Amplifier for Linear Recording of Oxygen Saturation and Dye Dilution Curves

By Curt Wiederhelm, B.S.

An amplifier system has been designed for use with commercially available oximeter earpiece or cuvette and a direct recording oscillograph. Linear response to changes in oxygen saturation and in vivo dye concentrations are obtained with a rise time less than 0.5 sec., noise level and drift less than 2.5 per cent and accuracy comparable to Van Slyke-Neill method. Standard error of estimate between Van Slyke-Neill manometric and cuvette oximeter amplifier-recorder systems is ±2 per cent.

The potential clinical value of oximetric technics and dye-dilution curves has been demonstrated repeatedly. However, the lack of commercially available instrumentation with satisfactory operating characteristics for continuous recording prevented their widespread use. Several instruments have been described, but all have characteristics which limit their application for routine clinical studies. Several exhibit a nonlinear response, which makes accurate extrapolation of the downslope limb of indicator curves difficult, and decreases accuracy of cardiac output determinations. Others have linear response, but do not use compensating circuits for cancelling out variations in either path length or total hemoglobin concentration. Since a photoelectric plethysmogram is superimposed on records when they are used as ear oximeters, their signal to noise ratio is poor. One oximeter provides a linear response and incorporates compensating circuits, but can only be used with one particular brand of photovoltaic cells.

CRITERIA

The following criteria were established as minimal requirements for performance of an improved system: 1. Linear response for oxygen saturations varying from 0 to 100 per cent and for T-1824 dye concentrations varying from 0 to 50 mg./L. 2. Reproducibility of the instrument readings comparable to that obtained with the cuvette and earpiece in the original circuit (S.D. ± 2.9 per cent for the earpiece and ±1.9 per cent for cuvette). 3. Adequate gain to produce full scale deflection on suitable recorder for a change of oxygen saturation from 80 to 100 per cent, or for dye concentration in whole blood of 50 mg./L. 4. Drift less than 2.5 per cent of full scale deflection over a half-hour period on the 0 to 100 per cent range, and less than 2.5 per cent of full scale deflection over a period of five minutes on the 80 to 100 per cent range. 5. Noise level less than 2.5 per cent of full scale deflection on the most sensitive range. 6. Speed of response 90 per cent of full scale deflection in 0.5 sec. 7. Simplicity of operation so that even relatively inexperienced personnel can manage routine maintenance and operation.

Both earpiece and cuvette modified by Wood use a compensated circuit. With low load resistances, the photocell current is a linear function of incident light. Since these earpieces and cuvettes are available commercially* and have been in use for several years, they were selected as basic components for a new instrument.

An oximeter amplifier meeting these requirements will be described. Calibration data will be presented using a cuvette.

DESCRIPTION

The circuit diagram of the amplifier is shown in figure 1. The amplifier can be divided into five subunits: A balancing circuit, B chopper amplifier, C logarithmic amplifier, D DC amplifier, and E metering circuit.

The balancing circuit consists of a potentiometer P1 and switch S1. P1 attenuates the potential from the red sensitive photocell. When properly adjusted, this potential just equals that of the infrared cell when the cuvette is filled with saline; thus, the resultant output of the cells is zero.

* Waters Corporation, Rochester, Minn.
FIG. 1. Circuit Diagram. **Linear potentiometers:** $P_1 = 10k\Omega; P_3, P_4 = 5M\Omega; P_2, P_5 = 1k\Omega$. **Tubes:** $V_1, 12AY7; V_2, 12AX7; V_3, V_4, 12AU7$. **Condensers:** $C_1, C_3, C_5, C_4, C_6 = .1\mu$farad; $C_7 = 150\mu$farads 150 V electrolytic; $C_8, C_9 = 10\mu$farads 150 V electrolytic; $C_{10} = 20\mu$farads 150 V electrolytic; $C_{11} = 2\mu$farad Paper. **Resistors:** $\frac{1}{2}$ watt $\pm 10\%$: $R_1, R_5, R_6, R_7, R_{10}, R_{13}, R_{14} = 47k\Omega; R_2, R_4, R_8, R_9 = 1k\Omega; R_3 = 27k\Omega; R_{11} = 4.7k\Omega; R_{12} = 1M\Omega; R_{15} = .56M\Omega; R_{16} = .3M\Omega; R_{17} = 2.7k\Omega; R_{18} = 1M\Omega; R_{19} = 10k\Omega; R_{20} = 1M\Omega; R_{21} = 2M\Omega; R_{22} = 15k\Omega; R_{23} = 33M\Omega; R_{24} = 47k\Omega; R_{25} = 3k\Omega; R_{26} = 9.1k\Omega; R_{27} = 5.6k\Omega$. **Misc.:** $C_{12}, C_{13}$ Leeds & Northrup Chopper 3338-10; $C_{14}$, Leeds & Northrup Chopper 3338-1; $F_1$ UTC 450 Hy Audio Choke; $B_1$, 6-Volt Dry Cell; $M$, 0-50 μammeter.

The input selector switch $S_1$ has three positions. In the "OFF" position, the input is grounded. In the "IR" position, the infrared sensitive cell is connected to the input with reversed polarity, and the bias voltage on the grid of the logarithmic amplifier is removed. The polarity of the meter $M_1$ is also reversed. The importance of these operations will be described later in the text. In the "READ" position ($R$), the photocells are connected in a bucking circuit and input to amplifier is then equal to the difference between the infrared and red cell potentials.

The chopper amplifier is a conventional resistance coupled amplifier with a gain control. The cathode resistors are not bypassed to provide gain stabilization. After synchronous rectification, undesired high frequency components are filtered out in a low pass LC filter. The rectifier is connected in such a manner that a negative output signal will result when a positive signal is applied to the input.

This signal is then applied to the grid of the logarithmic amplifier. This amplifier operates on the principle that the current passing through a diode will be an exponential function of the plate voltage at low plate currents (typically from 10 to 100 μA). In the circuit described here, the grid of the logarithmic amplifier functions as a diode plate. This grid is kept at a positive potential by a bias battery $B_1$. With the 1 megohm series resistor $R_{20}$ in the grid circuit and tube characteristics as described above, the grid voltage becomes pro-
portional to the logarithm of the applied voltage. This amplifier maintains its logarithmic response over more than two decades.

The output of the logarithmic amplifier is approximately 150 mv/decade. A change in oxygen saturation from 100 per cent to 80 per cent produces an output signal of only 15 mv. Since the recorder, with which the amplifier was intended to work (Sanborn polyviso), requires 100 mv for full scale deflection, one stage of DC amplification was added. This amplifier is a bridge circuit differential amplifier with one grid grounded. It also functions as a phase inverter and supplies a push-pull output to the recorder. The potentiometer $P_3$ in the grid circuit adjusts the bias on the input grid and serves as a meter zero control. The potentiometer $P_1$ functions as a shunt attenuator.

The metering circuit consists of a cathode follower, which operates as an impedance matching device between the high impedance plate circuit and the relatively low impedance of the microammeter $M_1$. Switch $S_3$ is the range switch, connecting a shunt across the meter on the 0 to 100 per cent range.

The power for the amplifier can be supplied from standard B batteries. However, for optimum performance and freedom from drift, a regulated power supply should be used. The power for the light source in the cuvette and for the filaments in the amplifier is supplied by a 6 volt 200 ampere-hour storage battery.

**Discussion**

The easiest way of visualizing the basic operation performed by this unit is to study the function of the logarithmic amplifier (fig. 2). This figure demonstrates that if a signal $IR_b$ of 7.5 volts is applied to the input of the amplifier, the output will be zero. If another signal $R_b$ of 6 volts is applied to the input, the output will be $-15$ mv. This output signal is proportional to $\log IR_b - \log R_b$ or $\log (IR_b/R_b)$. Similarly, if another voltage $IR_s = 10$ volts is applied to the input, the output will be proportional to $\log IR_s - \log IR_b$, or $\log (IR_s/IR_b)$. Thus the logarithmic amplifier makes it possible to measure the logarithm of the ratio of two voltages if one of these voltages is kept constant.

The following symbols are used: $E_{Hb}$ = extinction coefficient for hemoglobin in the infrared range; $E_{Hb}$ = extinction coefficient for reduced hemoglobin in the red range; $E_{HbO_2}$ = extinction coefficient for oxyhemoglobin in the red range; $IR_s$ = infrared photocell potential with saline in light path; $IR_b$ = infrared photocell potential with blood in light path; $R_b$ = red photocell potential with saline in light path; $R_b$ = red photocell potential with blood in light path; $R_b = IR_b$; $R_b$ = adjusted red photocell potential with blood in light path; $R_b = IR_b$; $u$ = gain in chopper amplifier; $G$ = gain in DC amplifier.

For a Wool oximeter cuvette the following relation holds true:

$$S = \frac{E_{\text{Hb}}}{E_{\text{HbO}_2} - E_{\text{Hb}}} \times \frac{\log \frac{R_s}{R_b}}{\log \frac{R_s}{R_b}} = \frac{\log \frac{R_s}{R_b}}{\log \frac{R_s}{R_b}} \frac{E_{\text{Hb}}}{E_{\text{HbO}_2} - E_{\text{Hb}}} \tag{1}$$

where $K_2$ and $K_1$ are constants. By subtracting the term

$$\frac{\log \frac{R_s}{R_b}}{\log \frac{R_s}{R_b}}$$

The figure shows the function of logarithmic amplifiers.
from both sides of equation (1), the following expression is obtained:

\[ S = \frac{\log IR_b}{K_b} - \frac{\log IR_s}{K_s} \]  

(2)

However in the balancing procedure, \( R_s \) is made equal to \( R'b \). Then the last term in equation (2) becomes zero and the equation becomes:

\[ S = K_2 - K_1 + K_3 \frac{\log IR_b}{IR_s} \]  

(2a)

When balancing the amplifier, the first step is to ground the input of the chopper amplifier by turning \( S_i \) to its “OFF” position, then adjust \( P_4 \) until the meter indicates its mechanical zero. With the input of the chopper amplifier grounded, the input voltage to the logarithmic amplifier is set at 7.5 volts (the voltage of \( B_3 \)). This adjustment establishes the output voltage of the logarithmic amplifier at zero for a 7.5 volt input voltage.

With \( S_i \) in the \( IR \) position, the 7.5 volts bias on the input of the logarithmic amplifier is removed. Adjusting \( P_2 \) for zero meter deflection with blood in the cuvette establishes \( u \times IR_s = 7.5 \) volts, where \( u \) is the voltage gain of the chopper amplifier and \( IR_s \) is the infrared cell voltage with saline in the cuvette.

The output voltage of the logarithmic amplifier is then proportional to \( \log (IR_s/IR_b) \). The DC amplifier gain control \( P_4 \) is then adjusted to obtain a predetermined meter reading \( M_0 \) which is the output signal to the logarithmic amplifier.

Substituting this value in equation (2a) gives:

\[ S = K_2 - K_1 + K_3 \frac{M_0}{IR_s} \]

The meter deflection produced by this signal will then be

\[ M = G \times \frac{IR_b}{IR_s} \]

but equation (2) says that

\[ G = \frac{M_0}{\frac{IR_b}{IR_s}} \]

Thus

\[ M = \frac{M_0 \times \log \frac{IR_b}{IR_s}}{\log \frac{IR_b}{IR_s}} \]

or the meter reading is a linear function of the saturation of the sample. The values of \( K_3 \) and \( K_4 \) are determined in the calibration procedure.

Balancing procedures are summarized in table 1.

When the system is used for dye-dilution curves a simplified balancing procedure is followed. The meter is set to its mechanical zero with \( S_i \) in the “OFF” position, \( u \times IR_b \) is made equal to 7.5 volts with blood in the cuvette by adjusting \( P_4 \) with \( S_i \) in the “IR” position. Next \( R_s \) is made equal

<table>
<thead>
<tr>
<th>( S_i ) position</th>
<th>Content of Cuvette</th>
<th>Control Adjusted</th>
<th>Operation performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>OFF</td>
<td>Blood</td>
<td>Meter Zero</td>
<td>Output = 0 for 7.5 volt input to log. amp.</td>
</tr>
<tr>
<td>IR</td>
<td>Blood</td>
<td>Chopper Amp. gain</td>
<td>( u \times IR_s = 7.5 ) volts</td>
</tr>
<tr>
<td>IR</td>
<td>Saline</td>
<td>DC Amp. gain</td>
<td>( G \times \log \frac{IR_s}{IR_b} = M_0 )</td>
</tr>
<tr>
<td>READ</td>
<td>Saline</td>
<td>Photocell balance (P)</td>
<td>( R_s = IR_s )</td>
</tr>
<tr>
<td>READ</td>
<td>Blood</td>
<td>Read saturation</td>
<td>( M = \frac{S - K_1}{K_4} )</td>
</tr>
</tbody>
</table>
to $IR_b$ by turning $S_i$ in the "READ" position and adjusting $P_i$ for zero meter deflection. The input to the logarithmic amplifier then is $7.5 - v \times (IR_a - IR_b) = 7.5$ volts. When dye passes through the cuvette, the adjusted red cell potential will decrease and the output of the logarithmic amplifier will then be proportional to $\log \frac{IR_a}{IR_b}$, which is the optical density of the blood sample, read against a background optical density of $\log \frac{IR_a}{IR_b}$.

**Calibration Methods**

**Oxygen Saturation.** The oximeter was calibrated against the Van Slyke-Neill apparatus. The following modifications were introduced in the Van Slyke method to reduce systematic errors due to oxygen physically dissolved in plasma.

Correction factors for physically dissolved oxygen were derived from Dill's oxygen dissociation curves* and subtracted from observed oxygen contents as follows: 0.2 volumes per cent was used for saturations between 98 and 92 per cent; 0.1 volume per cent for saturations ranging between 92 and 42 per cent; no correction factor was used for saturations lower than 42 per cent; the oxygen capacity of the sample was determined by usual methods. The correction factor for physically dissolved oxygen subtracted from the oxygen capacity varies from 0.60 to 0.67. Capacities and contents were run in duplicate and determinations were repeated if results did not agree within 0.5 volumes per cent.

Oxygen saturations as determined by the oximeter were compared with saturations determined by the Van Slyke-Neill method. Arterial and venous samples of human blood were withdrawn anaerobically into heparinized syringes and stored under refrigeration for analysis. Oximeter readings were determined at the time of gasometric analysis to avoid errors introduced by transformation of inactive hemoglobin derivatives into active form and changes in temperature.

**T-1824 Dye Concentration.** A Beckman DU spectrophotometer was used for calibrating response of the system to varying concentration of T-1824 in whole blood.

Samples were centrifuged at 3500 rpm for 20 min., the serum withdrawn and optical density read against serum blanks at 620 m/ in 1 cm. cuvettes. Hematocrit values (determined by Wintrobe's method) were used for converting concentrations of T-1824 in serum to whole blood concentrations.

Linear response of the system to varying concentration of T-1824 in whole blood was demonstrated in vivo in dogs. The animals were anesthetized with Nembutal (30 mg./Kg. bodyweight) and trachea was intubated. The endotracheal tube was connected to a spirometer containing 100 per cent oxygen to maintain arterial saturation at a constant level. The right femoral artery and vein and the right external jugular vein were exposed and cannulated. Ten milligrams of heparin were administered intravenously before the cuvette was connected as an arteriovenous shunt between the femoral artery and vein.

The instrument was connected to a recorder, and after the baseline had stabilized, 3, 4 or 5 rapid successive injections of 1 or 2 ml. of 0.5 per cent

![Fig. 3. Comparison of oxygen saturations as determined by cuvette oximeter and Van Slyke-Neill methods in 83 venous and arterial blood samples. Standard error of differences is ±2.0 per cent and coefficient of correlation is 0.995.](image)

![Fig. 4. Relationship between recorded deflection of pen in mm. (ordinate) and equilibrium concentrations of Evans blue dye in mg./L determined by spectrophotometric analyses (abscissa). From 3 to 5 successive injections were administered to each of 9 dogs. Samples for analyses were withdrawn after each injection. Standard error of differences is ±1 mm.](image)
WIEDERHIELM

T-1824 were administered by the jugular vein. Samples were withdrawn through the cuvette for spectrophotometric analysis 20 to 30 sec. after each injection. The difference between the original baseline and the pen deflection at the moment the samples were withdrawn was taken as a quantitative measure of the T-1824 concentration.

RESULTS

Comparison of Oximeter and Van Slyke-Neill Methods. Eighty-three determinations were made of oxygen saturation in patients by oximeter cuvette-amplifier readings and Van Slyke-Neill chemical analyses in vitro (fig. 3). Standard error of estimate was ±2.0 per cent saturation.

Linearity and Correlation of Concentrations. Thirty-five arterial blood samples were obtained from 9 dogs during the course of multiple intravenous injections of T-1824. Linear relationship existed between recorded pen deflection of dye concentration in cuvette and dye concentration in plasma, as determined by Beckman spectrophotometric analysis for each animal (fig. 4). Individual variations in slope of this relationship were not due to differences in hematocrit, but probably reflected differences in rate of blood flow through cuvette.

Standard error of estimate between observed pen deflections and calculated values derived from regression line for data from each animal were ±1 mm. This represented 2.5 per cent of full scale deflection for Sanborn polyviso.

SUMMARY

An amplifier is described for use with Wood's modified oximeter cuvette and earpiece. Linear response was obtained over a wide range of oxygen saturations and concentrations of T-1824 dye.

Standard error of estimate for oxygen saturations using cuvette was ±2 per cent. The standard error of estimate for T-1824 dye concentrations was ±2.5 per cent of full scale deflection.

It is concluded that this new amplifier meets requirements for clinical oximetry.

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SUMMARIO IN INTERLINGUA

Es describite un amplificator disveloppate pro le uso in conjunction con le modificate cuvette e auricular oximetric de Wood. Responses linear eseva obtenite pro un extense scala de saturationes oxygenic e de concentraiones de blau de Evans.

Le deviation standard pro saturationes oxygenic, in usar le cuvette, esseva ± 2 pro cento. Le deviation standard pro le concentraiones de blau de Evans esseva ± 2,5 pro cento del deflexion a scala complete.

Nos conclude que iste nove amplificator satisface le requirimentos del oximetrica clinic.

REFERENCES


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