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Biomedical Implantable Microelectronics

James D. Meindl

Summary. Innovative applications of microelectronics in new biomedical implantable instruments offer a singular opportunity for advances in medical research and practice because of two salient factors: (i) beyond all other types of biomedical instruments, implants exploit fully the inherent technical advantages—complex functional capability, high reliability, lower power drain, small size and weight—of microelectronics, and (ii) implants bring microelectronics into intimate association with biological systems. The combination of these two factors enables otherwise impossible new experiments to be conducted and new prostheses developed that will improve the quality of human life.

The key ingredient of the present electronics revolution has been the microelectronic integrated circuit or microchip (*1*, *2*). From 1960 to 1980 the number of transistors fabricated in a microchip increased from one to more than 10,000, while the cost of the chip remained essentially constant and its reliability improved. This rate of progress is projected to diminish only modestly during the next two decades, and it is likely that innovative applications of microchips in implantable biomedical instruments will result in new opportunities for improving the quality and availability of health care.

Biomedical instruments can be classified according to their orientation relative to the subject and their function (*3*). In the matrix shown in Table 1, implantable instruments installed during surgery (shown in the row marked "subcutaneous") offer a singular opportunity for advances in medical research and practice for two salient reasons: (i) Beyond instruments of all other types, implants exploit fully the inherent technical advantages—complex functional capability, high reliability, low power drain, small size and weight—of microchips. (ii) Implants bring the microchip into a uniquely intimate association with the biological system, thereby enabling otherwise impossible measurements and prostheses.

In most instances custom-designed as opposed to standard integrated circuits and sensors are required for implantable applications. Thus some of the outstanding benefits of low-cost standard microchips are sacrificed. With regard to function, research with implantable instruments is confined almost entirely to animals, whereas diagnostic, monitoring, therapeutic, and prosthetic uses of implants are largely pertinent to human patients and therefore clinical practice. The generic performance requirements imposed on implantable instruments include: (i) small size and weight, (ii) low energy consumption, (iii) low supply voltage, often a single cell battery, (iv) long operating life, (v) high reliability, (vi) very novel sensors and transducers, and (vii) biological compatibility.

Implantable Instruments in Research

Animal models of human disease are indispensable in biomedical research for a host of ethical, legal, scientific, and economic reasons. Implantable telemetry systems are invaluable in animal models because they enable investigators to collect data that are not available from the surface of the body, and to obtain these data over prolonged periods of time when the animal is not anesthetized, restrained, or interfered with in any way. In such research, automated storage techniques can be used for 24-hour data collection. Totally implantable telemetry and telestimulation systems offer an absolute minimum of interference with and by the subject with no risk of infection from percutaneous wires in physiological, pharmacological, and pathological studies of animals. In addition, they provide an essential step in the development of new implantable instruments for use in man.

A block diagram of a general-purpose multichannel telemetry system that is totally implantable is shown in Fig. 1 (*4*). This system is capable of accepting input signals from a variety of transducers in-

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cluding pressure, strain, acceleration, electrical potential, temperature, and *p*H sensors. The subsystem represented within the dashed rectangle is implanted within the body of a laboratory animal. The remainder of the system is externally located, typically within a range of 3 to 10 meters of the animal during periods of data collection. The signal outputs are displayed on a cathode-ray tube and recorded on magnetic tape or a paper strip chart.

Internally, the six input-stage preamplifiers and the 10- to 15-kilohertz oscillator and its output stage are implemented in a single custom-made microchip. The radio-frequency (RF) telemetry transmitter is a second custom-made chip that transmits at frequencies up to 125 megahertz using either frequency or pulse modulation. The counter is a commercially available chip. The command receiver is an RF controlled elapsed-time power switch operating in the 27-MHz citizens band. Its standby power drain is relatively small (7 microwatts). Upon activation by a 0.5-second RF burst from the external command transmitter, the

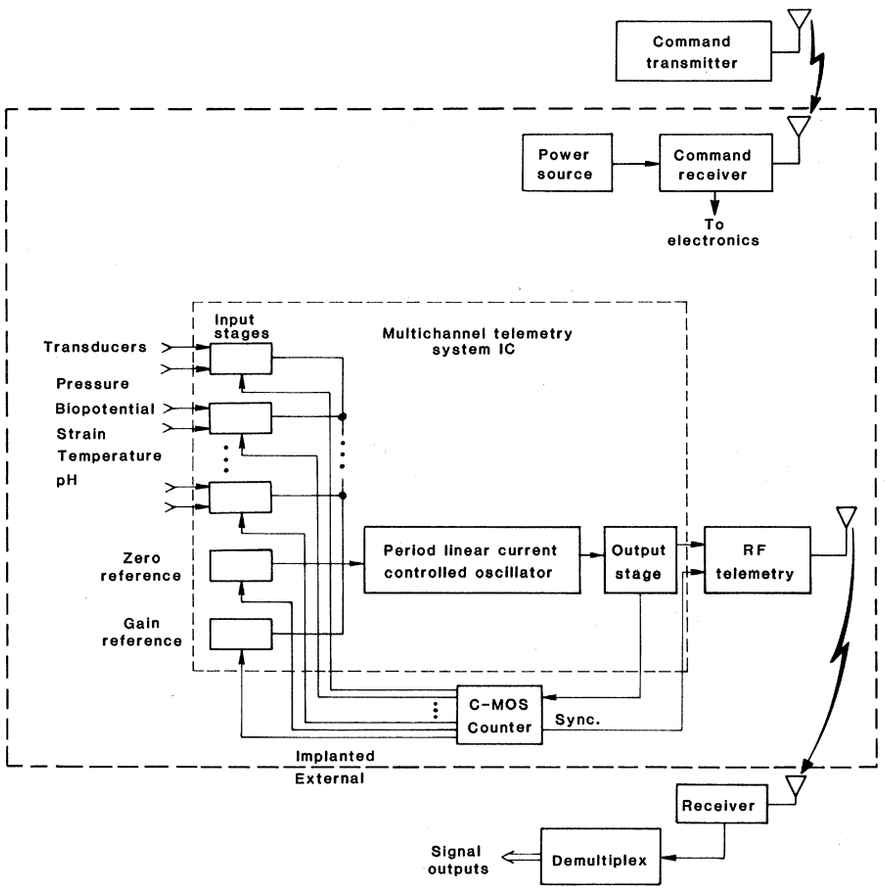

Fig. 1 (left). Block diagram of a multichannel telemetry system. Fig. 2 (right). Elapsed-time power switch.

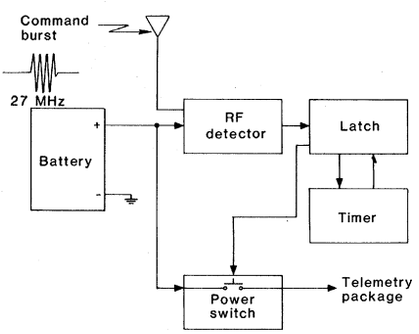

Table 1. Biomedical instrument matrix.

Location	Function				
	Research	Diagnostic	Monitoring	Therapeutic	Prosthetic
Subcutaneous	Microelectronics for totally implantable telemetry of flow, pressure, and dimension, for example	Totally implantable telemetry for coronary bypass graft monitoring	Cerebral pressure telemetry microtransducers and electronics	Microelectrodes for neural stimulator for pain relief	Cardiac pacemaker microelectronics; auditory prosthesis microelectronics
Supercutaneous	Microtransducers for animal backpack telemetry of flow and pressure, for example	Ingestible *p*H telemetry capsule	Ambulatory care ECG telemetry with active microelectronics	Microelectrodes and electronics for bladder stimulator	Hearing aid
Percutaneous	Implantable biopotential and temperature microtransducers with externalized leads	Catheter-tip blood gas sensor	Transvenous pacing lead for monitoring and stimulation; catheter-tip pressure sensor	Electrical stimulation of bone for enhanced healing	Microsensors for left ventricle assist device
Transcutaneous	Gamma ray microtransducer arrays for radioisotope imaging; blood pressure sensor array with piezoresistive microtransducers	Computerized x-ray tomography detector arrays	Piezoelectric transducer arrays for ultrasonic imaging; blood gas monitor microsensors	Microtemperature sensors for hyperthermia; microsensors for defibrillators	Microoptical sensors and tactile stimulators for optical-to-tactile reading aid for the blind
Extracutaneous	Electron microscope	Mass spectrometer; cell sorter	Miniature silicon gas chromatograph for breath analysis	Microsensors for kidney dialysis machine	Voice-actuated wheelchair controller

power switch serves to connect the single cell lithium-iodide power source to the telemetry electronics for a preselected self-timed data collection interval of several minutes after which the switch automatically disconnects the power source. A block diagram of this elapsed-time power switch is illustrated in Fig. 2. A low duty cycle enormously prolongs the useful operating life of the implanted unit. Colocation of the command receiver in the throwaway sealed assembly with the battery precludes leakage current in the cable to the telemetry electronics during quiescent periods. The telemetry electronics itself is hermetically sealed in a 2.5 by 2.5 by 0.4 centimeter flat package typically used for artificial pacemaker electronics.

For long-term measurements of blood pressure, a stable miniature transducer is particularly important. A capacitive transducer with on-chip microelectronics is a promising new approach illustrated in Fig. 3 (*5*). A thin silicon diaphragm approximately 1.0 millimeter in diameter and 5.0 micrometers thick is etched in the 3.0 by 3.0 mm chip and serves as the deflecting plate of a variable capacitor with the fixed plate deposited on the glass cap which forms with the silicon chip a hermetically sealed evacuated reference chamber. Signal preprocessing electronics are incorporated in the chip with the diaphragm to convert the change in capacitance to a change in frequency, thereby eliminating noise and drift caused by leakage in the cable connecting the sensor chip and the nearby telemetry electronics package.

Among the major physiological parameters not yet telemetered with narrow bandwidth multichannel systems such as illustrated in Fig. 1 are blood flow and dimensions (volume and velocity). Ultrasonic transducers appear to hold the most promise for these measurements. [Totally implantable electromagnetic flowmeters are precluded in many applications by their very large current requirements and baseline instability (*6*).] A key requirement of ultrasonic flow and dimension measurements is the relatively large bandwidths of the "video" signals present prior to signal demodulation; demodulation is done externally because of the complexity and bulk of the necessary circuitry (*4*). To achieve sufficient range resolution or accuracy in the measurement of either blood velocity profiles by means of a pulsed Doppler ultrasonic flowmeter or dimensions by transit time of ultrasonic pulses, typical pulse lengths must be less than 1.0 microsecond corresponding to a distance of 1.5 mm in tissue. These pulses are transmitted across the skin by a short-range (3 to 10 cm) inductively coupled data link rather than an RF link. With the use of more advanced integrated circuits, internal signal demodulation may be feasible in the future. This would reduce the telemetry bandwidth to the narrow 0.1- to 20-hertz range of most physiological measurements.

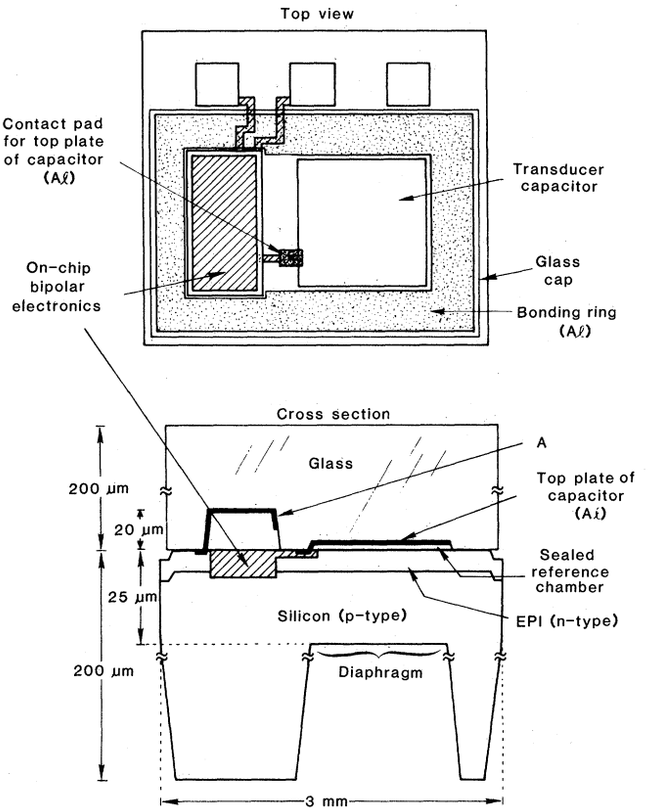

Fig. 3. Structure of capacitive pressure sensor.

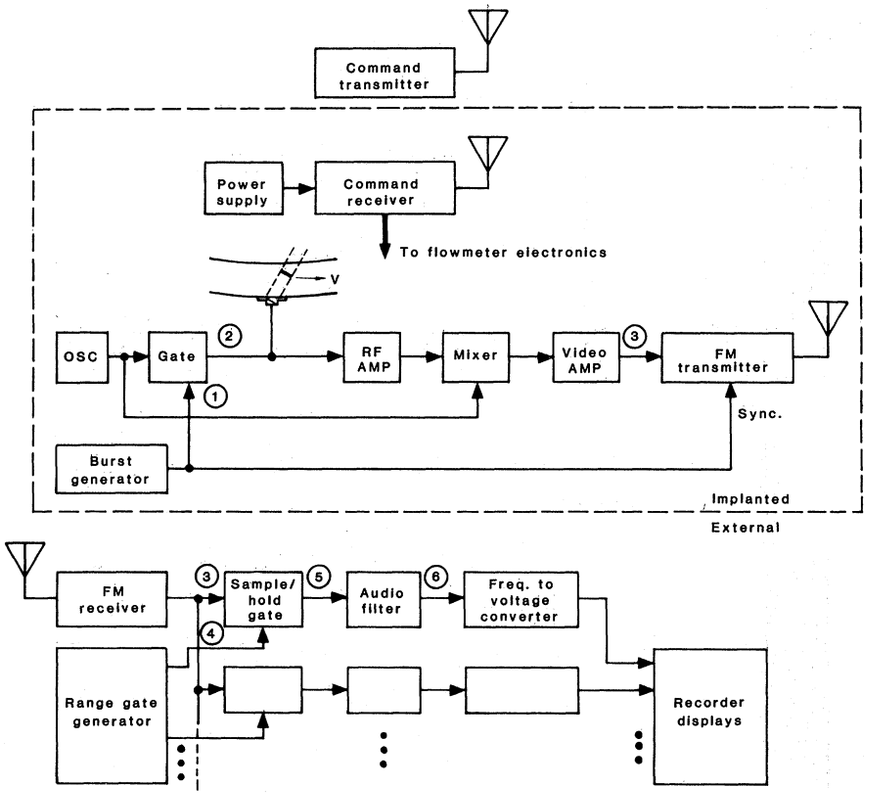

Fig. 4. Block diagram of an implantable flowmeter.

A block diagram of an implantable bidirectional ultrasonic flowmeter capable of measuring instantaneous blood velocity profiles and hence volume flow is illustrated in Fig. 4 (*4*). In this instrument the oscillator, gate, and burst generator provide a short (1.0 μsec) burst of high-frequency (6.0 MHz) excitation to the single piezoelectric transducer. For a relatively long interval (50 μsec) after each transmitted pulse, the scattered and Doppler-shifted signals returning to the transducer as the ultrasonic pulse traverses the vessel are processed by the RF amplifier, mixer, and video amplifier and then telemetered to the external electronics. Because the velocity of sound in blood is well known, the Doppler frequency shift in the returning signals at any instant corresponds to blood velocity at a particular point of the lumen. Instantaneous recordings of blood velocity from eight different points across the aorta of a dog with a transplanted heart are illustrated in Fig. 5. The area integral of the velocity profile gives an accurate estimate of volume flow.

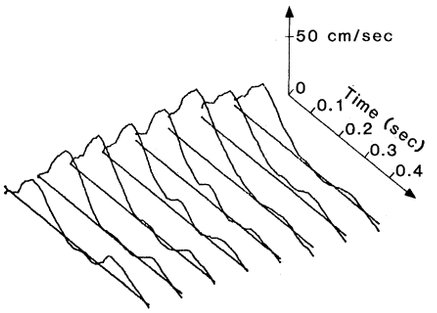

Fig. 5. Instantaneous blood velocity at eight different points across the aorta of a dog with a heart transplant.

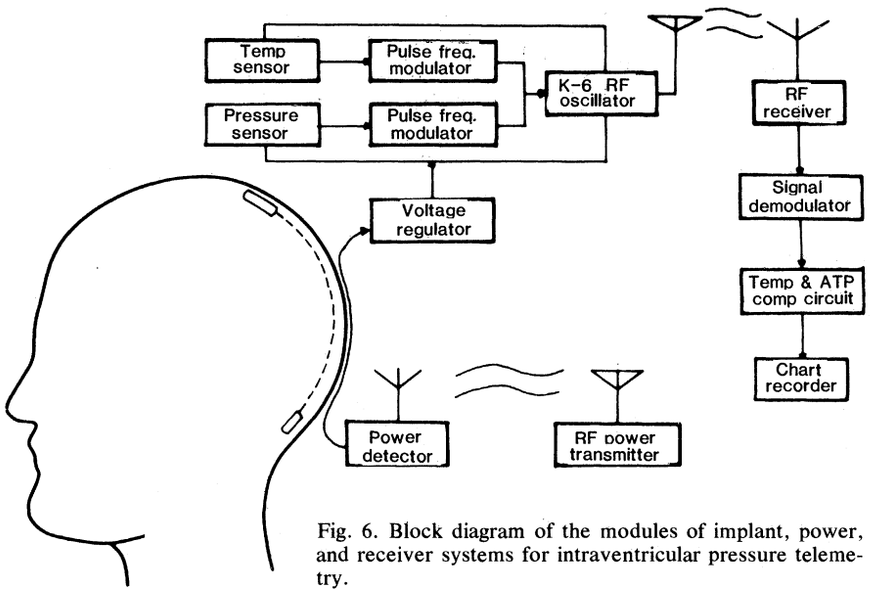

Fig. 6. Block diagram of the modules of implant, power, and receiver systems for intraventricular pressure telemetry.

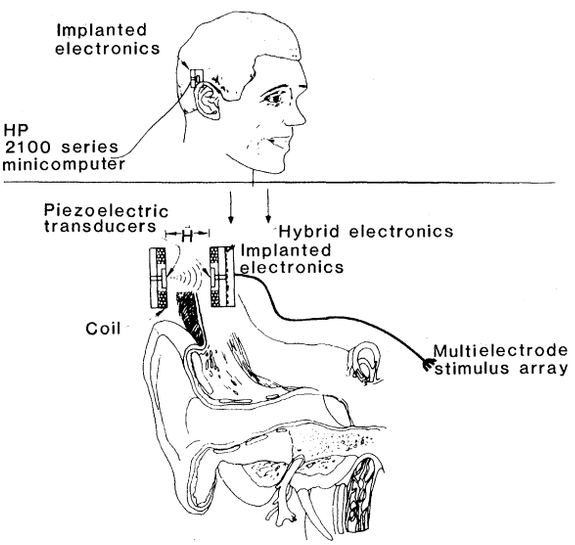

Fig. 7. Physical configuration of auditory prosthesis.

Implantable Instruments in Practice

In medical practice, the ideal diagnostic instrument provides definitive data on the condition of a patient, causes the patient no harm or discomfort, and is convenient, reliable, and economical for a medical practitioner to use. Since implants do not readily satisfy these criteria, they are not ordinarily used for diagnosis per se. However, ingestible telemetry pills, although not implanted, are used for diagnostic purposes, and, since they are entirely enclosed by inner surfaces of the body, they are subject to a set of performance constraints very similar to those of implants (*7*).

In addition to fulfilling all the requirements of an ideal diagnostic instrument, the ultimate monitoring instrument imposes the stringent requirement of virtually total freedom from the need for attention of a human for extended periods of time. Because of their invasive character, implants are most frequently used for monitoring patients who have had surgery. For example, an implant can avoid the necessity for periodic skull surgery for measurement of intracranial fluid pressure in a hydrocephalic child with a surgically installed shunt (*8, 9*). A block diagram of a batteryless implantable system for long-term monitoring of intraventricular pressure after neurosurgery is illustrated in Fig. 6. Inductive power at 3.5 MHz is beamed into a power detector, and pressure and temperature modulated RF is returned by way of the 120-MHz oscillator. The receiving system provides readout of intracranial pressure and transducer temperature in order to compensate for temperature changes.

Implants are used for therapeutic purposes to provide chemical, electrical, and mechanical stimuli designed to have remedial functions. Typical examples are (i) small electric currents to accelerate bone healing (*10*), (ii) strain gages to measure axial forces in Harrington rods for correction of scoliasis (*11*), and (iii) spinal cord electrical stimulation for relief of chronic pain (*12*).

By a wide margin, the most common implantable electrical prosthesis is the artificial cardiac pacemaker, a device that is vital to many patients (*13*). This battery-powered electronic device has been used in patients for treatment of chronic heart block since 1960. It is estimated that over 100,000 are installed annually in the United States alone. The earliest artificial pacemakers were simple regenerative pulse oscillators which applied fixed-rate asynchronous electrical stimulation to the heart. An early ex-

tension of this basic asynchronous system was the provision of rate adjustment by use of a magnet held against the skin. Following this, the synchronous pacemaker was introduced. Essentially, it is an electrocardiogram (EKG) preamplifier plus a pacemaker pulse generator that uses an extra sensing electrode. The EKG preamplifier senses a central nervous system signal, at the atrium, and responds by triggering the pulse generator, causing it synchronously to stimulate the ventricle.

A third approach to pacing is represented by the demand pacemaker. It senses the presence of a natural EKG signal. Should this signal exist, the demand pacemaker becomes inhibited for about 1.0 second, after which it fires asynchronously if a second natural EKG cycle is not in progress. Thus, the device operates on demand and does not stimulate in response to atrial arrhythmias as the synchronous pacemaker may. More recent pacemaker developments have included a dual-demand pacemaker which is designed to perform sequentially both atrial and ventricular sensing and stimulation. Transcutaneous programming of rates and stimulating currents is also coming into use. Modern pacemakers rely heavily on microchips for their advanced performance.

Other clinical applications of chronically implantable electrical stimulation systems include (i) bladder (*14, 15*) and muscle (*16*) stimulators for paraplegic patients, (ii) carotid-nerve stimulators for alleviation of hypertension (*17*), and (iii) dorsal column stimulators for electrical inhibition of pain (*12*). In these applications the stimulation can either be applied intermittently or can be temporarily suspended without grave consequences to the patient. Thus, the use of batteryless implants with transcutaneous inductive coupling of electrical power is common. Major concerns in such stimulators include the electrodes and the possibility of tissue damage (*18*). Requirements for metal electrodes include (i) minimal corrosion in the body, (ii) good fatigue resistance, and (iii) minimum body reaction to limit the increase of threshold. Electrical stimulation with "nontoxic electrodes" can cause tissue damage as a result of (i) gas generation brought about by large current density, (ii) heat generation at the electrode site, (iii) toxic material generated by an electrode-chemical reaction at the electrode site, and (iv) mechanical stress induced by the electrode assembly.

Opportunities for the use of advanced electrical stimulation systems as neural prostheses can be enhanced substantially by using integrated-circuit technologies to produce microelectrode arrays (*12–21*). Such arrays are being applied to a cochlear prosthesis for the profoundly deaf (*22–24*). As illustrated in Fig. 7, this implantable system uses the unusual approach of an RF link for transcutaneous power transmission and an ultrasonic link for information transmission in order to reduce interference between the two links.

Feasibility studies of a visual prosthesis incorporating multielectrode stimulation of the visual cortex have been reported (*25–27*). Substantial advances on many fronts are required for such a prosthesis to become practical.

In addition to neural prosthetic devices, a variety of other types using electronics are being pursued. Among them are artificial hip telemetry devices (*28*), the artificial heart (*29*), and the artificial pancreas (*30, 31*).

For many humans the quality of life is greatly diminished by loss of some natural function. Heart block, paralysis, chronic pain, loss of a limb, deafness, and blindness are afflictions suffered by many. The powerful and compact sensory, computational, and display capabilities of microelectronics make possible exciting new avenues for prostheses to remedy these functional deficiencies.

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