Optimization of the dwell-time for the quantitative analysis by gas chromatography–mass spectrometry

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Abstract

In this paper, the signal path in a mass spectrometer used as a detector for gas chromatography in the selected ion monitoring mode is analyzed. The process involved an accumulation step that can be considered as a digital filter. Thus the Nyquist criterion alone is to be taken into account for the acquisition, by contrast to what appends with other detectors which require a higher number of acquired points to minimize the error during peak integration. This theoretical assumption was tested and accepted for three different levels of signal-to-noise ratio.

1. Introduction

Signal acquisition of chromatographic profiles has been extensively discussed for the past 20 years, especially when personal computers became part of the common equipment of the laboratories. Computer acquisition implies two types of operation: time sampling of the signal, and digitization of the signal. Both have been extensively discussed on the basis of experimental results or theoretical background [1–7]. The digitization process cannot be perfect, but is regarded as satisfactory if the step of digitization is close to the standard deviation of the noise, or smaller. On the other hand, the Nyquist theorem states that sampling does not involves any loss of information as long as the sampling frequency is at least twice as high as the highest frequency in the signal. From this statement, one can derive that six

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points or more are required for the unbiased sampling of a perfect Gaussian chromatographic peak. In the real case, the signal is noisy. A non-adequate sampling of the noise might have two consequences: first, a bad estimation of the noise which may be an overestimation, secondly, difficulties in the detection of the start and the end of the chromatographic peaks especially since real peaks may tail or front. For these reasons, most authors recommend that at least 20 points [1–3] or even more [4–7] should be sampled to calculate a peak area if the signal is not corrupted by the acquisition process. It is possible to achieve this with the classical flame ionization detector. This detector never switches between several signals as a mass spectrometer does between m/z values, so that analog filtering applied to its signal. In this case, further low-pass filtering by smoothing over the sampling interval does not always improve the signal-to-noise (S/N) ratio, and this ratio may appear to be independent of the sampling period,

even if it is short. On the contrary, in the case of the mass spectrometry, which has become a widespread detector since the introduction of commercial bench-top GC–MS instruments, the acquisition period and the S/N ratio are strongly related.

2. Theory

2.1. GC–MS data handling in the selected ion monitoring (SIM) mode

In this mode, the signal $s(t)$ coming from the detector is amplified and filtered by a pure analog device. It is then acquired and digitized at a high frequency $v_a = 1/t_a$ to give $s_a(t)$. $s_a(t)$ is accumulated in a buffer for a so-called 'dwell time' t_d. The buffer content is in its turn sampled with a sampling period $t_s = t_d + t_t$. t_t is the time used to transfer the signal from the buffer to the data storage plus, if more than a single ion is monitored, the time to acquire the signal of the other ions. The mathematical model for an accumulation is a convolution by a boxcar function $b_{t_d}(t)$ with a width t_d and the model for the sampling is a multiplication by a 'Dirac comb' $\Pi_{t_s}(t)$ with a period t_s. Finally, the SIM signal $sim(t)$ can be described as:

$$sim(t) = [s_s(t) \otimes b_{t_d}(t)]\Pi_{t_s} \tag{1}$$

where $\otimes$ denotes the convolution product. The effect of this process will be easier to discuss in the frequency domain, using the same type of approach as Guiochon [1]. The Fourier transform of $sim(t)$ is calculated on the basis of the convolution theorem (lower case are used for the time domain functions and upper case for their Fourier transforms, that is in the frequency domain):

$$SIM(v) = [s_s(v)B_{t_d}(v)] \otimes \frac{1}{t_s} \Pi_{1/t_s}(v) \tag{2}$$

The Fourier transform of the boxcar accumulation function is a 'sinc' function:

$$B(v) = \frac{\sin(\pi v t_d)}{\pi v t_d} \tag{3}$$

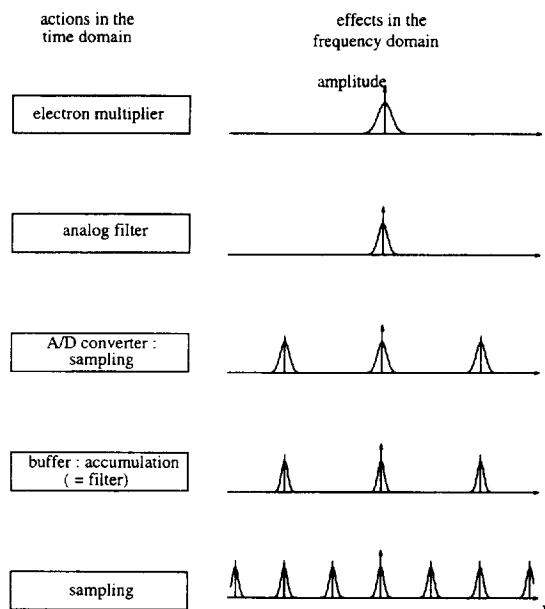$B(v)$ decreases at high frequency and, as expected, accumulation has the effect of a low-pass filter.

Fig. 1. Signal path in a GC–MS system.

Finally, changes in the signal can be summarized as shown of Fig. 1.

2.2. Error evaluation

When the noise is non auto-correlated, that is when the noise at any given time is independent of the noise at any other time, the error in a measurement is inversely proportional to the square root of the number of accumulated data: this is the reason why high sampling frequency has been recommended for the acquisition of chromatographic signals. In fact, the error e in surface evaluation of a chromatographic peak is only a function of the S/N ratio of the signal and of the square root of its number of points k:

$$e = \frac{\lambda}{S/N\sqrt{k}} \tag{4}$$

λ being a constant.

We could verify this relationship by simulating a chromatographic peak with various levels of noise and by integrating it. Here, the level of the S/N ratio is independent of the number of sampling points, as at the output of the electrometer of a flame ionization

detector. It should be noted that below six points per peak, that is if $1/\sqrt{k} > 0.4$, the error does not follow Eq. (4) and increases much faster, as can be seen from the slopes of the curves in Fig. 2. In fact, the Nyquist criterion is then no longer obeyed above 0.4 so that an error coming from the poor acquisition of the peak is added to the error due to the noise; as can be seen in Fig. 2, this error exists even when the S/N ratio is infinite.

In GC–MS the S/N ratio and the number of points acquired are not independent. On the one hand, a long accumulation step acts as a low-pass filter and improves the S/N ratio; on the other hand, as the final sampling period is longer than the accumulation time, long accumulation means few acquired points. It therefore is necessary to investigate the relation between t_d, the S/N ratio and k.

If $n(t)$ denotes the noise as a time function then the total power P_n of the noise is given by Eq. (5):

$$P_n = \int_{-\infty}^{+\infty} |n(t)|^2 dt \qquad (5)$$

P_n may seem to be infinite, but is not because if the noise is white, that is if $n(t)$ is uncorrelated with $n(t + \delta t)$, whatever is δt, then P_n is equivalent to the integral of an impulse function and is finite [8]. If it is not white, then it has a finite spectrum and Fourier analysis shows that it is limited in time: P_n is finite again. Thus, P_n can be written: $P_n = A_n^2$.

In fact in a mass spectrometer, the noise of the electron multiplier is white with respect to the time

Fig. 2. Error on the estimation of the surface of a peak (average value for 400 simulations).

scale of chromatography [9]. For instance, in the spectrometer we used (see experimental section), its maximum frequency is set by the analog filter at about 5 kHz, while the highest frequency of a chromatogram is around 1 Hz. We can suppose that the analog filter is a Butterworth filter of order one and relaxation time a, a basic low-pass filter with an impulse response $(1/a) \exp(-t/a)$. This hypothesis is only necessary to achieve a full calculation, but this does not change the meaning of the results. Then we have:

$$P_n = A_n^2 \int_{-\infty}^{+\infty} dt \left[\frac{1}{a} \exp\left(\frac{-t}{a}\right) \otimes b_{t_d}(t) \right]^2 \qquad (6)$$

$\exp(-t/a)$ is replaced by 0 for negative times because the filter is analog and therefore causal. Thus the convolution product can be calculated:

$$\begin{cases} \frac{1}{a}\exp\left(\frac{-t}{a}\right)\otimes b_{t_d}(t) = 0; & \text{if } t \le \frac{-t_d}{2} \\ \frac{1}{a}\exp\left(\frac{-t}{a}\right)\otimes b_{t_d}(t) = \left(\frac{-t}{a}\right)\left[\exp\left(\frac{t_d}{2a}\right) - \exp\left(\frac{t}{a}\right)\right]; & \text{if } \frac{-t_d}{2} < t < \frac{t_d}{2} \\ \frac{1}{a}\exp\left(\frac{-t}{a}\right)\otimes b_{t_d}(t) = \left(\frac{-t}{a}\right)\left[\exp\left(\frac{t_d}{a}\right) - \exp\left(\frac{t}{2a}\right)\right]; & \text{if } t \ge \frac{t_d}{2} \end{cases} \qquad (7)$$

$$P_n = A_n^2 \frac{t_d - a + a \exp(t_d/a)}{t_d^2} \qquad (8)$$

The S/N ratio is inversely proportional with respect to the square root of the power of the noise.

k, in turn, depends only on the width W of the peak and of the sampling period $t_s = t_d + t_t$

$$k = \frac{W}{t_d + t_t} \qquad (9)$$

Finally, using Eq. (8) for the noise and Eq. (9) for k, the error as expressed in Eq. (4) should take the following form:

$$e = \frac{\lambda' \sqrt{t_d - a + a \exp(t_d/a)}}{t_d} \frac{\sqrt{t_d + t_t}}{W} \qquad (10)$$

λ' being a constant.

3. Experimental

The mass spectrometer used was a Hewlett-Packard 5971 mass-selective detector (Hewlett-Packard, Palo Alto, CA, USA) interfaced to an HP 5890
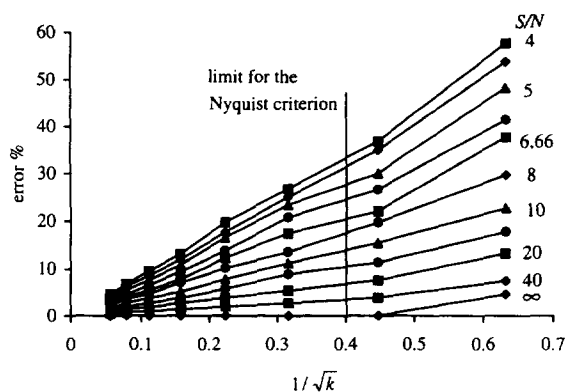
Table 1
Experimental mixture

Alkane	Concentration (mmol l^{-1})	Amount injected (approx.) (ng)	S/N (approx)
Dodecane	1.7	3	1200
Tridecane	0.17	0.32	120
Tetradecane	0.05376	0.11	38
Pentadecane	0.017	0.037	12

Series II gas chromatograph (Hewlett-Packard, Avondale, PA, USA). The mass-selective detector parameters were set to the values determined by the automatic tune procedure included in the Chem-Station, which is the software provided by Hewlett Packard. The column (25 m×0.1 mm, coated with 0.125 µm 100% methyl cross-linked silicone gum, SGE, Ringwood, Australia) was directly plugged into the ion source of the mass spectrometer. The flow-rate of the carrier gas (hydrogen) was set at 50 cm/s and the chromatograph temperature set at 140°C. A solution of *n*-alkanes described in Table 1 was injected and the signal recorded at $m/z = 57.1$ uma. The volume injected was approximately 1 µl and the split ratio set to 1/100.

The peak of dodecane had a very high S/N ratio because of the large amount injected. Dodecane was chosen as an internal standard and always recorded in the same conditions: $t_d = 100$ ms and about 30 points per peak. The signal for the other alkanes was recorded with variable dwell time in order to study the effect of this parameter. 15 repetitions of each chromatogram were performed. The chosen dwell times were: 25, 50, 100, 200, 400 and 800 ms. The S/N ratio was estimated as the peak height divided by the standard deviation of the background noise when it is not filtered, that is when the dwell time is set to its minimum value: 10 ms. Finally the quality of surface estimation was determined by calculating the variance of the response given by internal standardization.

4. Results and discussion

For small values of a as the one found in the HP5971 mass-selective-detector, i.e. 0.1 µs, the power of the noise depends only upon the dwell time. Eq. (10) may then be simplified to give:
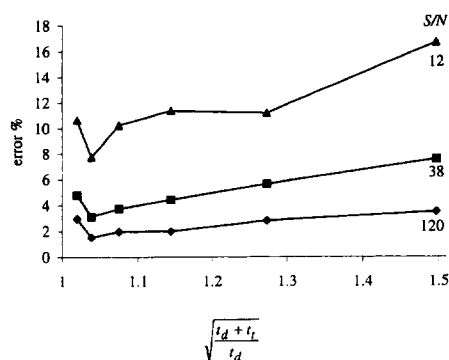

Fig. 3. Measured error on the evaluation of the surface of a chromatographic peak for three different signal-to-noise ratios and six different dwell times.

$$e = \frac{\lambda'}{W} \sqrt{\frac{t_d + t_t}{t_d}} \qquad (11)$$

Experimental results show a good agreement with the model. Fig. 3 shows the coefficient of variation for tridecane, tetradecane and pentadecane analyzed 15 times as explained in the experimental section. The precision is better for high values of t_d as long as six points at least are sampled in the peak. Eq. (11) tends to show that the longer t_d, the smaller the error. This comes from t_t which is the time during which the information is not recorded, i.e. which is 'lost time'. For the HP5971, $t_t = 31$ ms. However, it is important that $t_s = t_d + t_t$ remains short enough so that the acquisition follows the Nyquist criterion of six points per peak, as shown by the change in the slopes of the curves of Fig. 2.

It then possible to state a more precise recommendation than the one found in the operating manual of the GC–MS system [10]: the dwell time must be maximum as long as six points per peak are acquired.

5. Conclusion

Especially in the case of a poor S/N ratio, the error in the determination of the area of a chromatographic peak acquired in the SIM mode of GC–MS can be minimized by increasing the dwell-time. A long dwell-time is better than a great number of points, because the accumulation is an efficient filter.

Thus, following the thought processes of chemometrics by analyzing the information and the noise content of the data in order to adapt signal processing, we demonstrated that the mass spectrometer requires a very slow acquisition speed by contrast to the classical GC detectors that were studied when microcomputers first appeared in laboratories. However, six points per peak must be acquired in any case to remain within the basic theorem of Nyquist applied to chromatogaphic profiles.

References

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