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Physical Methods of Respiratory Gas Analysis

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Chemical methods for gas analysis (3, 14, 18) have certain disadvantages. For example, there are no satisfactory chemical methods for analysis of helium, nitrogen or nitrous oxide, which are frequently used in tests of pulmonary function; chemical methods for analysis of other gases are laborious (hydrogen) or, by the usual methods, slow (oxygen, carbon dioxide, carbon monoxide). By contrast, the physical methods for gas analysis (10) are rapid, continuous, can be automatically recorded and the sample is unchanged during analysis, thus making sequential analyses possible. By proper choice of a physical method, any gas can be measured accurately; this applies even to isotopes of inert gases. The analysis procedure is relatively simple, once the apparatus has been calibrated. Some apparatus for physical methods are not available commercially, and all are expensive compared to ordinary apparatus for chemical analysis; many, however, may be constructed in a laboratory shop at a fraction of the commercial cost.

The physical methods to be described have many uses in the analysis of pulmonary function. They are particularly valuable for continuous measurement and recording of rapid changes in gas composition that occur during all phases of each respiratory cycle; for this purpose, it is necessary to use analyzers with minimal latency interval and response time (10). However, all physical methods, including those that are relatively slow (0.5-10 sec between sampling and recording), are often valuable for continuous recording of the composition of respired gases even though the full magnitude of composition change will not be recorded if the fluctuations are rapid. Many of the physical methods were originally designed for nonbiologic purposes, in which extremely rapid

analysis is not essential. Nevertheless, by developmental work, most of the currently "slow" analyzers may be speeded up by decreasing the volume of the sampling system and analysis chamber and by providing more sensitive devices for analysis. However, when a nonspecific method (below) is used to analyze gases present in a mixture of 3 or more components, very rapid analysis is often impossible because of the need for preliminary chemical absorption of 1 or more of the components.

For purposes of this discussion, physical methods are divided into the nonspecific and specific methods. Each of the nonspecific methods utilizes some property which is common to all the gases in the sample, yet which differs in amount for the individual components. For a sample containing only 2 components, the magnitude of the property analyzed is uniquely related to the composition. However, if a 3d component is also present, several samples containing each of these 3 components in different proportions can yield the same measured value; therefore samples with 3 or more components must 1st be simplified to a 2-component system by specific chemical or physical removal of the other gases.

Specific methods, on the other hand, measure the value of some property of a gas which is unique for that particular gas and is not appreciably influenced by presence of other gases in a mixture.

Since many of the physical methods for gas analysis are still in the developmental stage so far as physiologic measurements are concerned, it would not be profitable to describe the apparatus in minute detail. However, it is desirable that physiologists be acquainted with the general principles, characteristics and present limitations of such techniques.

NONSPECIFIC METHODS

a) Thermal conductivity.—This method (2) depends on the fact that different gases conduct heat at different rates. Two wires are heated equally by a constant electric current; a reference gas, such as dry air, is drawn past 1 and an unknown gas past the other. These 2 wires are connected in a Wheatstone bridge circuit. If the unknown gas has a lower thermal conductivity than the reference gas, heat will be conducted away at a lower rate from the wire over which it is flowing, and the temperature and hence electrical resistance of the wire will increase, thus unbalancing the Wheatstone bridge a definite amount. After an empiric calibration of the apparatus, analyses may be performed with an accuracy of ± 0.03 per cent CO_2 and O_2 . In mixtures containing 3 or more

components, water vapor and/or CO_2 must be absorbed first. Since the thermal conductivity of CO_2 is much higher than that of other respiratory gases, large errors can be introduced by incomplete absorption of CO_2 . Temperature balance is of 1st order importance.

Analyses with the present models* require 15-20 sec, hence the full extent of rapid fluctuations in gas composition cannot be detected.

b) Refractive index, visible light (interferometer).—The refractive index of all gases is so close to the value for air that the usual method for its determination, as for a solid or liquid, is not suitable. However, by employing interference phenomena using visible light, it is possible to construct a refractometer of such sensitivity that useful measurements can be made (5, 20). A beam of light is divided into 2 by a lens and a pair of parallel slits. One beam is passed through a cell containing a reference gas, usually air; the other, through the unknown gas. The 2 beams are recombined by a lens and are observed with a microscope eyepiece. Because of mutual interference of light from the 2 slits, a set of interference fringes is formed at the eyepiece. The displacement of this set of fringes is a function of the differences in refractive index of the gases in the 2 cells.

If O_2 - N_2 mixtures are to be analyzed, CO_2 must be completely absorbed or its presence will cause large errors. The instrument** must also be carefully built to equalize 1st order temperature effects. It can measure CO_2 to as low as 0.01 per cent in dried air and can measure O_2 or N_2 to as low as 0.05 per cent in dried, CO_2 -free O_2 - N_2 mixtures. Several hundred ml is required for the analysis.

c) Other nonspecific methods measure gas composition by determinations of viscosity or density or by the effect of the gases on the velocity of sound (4, 7) or absorption of sound.

SPECIFIC METHODS

a) Magnetic susceptibility of O_2 (Pauling meter).—The apparatus***(13) indicates the partial pressure of O_2 in a mixture of respiratory gases. This analytic method depends on the strong

*Obtainable from Cambridge Instrument Company, New York 17, and Leeds & Northrup Co., Philadelphia.

**Constructed by Baird Associates, Cambridge, Mass.

***Obtainable from National Technical Laboratories, Pasadena 2, Calif.

paramagnetic susceptibility of O_2 ; the other respiratory gases are diamagnetic and their susceptibility is less. The unknown gas mixture is passed at a rate of a few ml/min into a chamber in which a small glass dumbbell is suspended on a stretched fused-silica fiber in a nonuniform magnetic field produced by a small permanent magnet. The dumbbell tends to turn into or out of the field, depending on the susceptibility of the unknown gas in comparison to that of the dumbbell, which the gas surrounds. The dumbbell position is measured by a mirror-light-scale system; the scale is calibrated directly in terms of pO_2 . Accuracy is about 1 per cent of the range covered, which may be from 0 to 160 or 0 to 800 mm Hg pO_2 . Temperature corrections are usually negligible when the instrument is used within a few degrees of the calibration temperature. Response time is about 6 sec. The chief delay is the time required to draw gas from its source into the instrument; the long response time is due to the slow flushing of the analysis chamber, required by the delicate structure of the dumbbell and suspension. A light-weight portable model is available, but it must be remembered that these instruments are delicate and require careful handling to achieve best results.

Rein (17) has used a similar principle in different form in which he measures the difference in flow resistance between 2 gas streams, 1 in a magnetic field. A modification of this instrument uses the difference in thermal conductivity of 2 streams, 1 of which is in a magnetic field; CO_2 and H_2O must be removed to obtain the highest accuracy.

b) Infra-red absorption.—Atoms of polyatomic molecules can vibrate in various modes. In general, for polyatomic compounds these vibrational modes have a variety of frequencies, and the compounds thus absorb infra-red radiation in a number of regions in the spectrum. The pattern of resulting absorption bands (position and intensity of bands) is unique for each compound and extends even to isomers of a given compound. Polyatomic molecules such as CO_2 , water vapor, CO , N_2O , ether, ethylene and cyclopropane have been measured by infra-red absorption; monatomic gases and symmetrical diatomic molecules such as O_2 and N_2 cannot be so analyzed.

In this method, a beam of infra-red radiation emitted by an incandescent material is passed through the sample, and the transmitted radiation is examined by spreading it out into a spectrum by a prism or diffraction grating (15). A small portion of this is allowed to fall on an infra-red detector; although delicate thermocouples may be used, greater sensitivity can be achieved

by use of a bolometer, which is a special type of resistance thermometer. Analysis time of the commercially available instruments* is about 6 sec.

Infra-red "analyzers,"** which are not true spectrometers but are analogous to filter photometers (colorimeters), require different gas-filled filters for different types of samples. Fowler (6) has designed an infra-red analyzer for CO_2 , with which 90 per cent of the maximal response is recorded in 0.1 sec over-all time; it possesses linear response from 0 to 9 per cent CO_2 and is insensitive to normal pressure and temperature variations.

c) Nitrogen meter.—Gases exposed to sufficient electrical excitation emit radiation (spark, arc or glow discharge) in different parts of the radiation spectrum. In the nitrogen meter (11) the gas to be analyzed is drawn continuously through an electrical discharge tube by a pump working against a leak at a narrowed inlet orifice; about 1.0 ml is drawn through per sec with pressure in the discharge tube maintained at about 2 mm Hg (Fig. 1). When a high potential difference is applied to the discharge tube electrode, the gas glows. Air glows with a bright pink color, O_2 a very faint green, N_2 a bright orange-pink, CO_2 a dim blue, and water vapor a rich red. The spectral region of 3100-4800 Å excludes the emission from O_2 and water vapor and almost all of CO_2 but includes some of the most intense N_2 bands. Consequently a light filter used to isolate this range is inserted between the discharge tube and a photoelectric cell. The cell is connected to a cathode follower and it, in turn, to an oscillograph galvanometer, movement of which is recorded on moving photographic paper. This instrument has the fastest response time of any known analyzer; it will sample, analyze and record a stepwise change in gas composition with 90 per cent of the full deflection occurring within 0.02 sec. Accuracy is ± 2 per cent. It requires a sample of about 1.0 ml/sec. It is not manufactured commercially, at present.

d) Mass spectroscopic methods (1, 12, 19).—If gases are ionized at a very low pressure (0.001 mm Hg) by a beam of electrons, the ions can be accelerated through an entrance slit by an electric field and then deflected by a magnetic field. The magnitude of deflection depends on the mass/charge ratios of the ions. Since the charge on most of the ions is a unit positive charge, and since the ions

*Infra-red spectrometers are manufactured by Baird Associates, Cambridge, Mass.; Perkin Elmer Corporation, Glenbrook, Conn., and National Technical Laboratories, Pasadena 2, Calif.

**Built by Baird Associates, Cambridge, Mass., and Leeds & Northrup Company, Philadelphia.

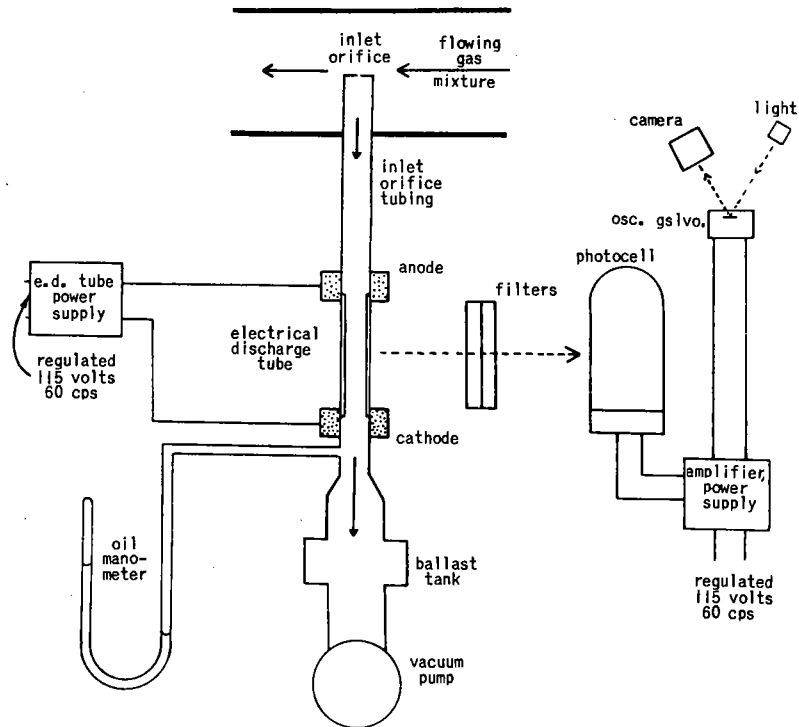


Fig. 1.—Nitrogen meter. (For details, see text.)

of greater mass are deflected less by a given magnetic field than those of a small mass, the beam of ions is spread out in space, forming a "mass spectrum." Ions of a given mass are selected by an exit slit and measured quantitatively by an ion collector which measures the charge or current carried by the ions. The entire mass spectrum can be measured by changing either the electric or the magnetic field in a uniform manner so that the desired range of the spectrum moves across the exit slit. If it is desired to measure several gases simultaneously and continuously, a slit and ion collector can be arranged for each of these gases in appropriate positions and the resultant currents measured individually (8).

The mass spectrometer* is capable of analyzing any gas, regardless of the composition of diluting gases, with a specificity,

*Manufactured by Consolidated Engineering Co., Pasadena, Calif., and by General Electric Co., Schenectady 5, N. Y.

sensitivity and accuracy that cannot be matched by any other known method of gas analysis. Commercial instruments are very expensive and not adapted for physiologic studies.

e) Nuclear properties methods.—Radioactive gases used as tracers and the methods of measurement were reviewed by Kamen (9) The gases are obtained from the Atomic Energy Commission Laboratories, Oak Ridge, Tenn. For simultaneous analysis of several gases, the β -ray and x-ray spectrometer (16) may be useful. Nuclear physics is being rapidly developed by physicists; new methods of gas analysis may become available as this field expands.

NOTE: This section was reviewed by E. J. Rosenbaum.

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