

Automated Peak Discrimination and Integration for Nonflame Atomic Absorption Analysis at Nanogram Levels

J. R. SARBECK and W. C. LANDGRAF*

Abstract □ A system for automated integration of nonflame atomic absorption signals is presented with improvements in the limits of detection reported for several typical elements. Theoretical considerations are developed to explain improvements in the signal-to-noise ratio as a function of high frequency noise rejection and filtering. Linearity of integration response curves is related to conventional peak height measurement.

Keyphrases □ Atomic absorption—automated integration of nonflame signals, improvements in detection limits □ Metal ions—automated integration of nonflame atomic absorption signals, improvements in detection limits for several metals

Recent studies in this laboratory indicated a good correlation between trace levels of transition metals and their influence on the degradation of chemical systems in use in the pharmaceutical industry. Frequently, one views these processes as being metal-ion catalysis of either an oxidative or a solvolytic nature, resulting in degradation of one or more compounds in that system. These conclusions resulted in a program of study for the determination of specific ions at low levels employing atomic absorption techniques. The principal objectives of this program were to simplify analytical procedures and to improve the limits of detection by atomic absorption techniques.

DISCUSSION

During the past several years, considerable effort has been expended for the improvement of higher levels of the ground-state species in atomic absorption analysis. Excellent use has been made of nonflame or graphite furnace techniques to increase significantly the population levels for ground-state atoms in atomic absorption analysis and to decrease extraneous species and other sources of noise. The use of nonflame methods for atomization has resulted in increases of two and sometimes three orders of magnitude (1-3). The improvement in radiation sources such as electrodeless discharge lamps has also resulted in better performance, especially when combined with nonflame furnace techniques (4-6).

A further improvement in overall signal-to-noise (S/N) ratios can be achieved by examining averaging techniques or perhaps by electronic data processing. A detailed discussion of possible methods including filtering, averaging, and linear transforms of signals was presented by Ernst (7). The distinction made by Ernst relates to the concept that filtering primarily affects the noise, leaving the signal undisturbed. Conversely, a transform of this signal does produce a significant change in the total signal, requiring further data processing. The accuracy of measurement of an integral for an absorption signal is limited by random noise, particularly its low frequency components (baseline stabilities). The integration process acts as a low bandpass filter and tends to eliminate high frequency components.

Noise is frequently considered to be a random function of time, $n(t)$, whose amplitude and duration are unknown. Past history of these noise components will not permit one to predict its future values; therefore, statistical methods are used to predict noise (or its components) in a signal. The probability distribution function, $P(t)$, specifies the likelihood that $n(t)$ will assume a value in the interval t_0 to $(t_0 + dt)$. A stationary random function is charac-

Table I—Detection Limits (Absolute Picograms)

Element	Reference 9	Reference 10	Reference 11	This Method
Ag	0.5	0.2	0.2	0.2
Cd	0.6	0.1	0.1	0.01
Cr	—	5.0	5.0	4.0
Cu	6.0	7.0	1.0	0.5
Hg	400.0	100.0	—	40.0
Ni	—	10.0	10.0	2.0
Pb	20.0	5.0	6.0	1.0

terized by a probability distribution function independent of time whose amplitude values are normally distributed; then $n(t)$ is equated to a Gaussian random function whose properties are described by average values. To secure the average, a sufficiently large number of samples in time is required. The time average of the quantity Q is $\equiv Q[n(t)]$; for a random function, $n(t)$ is defined by $(Q[n(t)])_{av} = \lim_{T \rightarrow \infty} (1/2T) \int_{-T}^T Qn(t) dt$. This ensemble average is obtained ideally from an infinite number of random functions, $n_1(t), n_2(t), \dots$ (having some common property). This ensemble average of the quantity Q at time t is defined by the average over the instantaneous values of $Q[n(t)]$ for different members, $N(t)$, of that ensemble and is expressed as follows:

$$\overline{Qn(t)} = \lim_{N \rightarrow \infty} (1/N) \sum_{i=1}^N Q[n_i(t)] \quad (\text{Eq. 1})$$

In many cases, it is permitted to replace the time average by the ensemble average or the converse. Such random functions for which time and the ensemble average can be equated are referred to as ergodic random functions. Since digital methods are considerably more accurate in the counting sense, the concept of ensemble average counting can be readily assigned to a minicomputer. Through a selection of the appropriate time windows, one can secure a good ensemble averaging of the noise and the signal. Furthermore, the selection and use of an appropriate algorithm permit discrimination against spurious signals either superimposed on the desired data or nonconcurrent with the signal.

EXPERIMENTAL

The atomic absorption analyses were performed on a spectrophotometer¹, employing standard hollow cathode lamps as wavelength sources. The atomization of the elements was performed by a carbon rod atomizer². The output of the photomultiplier detector was coupled directly into the interface of a unit³ where the A/D (analog-to-digital) conversion was completed. Since the carbon rod atomizer has three independent operating cycles, one can readily vary each independently for its optimum performance. The atomization cycle can be varied for 0-10 sec in either the pulse or ramp mode. In the present work the pulse mode of operation was used exclusively, with 2 sec being the typical operating cycle time for this parameter.

The operational sequence is as follows. Standard solutions of the metal of interest (Fisher certified atomic absorption standards) are diluted with water (previously shown to be essentially free of the metal). Dilution of the standard is such that the limiting, detectable amount is contained in 1-5 μ l of solution. A 1-5- μ l portion of this solution is transferred to the carbon rod using a microliter syringe equipped with an inert plastic tip. Thereafter, the automatic sequence is initiated.

¹ Perkin-Elmer model 305.

² Varian Techtron model 63.

Table II—S/N Improvement versus Wavelength

Element	Wavelength, nm	Relative Improvement
Cd	228.8	10
Ni	232.0	20
Hg	253.8	2.5
Pb	283.3	10
Cu	324.7	10
Ag	328.1	5
Cr	357.9	1.25

The resulting ground-state population is measured directly by the photomultiplier and integrated³. For descriptive purposes, the peak absorption due to the carbon rod atomizer can be envisaged to be triangular in shape (8) with a rapid exponential decay of this peak. Since this parameter is perhaps the most critical element in the operating sequence, it was optimized with considerable care (Fig. 1). Furthermore, the capability of precisely selecting the onset of this signal and terminating its integration was used judiciously. This ability to discriminate against spuriously generated noise and nonpertinent signals adds greatly to the increased S/N ratios of this combination. An additional feature of this unit is the ability to reject significant noise "spikes" in the signal while processing the data.

RESULTS

The limit of detection for this work is defined as the amount of analyte that produces an integrated signal area equal to twice the average area for the noise peaks occurring during the atomization step. In general, results reported are for the average of at least six S/N pairs.

For an indication of the limits for detection, a table of data was collected to show how the current method compares to previously reported data on a number of selected elements. As Table I illustrates, the lowest limit for detection is not uniformly improved by this technique; some special source of noise may be involved for these determinations. Table II gives an indication of the relative improvement in lowest detection levels permitted by this operational sequence.

Several points are clearly evident upon closer inspection of these data. With the exception of the mercury data, one sees a general inverse trend for relative improvement in S/N ratios as the wavelength for detection increases. This tail-off in sensitivity improvement may be a reflection of the increase in emission for the carbon rod at longer wavelengths. One may envisage the carbon rod as being equivalent to a blackbody where significant radiation increases beyond the 350-nm wavelength region. This type of radiation constitutes "background" or "scatter" radiation and may define a lower limit for detection of elements in the regions of longer wavelength (6)—e.g., calcium, sodium, and potassium—

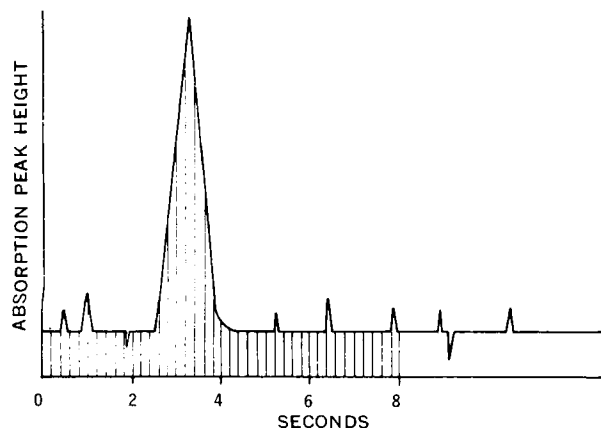


Figure 1—Typical absorption peak; example of data bunch rate. Selected peak width = 2 sec. Bunch rate = 5/sec.

³ Spectra-Physics Autolab IV.

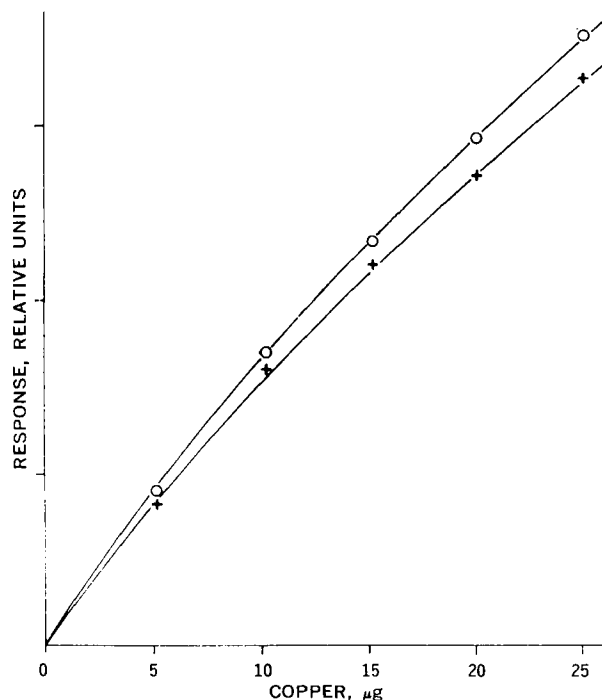


Figure 2—Analysis of copper samples by peak area method (O) and peak height method (+).

since neither integration nor peak noise rejection eliminates this condition.

Another point relates to the lower relative improvement in the current method for mercury detection. This problem may reflect the idea that with carbon rod atomization, the ground-state residence time of the mercury atom in the atomizer is relatively short and the current time window is not optimized. This parameter could be improved by choosing a lower atomization temperature by decreasing the inert gas flow (6) through an optimization of the integration time window or by selecting a faster A/D converter where the 100-msec limit is no longer a serious handicap for integration purposes.

The aspect of linearity for the analytical curves obtained by the integration method previously described was compared to data obtained by simple peak height measurements. A series of subnanogram level samples of copper was evaluated by a comparison of integration and peak amplitude information recorded simultaneously (Fig. 2). In terms of linear response, the slight difference between the two curves is attributed to scaling factors for assigning graphical values. This similarity of the data lends support to the concept that the peaks are approximated by triangles with short and constant bases (8).

The described system has been routinely applied to the determination of iron in propylene glycol. The application is straightforward and allows for increased sensitivity as well as decreased analysis time due to the automation of peak discrimination and data acquisition.

Further studies are designed to investigate peak shapes and the factors influencing them as a means of improving S/N ratios. A study of different elements using the current technique also will be undertaken in extreme regions of the atomic absorption spectrum.

REFERENCES

- (1) T. West and X. Williams, *Anal. Chim. Acta*, **45**, 27(1969).
- (2) S. Dipierro and G. Tessori, *Talanta*, **18**, 707(1971).
- (3) J. Alder and T. West, *Anal. Chim. Acta*, **51**, 365(1970).
- (4) J. Winefordner, *Spectrosc. Lett.*, **5**, 311(1972).
- (5) B. Patel, R. Browner, and J. Winefordner, *Anal. Chem.*, **44**, 2272(1973).
- (6) R. Reeves, B. Patel, C. Molnor, and J. Winefordner, *ibid.*, **45**, 346(1973).
- (7) R. Ernst, in "Advances in Magnetic Resonances," vol. 2, J. S. Waugh, Ed., Academic, New York, N.Y., 1966, pp. 1-121.

(8) K. Aldous, D. Mitchell, and F. Ryan, *Anal. Chem.*, **45**, 1990(1973).

(9) J. D. Winefordner and R. C. Elser, *ibid.*, **43**(4), 24A(1971).

(10) "Carbon Rod Atomizer," Varian Techtron Corp., Palo Alto, Calif., Dec. 1970, p. 4.

(11) "High Sensitivity Sampling Systems for Atomic Absorption," RG 67210, Perkin-Elmer Corp., Norwalk, Conn., 1972, p. 3.

ACKNOWLEDGMENTS AND ADDRESSES

Received November 12, 1973, from the Applications Research Department, Quality Control Division, Syntex Laboratories, Inc., Palo Alto, CA 94304

Accepted for publication February 12, 1974.

* To whom inquiries should be directed.

Factors Affecting Water Vapor Transmission through Polymer Films Applied to Solid Surfaces

ANTON H. AMANN*, RICHARD E. LINDSTROM, and JAMES SWARBRICK*

Abstract □ The permeation of water vapor through cellulose acetate phthalate polymer films applied in a variety of ways to hygroscopic solid surfaces was determined at several different temperatures. The systems investigated consisted of films: (a) placed against a flat solid surface, (b) sprayed onto a flat solid surface, and (c) sprayed onto tablets in a rotating coating pan. The data indicate that the activation energy of the absorption process is determined by the film, while the method of film application affects the actual rates of permeation at a given temperature. The physical properties of the material being coated also affect the water vapor absorption rate.

Keyphrases □ Films, cellulose acetate phthalate polymer—water vapor permeation on hygroscopic solid surfaces, comparison of application methods and temperatures □ Permeation, water vapor—polymer films applied to solid surfaces, effects of temperature and application method □ Absorption, water vapor—solid dosage forms, effects of film application method and film material

A previous paper (1) presented the relative characteristics of water vapor permeation through free-standing hydrophilic and lipophilic polymer films used to coat pharmaceutical solid dosage forms. It was shown that the permeation coefficients for the lipophilic films were unaltered by the presence of water vapor on the distal surface of the film. In contrast, water vapor permeation through the hydrophilic films was dependent on whether the vapor pressure gradient resulted from water vapor on one or both sides of the film. This behavior was rationalized on the basis of plasticization of the film by the permeating water vapor. With water vapor present on only one side of the film, dehydration was postulated to occur. This would reduce permeation, an effect noted in earlier work (2).

The present report extends previous work to include the water vapor permeation through hydrophilic cellulose acetate phthalate films when applied to the surface of solid systems having a potential to absorb moisture. In this manner, it was hoped to evaluate the relationship between free-standing films and those applied to solid dosage forms in terms of their water vapor permeability properties. Several

Table I—Water Vapor Permeation through Various Applied Films of Cellulose Acetate Phthalate^a

System	Temperature	Permeability Coefficient P^0 , $\text{g hr}^{-1} \text{cm}^{-1} \text{mm Hg}^{-1} \times 10^{-7}$
Cast film placed onto disk	20°	4.12 ± 0.71 ^b
	30°	3.54 ± 0.83
	40°	2.37 ± 0.22
Sprayed film on disk	20°	2.64 ± 0.11
	30°	1.99 ± 0.18
	40°	1.52 ± 0.13
Film-coated tablet	20°	0.31 ± 0.06
	30°	0.18 ± 0.07
	40°	0.09 ± 0.02

^a Vapor pressure of 16.5 mm Hg. ^b A 95% confidence interval.

model systems were thus established to create a series of conditions intermediate between permeation through a free film and one applied to a tablet. Accordingly, moisture permeation was studied in systems in which: (a) a film of cellulose acetate phthalate was simply placed in contact with a flat disk containing calcium chloride; (b) the same polymer, in solution, was sprayed onto one surface of a flat disk containing calcium chloride; and (c) the polymer solution was used to spray coat the entire surface of conventionally shaped convex tablets containing calcium chloride.

EXPERIMENTAL

Preparation of Disks and Tablets Containing Calcium Chloride—The powder mixture used for compression contained calcium chloride USP (33%) in microcrystalline cellulose¹. Magnesium stearate (1%) was present as a lubricant. The compressed disks were prepared using flat-faced punches and die, 1.60 cm in diameter, and a press² set at 1816 kg (4000 lb). Under these conditions, the formation pressure was approximately 13,000 psi. The average weight of the disks was 1.586 ± 0.001 g.

Tablets were prepared from the same powder mixture using a single-punch tablet press³ fitted with deep concave punches, 0.96

¹ Avicel, F.M.C. Corp.

² Carver.

³ Stokes model E.