operating concept. Customers can easily reconfigure the system for other determinations or modify the method sequence of existing applications.
- a system that is rugged and reliable and that operates with low maintenance in spite of the intricacy of the connecting tubes, cables and peripheral instruments. The system has now been in full operation for about nine months. During this time it has operated perfectly to the full satisfaction of the customer.

In summary, this is yet another example that shows how METTLER TOLEDO DL70ES or DL77 titrators (with the appropriate auxiliary instruments) can solve almost any titration problem – try them out yourself!

We automate almost everything.

METTLER TOLEDO continues to expand its range of automated solutions for titration:

The new QUANTO aliquot and QUANTO direct titration systems are specially designed for very high sample throughput applications. Together with a DL58, DL70ES or DL77 titrator, they can completely automate the titration process including sample preparation for up to 60 samples.

QUANTO aliquot is the specialist for applications in the water and beverage industries. The instrument can in fact be used for any applications where a large number of liquid samples have to be determined efficiently without intervention by the user.
Since QUANTO aliquot itself measures the required sample volume, all you have to do is to fill the 60 sample tubes with the approximate volume of sample before the measurement. The tedious and time-consuming work of measuring an exact sample volume is no longer necessary.

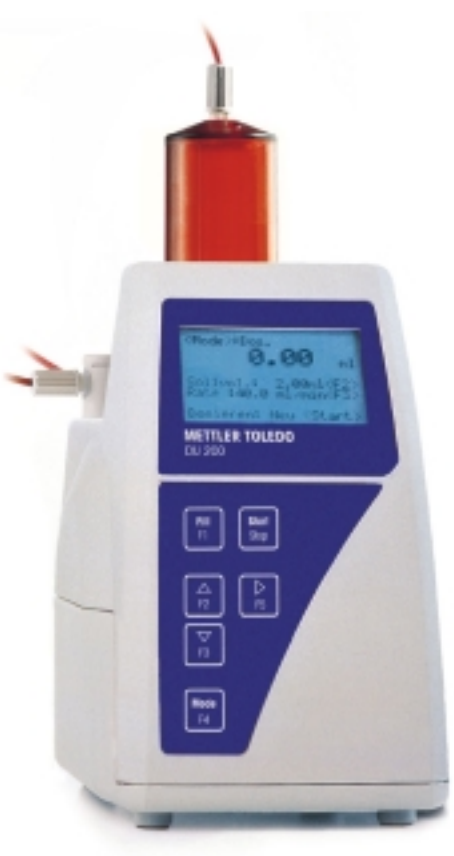
QUANTO direct

QUANTO aliquot

QUANTO aliquot can operate almost unattended thanks to the large solvent reservoir, the integrated level sensor and the various pumps that are available. So there is nothing to stop you letting it run overnight.
For conductivity measurements, a special optional conductivity cell can be added and used with the various METTLER TOLEDO conductivity sensors.

QUANTO direct is the choice for applications where a large number of samples first have to be dissolved, reduced in size or otherwise prepared in some way. The instrument is therefore an ideal solution for many different pharmaceutical applications and in particular for nonaqueous analyses such as TAN/TBN. The titration head

is equipped with the PowerShower™ rinsing system. This guarantees optimum rinsing of the electrodes even when sticky or viscous samples are analyzed.
Included with QUANTO direct is the FlipRack™, which can be positioned to accept either sixty 50 ml beakers or forty 100 ml beakers.
The next edition of UserCom will present a number of applications that illustrate the advantages of QUANTO aliquot and QUANTO direct.



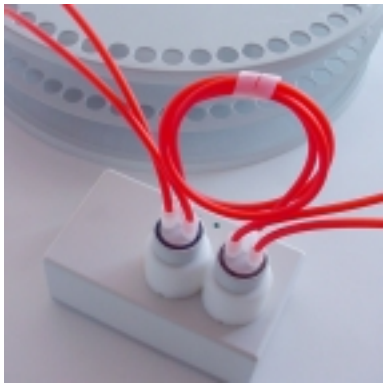
METTLER TOLEDO DU200 Dispenser

Automated dispensing – the DU200

METTLER TOLEDO titrators can be expanded to 2 or 4 burette drives depending on the type. If an additional burette drive is required for dispensing a solution, for example in a back-titration, a very simple and elegant solution is now available - the METTLER TOLEDO DU200 Dispenser.
This instrument allows 0.01 mL to 999 mL of solution to be accurately dispensed in combination with a DL50 Graphix, DL53, DL55, DL58, DL70ES or DL77 titrator. The dispensing accuracy meets the requirements of the new ISO 8655 standard and is therefore equivalent to that of the titration burettes.
The DU200 is supplied complete with all the necessary tubing for connection to the above-mentioned titrators. The command for dispensing is integrated directly in the titration method. Control is via the TTL I/O (DL5x) or auxiliary outputs (DL7x) of the titrator.
The DU200 can also be used as a highly accurate stand-alone dispenser.

Extremely accurate sampling- the SU24

The SU24 sampling unit can be used in any applications where exactly the same volume of sample has to be repeatedly dispensed. An excellent example of the use of the SU24 in a complex automated application can be found on page 14 in this edition of UserCom.


Sampling unit METTLER TOLEDO SU24

Six outputs – AOE06

Comprehensive automated applications demand a variety of external control possibilities. That is why the 3 auxiliary outputs of the DL70ES and DL77 sometimes need to be supplemented. The AOE06 converts each auxiliary output into six new outputs. Two AOE06 units enable up to 12 different instruments to be independently controlled from a DL77/DL70ES!

METTLER TOLEDO AOE06

Publications

The application chemists of the Analytical Chemistry market support group have prepared several publications and a series of application brochures to support customers in their routine work in the laboratory. Each brochure is dedicated either to a particular branch of industry (such as paper and pulp, petroleum and beverages), a particular titrator or a specific analysis technique. The following list shows all the publications together with their order numbers. They are available from your local METTLER TOLEDO marketing organization.

Publications, reprints and applications		German	English
Titration in routine and process investigations		51724658	51724659
Basics of Titration		51725007	51725008
Fundamentals of Titration		704152	704153
Applications Brochure 1	Customer Methods	724491	724492
Applications Brochure DL70	Gold and Silver		724613
Applications Brochure 2	Various Methods	724556	724557
Applications Brochure 3	TAN/TBN	724558	724559
Applications Brochure 5	Determination in Water	51724633	51724634
Applications Brochure 6	Direct measurement with ISE	51724645	51724646
Applications Brochure 7	Incremental Techniques with ISEs	51724647	51724648
Applications Brochure 8	Standardization of titrants I	51724649	51724650
Applications Brochure 9	Standardization of titrants II	51724651	51724652
Applications Brochure 11	Gran evaluation DL7x	51724676	51724677
Applications Brochure 12	Selected Applications DL50	51724764	51724765
Applications Brochure 13	Nitrogen Determination by Kjeldahl	51724768	51724769
Applications Brochure 14	GLP in the Titration Lab	51724907	51724908
Applications Brochure 15	Guidelines for Result Check	51724909	51724910
Applications Brochure 16	Validation of Titration Methods	51724911	51724912
Applications Brochure 17	Memory card "Pulp and paper"		51724915
Applications Brochure 18	Memory card "Standardization of titrants"	51724916	51724917
Applications Brochure 19	Memory card "Determination in Beverages"	51725012	51725013
Applications Brochure 20	Petroleum		51725020
Applications Brochure 22	Surfactant Titration	51725014	51725015
Applications Brochure 23	Edible oils and fats		51725054
Applications Brochure 24	KF Titration with DL5x		51725023
Applications Brochure 25	Pharmaceutical Industry	51710070	51710071
Applications Brochure 26	METTLER TOLEDO Titrators DL31/38 *	51709854	51709855
Applications Brochure 27	KF Titration with Homogenizer		51725053
Applications Brochure 29	Applications with the METTLER TOLEDO Rondo 60		51710082
Applications Brochure KF	Chemical	724353	724354
Applications Brochure KF	Food, Beverage, Cosmetics	724477	724478
Applications Brochure KF	10 DL35 Applications	724325	724326
Applications Brochure DL18		724589	724590
Applications Brochure DL12			724521
Applications Brochure DL25		724105	724106
Applications Brochure DL25	Food	51724624	51724625
Applications Brochure DL25	Petro / Galva	51724626	51724627
Applications Brochure DL25	Chemical	51724628	51724629

* Also available in French (51709856), Spanish (51709857) and Italian (51709858)

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