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The design of Flow Injection manifolds to give the best detection limits for methods involving on-line chemical derivatisation

Part 1. Theoretical basis for high sensitivity

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The criteria to be considered when designing a flow-injection manifold for the highest sensitivity for a method based on measurement of the peak height corresponding to a derivative formed on-line between the injectate and a reagent. These criteria include the ratio of reagent concentration to determinand concentration at the peak maximum, the concentration of the top standard and the reagent composition. These three parameters can be combined to give a single parameter referred to as the α-value being the ratio of the determinand to reagent dispersion coefficients at the peak maximum for the top standard. It is shown, on the basis of the single, well-stirred tank model that the required dispersion coefficient is (1 + α) for both a single-line and a double-line manifold. It is further shown that the throughput for the former manifold would be higher than that of the latter.

Keywords: *Flow injection analysis, manifold design, dispersion coefficient, sensitivity, throughput, well-stirred tank model.*

In any analytical procedure there are two factors which significantly affect the detection limit. These are the magnitude of the analytical signal and the magnitude of the noise. The procedure to be adopted to obtain the best limit of detection is therefore, to maximise the signal and minimise the noise. In the case of flow injection analysis (FIA), the magnitude of the signal depends on the dispersion in the system, this is in turn dependent on the choice of manifold design and operating conditions.

Many flow injection methods are based on monitoring the extent to which an on-line chemical derivatisation reaction has proceeded as the dispersed injectate zone passes the downstream flow-through detector. Of such methods, the use of the measurement of a reaction product peak maximum by molecular absorptiometry in solution is the most widely reported.

For measurements based on peak height, it is important to ensure that mixing to produce a sufficient concentration excess of reagent over determinand across the entire sample profile to give the desired degree of reaction at the peak maximum occurs.

Thus the requirement is to design a manifold which allows such mixing without introducing an undue amount of dispersion or dilution. This paper describes a method of comparing flow-injection (FI) manifold types on the basis of achieving maximum sensitivity. A simple model for dispersion is used based on the well-stirred mixing chamber concept. A theoretical treatment of the various sources of noise is not possible and this aspect of the design requirements for low detection limits will be discussed in a subsequent paper [1].

Manifold Design

Two types of FI manifold (see Fig. 1) may be distinguished based on the mechanisms by which reagent and determinand are mixed. In the first type, mixing occurs primarily as a result of the inter-dispersion of injectate and carrier stream. This inter-dispersion is due to the various hydrodynamic regimes produced in the particular manifold. In the case of open tubular reactors (OTRs), the predominant hydrodynamic process is convection and this is accompanied by diffusion across the radial concentration gradients so generated to an extent governed by the magnitude of the gradient, the diffusion coefficient of the species concerned and the residence time. Provided that the diffusion coefficients of species in the carrier stream and in the injectate solution are similar, the concentration gradients of reagent and determinand due to physical dispersion processes may be considered to be «mirror» images of each other. Obviously, the concentration gradients are greatly affected by chemical reaction.

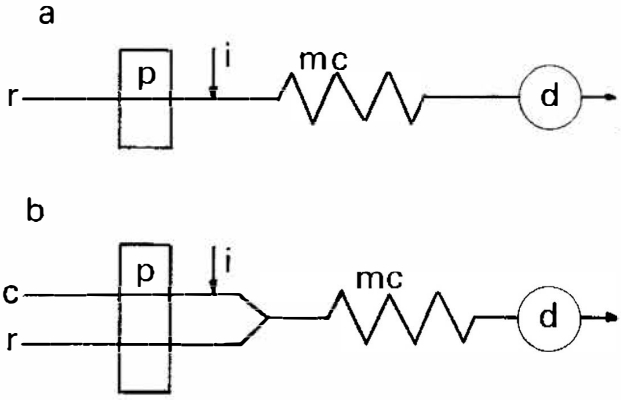

Figure 1. Conventional representation of the two basic types of flow injection manifolds, (a) single-line manifold and (b) double-line manifold; c determinand carrier stream, d detector, i injection point, mc manifold components, p pump and r reagent stream.

Manifolds of this type are those in which a single line connects the injection valve to the detector. Prior to the injection valve there may be, of course, a number of merging streams in which, for example, an unstable reagent may be synthesised.

In the second type of manifold, in addition to convection and diffusion, the extent of mixing is governed by the relative flow rates of streams merging at confluence points. The simplest form of this manifold is the two-line manifold in which the sample is injected into a non-reactive carrier stream which is subsequently merged with the reagent stream. In general, such manifolds may have several confluence points and are referred to as multi-line manifolds. In practice both types of manifold may contain additional components, which will produce a variety of hydrodynamic regimes, such as packed bed reactors (PBRs), contorted OTRs, mixing chambers, right-angle bends, step changes in diameter etc.

Previous discussion [2-4] of the relative merits of the single-line manifold and the double (or multi-line) manifold have indicated that the latter type allows a high sensitivity version of the former because to increase the sensitivity the most obvious approach is to increase the volume injected. However with a single-line manifold, increasing the volume injected eventually leads to the formation of double peaks. Provided that the flow rate ratio of the injectate carrier stream and the reagent carrier stream was not too large, conventional peak shapes would be obtained with a multi-line manifold. There is, of course, no inherent reason why flat-topped peaks (the multi-line manifold equivalent of the double peak) should not be obtained with this manifold. Their appearance depends on the concentration ratio of determinand and reagent and the relative flow rates.

Basis for Comparison

As the intention is to examine the relative sensitivities produced by the two types of manifold, a simple model for dispersion may be used and applied to each manifold. The model used is based on the passage of step concentration changes through a single well-stirred tank [5]. This model has been applied to the dispersion produced in single-line manifolds for solution spectrophotometry and atomic absorption spectrometry and the relevant equations for the relationship between peak height [6,7], peak width [7,8] and peak area [9] have been derived. The peak width relationship has also been derived for a merging-stream manifold in which the injectate passes through mixing chamber before merging with the reagent at the confluence point [7]. The model manifolds are shown in Fig. 2, from which it can be seen that the merging stream manifold is modelled by mixing at the confluence point before passage through the tank.

A key concept in comparison is the the ratio of the reagent to determinand concentration at the peak maximum, $R_p^{r/d}$. Many spectrophotometric

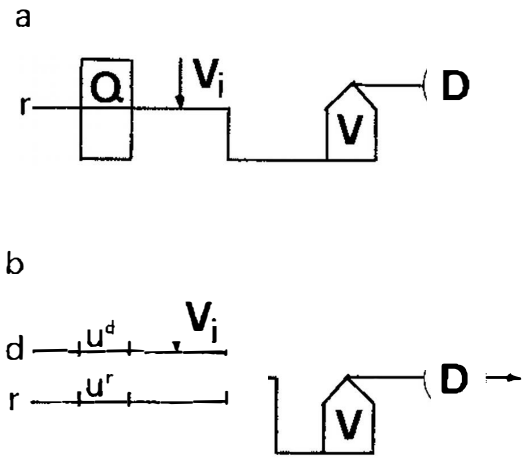

Figure 2. Model manifolds, (a) single-line manifold, (b) double-line manifold. Plug flow is assumed between the point of injection and the single-well stirred mixing chamber and between the mixing chamber and the detector. The volume injected is V_i, the volumetric flow rate is Q, the tank volume is V, D is the detector, r is the reagent stream and d is the determinand carrier stream (flow rate u^d). The flow rate of the reagent stream in the double-line manifold is u^r.

methods are based on the use of reaction conditions in which a large excess of reagent is used, so that even if the equilibrium constant for the reaction of interest is not very large the concentration of the product formed is directly proportional to the concentration of the determinand. This ratio has a minimum value at the peak maximum for any flow injection manifold in which the determinand is injected. Thus it is necessary as part of the method design to specify a value for this ratio appropriate for the top standard in the calibration sequence.

Single-Line Manifold

The dispersion coefficient at the peak maximum is given by

$$D = [1 - \exp(-V_i/V)]^{-1} \quad (1)$$

where V_i is the injected volume and V is the volume of the hypothetical well-stirred tank. The ratio of the concentration of the reagent stream to that at the peak maximum may be referred to as the reagent dispersion coefficient, D^r. For a single-line manifold the determinand and reagent dispersion coefficients are related by the equation[7]

$$D = D^r / (D^r - 1)$$

The ratio of reagent to determinand at the peak maximum is thus given by

$$R_p^{r/d} = R_m^{r/d} (D - 1) \quad (2)$$

where $R_m^{r/d}$ is the ratio of pumped reagent concentration to injected determinand concentration [7].

Merging-Stream Manifold

To derive the equation for the concentration at the peak maximum and hence the dispersion coefficient, it is necessary to derive the equation for the concentration rise as the diluted injected plug flows into the mixing chamber and to substitute into this the expression for the time taken for the rear of the diluted injection volume to enter the tank. If the flow rate of the injectate carrier stream and the reagent stream are u^d and u^r, them the determinand concentration injected, C_m^d, is diluted to $C_m^d Cu^d/(u^d + u^r)$] ie $C_m^d f^d$ where f^d is the fraction of the total flow, Q, due to the determinand stream. The change in concentration with time for the well-stirred tank is given by

$$dC/dt = C_m^d f^d Q/V - CQ/V$$

Separating the variables and integrating gives

$$\ln(C_m^d f^d - C) = -Qt/V + k$$

where k is a constant of integration which is evaluated by substituting the boundary conditions $C = 0$, $t = 0$. This gives $k = \ln C_m^d f^d$. Therefore

$$t = (V/Q)\ln[C_m^d f^d/(C_m^d f^d - C)] \quad (3)$$

This can be rearranged to give

$$C = C_m^d f^d[1 - \exp(-Qt/V)] \quad (4)$$

The trailing edge of the diluted sample plug enters the tank at time t_p given by $t_p = V_i/u^d$ when the concentration in the tank is C_p^d. Substituting in equation 4 gives

$$C_p^d = C_m^d f^d[1 - \exp(-V_i/Vf^d)] \quad (5)$$

and thus

$$D = [f^d[1 - \exp(-V_i/Vf^d)]]^{-1} \quad (6)$$

The reagent concentration remains at a constant value after the step change at the confluence point at $C_m^r f^r$. Where f^r is the fraction of the total flow due to the reagent stream. Thus the ratio of the reagent concentration to the the determinand concentration at the peak maximum is given by

$$R_p^{r/d} = R_m^{r/d} D f^r \quad (7)$$

The relationship between concentration and time for the fall curve is obtained in exactly the same fashion as was done for the single-line manifold [7] and is given by:

$$C = C_p^d \exp[-Q(t - t_p)/V] \quad (8)$$

Design for Highest Sensitivity

The requirement is to obtain the smallest value of D for a given value of the reagent to determinand concentration ratio at the peak maximum, $R_p^{r/d}$. This value will be a minimum for a given reagent composition when the most concentrated standard in the calibration sequence is considered. Thus the reagent composition and top standard fix the value of $R_m^{r/d}$. The ratio, α, of these values is, therefore, also fixed and is given by

$$\alpha = R_p^{r/d}/R_m^{r/d} \quad (9)$$
$$= D/D^r$$

For the single-line manifold, the α-value fixes the D value. From equation 2,

$$\alpha = D - 1$$

and

$$D = \alpha + 1$$

However, for the double-line manifold, the situation is not so immediately obvious as the corresponding relationship for the single-line manifold is. From equation 7,

$$\alpha = Df^r$$

ie

$$\alpha = D(1 - f^d) \quad (10)$$

As can be seen from equation 6 the D-value for a double line manifold is a function of the fractional flow-rate (as well as the volume injected and the volume of the tank). Substitution in equation 6 gives

$$(1 - f^d)/\alpha = f^d - f^d\exp(V_i/f^dV)$$
$$\ln(1 + 1/\alpha - 1/f^d\alpha) = -V_i/f^dV$$

For this equation to be solved for realistic values of the variables concerned, the logarithmic term on the left hand side must be negative, ie

$$0 < (1 + 1/\alpha - 1/f^d\alpha) < 1$$
$$1/(\alpha + 1) < f^d < 1$$

From equation 10, it can be seen that the smallest value of D is obtained when the smallest allowable value of f^d is selected. From the inequality above, this value is $1/(\alpha + 1)$ and thus the D-value for the double-line manifold is given by

$$D = \alpha + 1$$

This value is the same as for the single-line manifold and thus regardless of which manifold type is selected, the same sensitivity will be obtained for the same chemistry.

For a given manifold (ie value of V), the experimental variable in this model is the volume injected. For the single-line manifold the required volume is given by,

$$V_i = V\ln[(\alpha + 1)/\alpha]$$

Whereas for the double-line manifold, the required volume is given by

$$V_i = V\ln(\text{infinity})$$

Thus the required volume is infinite. To minimise the value of D with this type of manifold the approach should be to inject a sufficiently large volume so that there are essentially no dispersion effects due to passage through the thank and all the dispersion is due to dilution at the confluence point. Under these operating conditions, D is equal to $1/f^d$. As f^d is given by $1/(\alpha + 1)$, the relative flow rates are governed by the α-value required. In practice it is possible to calculate a value for the volume injected which will give any desired fraction of the D-value corresponding to infinite volume. For example the volume injected giving 0.99 of the infinite-volume value is $4.605V/(1 + \alpha)$.

This result (that the single-line and double-line manifolds give the same maximum sensitivity) is perhaps not so surprising when the factors controlling the dispersion coefficient of a double-line manifold are considered. Regardless of the volume injected, the dispersion coefficient can never be smaller than the value set by the flow rate ratio and thus the approach to minimising the D-value must be based on the injection of an infinite volume.

The manifold designs may be further compared on the basis of through-put. It is possible calculate a parameter related to the through-put for each manifold. One of the simplest of such peak width values is the half-width, $t_{½}$.

For the single-line manifold.

$$t_{½} = (V/Q)\ln[\exp(V_i/V) + 1]$$

and thus when $V_i = V\ln[(\alpha + 1)/\alpha]$, $t_{½} = (V/Q)\ln[(2\alpha + 1)/\alpha]$.

For the double-line manifold, the half-width is given by

$$t_{½} = V/Q\ln[\exp(V_i/Vf^d) + 1]$$

Thus if the volume injected is that required to give 0.99 of the infinite volume D-value and f^d is equal to $1/(\alpha + 1)$, $t_{1/2} = 4.605V/Q$ (assuming 1 may be neglected compared with exp 4.605).

It is only in cases where α is very small (of the order of 0.01) that the peak widths would be comparable. Under other, more usual, circumstances the single-line manifold would give a higher through-put for the same α-value.

Conclusion

In the design of a manifold for a flow injection method of analysis in which the peak height, corresponding to the product formed on-line by the interdispersion of injectate and reagent, is monitored as the analytical parameter the same maximum sensitivity may be obtained from either a single-line manifold or a double-line manifold. For the double-line manifold a sufficiently large volume must be injected to obtain essentially infinite volume conditions and the desired dispersion coefficient is obtained by a suitable selection of flow rate ratio. This means, in general, that the single-line manifold will have a higher through-put than the double-line manifold giving the same dispersion coefficient.

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