a normal cell (*a*), a cancer cell (*b*), and a cluster of cells (*c*). The output of the photomultiplier tube consists of three pulses of differing amplitude and width which correspond to the intensity and the distribution of the light in the fluorescing cells. After amplification the pulse-width discriminator rejects pulse *c*, derived from the cluster of cells. The remaining pulses, *a* and *b*, are led into the pulse-height discriminator, whose level, *h*, is set above the height, *a*, of the normal pulse. A portion of pulse *b*, derived from the cancer cell, then energizes the counting circuit, and the presence of a cancer cell is recorded.

*Oscilloscope presentation.* The voltage pulse can be led from the preamplifier to a cathode-ray oscilloscope (Sylvania Model 400) for presentation on an observation screen (Fig. 2). The fluorescence and phase photomicrographs and the voltage pulses for various cells that exfoliate from the cervix uteri and the pleura are given in Fig. 3. The cytological criteria and the classification of Papanicolaou (*8*) are used. The voltage pulses are photographically recorded from the oscilloscope screen as each cell is scanned. Representative normal cells of the vaginal smear (squamous and parabasal epithelial cells) and of the pleural fluid (mesothelial cells and histiocytes) have voltage pulses of the order of 0.1 v. Cancer cells of the vaginal smear (Class IV) and the pleural fluid (Class V) have voltage pulses of 0.2 and 0.3 v, respectively. Abnormal cells (Class III) in the vaginal smear with morphological features suggestive of, but not conclusive for, cancer have intermediate values, of the order of 0.15 v. The fluorescence intensities of the cells in Fig. 3 are approximately representative of the average for samples of the order of 100 cells. The statistical evaluation of this material, which will appear in a forthcoming publication (*4*), indicates that 20 per cent of cells of Class III, 60 per cent of Class IV, and 83 per cent of class V have fluorescent light intensities above the maximum for the normal cells in a smear.

In view of the foregoing consideration, the development of a microfluorometric scanner for the automatic searching and detection of cancer cells in preparations of exfoliated cells appears to be feasible. This instrument, it is hoped, will serve as an adjunct to the Papanicolaou technique in the screening of the population for certain types of neoplastic diseases. Moreover, with modifications in technical and staining protocol to be described elsewhere, such an instrument has potential application in other fields: (*a*) clinical hematology, for the differential counting of cells of the peripheral blood and the bone marrow; (*b*) biology, in the counting of the relative numbers of resting, dividing, and polyploid cells in a fixed tissue culture, a spread of whole cells, or a preparation of isolated nuclei; and (*c*) radiology, for the study of the degenerative change in the nuclear chromatin of radiated cells that exfoliate from the serous and mucous membranes.

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# *Technical Papers*

## Series-Aiding Phototube Bridge[1]


**L. G. Glasser**

***Engineering Department, Applied Physics Section, E. I. du Pont de Nemours & Company, Wilmington, Delaware***


The series-aiding phototube bridge circuit, in conjunction with a light source, comprises a photometer that is ideally suited for measurements of light absorption with very high precision and sensitivity. The circuit schematically consists of a Wheatstone bridge arrangement of two resistors and two phototubes. The tubes are connected anode-to-cathode with a vacuum-tube voltmeter connected from a point between the resistors to the common connection between the phototubes. A small battery or dry rectifier can supply the bridge potential. In this circuit, the dynamic resistance of one phototube acts as a load resistance for the other phototube so that very large output voltages are obtained for small changes in relative light intensity on the tubes. Such a circuit measures the ratio of the light intensity on the two tubes and hence is independent of the intensity of the light source. When Type 935 phototubes are used, a sensitivity of 1 v for 1% change of light intensity is achieved when a total of 30 v potential is applied across the bridge. At 90 v the sensitivity is 7 v/%. Thus a high voltage is provided for a small change in light intensity. The vacuum tube voltmeter that operates in connection with this bridge must operate on circuit resistances ranging from $10^7$ to $10^{13}$ ohms.

Best performance of the photometer employing this

[1] Abstract of a paper presented at the Gordon Research Conferences, New London, N. H., on Aug. 1, 1951.

circuit is obtained when the light intensities on the two phototubes are maintained at a constant ratio close to unity. Constant intensity ratio in an absorption photometer is achieved by employing a light gate to adjust the intensity in at least one of the light beams. When a light gate is employed, light absorption measurements can be made over the full range from 0 to 100% absorption. When a light gate is not employed and only the unbalance voltage of the bridge is measured, the range is restricted to 10 to 30% absorption, depending on the magnitude of the bridge potential. The calibration of the electrically unbalanced photometer is nearly linear over the useful range described, and the sensitivity drops off rapidly beyond this range. Measurements of light absorption with this circuit of the order of 0.001% can be reproducibly recorded.

The circuit is remarkably free from instability and drift. If the two phototubes have identical slopes and heights for the saturation portion of their characteristics curves, then when the relative illumination on the two tubes is maintained at a constant ratio, the output reading of the photometer is independent of bridge voltage. With commercial tubes, slight differences in slope and in height (or sensitivity) occur. The sensitivity difference is accommodated by using light intensities on the two tubes that are in inverse proportion to sensitivities of the tubes. The slope difference introduces a small voltage coefficient into the zero reading. This can be compensated by rapid trial-and-error selection of the relative values of the two bridge resistors.

A source of large drifts stems from the dependence of phototube response on absolute temperature. Although the effect is quite small by ordinary standards, it introduces errors when light absorption is measured over narrow ranges, such as 0 to 1%, or when stability over long periods of time, such as 24 hr, is required. The difference in the temperature coefficients of sensitivity between randomly selected Type 935 phototubes is often so large that a spurious absorption reading of 0.05% is introduced for 1° C change in temperature. This effect can be minimized by preselection of tubes, by thermal jacketing and temperature control, or by frequent zeroing of the photometer.

Major drifts and instabilities encountered in the use of this bridge are often caused by associated components. Changes in the color or color temperature of the source will unbalance the bridge, when the two phototubes have different spectral sensitivities. Many temperature effects may occur, including change in transmission of color filters, thermal expansion of mechanical members in the light paths, and drift of the voltmeter. Other sources of error are accumulation of dust at different rates on members in the two light beams, and accumulations of light-absorbing gases or vapors in different amounts in the two light paths. These difficulties can be minimized by good design of the apparatus, and the full capabilities of the series-aiding phototube bridge can be realized.

# A Simple Instrument for the Determination of ACH[1]

J. B. Davidson[2]

*Instrument Department,*
*Oak Ridge National Laboratory, Oak Ridge, Tennessee*

The use of the contraction of the *rectus abdominus* muscle of the frog for the determination of acetyl choline is well known (*1*). The simple instrument described here eliminates the traditional smoked-drum kymograph and in its place uses a lightweight cantilever beam equipped with resistance wire strain gauges in a bridge circuit. The output of the bridge is recorded on a Brown strip chart recorder.

The strain gauges are of the paper kind (Baldwin Locomotive Works, Type A-7) and have a resistance of 120 ± .3 ohms and a gauge factor of approximately 1.92 ± 2%. Four of them are mounted on a Starrett feeler gauge which serves as the beam. The feeler gauge is of steel, 6″ long, ½″ wide, and .008″ thick. The width tapers from ½″ in the center to about ¼″ at one end. The beam is mounted between two pieces of brass of dimensions 4″ × 1″ × ¼″ (Fig. 1). About

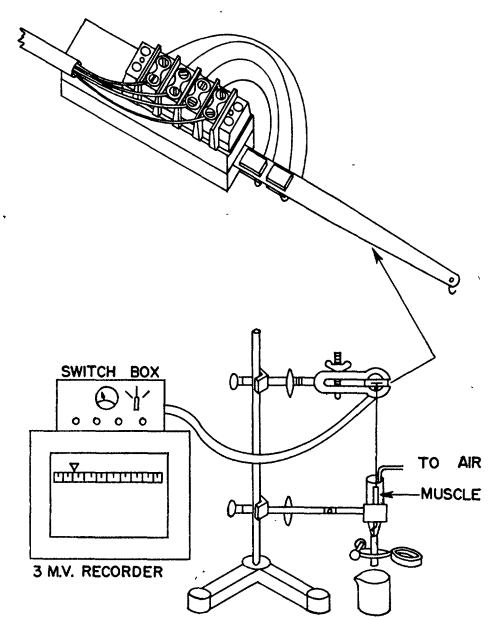


FIG. 1. Arrangement of strain gauge beam and frog muscle for ACH determination.

¼″ of the beam is clamped between the brass mounts. The four strain gauges are cemented to the beam (two on top and two on the bottom) ⅛″ from the clamped end, with Duco cement, according to the instructions of the manufacturer. After the gauges have dried thoroughly they are connected in a bridge circuit so

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