INTRAOCULAR PRESSURE

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The condition of glaucoma is generally accepted by ophthalmologists to be related to excessive internal eye pressure. The intraocular pressure is surprisingly well regulated in the normal human eye to approximately 15 mm Hg (average) above atmospheric pressure, although it is not known whether the system achieves pressure control by controlling the mechanism whereby fluid is added to the eye or by venting fluid through the channels near the edge of the cornea. The measurement of small pressure differences and reliable flows in the animal eye is the subject of investigations that have been undertaken by APL in cooperation with staff members of the Wilmer Institute of The Johns Hopkins Medical Institutions.

The pressure-flow characteristics of the eye have been studied in various specimens, such as rabbits and monkeys, for many years, principally using a graduated pipette attached to a length of plastic tubing connected to a hypodermic needle that can be inserted through the wall of the eye. By elevating the pipette a specified distance above the eye, the intraocular pressure may be slaved to a known fixed value. By observing the change in volume of fluid in the pipette over some interval of time, a measure of additional fluid flow to sustain the

A closed-loop servo system has been developed for studying the pressure-flow characteristics of the eye. The system greatly increases the resolution with which one can control the rate of adding fluid to or removing it from the interior of the eye. It may also be used to slave the eye to a prescribed intraocular pressure and to measure, with high resolution, the rate of fluid flow into the eye required to sustain that pressure.

CONTROL SYSTEM

specified pressure is obtained. This instrumentation technique is very limited in its resolution of flow measurement since the range of flow is so small—typically 1 to 10 μliters/min. Several minutes are required to accumulate sufficient volume change to be read with accuracy. This, of course, raises the question of whether the flow is sufficiently steady for such long-time measurements to be meaningful.

The system described in this paper is an attempt to apply closed-loop servo techniques for measuring flow with much greater precision in very much shorter intervals of time. It also permits an experimenter to choose either pressure or flow as the controlled variable and to observe the behavior of the other. Investigators are also interested in the system for its ability to measure the elastic properties of the eye by the transient response to a step-function change in controlled pressure.

The intraocular pressure control system (Fig. 1), developed by the Applied Physics Laboratory, consists of three basic subsystems: the system of sensing devices; the system of controlling devices and circuitry; and the readout circuitry. These will be described separately and then as they function in the control loops of the system. The system has been developed, tested, and calibrated and is now available for experimental use with animals in the further study of pressure-flow relationships and pressure regulation at the Wilmer Institute.

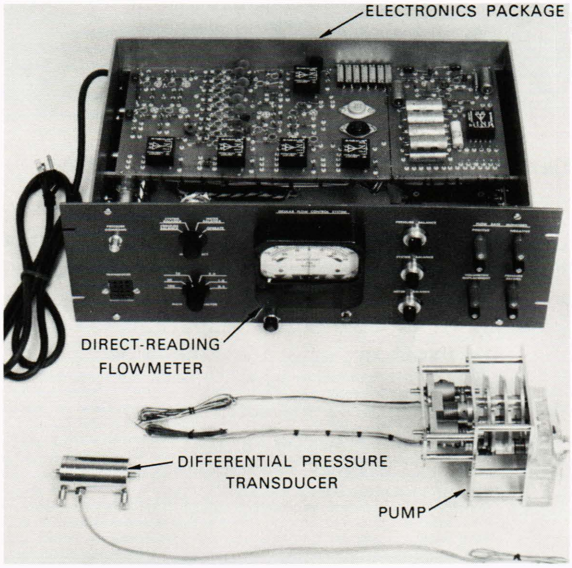

Fig. 1—Intraocular pressure control system.

System of Sensing Devices

Differential Pressure Sensor—The differential pressure sensor provides a measurement of the difference between intraocular pressure P and a known external reference pressure P_0. Development of this unit was based on the principle of unbalancing a reactance bridge by a differential pressure. For this unit, variable capacitance was chosen for the variable arms of the bridge circuit, Fig. 2.

The bridge circuit is excited by a 2-MHz transistorized sine wave oscillator, and the unbalance of the bridge is indicated by means of two halfwave rectifiers and associated filters. The DC voltages associated with each rectifier-filter unit are summed

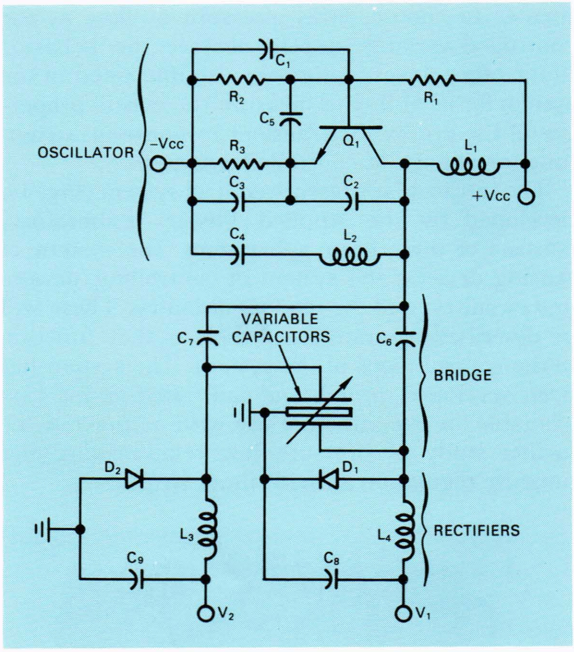

Fig. 2—Internal circuitry of pressure transducer.

algebraically to form a difference voltage indicative of the differential pressure. The use of this voltage will be discussed later in the closed-loop discussions.

As shown in Fig. 3, the capacitance pick-off units are made up of a movable ground plane capacitor plate and two opposing fixed capacitor plates. The former is part of a central shaft that is suspended at each end of the unit by bronze bellows. These bellows are connected directly to the pressure sources P and P_0 so that their difference $(P–P_0)$ will change the spacing between the fixed and movable plates and result in a change in capacitance.

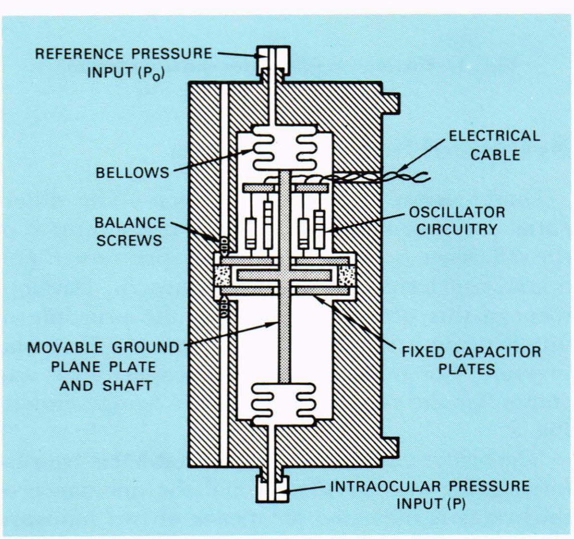

Fig. 3—Differential pressure sensor.

Motor Speed Sensor—The motor speed sensor was developed primarily as a feedback element, necessary to achieve the required dynamic range of fluid flow.

Motor speed indication is achieved by coupling a shaft encoder directly to the drive motor. This encoder produces eight pulses per revolution of the motor shaft, which provides a measure of motor speed in terms of pulse frequency. The pulses produced are generated by rotating two cylindrical capacitor plates past two fixed cylindrical capacitor plates and detecting the rise and fall in voltage that results from the variation in reactance of the elements. A simple logic network between the shaft encoder and the input to the control system determines the motor rotation direction. The eight pulses per motor-shaft revolution are derived from two outputs of the motor speed sensor system, one output representing clockwise rotation and the other, counterclockwise. These two separately phased pulse trains are also filtered to provide the approximate instantaneous readout of fluid flow.

System of Controlling Devices and Circuitry

Fluid Displacement Drive Motor—The drive motor is a 12-volt DC motor that is excited by a push-pull DC power amplifier. This motor serves the following three functions within the system:

1. Mechanical displacement of the pump bellows through a gear reduction of 25,000:1 between the motor shaft and the bellows.
2. Direct drive of the shaft encoder just discussed.
3. Mechanical drive of a dual-ganged readout potentiometer, coupled through a gear reduction of 2600:1 between the motor shaft and the potentiometer shaft.

Fluid Displacement Pump—The fluid displacement pump has a flexible bellows used as a variable capacity storage tank and includes one control port and one deaeration port. This bellows is mounted on two ball screw nuts at one end, with the opposite end secured to a fixed mounting plate, as shown in Fig. 4. As can be deduced from study of Fig. 3, any excitation of the drive motor (not shown) is transferred to the ball drive gears, which in turn rotate the ball screws. This rotary motion is converted (within the ball nuts) to a motion along the axis of the bellows, which causes expansion or contraction of the fluid-filled bellows to form the pumping action.

Shaft Encoder—The shaft encoder was

developed with two purposes in mind. Primarily, this device is used as a servo feedback control element that diminishes motor deadspace for low

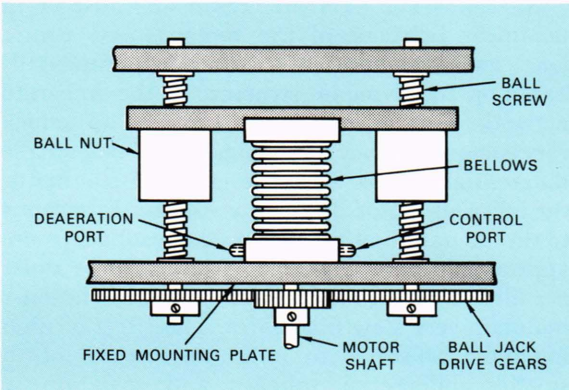

Fig. 4—Ball screw and bellows mechanism of the fluid displacement pump.

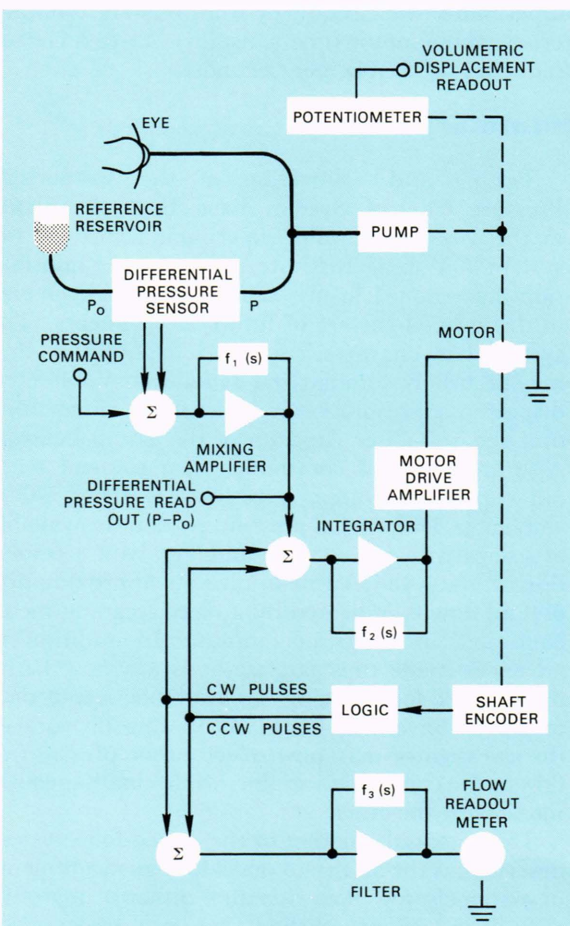

Fig. 5—Schematic of the subsystem of controlling devices.

fluid flow rates. As the motor shaft rotates, pulses are produced by the shaft encoder and interface logic. These pulses are fed back to the input of a control voltage integrator where they subtract from the integral of the input command. Thus, by integrating minute input signals to an output level above the breakaway voltage of the motor, flow can be initiated. In response to this flow, the feedback pulses have a limiting effect by reducing the voltage available to the motor drive amplifier. By this technique, the range of flow control has been expanded by a factor of three.

Secondly, the pulses generated are representative of the flow, both in magnitude and direction, and when summed over time they represent the volume of fluid displacement. The two previoulsy mentioned outputs of the motor speed sensor system differentiate between fluid flow into and out of the eye. Figure 5 depicts the controlling devices and their functional relation to the remainder of of the system.

Readout Circuitry

Volumetric Displacement Readout—As indicated in the discussion of controlling devices and circuitry, each pulse generated by the shaft encoder represents an increment of fluid displacement, to or from the eye, of 3.14 x 10^{-3} μliter; thus, a total of 318 pulses would indicate one μliter of displacement. These two channels of pulses are available at the system front panel for recording or further processing.

A continuous history of the displaced fluid is provided by a dual-ganged potentiometer driven by the control motor. The resistive elements of the two potentiometers are offset by 180° so that one potentiometer is rotating through its linear range during the recycling event of the other potentiometer. The circuitry was developed to select the two linear portions of the potentiometers and to combine these 180° portions to provide two voltage ramps for every 360° of potentiometer shaft rotation. Each 20-volt ramp represents 30 μliters of fluid displacement, hence the readout sensitivity is 1.5 μliters per volt.

Differential Pressure Readout—As shown in Fig. 5, the differential pressure $P–P_0$ can be recorded from the output of the mixing amplifier. Figure 6 shows the relation $P–P_0$ (in volts) plotted against changes in P over the usable range of the pressure sensing element. From these data, a sensitivity K_1 equal to 0.645 volt/mm Hg was derived, which was used as an original design figure around which the control loop was developed. By increasing the voltage gain of the mixing amplifier, we were able to use the more linear portion of the pressure sensor range.

FLOW READOUT—Approximate fluid flow readout is made available by filtering the shaft encoder pulses and displaying this voltage as a front-panel meter reading. Hence a quantitative indication of fluid rates can be observed at any phase of an experiment.

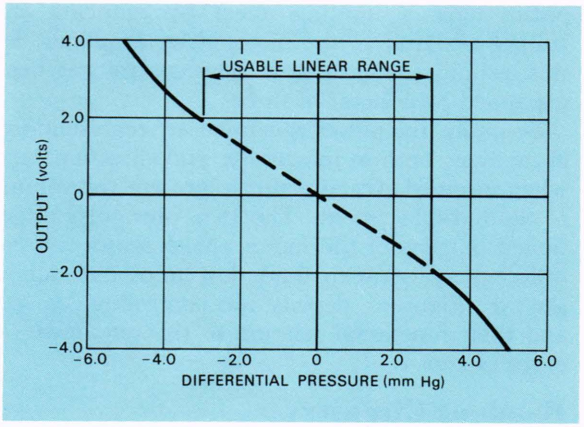

Fig. 6—Sensitivity of differential pressure transducer.

System Control Loops

FLUID DISPLACEMENT CLOSED LOOP—The fluid-displacement control loop consists of the pressure-sensing device, a mixing operational amplifier, an integrator (operational amplifier), a power drive amplifier, and the displacement elements (motor, gears, and pump).

For simplicity we shall assume that the system has been statically balanced, with P adjusted to P_0. The system is then in a null state and will react only to small perturbations around the intraocular pressure P and to small fluctuations due to the minimum velocity control deadspace associated with the integrating circuit.

Now let us make a change in P_0 to a value $P_0+\Delta P$. This change in pressure, ΔP, will result in a differential voltage at the output of the mixing amplifier. It follows that the integral of this voltage will in turn activate the motor and drive the pump mechanism. The action of the pump is such as to increase the volume of fluid on the specimen side of the system, thus increasing the intraocular pressure to a value $P+\Delta P$. After this condition of balanced pressure is realized, the action of the system will be to replace the specimen fluid commensurate with the increased intraocular leakage rate that is caused by the increased intraocular pressure.

The previous discussion does not account for the action of the feedback pulses and their influence in extending the range of fluid rates; however, this extension can be described by next considering the function and development of the motor speed control loop.

MOTOR SPEED CONTROL LOOP—Because of the nonlinear behavior of the motor speed control loop, its closure was determined experimentally, based on the dynamic structure of the integrator network. This network was developed to achieve very slow fluid rates by integrating the smaller differential signals, with the effect of eliminating the inherent motor deadspace voltage. In response to the excitation of the motor, the feedback pulses appear as inputs to the integrator. These pulses are filtered by a time constant properly chosen to maintain very slow fluid rates. The effect of filtering these pulses is to limit the integral of the smaller differential voltages and maintain an average motor excitation voltage just outside of the motor deadspace voltage.

Additional shaping circuitry was developed around the basic integrator, which extends the upper half-power frequency from 0.68Hz (characteristic of the motor time constant) out to a corner frequency of 2.5Hz per second.

Summary

Testing and calibration of the Intraocular Pressure Control System have been completed in the laboratory, and experimental use of the system at Wilmer Institute has provided information that should insure significant improvements in the state-of-the-art of future experiments. The system has characteristics and capabilities that may be briefly summarized as follows: Volumetric displacement resolution is 3.14×10^{-3} μliter/pulse over the 500-μliter capacity of the pump bellows. Also provided is a continuous displacement readout capability whose sensitivity is 0.667 ± 0.01 volt/μliter. Differential pressure readout is available at a sensitivity of 0.645 volt/mm Hg, with a resolution of ± 0.01 volt. An instantaneous approximation of fluid flow is indicated by a direct-reading meter calibrated in μliters per minute. In addition to advances made thus far, methods are now being investigated for reducing the available output data to more convenient forms. With this instrument the investigator may now select either pressure or flow as the controlled variable, while simultaneously monitoring the other.

The potential inherent in the closed-loop system described is the ability to make flow measurements in extremely low flow domains hitherto unattainable. It is well established that requirements for such a capability have long existed in branches of medicine other than ophthalmology as well as in other areas concerned with minute fluid flow.