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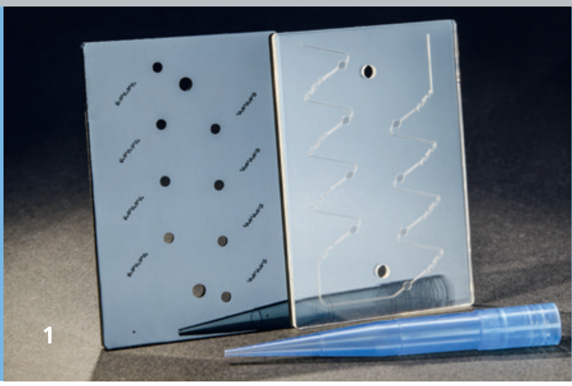

1 *Chip for continuous µ-titration*

LAB-ON-A-CHIP FOR QUANTITATIVE SIMULTANEOUS TITRATION

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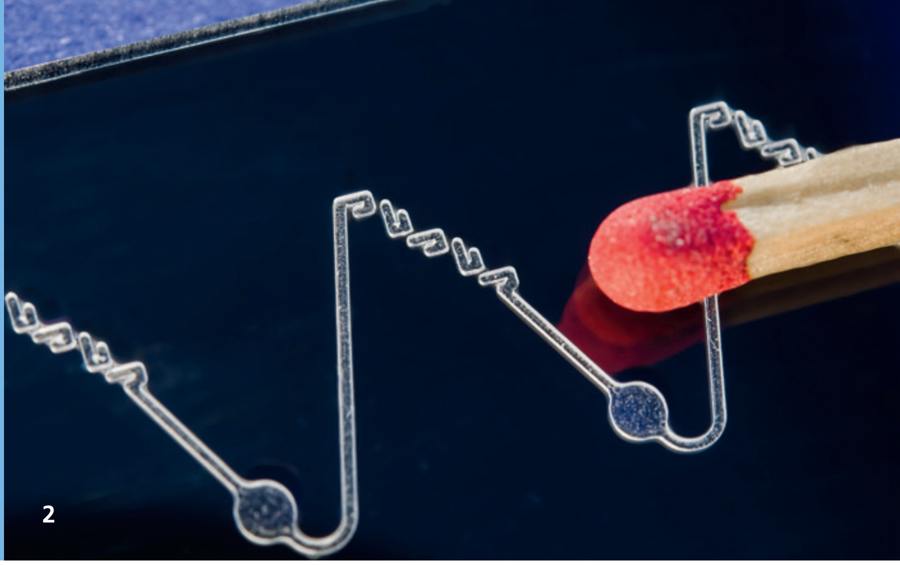
Introduction

Titration is a common method for concentration analysis in all industrial sectors. A reagent, called the titrant or titrator, of a known concentration (a standard solution) and volume is used to react with a solution of the sample, whose concentration is not known. Using a linear, volumetric method the titrant is added to the sample in sequential steps. From the equivalent point (i.e., inflection point) of the titration curve the concentration is calculated. Volumetric titration processes generally consist of six individual steps to be carried out: sample preparation, sampling, addition of titrant, mixing, metering, and evaluation. These steps determine the total analysis time and the reagent consumption for each quantitative analysis.
A multichannel Lab-on-a-Chip-System was developed, that allows for flow-through "continuous" titration. It is based on a simultaneous data acquisition working principle providing results continuously during operation. Basically, the volumetric scale (x-axis) of the "classic" titration curve undergoes a transformation into a length scale corresponding to the measuring points of the indicator electrodes or sensors distributed along the flow channel. Notably, the reagent as well as the sample consumption is considerably low with approx. 3 ml/h (or approx. 3 l/month) compared to 5 to 20 ml per titration required in the conventional method (or 7-30 l/month based on 50 titrations/day).

Flow concept and chip design of continuous µ-titrator

The core item of the LOC system consists of a polymeric microfluidic chip holding integrated miniaturised indicator electrodes or sensors, arranged in series equidistantly along a flow through channel which is filled



with a mixture of analyte and titrant. The respective titrant injection points are located in front of the titrating units consisting of mixer and sensor. The flow concept allows simultaneous addition of equal titrant aliquots to the sample flow and simultaneous recording of measuring points. The unit can be easily calibrated by two point method, e.g., using reference samples as reagents adjusted to two known pH values. Modern algorithms, like dynamic titration, are possible with different distances and numbers of reagent channels.

- Transfer of macro-scale analytical assay to chip format
- Prototyping of automated device for lab-on-a-chip operation

Results and applications

In a patent [1] a continuous titration is described, where the curve is continuously pending. The resulting titration curves resemble the classical ones, but show the true status of the sample (i.e., concentration) during operation thereby enabling online process monitoring. As can be seen in the graph shown below the titration curve moves according to the change in sample concentration. The equivalent point can be calculated from the inflection point of the curve. The response time for concentration change is dependent on the flow rate of sample.
It is typically in the range of approx. 20 s. The chip-based continuous µ-titrator can be used in on-line process control in chemical industry. As there is only a significant small amount of sample and reagent necessary, it is a perfect solution for micro processing units. In our days we know about the influence and importance of the pH, e.g., on the yield of chemical processes, on production of pharmaceutics or analysis in food industry. The concept is however not limited to pH titration of acids and bases. It is possible to use a silver sensor instead of the pH sensor to cover titration of halides like chloride or bromide. The chloride application is one of the most used titration methods, especially in chemical, food and beverage industry. The most general method is the redox titration. The iodometry as an example is used in the whole titration market in all industry fields. Other titration reactions are also possible. Only the indicatior electrodes or sensors must be adapted. ISE (Ion Sensitive Electrodes) would expand the field of applications.

Which sensors can be incorporated:

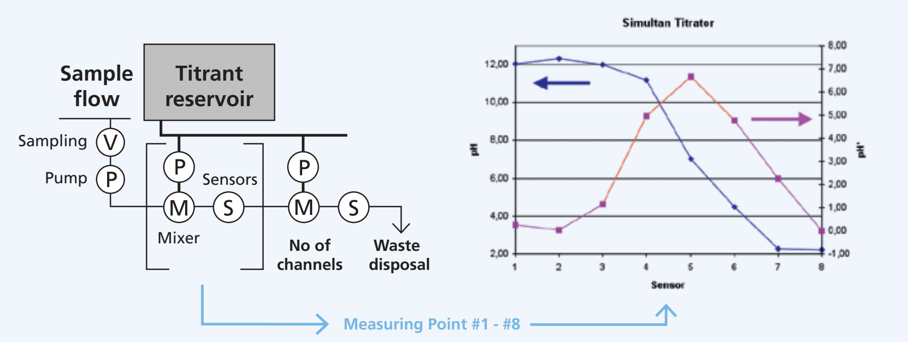
- pH sensors, glass electrodes
- Conductivity cells
- Redox electrodes (e.g., Pt)
- Metal electrodes (e.g., Ag, Cu)
- Double Pt electrodes biamperometric detection
- Ion sensitive electrodes
- Optical sensors
- Temperature sensors

References

[1] Vorrichtung zur kontinuierlichen Titration. Peters Dr. Jürgen; Tauber Dr. Günter, DE, 6672002, 19.04.2002

Project Partner
SI Analytics GmbH

µ-Titrator – working principle



2 *Microfluidic channel structure in polymer representing the flow concept*