294. An Alternative to Automatic Titration

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Summary

Automatic titrators are designed to do exactly what a lab-technician used to do. Much more sophisticated automation of volumetry is possible. Omegaphoresis [3] in buffer-free [2] sample solutions automatically creates a stationary multiple component titration curve or zoned pattern with normalized concentrations of each separated species. An automatic measurement of each zone length yields their quantity. Simultaneous automatic detection of all the zones in a 10–20 component solution in less than 2 minutes, with a precision of $\pm 2\%$, a required amount of the order of less than one nanomol and a resolution of $\Delta pK < 0.01$ replaces acid-base, complexometric, and certain types of redox-titrimetry. An option of the method allows identification of the components as well.

1. For more than 150 years chemists have used volumetric analysis, *i.e.* determined equivalent reaction volumes of a standard and an 'unknown' solution by detection of an abrupt change of a physical property near the equivalence point, *e.g.* colour, smell, extinction, electrode potential, conductivity, current, temperature, turbidity, etc. Since barely anything happens during most of a titration, people became bored with routine titration. Criteria for endpoint detection were mathematically analyzed and put to work in an automatic titrator. This is a device using an electromagnetic valve (instead of a stop-cock and fingers), a cylindrical volume with an electromechanically driven piston, and a probe which senses the 'endpoint' in advance in order not to overshoot it. Finally, the equivalent volume is printed out by a counter which records the number and fraction of turns of the piston screw. Then another part of the device, not unlike a washing machine, rinses the titration vessel, admits the next sample and starts the titrator. All in all: A perfect automation, step by step, of what a lab-technician used to do. Yet there is *McGovern*'s law [1]: 'For automation of a process never imitate its manual form you want to replace. Identify the variables and the parameters of the system and adapt them to a new synthesis with the elements of automation.'

2. In fact, the automated titration has not really advanced the analytical art. It is still difficult or impossible to titrate more than two to three components in a sample in one operation; handled volumes (a few ml) and samples (a few milligrams) are

large; endpoint detection is not better; selectivity has not improved; a titration lasts minutes, and the necessary operations to prepare a sample for titration are the same as in the old days, unless the expensive automated wet laboratory [1a] is used which contains procedures for a few routine titrations performed in large number every day.

3. We propose to do away with most types of automatic titrations for analytical purposes. They can be replaced with a physicochemical method published 1964 [2] and improved for automation in the last three years [3] [4], for which we have proposed the name of omegaphoresis [4]. A straightforward implementation of the automatic, multiple component microanalyzer is now in construction [5]. The idea is very simple. Suppose we have to analyze a water solution of 10 different acids with first pK-values below 5. The pH of the sample may be anywhere, the acids may be mono- or polyprotic, and their first pK-values pairwise between $\pm$ 0.01 units. The total amount of material is about one nanomol – the extract of one drop of a sweat mark which a criminal left as fingerprint. The quantity of each acid must be determined to $\pm$ 2% precision and within three minutes at most. The pattern of acid concentrations in the sweat has to be compared with police records in order to identify the fugitive. – This task will horrify any manufacturer of automatic titrators: it just cannot be done, and by a very large margin.

4. In our manual omegaphoretic device it has been done in three minutes [3] [4]. With our microprocessor-controlled automated system, we will be able to display simultaneously the quantity and identification of 10 to 20 components within less than 2 minutes. We simply use the fact that the electrical conductivity of a solution with a normalized concentration of each acid A_i of the sample depends on its pK-value(s). The normalization is automatically accomplished by using a buffer free system and moving boundary conditions with a fixed concentration c_L of the leading electrolyte, which plays the role of a standard solution in titration. *Kohlrausch*'s regulating function ω then guarantees a stationary state which is characterized by a precisely constant ratio of any component concentration c_i in the sample to c_L [2] [3]:

$$c_i = a_i \, c_L \tag{1}$$

where $a_i = u_i/u_L$, u: transport coefficient

The a_i's are qualitative criteria which can be measured and used for component identification. c_i is known from (1) and the quantity m_i of the component A_i is then given by the volume ($\propto$ zone length) which the separated acid A_i occupies between its two moving boundaries. The detection of the moving boundaries is similar to endpoint detection in titrimetry. Each boundary between a pair of acid i/acid j is marked by a sudden change in a number of physical properties: conductivity, electrical field-strength, refractive index, pH-value, temperature etc. This can easily be detected manually [3] [4] [6] or, preferably, with an automatic device.

5. One embodiment is the following (simplified): An array of a few hundred very fine gold-electrodes is evaporated through a mask onto the rectangular trough of the omegaphoretic device. Each electrode is connected through a highohmic network to an input port of a microprocessor's RAM. During a run, the microprocessor scans each pair of adjacent electrodes in turn for a preset voltage difference. If this is larger than the given threshold, which may be changed automatically by a software

algorithm in the microprocessor's ROM in order to get the best possible discrimination, a bit is set to mark that electrodes address as boundary location. The approach of the omegaphoretic pattern towards the stationary state is automatically stopped when the differences between the marked addresses have become constant (*i.e.* ± 1 channel address among ~ 500). The isotachophoretic state [2] is then reached and the analysis terminated. With the simple relation (1), a table of the a_i's, and the differences between the marked addresses, the quantity m_i of each resolved component A_i is determined. If the a_i's are not known, an option at system initialization automatically calibrates the device once and for all components and thus generates the table a_i in the RAM. These constants reflect pK_i, and transport coefficients u_i of each A_i for a given c_L, u_L standard. They are qualitative properties of a component and determine its location in the linear pattern of zones. The resolution (=selectivity) depends on the current density in the device, which defines the boundaries' thickness. Two acids with $\Delta pK = 0.005$ can be resolved. This is about a factor of 10^3 better than the endpoint discrimination in conventional titration. The omegaphoretic pattern of all the components develops in a time proportional to the current density. It can be as short as one minute and is limited only by the finite heat conductivity from the omegaphoretic trough to the cooling fluid.

Other embodiments use *e.g.* fiber optics and the jump of the refractive index at each boundary.

6. The method can be adapted to most types of titration and has been tested with the following classes of substances:

- protonic acids $-8 < pK_a < 5$ 14 components [2] [3] [4]
- protonic bases $-10 < pK_b < 5$ 10 components [3]
- ampholites: polypeptides, amino acids 8 components [4]
- metal ion complexometric titrations (*e.g.* EDTA, NTA, triphosphates): *e.g.* the whole series of rare earths or actinides (Ac to Fm) [5] [6]
- traces in water
- photographic processing solutions

7. The system can easily be expanded for automated sampling with sample changers. Because volumes are small, very simple devices are realizable. Sample preparation does not require the usual exacting conditions.

LITERATURE

[1] *J. E. McGovern*, pers. comm.; to be published in J. for Comm. Sens. in Measurement; see also E. Schumacher, Mittlg. Geb. Lebensm. Hyg. *67*, 21 (1976).

[1a] *R. W. Arndt & R. Werder*, Fresenius Z. analyt. Chem. *287*, 15 (1977).

[2] *E. Schumacher & T. Studer*, Helv. *47*, 957 (1964); *T. Studer*, Diss. Univ. Zürich 1965.

[3] *P. Ryser*, Diss. Univ. Bern 1976. – Omegaphoresis is a special version of moving boundary electrophoresis with constant zone-speed as invented in [2]. The solutions must be free of buffers which is not the case with the type of isotachophoresis described *e.g.* by *F. M. Everaerts, J. L. Beckers & Th. P. E. M. Verheggen*, Elsevier, 1976.

[4] *P. Ryser*, Mitt. Geb. Lebensm. Hyg. *67*, 56 (1976); *E. Schumacher & P. Ryser*, Chimia *30*, 105 (1976).

[5] Description and results will be submitted for publication in Analyt. Chemistry.

[6] *W. Thormann*, Diplomarbeit Univ. Bern 1977.