An in vivo fiber-optic cardiac blood-flow meter

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ABSTRACT

This paper describes the design and construction of an organ blood-flow meter which uses an indwelling venous fiber optic catheter and an infrared absorbing indocyanine dye. The instrumentation design consisted of: a light source, fiber bundles, couplers, a photodiode sensor, an electronic filter, and an analog-to-digital conversion circuit. Static tests were done to demonstrate a technique sensitivity for detection of the dye in concentrations as low as
3.1 mg per liter of blood.

1. INTRODUCTION

The purpose of the project is to measure blood perfusion of individual organs. A double fiber-optic/injection catheter uses injection of a light absorbing dye into the inferior vena cava to provide a timed appearance of the dye in the venous blood that returns to the vena cava from individual organs.

An in vivo fiber-optic blood-flow meter measures the change in the concentration of a dye in blood at the tip of a cardiac catheter after injection of the dye upstream. The cardiac catheter contains a bundle of optical fibers, the tip of which is placed in the vena cava. The other end of the fiber bundle is split into two halves. One half is connected to a light source which emits pulses of light at two different wavelengths, a pulse at 820nm followed immediately by a pulse at 940nm. The other half of the fiber bundle is connected to a photodiode amplifier sensitive to light at both wavelengths. The light is carried by these transmitting fibers to the tip of the catheter where it is reflected by the blood back into the receiving optical fibers. The receiving fibers carry the light back to the photodiode sensor. Increases in blood flow will increase the rate of decline in the concentration of indocyanine dye[1] at the catheter tip. From this decreasing curve of dye concentration, the cardiac output can be determined[2-7].

The most appropriate dye is indocyanine green which absorbs light at wavelengths from 760 nm to 830 nm, but not above 900 nm[1]. In order to determine dye concentration, the reflected shorter wavelength light pulse is compared to the longer wavelength reference light pulse. The smaller the ratio of the shorter reflected wavelength to the longer, the greater is the concentration of indocyanine green at the catheter tip.

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2. THE LIGHT SOURCE

The design of the light source is centered around two high- powered infrared light emitting diodes (Fig. 1). Each LED is pulsed on for 20 sec at a frequency of 100 Hz for a duty cycle of less than .2%. The 940 nm LED is pulsed on first, followed .006 seconds later by the 820 nm LED.

Each LED is switched using a darlington transistor pair. The beta of 2400 allows the transistor to be driven by a 7416 invertor chip with an open collector output. Three invertors are wire ANDed together in order to increase the high level output current (I_{OH}).

As shown in figure 1, the L1854 timing is controlled by a dual 74LS123 multivibrator chips. The inverted output of the second is inputed to the first. This configuration provides a continuous output of 20μsec pulses at 100Hz. The OD-820L is controlled by the second multivibrator chip. The chip is set up in a delay configuration triggered by the pulse controlling the L1854.

3. THE LIGHT SENSOR

3.1 The photodiode amplifier

The photodiode amplifier utilizes a high speed pin photodiode (Fig 2). The first stage of the photodiode amplifier is a current-to-voltage converter with the photodiode in photovoltaic or zero bias mode. The second stage of the circuit is a non-inverting amplifier with a voltage gain of 12. From this stage the signal is fed into an electronic filter.

3.2 The electronic filter

The signal from the photodiode amplifier is shown in figure 3. The response of the photodiode amplifier to the 20μsec pulse from the LED is a peak with a width of 30μsec. Because the signal is not sinusoidal it is important that the filters be as phase-linear as possible in order to prevent distortion of the signal.

The filter arrangement chosen is a high pass filter cascaded with a low-pass filter. Each filter is buffered at input and output by an LM310 unity gain amplifier.

After filtering, the signal is amplified by a non-inverting amplifier with a gain of 3.7. From this point the signal is fed into a sample and hold circuit and eventually to an A/D converter.

4. THE SAMPLE AND HOLD CIRCUIT AND A/D CONVERTER

In order to analyze the amount of reflected light emitted by LED it is necessary to separate the train of pulses issued by the photodiode amplifier and create two continuous signals. One signal represents the amount of light reflected off the blood at 820nm while the other represents the amount reflected at 940nm. The signals are then compared using a differential amplifier. The resulting continuous signal portrays the difference in reflected light intensities over time.

The two continuous signals are created using two sample and hold amplifiers which sample the signal from the photodiode amplifier at the peak of a pulse (Fig. 4). Each sample and hold is only activated if the pulse of light is from the particular LED whose reflection signal it is supposed to output. Because there is a delay between the pulse that activates the LED (the pulse from the light source) and the signal emitted by the photodiode sensor (Fig. 4), the pulse cannot be used to activate the sample and hold directly. A peak detector was built which finds the peak of the pulse from the light sensor and then is used to activate the appropriate sample and hold amplifier.

4.1 The peak detector

The peak detector circuit utilizes the analog signal from the light sensor along with the two digital signals (from the light sensor) which indicate when an LED has been activated. When a peak is detected it emits a 2μsec pulse, the leading edge of which is at the analog peak. The circuit used is shown in figure 5. Note that the input signals are on the right and the output signals are on the left.

The PK signal from the AND gate is fed into a J-K flip flop. The flip flop is set high by the PK signal and is cleared only by a signal from the OR gate. The OR gate inputs are the Vled1 and Vled2 signals which indicate that an LED is on. The PK2 signal from the flip flop triggers the 74LS121 multivibrator chip which emits a 2μsec pulse. This is the pulse length recommended for activation of the sample and hold amplifier which is described in the next section.

The Vled1 and Vled2 signals from the light source are also fed into the J and K inputs of a J-K flip flop. The Q output of the flip flop goes high at the leading edge of the pulse from the 820 nm LED. The Q output goes high at the pulse from the 940 nm LED. In this way Q and Q' indicate which LED has just been activated.

4.2 The sample and hold amplifier

As discussed earlier, the sample and hold circuit receives the analog signal from the electronic filter along with three digital signals from the peak detector circuit. It outputs a continuous signal which represents the ratio of the 820nm reflected light over the 940nm reflected light. The circuit is depicted in figure 4. The chips used are two AD 585 high speed precision sample and hold amplifiers. The 585 has an aperture delay time of 5μsec. The aperture delay time is the time it takes to switch from sample to hold. The 5μsec delay time includes a 3μsec acquisition time meaning the 585 can acquire a signal to .01% within 3μsec.

Each 585 in the figure is triggered by a positive pulse from an AND gate. The sample function of the upper chip is activated when both the Q signal and PEAK signal are high. The lower chip is triggered when Q' and PEAK are high.

The outputs from the 585 chips are fed into a 4214 multiplier divider chip set up in division mode. The signal representing the 820nm reflection is divided by the 940nm signal.

4.3 The A/D conversion circuit

The analog to digital conversion is accomplished using a MN574A 12 bit A/D converter chip (Fig. 6). The analog inputs are set for unipolar operation at a range of 0 to 20 volts. The 12 bit A/D converter was chosen because it allows for improvement in noise reduction.

The MN574A has five control pins. They are: chip Enable (CE), chip select (CS'), read/convert (R/C'), byte address (A0) and data mode select (12/8'). In read mode when the A/D chip is interacted with an 8 bit data bus, a low A0 accesses the high byte of data and a high A0 accesses the trailing 4 least significant bites. A high data mode select pin enables the 12 data output pins simultaneously, while a low one will enable either the high byte or 4 lease significant bytes (depending on the value of A0).

4.4 The A/D control circuit

The A/D converter illustrated in figure 6 converts the continuous signal from the divider chip. The computer is in full control of the sampling rate of the A/D.

A convert operation is performed by first setting the A0 and R/C' pins to the desired level. The chip select is then set low to initiate the conversion.

The data mode select pin of the MN574A is set to 8 bit operation in order to interface with an 8 bit microprocessor. For this reason the lower four least significant bits are tied to the four most significant bits. A0 is used to determine whether the lower four bits or the upper eight are being read.

The read operation is performed in the same manner as the convert operation. After check the status line to insure that it is low and the conversion is over the A0 line is set low to access the high byte of data and the R/C' pin is set high. Then the chip select is set low and the information is accessed on the data bus. If the lower four bits of data are also required the operation is performed again with the A0 pin set high.

The problem with this circuit is that it is subject to the voltage drop of the sample and hold amplifier multiplied by the divider error. An alternative circuit eliminates the error by doing the division in the software and utilizing interrupts.

4.5 An alternative A/D control circuit

The circuit depicted in figure 7 utilizes only one sample and hold amplifier which is triggered by the PEAK signal. The PEAK signal also initiates the conversion function of the A/D converter. The sample and hold amplifier simply acts to hold the value at the peak long enough for the MN574A to convert it.

Once the conversion from analog to digital is completed the status signal of the MN574A goes low. The status signal, in conjunction with the LED1 signal can be used to initiate interrupts for the

microprocessor. The A0 pin is tied low and the 12/8' pin is tied high in this circuit which means that the conversion is a 12 bit conversion and the data output is across all 12 data lines. This can be changed and placed under the control of software as long as the A0 line is stable 120 ns before a read or convert operation.

5. STATIC CONCENTRATION TESTS

The photodiode sensor and light source were tested using various static concentration of dye and blood. The tests were used to give an indication of the sensitivity of the instrument to small concentrations of dye. Six concentrations of dye and blood were used, starting with 24 mg/L and ending with 3.1 mg/L.

Two separate identical dye mixtures were prepared. The first was tested at the six concentrations for a total of three times. This procedure was replicated with the second dye mixture.

Along with the solid indocyanine green an aqueous solvent, distilled water, bovine albumin and dog blood were mixed to make the various dye concentrations. The aqueous solvent is packaged with the indocyanine green and is simply sterile water at a typical pH of 6.0. The bovine albumin is used to stabilize the dye. The albumin is available in crystallized form and is dissolved in the distilled water before mixing with the dye. The dog blood is refrigerated blood which had been extracted one month before the test date. Heparin is used as an anticoagulant.

6. RESULTS AND CONCLUSIONS

The results are in the form of three graphs shown in figures 8-10. Figures 8 and 9 are graphs of the 820/940 ratio versus the dye concentration for each replicate. There are three data points representing the 5 ml blood samples tested at each blood dye concentration. Figure is a composite graph of the mean ratio and standard deviation at each concentration.

The correlation between the 820/940 ratio and the concentration appears linear up to the 16 mg/L concentration and then begins to level off. This agrees with other research data which found that the linearity dropped off at 20 mg/L. The points from all three graphs fit the polynomial:

$$(V_{820}/V_{940}) = 1 - .04547C + .001C^2$$

$$C = \text{blood-dye concentration}$$

The small value of the coefficient multiplied by the C^2 term explains the linearity up to the 16 mg/L concentration.

There are several possible sources of error in these tests. If the depth of the tip of the bundle is off only slightly from the previous measurement the ratio can differ as much as 10%. The reflection of light off the inner walls of the test tube is also a source of error. Bending loss of the optical fibers can cause the output of the LEDs at the tip to differ slightly if the bundle does not remain in the same position throughout the test. Better results can be obtained in tests where the

bundle remains static and is not moved from test tube to test tube.

Another source of error is the settling of the blood. The data points in the second two graphs (Figs. 9 and 10) are much closer together, because the blood was mixed thoroughly immediately before testing, and greater care was taken in the placement of the fiber bundle.

The data obtained does clearly indicate that the presence of even minuscule amounts of indocyanine green in blood can easily be detected.

7. ACKNOWLEDGMENTS

This research was performed at the Center for Applied Microcirculatory Research of the University of Louisville. The authors wish to thank Dr. Patrick Harris and Mr. Cary Schooley for their expert guidance throughout the project.

8. REFERENCES

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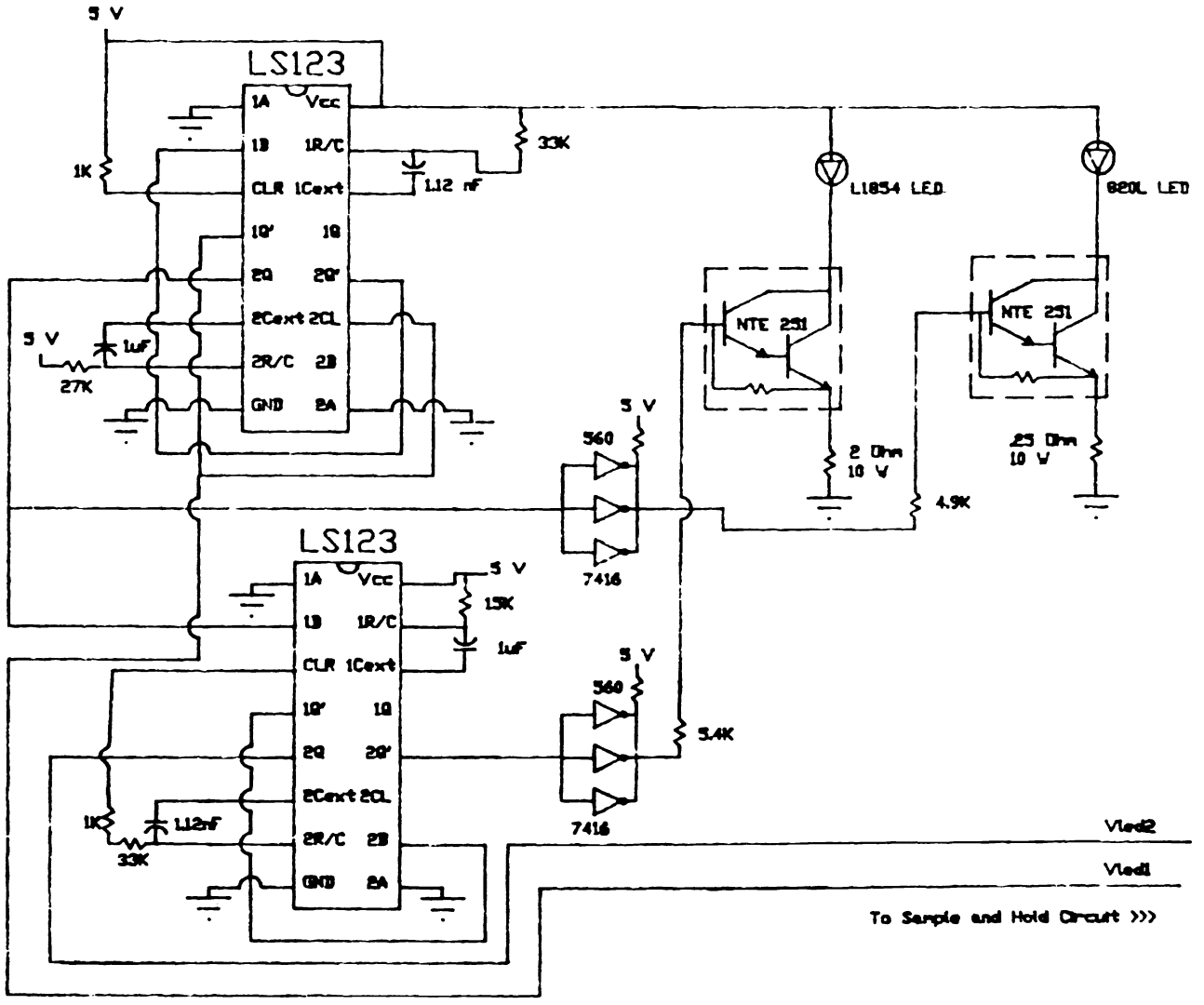

Fig. 1. The schematic of the light source.

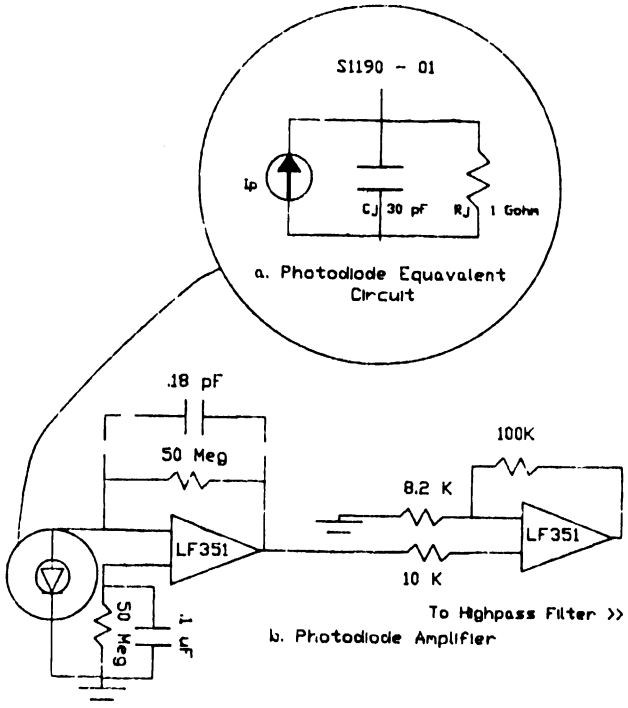

Fig. 2. The photodiode amplifier.

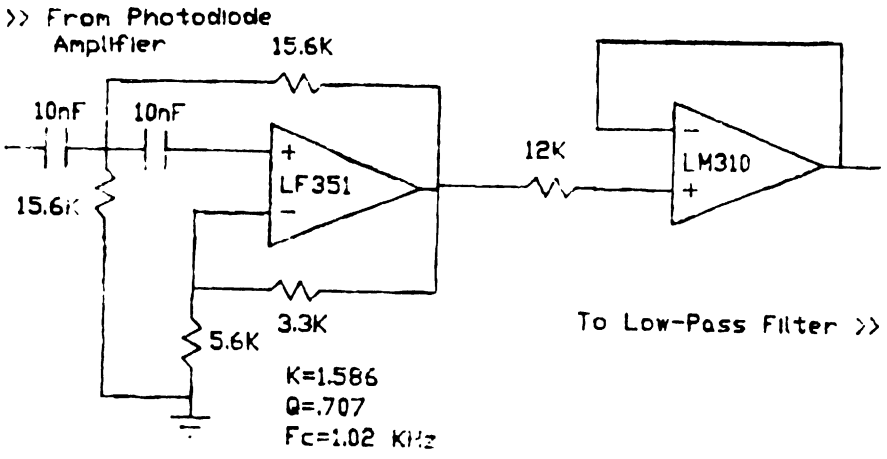

Fig. 3a. Second-order Butterworth high-pass filter.

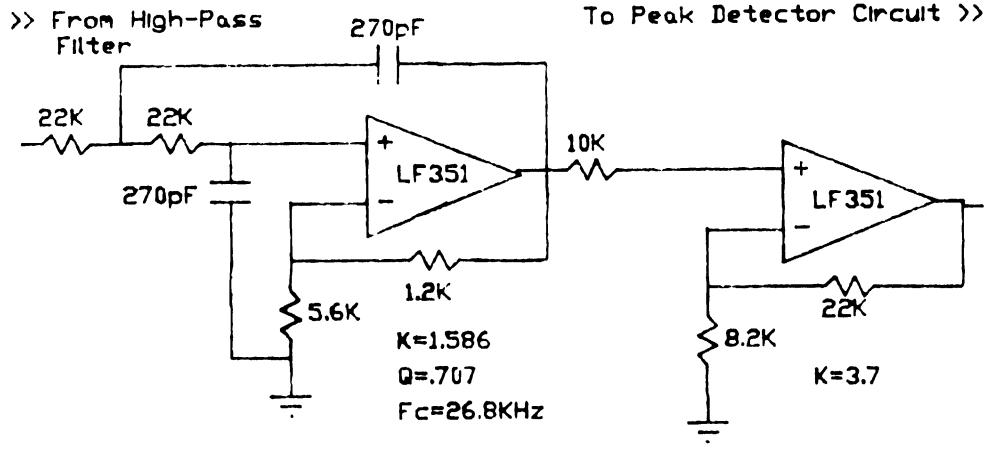

Fig. 3b. Second order Butterworth low-pass filter.

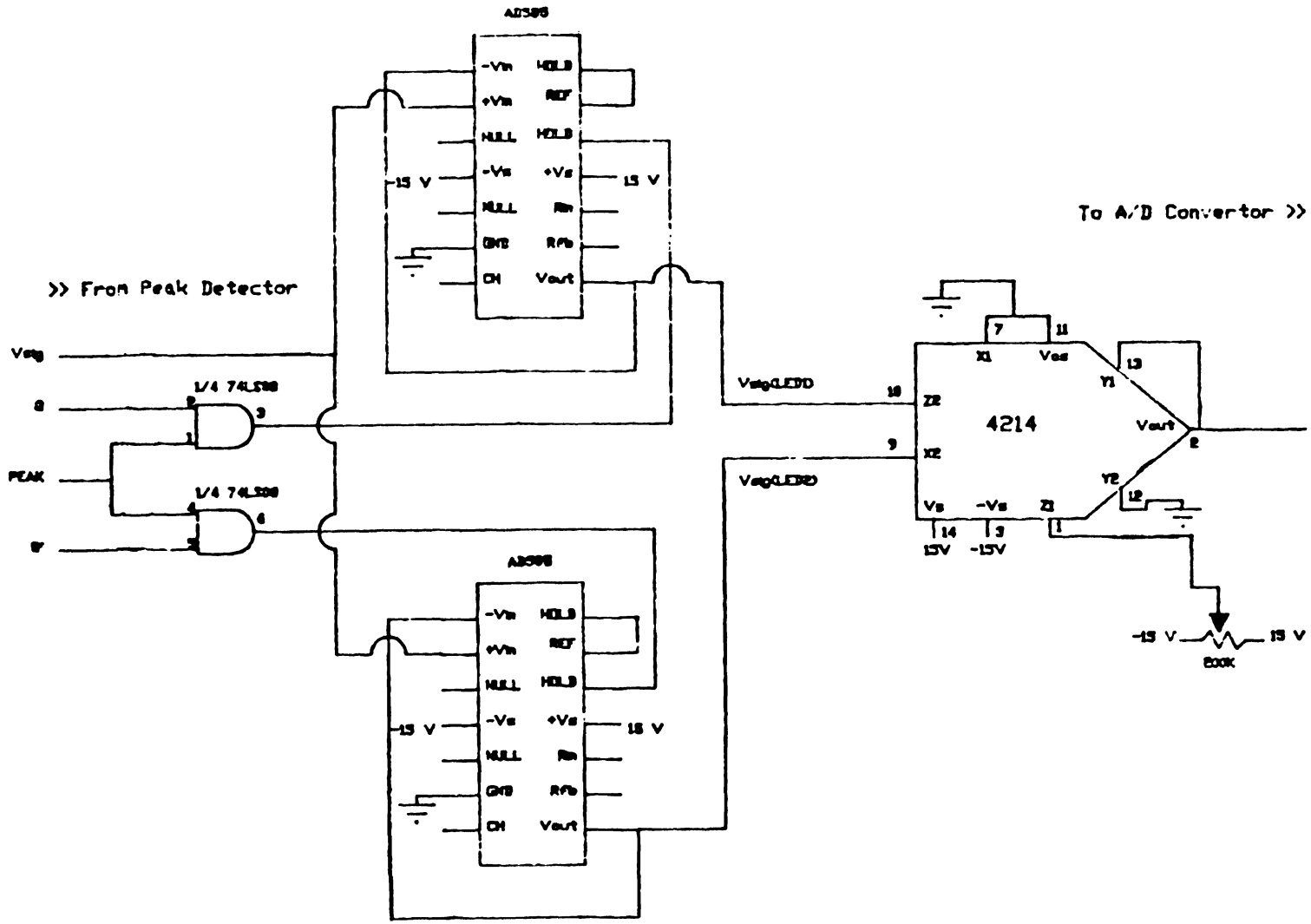

Fig. 4. The sample and hold circuit.

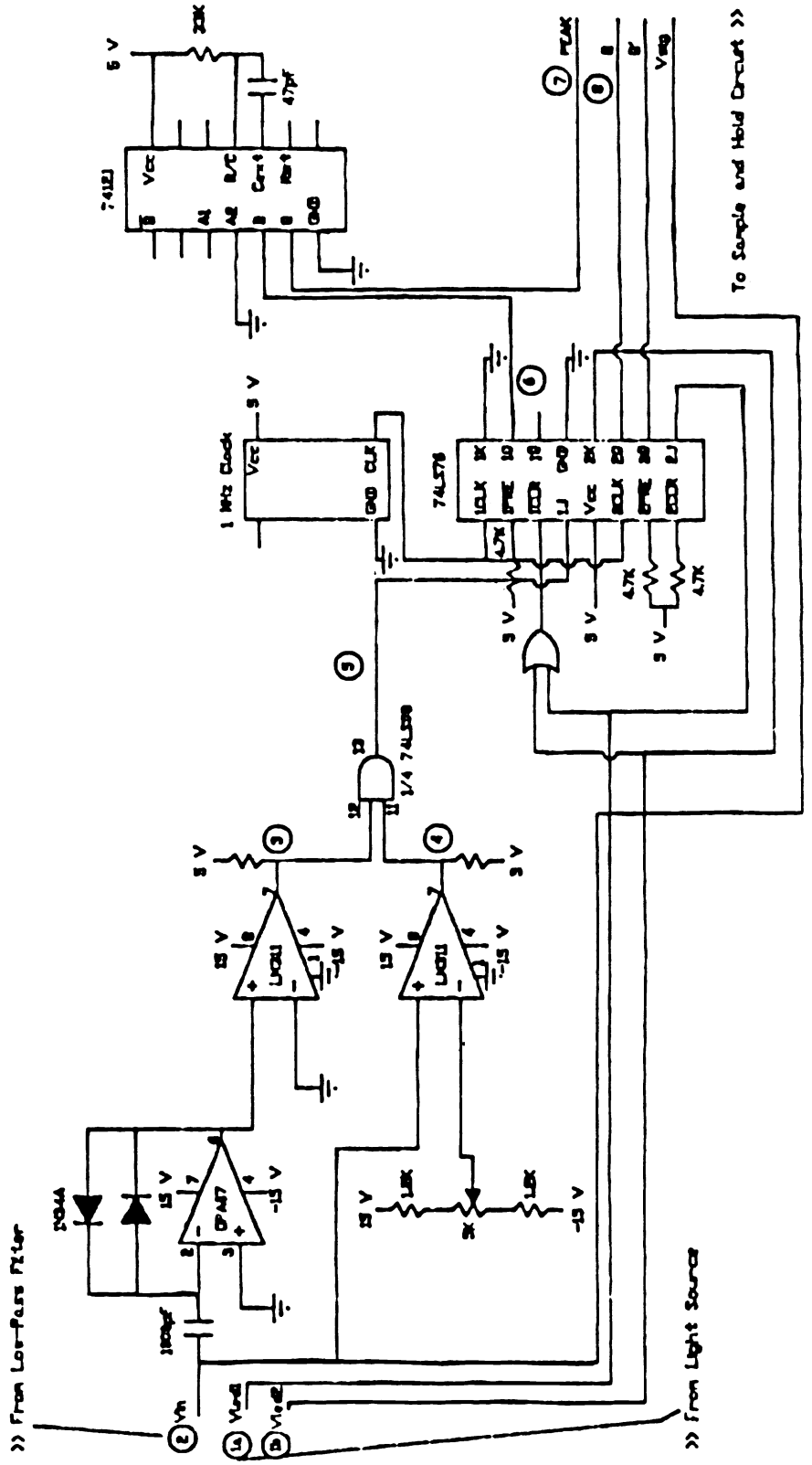

Fig. 5. The peak detector circuit.

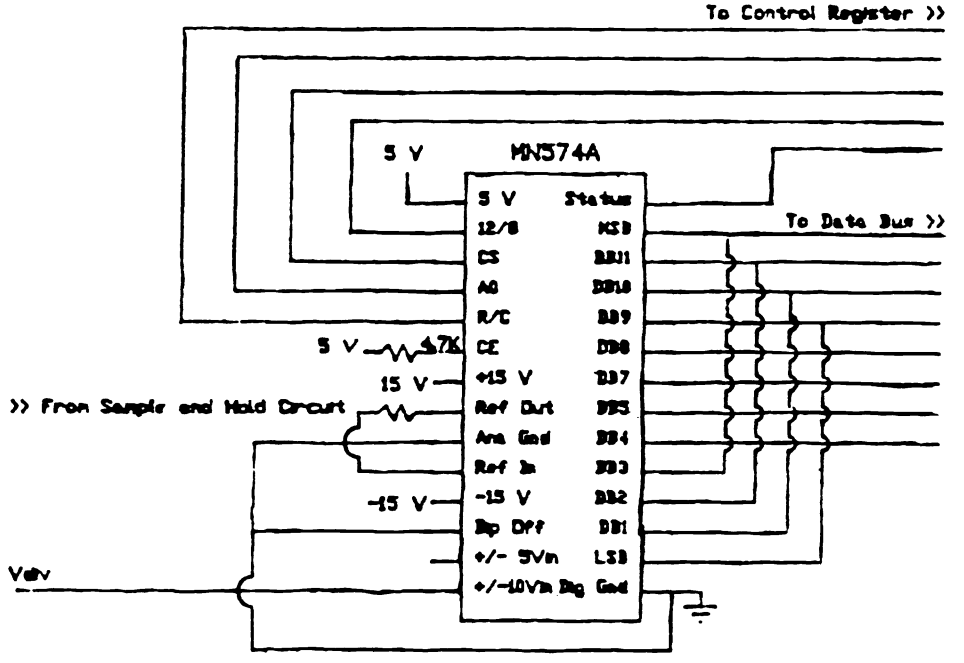

Fig. 6. The A/D control circuit.

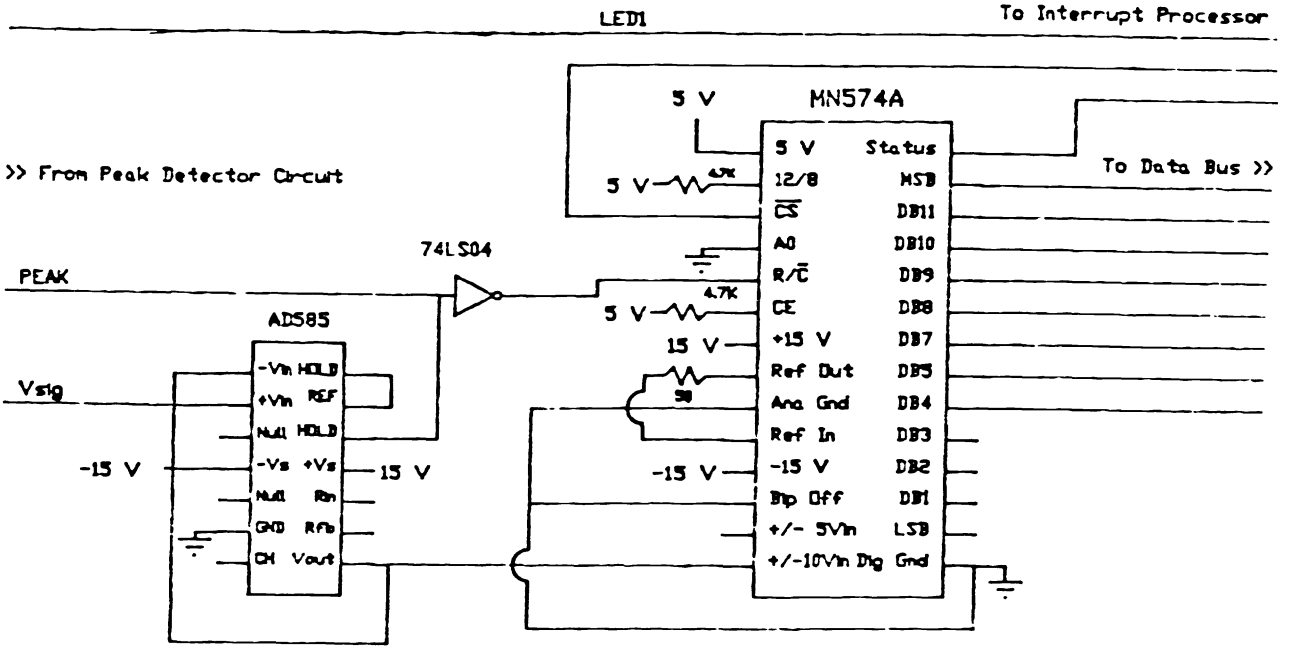

Fig. 7. An alternative A/D control circuit.

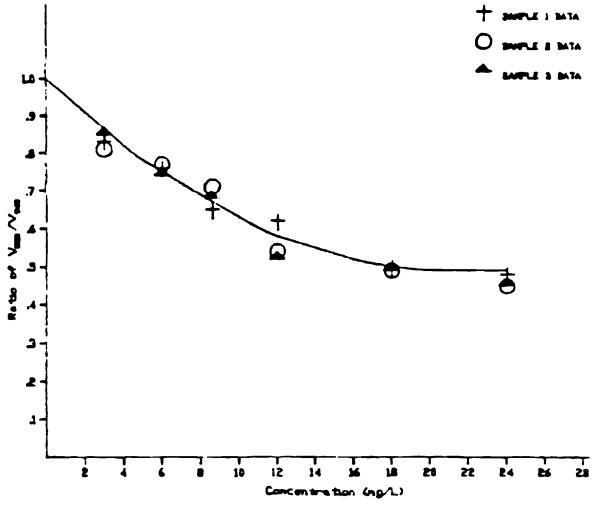

Fig. 8. Data from first replicate.

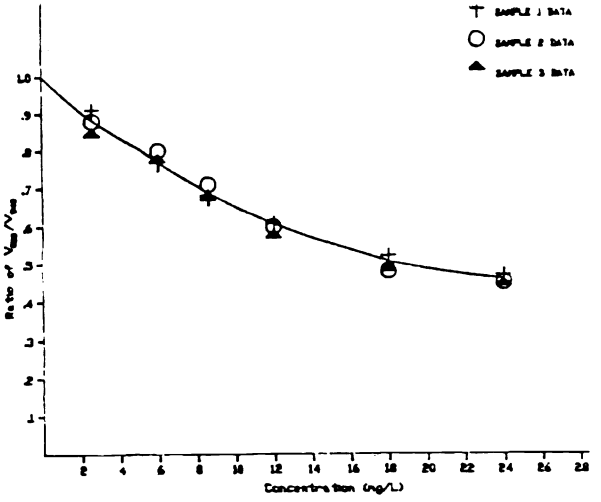

Fig. 9. Data from second replicate.

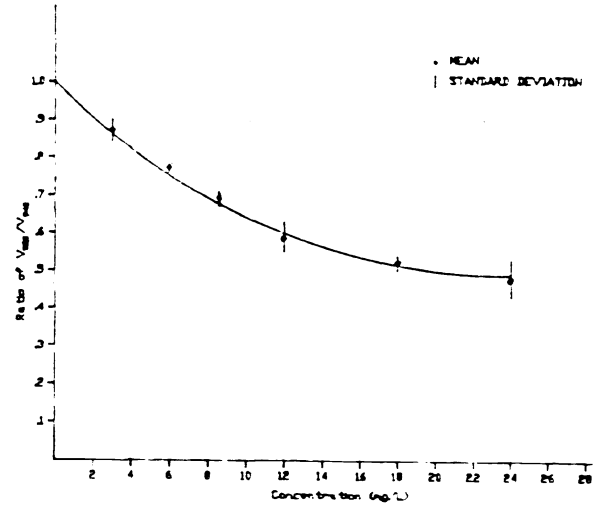

Fig. 10. Mean and standard deviation.