AN AUTOMATED INTERFEROMETER FOR THE ANALYSIS OF ANAESTHETIC GAS MIXTURES


As part of the design and development of a new microprocessor-controlled anaesthetic machine [1-3] it was necessary to design apparatus for the analysis of mixtures of anaesthetic gases and vapours (in the fresh gas system) such as oxygen, nitrous oxide, carbon dioxide, air, halothane, enflurane, isoflurane and possibly trichloroethylene. Analyses of ether and cyclopropane were excluded because of the problems of designing an apparatus which would cope with their flammability.

The overall philosophy of the new anaesthetic machine was that each control should be "calibrated" so that a "set" value could be selected, and which would in turn program the microprocessor. The net result is that a "set" value and a "measured" value are displayed, leaving the anaesthetist to compare their values visually and so satisfy himself that the machine is functioning correctly. An alarm system gives a warning of any large excursion of "measured" from "set" values, by flashing the "measured" display and displaying a message on the central control monitor panel. The gas/vapour analyser would thus form a critical part of the anaesthetic machine, and would ensure the safety of the delivered gases. To ensure this safety, we decided that the analyser must satisfy the following criteria:

**Reliability.** There should be a low probability of failure (preferably less than 0.001), that is, that a fault will arise during a typical working day of, say, 10 h.

**Stability.** Output drift should be less than, say, 25% of the required intrinsic accuracy (see below) over the same period.

**Response time** should be minimized to less than, say, 15 s to form a safe warning of low oxygen content. Preferably, the response time should be a few seconds.

**Accuracy** should be adequate for clinical requirements, but should not be enhanced in preference to the first three criteria. We considered the clinically acceptable accuracy figures to be: oxygen ±2% v/v; halothane etc. 0.1% v/v, at low concentration.

An investigation into methods of achieving...
AUTOMATED INTERFEROMETER ANALYSIS OF ANAESTHETIC GASES

TABLE I. Assessment of the suitability of different types of analysers for use as part of a microprocessor controlled anaesthetic machine. An infra-red analyser is now available which, in addition to analysing vapours, will measure the nitrous oxide concentration so that oxygen concentration may be deduced. However, the instrument is unsuitable for our purposes because of its very high cost.

<table>
<thead>
<tr>
<th>Analysers</th>
<th>Piezoelectric crystal</th>
<th>Interferometer</th>
<th>Mass spectrometer</th>
<th>Ultra violet</th>
<th>Infra-red</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small size</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ability to analyse all anaesthetic agents</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Reasonable cost</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Possibility of analysing O₂ as well as vapour</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
<td>✓</td>
</tr>
</tbody>
</table>

these objectives included the cost of the analyser and its complexity. Various methods were rated against all the important factors (table I) and as a result interferometry emerged as the most suitable for further investigation.

METHODS OF ANALYSIS

The interferometric method of analysis, by detecting relative refracted indices of two gas samples is well established in anaesthesia [4—6]. Practical instruments differ in detail, but show the common principle that a beam of light from a single source is split by partial reflection/partial refraction on a glass plate or prism into two beams which are then recombined by a similar device (fig. 1). If the optical path length of one light path differs from the other by a whole number of wave lengths of light, the two beams will be additive in brightness; if one path is half a wavelength from the other, then destructive interference will cause the brightness to decrease. By imposing a very small degree of non-parallelity between the beam splitters, an image in the form of dark lines on a bright background can be produced. By using a white light source, dispersion will result in one bright and two dark strips which can be easily distinguished from less distinct, and in any case coloured, lines on either side. These dark lines can therefore be used as an optical pointer, as in the Riken Refractometer [5].

If each beam is arranged to pass through a sampling cell, any difference of refracted index between the gases in the two cells will displace the lines, and this displacement, Δx, is proportional to the difference in refracted index Δµ, according to the equation:

$$\Delta x = \frac{k \cdot L \cdot \Delta \mu}{\lambda}$$

where L is the length of the cell, λ is the wavelength of light and k is a constant depending on the geometry of the system.

The major advantage of using the refractive index of gases and vapours as the analysis factor, is that each gas has a specific value and that these values are strictly additive in any mixture of gas and vapour (assuming that chemical reactions are not occurring).

The refractive power of a gas, f, is related to its refractive index, µ, by the formula:

$$\beta = (\mu - 1) \cdot 10^6$$

Values of β or µ are usually quoted at STP (273 °K, 101.3 kPa). β is proportional to density and therefore, for a perfect gas at temperature T₁ and ambient pressure P₁:

$$\beta_{P_1, T_1} = \beta_m \cdot \frac{P_1}{101.3} \cdot \frac{273}{T_1}$$

Anaesthetic vapours, in the concentration range used clinically, behave sufficiently like true gases for non-perfect gas errors to be ignored. Under these conditions, for a mixture of gases of partial pressures P₁, P₂, P₃..., with refractive powers, β₁, β₂, β₃..., the refractive power of the gas mixture, βₘ, is related to the total gas pressure in the mixture, Pₘ, by the formula:

$$\beta_{m, P} = \beta_1 \cdot \frac{P_1}{P_m} + \beta_2 \cdot \frac{P_2}{P_m} + \beta_3 \cdot \frac{P_3}{P_m} + ...$$
Table II. Refractive powers of common anaesthetic gases. * Measured values not available

<table>
<thead>
<tr>
<th>Source of data</th>
<th>Carbon dioxide</th>
<th>Air</th>
<th>Oxygen</th>
<th>Nitrous oxide</th>
<th>Water vapour</th>
<th>Nitrogen</th>
<th>Halothane</th>
<th>Enflurane</th>
<th>Trichloroethylene</th>
<th>Methoxyflurane</th>
<th>Isoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 °C, 760 mmHg</td>
<td>451</td>
<td>293</td>
<td>272</td>
<td>510</td>
<td>257</td>
<td>299</td>
<td>1582</td>
<td>1582</td>
<td>*</td>
<td>*</td>
<td>1534</td>
</tr>
<tr>
<td>22 °C, 760 mmHg</td>
<td>418</td>
<td>271</td>
<td>252</td>
<td>477</td>
<td>238</td>
<td>277</td>
<td>1465</td>
<td>1425</td>
<td>1652</td>
<td>1696</td>
<td>1534</td>
</tr>
</tbody>
</table>

Table II shows the refractive powers of the common anaesthetic gases, together with the respirable gases.

Since anaesthetic machines usually define gas mixtures in terms of % v/v, equation (4) can be readily expressed in % v/v terms by remembering that, for gas 1, in the above mixture:

$$P_1 = \frac{\% \text{ v/v gas 1}}{100}$$

and the same relationship holds for every other gas in the mixture. Therefore, equation (4) can be expressed as:

$$\beta_m = \frac{1}{100} \left[ B_1 \cdot \% \text{ v/v gas 1} + \beta_2 \cdot \% \text{ v/v gas 2} + \cdots \right]$$

Principle of automation

In laboratory interferometers, the dark interference fringes are viewed through a microscope eyepiece either against a split image (Rayleigh) which is used as a zero against which movement can be measured, or against a transparent calibrated scale [4, 5].

In our instrument, the movement of the fringes is detected electronically using a detector consisting of an array of photosensitive elements, such as photodiodes or charge-coupled devices. The photosensitive material is subdivided into 256 elements (referred to as pixels) at 25-μm centres (arrays of 128 pixels may also be used for certain applications requiring less sensitivity). Each pixel is electrically independent of the others. The dark interference fringe results in a low signal output from the pixels on which it falls, and bright interference areas give high pixel outputs.
amplified and held by a fast peak detector, or sample-and-hold circuit, which is also controlled by the timing circuit. Whilst the peak value is held between the clock pulses, an analogue-to-digital converter circuit converts it to a digital indication. Thus the intensity pattern is converted into a series of 256 numbers. These digital values are read into and stored by a microprocessor, which also performs all of the calculating functions and controls the lamp.

**Principle of measurement**

If the relative position of the principal maximum (fig. 2) is measured with pure oxygen in the sample cell, its digital signal is recorded as "0" in a microprocessor, and the equivalent position with pure nitrous oxide in the cell is recorded as equivalent to nitrous oxide–oxygen = 225 units of refracted power (at 20 °C), the instrument is calibrated to read in terms of per cent nitrous oxide. A linear relationship then holds for all other oxygen–nitrous oxide gas mixtures, because of the linearity of the refractive power relationship. The interference pattern can be adjusted by optical means, so that when it is imaged on the array of photosensitive elements the distance between two peaks corresponds to a sufficient number of pixels, typically 10–20, to provide fine resolution. The sensitivity of the instrument (deflection for unit change in concentration) is determined by the optical path length of the sample cell. It is also necessary to select the length of the array so that all anticipated movements of the intensity pattern can be detected within it. Mathematical correlation procedures enabled the geometric position of the principal maximum to be located by the microprocessor to an accuracy of 0.1 pixels.

From standard tables, the refractive powers of the anaesthetic agents are held in the microprocessor relating the relative shifts produced by 1 % v/v of these agents, in a particular carrier gas, to that of 100 % nitrous oxide.

Taking halothane as a typical example, and taking the distance between two peaks as approximately 20 pixels, with a 1-cm cell length, each fringe will represent about 4 % v/v of halothane in oxygen. Therefore, one pixel is approximately 0.25 % v/v halothane. By using the calculating power of the microprocessor to estimate the centroid of the area under the principal peak, it is possible to estimate the peak of 0.1 of a pixel, so giving an instrument resolution considerably better than 0.1 % v/v. Similarly, a 1 % v/v resolution of nitrous oxide in oxygen–nitrous oxide gas mixtures is possible.

**GAS SAMPLING**

The gas sampling system is shown schematically in figure 4. The gases are sampled sequentially through the valve and pump arrangement. The microprocessor software controls the valve timings to allow the sample cell to fill with the gas of interest. After each gas has been introduced to the sample cell the pressure is allowed to equilibrate with atmosphere via V5, then the peak of the intensity pattern is calculated and stored.

Pure oxygen is sampled first via valve V1. This gives a zero position and, therefore, helps to compensate for any overall shift in fringe position as a result of mechanical or temperature-related effects. On the initial start up and at approximately 20-min intervals, this is followed by a calibration cycle where 100 % v/v nitrous oxide is sampled via the other port of V1. A microcomputer-controlled gas mixing system [1] produces the oxygen–nitrous oxide gas mixture which is sampled via the electromagnetic solenoid valve V2 next. Finally, the interferometer samples, via V4, the complete mixture of oxygen, nitrous oxide and vapour as supplied by the gas mixer–vaporizer.
system. Solenoid valve V3 is used as a means of isolating the gas supplies from V1 and V2 from the cell.

After all the samples have been taken and the microprocessor has stored the peak positions, the calculations are performed. The difference between the peak positions from pure oxygen and nitrous oxide is used as a calibration factor, and verification is also made that it lies within certain predetermined limits. Next, the difference between the peak positions for pure oxygen and the oxygen–nitrous oxide mixture is used to calculate the nitrous oxide concentration and, hence, to deduce the oxygen concentration. Finally, the difference between the last two positions can be used to calculate the vapour concentration. The particular vapour in use is identified by the operator via a manual input control to the microprocessor. The measured oxygen and vapour concentrations are then displayed on the front panel of the instrument.

It is fortuitous that the shifts in interference pattern for gas and vapour concentrations in common anaesthetic practice (namely 70% nitrous oxide, and less than 5% halothane) make analysis of both nitrous oxide and vapour possible with the required degree of accuracy. The fringe shift produced by 5% halothane is approximately equal to that produced by 30% nitrous oxide. This means that, if the nitrous oxide concentration can be read to an accuracy of 1% v/v, then the accuracy obtainable for vapour will be 0.15% v/v. It is, therefore, necessary to obtain a slightly greater accuracy on the nitrous oxide measurement in order to be able to read vapour concentration to 0.1% v/v. The refractive powers of the other agents in common use (eg. isoflurane and enflurane) are of the same order (table II), so that this applies to them also.

The output of gas from the pump may be diverted to atmosphere or a scavenging system, or returned to the patient circuit as shown in figure 4.

**EVALUATION**

*Stability and repeatability*

The stability and repeatability of the system were verified over prolonged periods using air, 100% oxygen, 50% v/v oxygen–nitrous oxide, and 100% nitrous oxide. The readings were determined in units of pixel numbers and were recorded every 14 s for periods of up to 14 h. Both the absolute values of the pixel numbers and the differences between successive readings were taken.

*Linearity and accuracy*

The linearity of the system was confirmed using mixtures of oxygen and nitrous oxide supplied by a Wosthoff gas mixing pump (type SA18/F). These mixtures were supplied to solenoid valves V2 and V4 whilst 100% oxygen was fed into solenoid valve V1. An average of 30 readings was taken and the maximum, minimum and standard deviation were recorded. The standard deviation gave a measure of the precision with which it was possible to measure nitrous oxide concentration. A graph of pixel shift against nitrous oxide concentration was plotted. The gradient of this
line gave a measure of the sensitivity of the instrument to nitrous oxide in oxygen. Verification of the linearity and sensitivity for different mixtures was made by supplying halothane in oxygen via solenoid valve V4 with pure oxygen supplied via valves V1 and V2, and then supplying halothane in nitrous oxide on V4 with oxygen on V1 and nitrous oxide on V2. The halothane was supplied by a conventional Abingdon anaesthetic vaporizer (Penlon, Ltd) and it was, therefore, impossible to maintain a completely constant concentration over the period of measurement. The concentration was monitored using a mass spectrometer (Centronic, MGA200) and the average value was used when plotting mean pixel shift (over 20 readings) against halothane concentration. The gradients of these two lines gave the sensitivity of the instrument to mixtures of halothane in oxygen or nitrous oxide. A check was then made to ensure that the relative sensitivities were in the proportions predicted in the Appendix.

Response time

The response time of the system depends on the volume of the tubing, the time for the pressure in the cell to reach a value equal to atmospheric pressure, and the time for the microprocessor to calculate the concentration values. The times were optimized by using a mass spectrometer to analyse the sample emerging from the pump and adjusting the times as necessary to ensure that readings were taken just after the cell and tubing were completely flushed by the gas of interest.

RESULTS

Stability and repeatability

Figure 5 shows how the position of the peak of the intensity pattern varied with time when air was being sampled over a 14-h period. \(x\), \(y\) and \(z\) are the absolute values of the peak positions when sampling via V1, V2 and V4, respectively. Figure 5 also shows the difference between \(y\) and \(x\), and \(z\) and \(x\); these are the values used by the microprocessor in calculating the gas concentrations. The absolute value of the peak position varies from pixel number 12.27 to 23.1; however, the maximum value of the difference varies from \(-0.24\) to \(+0.28\), with a mean of 0.000 and a standard deviation of 0.065.

Figure 6 shows how the position of the peak of the intensity pattern varies when oxygen is sampled through V1, 50% v/v oxygen—nitrous oxide is sampled through V2 and pure nitrous oxide is sampled through V4. The mean of the difference in pixel numbers is 57.9 for the 50% mixture, and the mean of the difference between pure nitrous oxide and the 50% mixture is 58.5. The standard deviations are 0.179 and 0.106, respectively.

Linearity and accuracy

Figure 7 is a plot of pixel shift v. nitrous oxide concentration. The value used for pixel shift is an average of 30 successive readings. The gradient of the line is 1.15. Figure 8 is a plot of pixel shift v. halothane concentration for halothane in oxygen and halothane in nitrous oxide. The gradients of the two lines are 6.4, and 4.9, respectively. These would correspond with gradients of 1.18 and 1.12 for nitrous oxide in oxygen, as shown in the Appendix.

Response time

The time taken for the system to update the halothane and oxygen concentrations was 14 s and this is the “response time” of the instrument. During this period the instrument flushes the cell through with three different gases, stores the...
![Diagram](https://academic.oup.com/bja/article-abstract/61/4/484/286626)

**Fig. 6.** Plot of peak position against time when pure oxygen is sampled via V1, 50% v/v oxygen in nitrous oxide via V2 and pure nitrous oxide via V4.

**Fig. 7.** Plot of pixel shift against nitrous oxide concentration.

**Fig. 8.** Plot of pixel shift against halothane concentration for halothane in oxygen (●) and halothane in nitrous oxide (○).

values of the pixel numbers for the peaks, and then performs the calculations.

**DISCUSSION**

Table III shows the means and standard deviations of the values of pixel shift for oxygen-nitrous oxide mixtures, together with the difference between the measured value and the value predicted from the best fit line shown in figure 7. This shows that the instrument gave results which were repeatable and stable to 0.1 pixel, corresponding to 0.12% v/v for nitrous oxide and 0.02% v/v halothane. If an error of this magnitude were to occur on all readings, both gas and vapour could be read to the required degree of accuracy. In most cases the accuracy will be even greater. Figure 8 shows inaccuracies in the vapour concentrations apparently greater than the required values. However, this was caused by the difficulty in obtaining a constant output from a standard vaporizer and the need to use an average value of vapour concentration. It is required that the instrument should read nitrous oxide to an accuracy of 1%, and halothane to an accuracy of 0.1%. The instrument complies with these requirements and, in the majority of cases, should be capable of an even higher degree of accuracy.

It would, in theory, be possible to use a hand-held interferometer for sequential analysis of
TABLE III. Mean pixel shift (average of 30 readings), standard deviations and difference between measured and predicted values for different concentrations of nitrous oxide

<table>
<thead>
<tr>
<th>N₂O concn (% v/v)</th>
<th>Mean pixel shift</th>
<th>SD</th>
<th>Difference between measured and predicted values</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>11.619</td>
<td>0.073</td>
<td>+0.119</td>
</tr>
<tr>
<td>20</td>
<td>22.851</td>
<td>0.043</td>
<td>-0.149</td>
</tr>
<tr>
<td>30</td>
<td>34.520</td>
<td>0.048</td>
<td>+0.020</td>
</tr>
<tr>
<td>40</td>
<td>46.528</td>
<td>0.080</td>
<td>+0.528</td>
</tr>
<tr>
<td>50</td>
<td>58.380</td>
<td>0.084</td>
<td>+0.880</td>
</tr>
<tr>
<td>60</td>
<td>69.563</td>
<td>0.076</td>
<td>+0.563</td>
</tr>
<tr>
<td>70</td>
<td>80.479</td>
<td>0.092</td>
<td>-0.021</td>
</tr>
<tr>
<td>80</td>
<td>91.980</td>
<td>0.055</td>
<td>-0.020</td>
</tr>
<tr>
<td>90</td>
<td>103.801</td>
<td>0.125</td>
<td>+0.301</td>
</tr>
</tbody>
</table>

emphasizes the importance of using a sample of 100% oxygen to provide the zero position.

This analyser is not, in its present form, capable of analysing an unknown mixture such as that in an anaesthetic rebreathing system. However, it can be used as a secondary standard to check the calibration of in-line analysers of a less stable, but more specific, nature and will be used in this way (British Patent Application no. 8415670) [7] in the development of the new microcomputer controlled anaesthetic machine, of which this instrument forms but a part [3].

APPENDIX

The shift in the interference pattern produced by 1% of gas 2 in gas 1 compared with gas 1 alone is given by:

\[ x = k(\beta_2 - \beta_1) \]

Therefore the gradient of the graph of pixel shift against concentration of nitrous oxide in oxygen, \( m_1 \), is given by:

\[ m_1 = \frac{k(477 - 252)}{225} \]

The gradient, \( m_2 \), of the graph of pixel shift against concentration of halothane in oxygen is given by:

\[ m_2 = \frac{k(1465 - 252)}{1213} \]

and, finally, the gradient, \( m_3 \), of the graph of pixel shift against concentration of halothane in nitrous oxide is given by:

\[ m_3 = \frac{k(1465 - 477)}{988} \]

Therefore \( m_1/m_2 = 0.185 \) and \( m_1/m_3 = 0.228 \)

REFERENCES