Lab Manager

TITRATORS RESOURCE GUIDE

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Introduction

Titration is a common laboratory method of quantitative chemical analysis that is used to determine the unknown concentration of an identified analyte. Since volume measurements play a key role in titration, it is also known as volumetric analysis. A reagent, called the titrant or titrator is prepared as a standard solution. A known concentration and volume of titrant reacts with a solution of analyte or titrand to determine concentration.

In most cases, titration is performed by a dedicated titrator, and different types of titrators are available depending on the specific analysis required.

3 Considerations for Choosing a Titrator

For laboratories with high sample volumes and an increased need for faster turnaround times, automating the titration process may be the way to go.

by Ryan Ackerman

What effect does non-routine analysis have on the type of titrator that should be used?

For laboratories running a wide variety of analyses on samples—such as is in the food and beverage or environmental industries—the configuration or type of titrator required may need to be more flexible. Typical systems such as Karl Fischer (water content), potentiometric (voltage), acid/base, stat, and single element titration can be combined into a multi-parameter system. This allows greater flexibility when more than one test is required, or if t he analysis is not routine.

Is it important to know if the analyte(s) of interest are trace level?

In the instance of some forms of titration—such as Karl Fischer for moisture determination—there are alternative options where lower detection limits are required. In volumetric titration, the titrant is added directly to the sample via burette, where the moisture content is determined from the titration volume. This works for high levels of moisture, but does not give as low a detection limit. Coulometric, on the other hand, has the titrant generated electrochemically in a titration cell, giving the ability to see much lower levels of moisture.

SAFETY TIP

As titration involves the use of chemicals, you'll want to follow some basic safety procedures, such as wearing safety goggles, a lab coat, and gloves. Wash any spills on clothing or skin immediately with plenty of water and inform whoever is in charge of the lab. For basic titrators, you'll want to lower the burette to a comfortable height when reading or filling it. You'll also want to use a funnel to fill the burette, and do so slowly in order to avoid splashing or spills.

How will the volume of sample throughput affect the titrator's installation?

For laboratories with high sample volumes and an increased need for faster turnaround times, automating the titration process is an important consideration. Many vendors offer a variety of automated solutions including the more common sample-changing robotics, all the way to fully automated systems that can weigh, change, and titrate automatically. In doing so, technicians and researchers can work on other processes, greatly increasing efficiency and turnaround times.

Troubleshooting a Titrator

When titration runs into trouble, history impacts the troubleshooting

by Mike May, PhD

Knowing How to Look for the Trouble Makes it Easier to Find

To find the concentration of an analyte in a solution, scientists turn to titration. Once a drop-by-drop-by-drop method, this can now be handled automatically with a titrator, but getting an accurate answer still takes some skill. Part of the needed skill depends on what is being tested. Nonetheless, some general information applies to virtually any titration situation.

According to industry experts, titration issues are typically either systematic or random. Systematic errors generate the same results, although incorrect, every time; random errors generate no results or various incorrect results without consistency. Since systematic errors generate the same problems every time, they are the easiest to figure out. To see whether a problem is systematic it is always advised before troubleshooting to run the sample or method with the issue multiple times to look for trends and to see the repeatability of the issue before attempting to address the problem.

Scientists in research and industry use titration in so many ways that variety alone creates a challenge. Depending on the type of reaction, whether it's an acid-based, a redox, a complexometric, or a nonaqueous titration, using the right electrode can make all the difference. Leading manufacturers have fine-tuned the electrode design for even the most difficult samples.

In search of the source

The goal of titration is finding the end point, but that can be elusive. There are many different reasons why an end point may not be obvious; however, here are a few simple questions you can ask yourself to identify the cause.

The questions include, is the correct titrant at the proper concentration being used? Is the electrode fully submerged in the sample? Is the sample completely dissolved, and is the analyte of interest available for titration? Are the increments in the titration method set properly? And did the titration just stop too soon?

Other experts also see users struggling at times with the titration end point. For titrations in which the user is looking for a visual end point, the most common issue is probably going to be overshooting the end point. This is usually caused by not completely mixing in each drop of titrant or dispensing drops that are too large. Even for titrations that require a pH-change end point, it can easily be overshot if the pH probe being used does not have a fast enough response.

Also, when titration runs into trouble, history impacts the troubleshooting. If a titration method and procedure have been used for some time with success, then that is the last thing one would want to modify; the fluctuations are most likely due to hardware, reagent, or sample inconsistencies.

Even the sample can contribute to the problem. With sample fluctuations, users should try to pretreat samples in a way that minimizes effects of interference, temperature, pH, etc., so that the results are consistent, according to industry specialists. Things like pH adjustment to a specified pH, dilution, and filtration are common pretreatment steps, and these will vary largely depending on the type of titration being performed.

Keep up the care

Perhaps the best way to deal with any fluctuations in system performance or sample results is to make sure you are taking care of your titration system, making sure the electrode is stored in the correct solution and calibrated properly will help reduce fluctuations. In addition, ensuring that your

dosing burettes are properly vented to the molecular sieve or ascarite will help protect the titrant concentration from degrading.

Diminished reproducibility can really destroy results over time. When reproducibility starts to fade, it's time to verify a few things. For one thing, inspect the electrode for wear or blockage. Two key components of every electrode system are the measuring membrane and the reference diaphragm, if either of these areas becomes slightly blocked or scratched, the electrode won't be able to respond properly and will give irregular results.

The other most common source of issues is the titrant or solvents used. Changing titrant strength due to varying temperature or contamination, improper storage and protection of titrants, or contamination of solvents are the typical issues regarding reagents. To find the source of this kind of problem, the user should exchange the reagents one by one and see whether that solves the problem.

It's also possible that the system that purifies the water used in titration needs maintenance.

To keep your automated titration running smoothly and accurately, it's always good to refresh your mind with how the electrode system works, because understanding the key functioning areas of an electrode will often lead you to the proper troubleshooting techniques. Additionally, review the different modes of titration and how changes in titration parameters affect the shape of your titration curve. To develop new titration knowledge or refresh it, some manufacturers host "Titration Bootcamp" courses. These courses can provide an excellent refresher to anyone working in the field of titration, regardless of their years of experience."

So keeping up titration knowledge and the condition of the equipment go a long way toward preventing problems. Even an automated titrator needs care and skill to ensure ongoing accuracy in the results. The level of skill needed, however, depends on the task at hand.

LINDA Says...

Good Laboratory Practices (GLP) is a broad term that encompasses best practices followed in many industries that use titrators. As long as you can demonstrate a year from now that you were following procedures that gave you the best chance for a correct answer, you are probably following GLPs. This means calibrating key components, maintaining a history of calibration and quality checks, and demonstrating that all users have followed the manufacturer's maintenance recommendations.

Meet LINDA

LINDA is a lab manager. Her job is to balance the scientific needs of her staff with the business needs of her lab. LINDA stands for:

Leadership
Informed
Negotiator
Decision-Maker
Accountable

Titrators: Myriad Methods for Quantifying Unknowns

Those whose only brush with titration came in a freshman chemistry lab may be surprised to learn the significance of titration in companies that manufacture materials, drugs, foods, and beverages

by Angelo DePalma, PhD

A titrator is best described as as a sophisticated delivery system that performs stoichiometry. It's a tool that provides better repeatability, accuracy, and efficiency than manual titration."

There are two major titrator types: potentiometric acid-based designs and Karl Fischer titrators. Those in the first group, which use a pH or redox probe, resemble pH meters in their ability to derive acid strength and total acidity; Karl Fischer titrators measure water content in foods, materials, biofuels, etc.

Most titration work occurs in quality control (QC) laboratories. A survey found that 75 percent of titrators are used in QC, 20 percent in research, and 5 percent in clinical labs. More than half of those surveyed had more than one titrator, with 10 percent owning four or more. Of specific titration modes, more than half fall under the "potentiometric" category, and 21 percent each for volumetric and coulometric Karl Fischer titrations.

All those surveyed considered instrument cost during the purchasing process. This is not unusual when you consider that everyone who performs titration professionally has at one time done it on the cheap with a burette, an Erlenmeyer flask, and either a colorimetric indicator, pH paper, or a pH meter. Dedicated titration systems range in price from about $5,000 to more than $100,000. Yet only 10 percent of those surveyed listed instrument cost as the top reason for choosing one titrator over another.

After price, our readers considered performance, reliability/maintenance, service, support, and ease of use when purchasing a titrator. Experience with a particular vendor or product line was the number-one factor (53 percent) in selecting a specific instrument.

Bucking the trend

The developments and trends in titration largely focus on "flexibility and versatility." Different industries have different titration needs, these range from low-cost, easy-to-use, single-type titrations to complex, multi-chemistry, multielectrode, multi-sample, and multireagent analysis. The point: Select your titrator with current needs in mind, and perhaps with a thought toward expanding future capabilities.

A major trend for lab instruments in general, and titrators in particular, has been to supply each instrument with a computer for data acquisition, logging, and massaging. Not all companies have gone along with this approach. There is no need to have a computer attached to each instrument in the lab, many instruments come with software for downloading and archiving data through an RS-232, a LAN, or USB interface, but the computer is not required to operate the instrument.

There are good arguments for not computerizing. Barring regulatory requirements, controlling all functions from the instrument itself minimizes cost and footprint, flattens the learning curve, and lowers costs. For those so inclined, complex, multichemistry titrations may be fully automated through standard, off-the-shelf equipment without customized software or programming – that is, provided the titrator possesses some "smarts." Analyticon's instruments store up to 80 pre- and user-defined methods that range from simple pH adjustment and pH microtitration to automated calibration, blank determination, and subsequent sample analysis, all from a built-in keypad.

When packaged with methods targeted to specific industries, titrators are a convenient way to consolidate several analyses with one investment. Because wineries are significant purchasers of titrators, one manufacturer has bundled

methods for analyzing pH and sulfur, two components that affect a wine's taste and longevity.

Methods are of varying value to customers, according to one manufacturer. About one-third of customers use their own methods; the remainder rely on vendor-supplied methods and training. The challenge is providing an instrument that cuts through widely disparate skill sets.

Versatility is key

One titration expert observes that "the days of single titrator analysis are fading fast. Purchasers want to maximize their investment and get as much as possible out of the instrument. Major vendors have overhauled user interfaces to include touch screens, and even stand-alone titrators can benefit from automation and sample prep tools, particularly in high-throughput settings (e.g., QC for foods or chemicals). Up to 40 percent of surveyed users employed an auto-sampler; leading sample preparation methods were homogenization (27 percent), drying (18 percent), and evaporation (12 percent).

Within the automation categories, sample changers and liquid handlers are the most common features. Some titrators come equipped with pipetting and dosing technology (in addition to the titrator itself), but addons like ovens are usually purchased separately.

Decisions to automate operations like dispensing and sample prep are not made lightly, because this equipment can be expensive. One tends to think of throughput as a crossing point: The more samples run per unit time, the greater the need to automate. A natural expectation from this line of thinking is that automation is always faster. That is not true. Sample prep and automation require some user input and have learning curves of their own, while some technicians are very fast.

The best arguments for automation and for sophisticated data acquisition tools are consistency, data quality, and data integrity. Instruments perform repetitive tasks faithfully and accurately, and they never tire of recording and tracking samples as even the best technician sometimes does.

Survey Results

Types of titrators used by *Lab Manager* readers

Potentiometric	62%
Karl Fischer Volumetric	35%
Karl Fischer Coulometric	29%
Other	15%

Titrator components used by *Lab Manager* readers

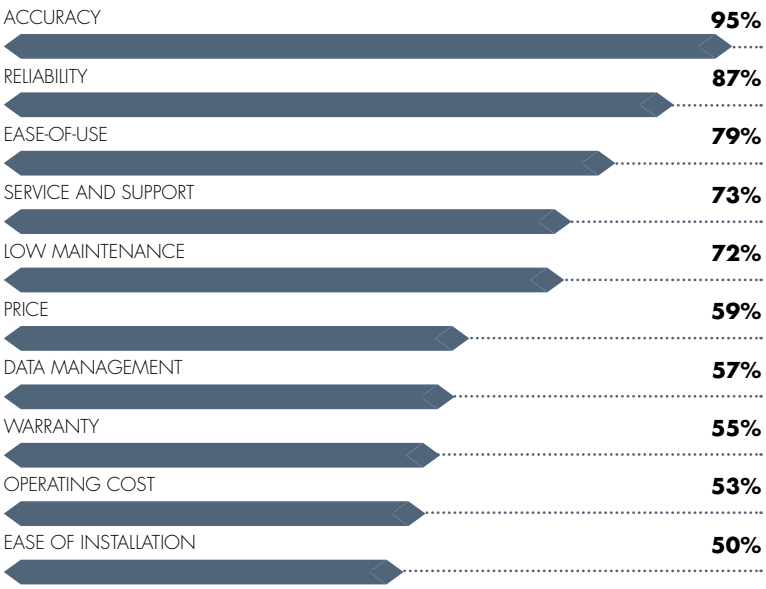
Autosampler	50%
Karl Fischer Oven	24%
Homogenizer	17%
Evaporators	13%
Other	23%

Are *Lab Manager* readers using manual or automated titration?

Manual titration	50%
Automated titration	24%

TOP 10 FEATURES/FACTORS

Respondents Look for When Purchasing a Titrator:



Titrators: Compliance Based on Best Practices

When the U.S. Food and Drug Administration promulgated its good laboratory practices (GLPs) for animal toxicology labs in 1979, the regulations were considered a breakthrough in compliance assurance.

by Angelo DePalma, PhD

As GLPs expanded to include all instrument and non-instrument operations, in tox labs and beyond, other U.S. agencies, most notably the U.S. Environmental Protection Agency, adopted the idea. The original GLPs spawned regulatory and standards practices worldwide whose goals were to improve quality through best practices.

Quality in, quality out

GLPs' inputs are best practices, and their output is data quality. A key component relates to 21 CFR Part 11, promulgated in 1997. Part 11 covers electronic records, signatures, and related computer systems. It is often considered as "the gold standard of compliance." Adhering to it, ensures compliance with most if not all U.S. regulatory bodies because Part 11 is a very stringent standard.

At one time, all recordkeeping and compliance recording were done by hand in paper notebooks and on forms. Today, even labs lacking a Lab Information Management System (LIMS) or an electronic lab notebook (ELN) are computerized.

For this reason, purchasers should look for systems with built-in traceability and compliance aids. Software and touch panel-controlled firmware can even assist with operations crucial to GLP compliance. It goes well beyond electronic signatures. The software can tell if you're using the right burette, electrode, reagents, even the right method. Many modern titrators have this ability built in.

Some manufacturers even embed microchips into components, peripherals, and systems to ensure that the right components are used with the right method. Parts identify themselves through unique serial numbers. Systems will not operate when components are incorrect or past their calibration dates. Users obtain the equivalent of a full system compliance audit every time they turn the titrator on. In the past you had to keep track of and record this information on paper. Now, the titrator does it for you and a computer is not even required in order to be in compliance.

GLP is a broad term that encompasses best practices followed in many industries that use titrators. As long as you can demonstrate a year from now that you were following procedures that gave you the best chance for a correct answer, you are probably following GLPs.

This means calibrating key components and maintaining a history of calibration and quality checks; for example, ensuring that burettes have been validated for dispensed volume within a timeframe specified by the protocol. And, importantly, demonstrating that all users have followed the manufacturer's maintenance recommendations.

Potential purchasers should also look to acquire software that handles most routine compliance tasks automatically. Users still need to make up and run standards, but the software should remind operators and management to complete those tasks, and to keep track of burette calibration, titrant standardization, and electrode calibration. Operators should not have to worry about these things.

Compliance software should interface with LIMSs and ELNs in both workflow directions. A LIMS, for example, can generate worksheets containing automated quality check standards and collect and process data as each sample runs, not only when the batch is completed.

The critical ingredient for such automation is simplicity. Otherwise, the benefits of automated recordkeeping are squandered through human error and/or lack of compliance.

Instrument tips

Experts agree that good compliance begins with good

recordkeeping and good instrumentation. The following instrument-related tips are a good start to facilitate GLP compliance:

- Electrodes: Record electrode(s) type, starting date of use, and manufacturer data such as lot number. These data provide reference points for documenting subsequent maintenance and testing activities.
- Burette: Record the starting service date and total dispensed quantities. For reliability checks, fill burettes with pure lab water and dispense quantitatively into an appropriate tared weighing vessel. Confirm repeatability and accuracy by measuring dispensed weight. Also, confirm operation of the burette sample changer.
- Calibration and error history: Saving past pH calibration data reveals the point in time when electrode malfunction began. It is advised that labs maintain a daily graph of calibration and error events.

Good Titration Practice (GTP) consists of five steps: evaluation of current and future analytical needs, instrument selection, installation, qualification, and operation. The company website provides a GTP "risk check" guide covering:

- Temperature fluctuation: A 5°> temperature change can affect volumes of non-aqueous titrants by 0.5 percent, while pH is also temperature-sensitive.
- Installation mode: Least desirable is self-installation; most desirable is vendor installation.
- Titration mode: The more automated the better, to reduce human error and free operator time.
- Documentation: Forget handwritten results. Consider a system that provides automated GLP-compliant printouts or, even better, that stores results in a compliant database.
- Training: GLP regulations do not specify training requirements. However, operators should be trained in titrator operation as they would be for any other instrument.
- Performance verification: Labs should calibrate periodically based on elapsed time or usage. Some systems lock when calibrations fall out of date or when titrants fall out of specification.

While some labs don't appreciate this level of intrusion, preferring simple automated reminders or acknowledgements that managers, one hopes, can act on. If changes are made to certain protocols, the software should provide a login password that demonstrates the operator has the authority to make those changes, and include a field to include reasons for the change.