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Authors
Wise, Kensall D
Angell, James B
Starr, Arnold

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An Integrated-Circuit Approach to Extracellular Microelectrodes

KENSALL D. WISE, MEMBER, IEEE, JAMES B. ANGELL, FELLOW, IEEE, AND ARNOLD STARR

Abstract—**This paper describes a new multielectrode microprobe which utilizes integrated-circuit fabrication techniques to overcome many of the problems associated with conventional microelectrodes. The probe structure consists of an array of gold electrodes which are supported on a silicon carrier and which project beyond the carrier for a distance of about 50 μ to allow a close approach to active neurons. These electrodes are covered with a thin (0.4-μ) layer of silicon dioxide which is selectively removed at the electrode tips using high-resolution photoengraving techniques to define the recording areas precisely. The processing sequence described permits any two-dimensional electrode array to be realized. Interelectrode spacings can be accurately controlled in the range from 10 to 20 μ or larger, and electrode-tip diameters can be as small as 2 μ.**

An equivalent-circuit model is developed for the probe structure which allows its performance to be predicted. The stray capacitance from electrode to ground (and corresponding signal attenuation) is very low for the present structure, and interelectrode coupling is virtually negligible. Preliminary tests using these probes in the brain have shown them to be well suited for recording from small populations of neurons, and they have successfully recorded spike discharges from isolated neurons in cat cortex.

INTRODUCTION

THE RECORDING of bipotentials generated by individual nerve cells has proved to be one of the most important techniques for research on the central nervous system at the cellular level, and the design of recording amplifiers and other instruments to aid in the processing and interpretation of these signals has received wide attention. The techniques for fabricating the microelectrodes used to couple the biological and electrical systems have changed little over the last twenty years, however, and the limitations imposed by these techniques are among the foremost instrumentation problems in neurological research. This paper reports a new multielectrode microprobe which utilizes the fabrication techniques of microelectronics to overcome many of the problems associated with conventional electrodes.

Presently used conventional microelectrodes may be classed as either metal electrodes or glass micropipettes; the tip configurations for these electrode types are shown in Fig. 1(a) and (b). For a metal electrode the recording area is confined to a small site at the electrode tip by a thin layer of insulation. The glass pipette is filled with a concentrated electrolyte and contacts tissue electrically through a fluid junction at the pipette tip. The construction of either of these conventional microelectrodes is generally considered to be "art," however, because the fabrication techniques used impose inherent limitations on the precision and reproducibility of the resulting tip sizes, shapes, and impedance levels. For comparison, Fig. 1(c) shows the glass-insulated gold electrode developed as part of the work to be described in this paper. This electrode differs from previously described glass-insulated metal electrodes [1], [2] in several respects, the most important of which is that, unlike conventional electrodes, its physical dimensions can be closely controlled using integrated-circuit technology and, in fact, can be designed for a given application. This control makes the microprobe structure suitable not only for single electrodes but for multielectrode probes as well.

This paper first reviews the microprobe design. Subsequent sections deal with the fabrication and electrical characterization of the probe structure and with the results of tests in which the microprobes have been used to record from single neurons in cat cortex.

A MICROPROBE USING INTEGRATED-CIRCUIT TECHNOLOGY

A. Design of the Microprobe Structure

The microprobe shown in Fig. 1(c) was designed specifically for extracellular biopotential recording in the brain. The gold electrode is formed on a SiO_2-covered silicon carrier, which provides the needed mechanical strength, and it is insulated from the extracellular electrolyte by a thin layer of deposited silicon dioxide. This deposited film is selectively removed at the electrode tip to form the recording area. The insulated electrode projects beyond the silicon carrier for a short distance (10 to 50 μ) to minimize tissue damage at the recording site.

Silicon is a good choice for the supporting carrier since its technology is well developed, and it has good mechanical strength. Silicon dioxide, a glass, occurs as its natural oxide and renders it passive in body electrolytes. In addition, it can be accurately shaped and is now commercially available in wafers as thin as 50 μ.[1] These wafers are strong enough to be processed without breakage and are well suited as a starting material for probe fabrication. The use of a silicon carrier is also compatible with the eventual integration of source-

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K. D. Wise and J. B. Angell are with the Department of Electrical Engineering, Stanford University, Stanford, Calif.

A. Starr is with the Department of Neurology, Stanford University, Stanford, Calif.

[1] For example, Monsanto Monthin Silicon, Monsanto Company, St. Louis, Mo.

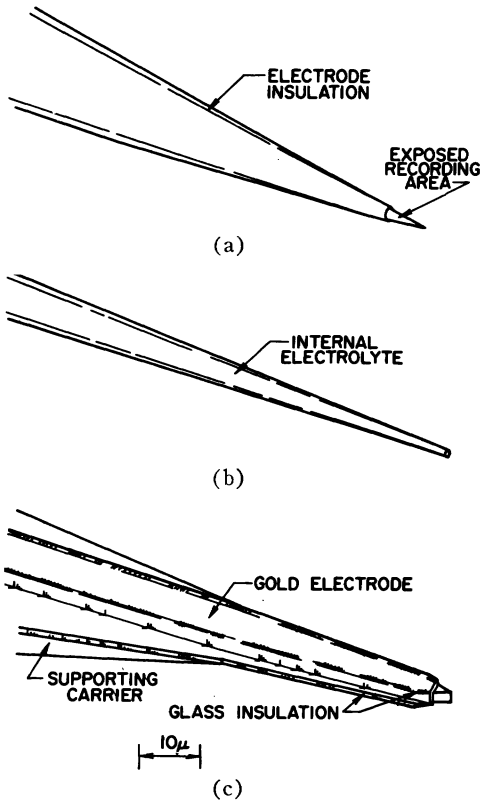

Fig. 1. Microelectrodes used for biopotential recording. (a) Metal electrode. (b) Glass micropipette. (c) Gold microprobe.

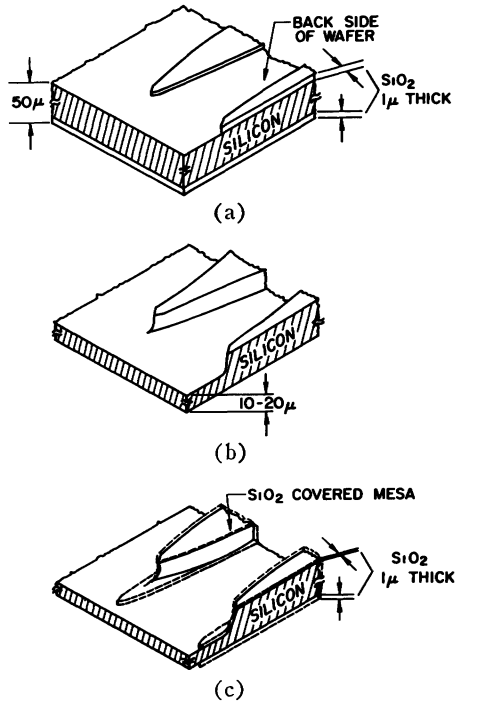

Fig. 2. Preparation of the silicon substrate. (a) Initial oxide mask. (b) Mesas formed. (c) Final substrate.

follower preamplifiers on the carrier with the electrodes. Such integration should minimize stray coupling and noise pickup and should virtually eliminate interelectrode coupling on multielectrode probes.

Gold was chosen as the electrode metal because of its low exchange-current density in biological fluids and its proven suitability for high-resolution electroforming. Although gold has been widely used for macroelectrodes, its low mechanical strength has not permitted its use for microelectrodes in the past. Since in the approach described here the electrode is supported by the silicon carrier, the low mechanical strength of the gold itself is no longer a problem. A thin film of nickel is used to join the gold electrodes to the silicon–dioxide base layer since the adherence of gold directly to silicon dioxide is weak.

The selection of silicon dioxide for electrode insulation is a natural one from both a biological standpoint and from processing considerations. Glass, of which silicon dioxide (fused quartz) is a highly purified form, has been used extensively as an electrode material in the past. In addition, it is one of the few insulating materials which can be deposited in thin uniform films and controllably etched using planar photoresist techniques.

The next section summarizes the processing steps developed to permit the realization of the microprobe structure with the precise dimensional control required in this application.

B. The Fabrication Sequence

The precise dimensional control realized for the microprobe structure is obtained through the use of photoresist, an acid-resistant light-sensitive lacquer. This material permits the high-resolution photoengraving and electroplating operations on which the processing sequence is based to be performed reliably. These same photoresist techniques are also a critical part of the fabrication of all integrated circuits and have now been developed to the point where dimensions can be controlled to a precision approaching 1μ.

The microprobe fabrication sequence basically consists of four parts: 1) substrate preparation, 2) metalization, 3) insulation, and 4) finishing. The starting point is a silicon wafer (50 μ thick) which has been thermally oxidized. Using a photolithographic process, registration marks are first placed on the two sides of the wafer in precise ($\pm 5\ \mu$) alignment with each other. These marks are used as points of reference in the positioning of all subsequent processing masks. Another photoresist operation is now used to define an oxide pattern in the shape of the eventual carrier on the back side of the silicon wafer [Fig. 2(a)], and this pattern is used as an etch mask as mesas are formed by etching the silicon to a depth of 25 to 35 μ [Fig. 2(b)].

The wafer is next reoxidized, and oxide patterns are defined on the two sides of the wafer as shown in Fig. 2(c). The topside pattern will form the insulating base for the electrode while the back-side pattern will be used as the final etch mask in shaping the silicon carrier. A photomicrograph of the reverse side of one wafer is shown in Fig. 3 at this stage in the processing. If active devices were to be integrated on the carrier, such integration would now proceed by the usual techniques. If, however, no such devices are to be included, then the wafer is ready for metalization.

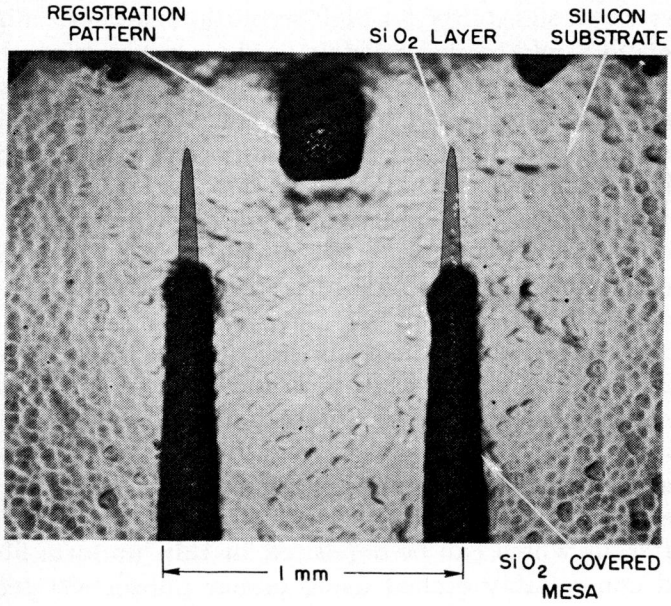

Fig. 3. Photomicrograph of a prepared substrate.

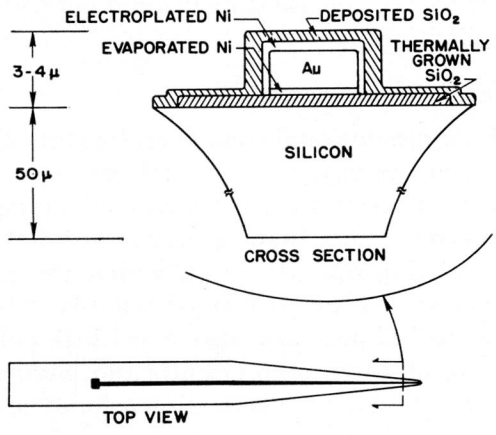

Fig. 4. Cross section of a single-electrode microprobe.

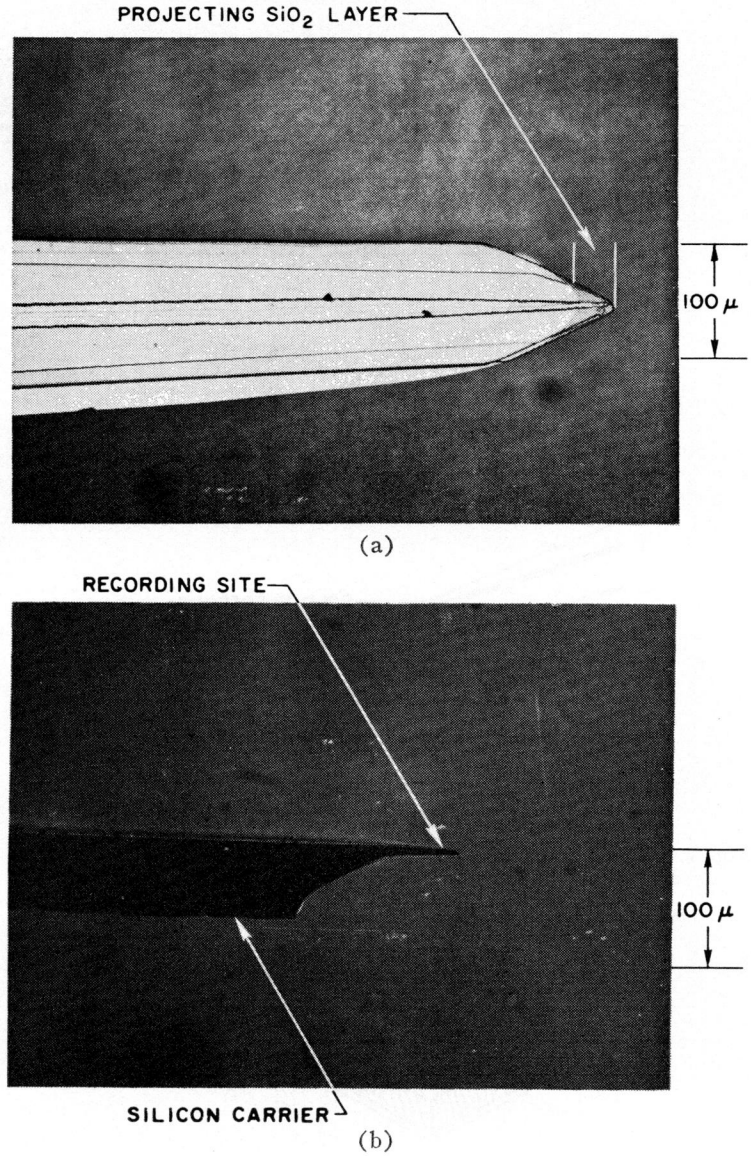

Fig. 5. Photomicrographs of a single-electrode microprobe. (a) Top view. (b) Side view (profile).

The metalization structure for a single-electrode probe, shown in Fig. 4, is realized as the result of a detailed sequence of plating and etching steps. It is important to point out here that since the electrode is defined by a photolithographic process, its size and shape can be closely controlled. Electrode tip diameters as small as 2 μ have been achieved. The thin (1000 to 1500 Å) nickel film surrounding the gold electrode in Fig. 4 is used to promote adherence between the electrode and the SiO_2 as mentioned earlier.

A thin layer of SiO_2 insulation is next deposited over the wafer using a radio-frequency glow-discharge system similar to that described by Swann *et al.* [3] This technique allows thin uniform films of high quality glass to be deposited at temperatures less than 300°C. Following the deposition, another photoresist operation is used to allow the selective removal of the deposited SiO_2 to form a recording site at the electrode tip. Since photoresist line edges can currently be controlled to within ± 1.5 μ, good adherence between the photoresist and the deposited oxide is especially important in achieving precise recording-area definition. The use of thin deposited oxide films is advisable to minimize etching times, and a film thickness of 3000 Å is typical of those used. Recording areas as small as 15 μ^2 have been realized by this technique.

The probes are now ready for a series of finishing operations in which they are separated from the wafer, attached to output wires, and mounted in a suitable handle. The microprobe is separated from the silicon wafer by chemical etching, and the cross section of an etched single-electrode probe has been shown in Fig. 4. The undercutting caused by the isotropy of the etchant[2] is important in that it allows the cross-sectional area and hence the probe volume to be minimized. This is especially important at the carrier tip as shown in the profile of an actual microprobe presented in Fig. 5. This profile can be controlled to within about 10 percent, while the carrier thickness can be of any desired value from 10 to the 60 μ shown here. The effect of tip size on the ability of a microprobe to record from single cells

[2] 10 percent (49 percent) HF—90 percent (70 percent) HNO_3 by volume.

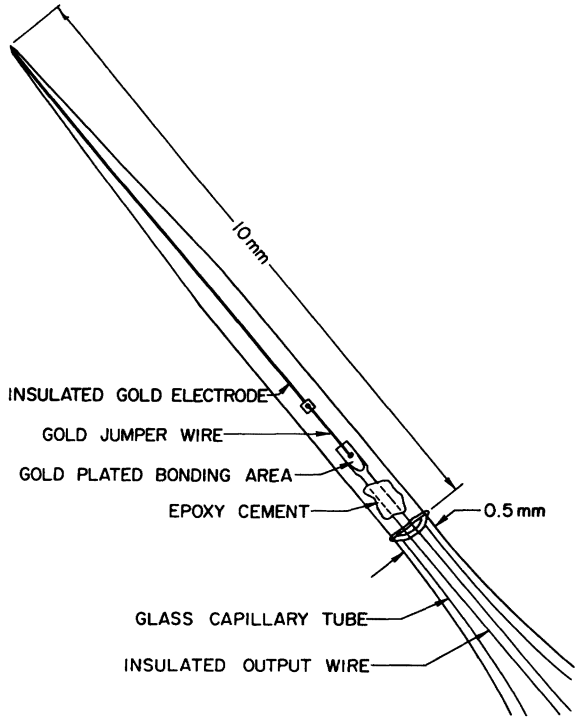

Fig. 6. Mounting arrangement for a finished probe.

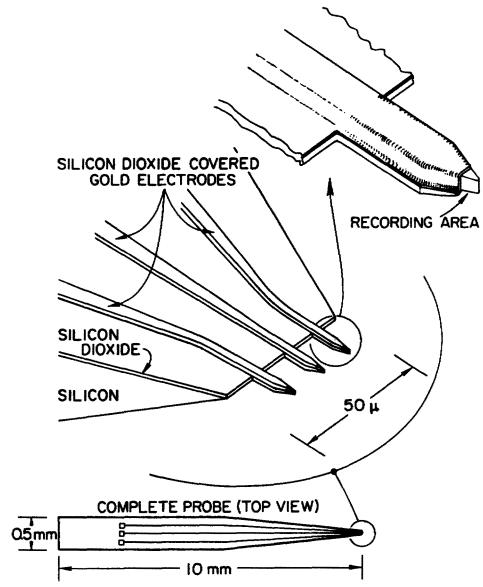

Fig. 7. A multielectrode microprobe for biopotential recording.

will be discussed in a later section.

The bonding and mounting scheme developed for the probe structure is shown in Fig. 6. Thermocompression bonding is used to make electrical connection between the metalization area and the 75-μ diameter output wire, and the probe is then mounted in the end of a tapered glass capillary tube as shown. To complete the fabrication process, the bonding areas are insulated from the biological electrolyte by coating the entire probe, except for its tip, with an insulating lacquer such as Mobil Stoner-Mudge vinyl, which has also been used to insulate conventional metal electrodes. With care, this lacquer can be routinely extended to within 100 to 150 μ of the electrode recording areas. Multiple coatings are used over the output wires to minimize stray capacitance to ground and ensure a high degree of isolation.

At the present time, the complete fabrication sequence represents between one and two man-weeks of work. Typically from 20 to 30 microprobes are realized from a single silicon wafer, however, and two to three wafers constitute a typical processing run. The fabrication time required per probe is therefore not excessive.

Fabrication of Multielectrode Probes

The fabrication techniques used for conventional metal and glass pipette electrodes are not easily extended to permit the realization of multielectrode arrays. Although concentric pipettes [2], [4] have been successfully fabricated and used, for example, to record simultaneously from inside and outside a cell, the fabrication of electrodes with small but controlled transverse spacings is more difficult. While double and multibarreled pipettes [4], [5] have been realized, intertip spacings here are generally either less than 1 μ or greater than 100 μ, depending on the fabrication technique used.

In those instances [6]–[8] where two electrodes have been realized with interelectrode spacings in the range from 1 to 100 μ, two problems have complicated their use. First, the interelectrode spacing frequently changes as the electrodes are inserted so that the recording separation is often unknown. Second, interelectrode capacitive coupling is usually high for these conventional structures.

Since in the approach described in this paper the electrodes are defined by photoengraving techniques, any two-dimensional array of electrodes can be fabricated with good control. One such structure is shown in Fig. 7. Once the photomasks have been made for the particular array desired, the remainder of the processing sequence is identical whether one electrode or a dozen are needed per probe. Interelectrode spacings are accurately controlled and can be as small as 10 μ using present techniques. Since these electrodes are rigidly fixed on the carrier, the interelectrode spacings can not change during use. Furthermore, as will be shown in the next section, the interelectrode coupling on the probe structure is virtually negligible. Fig. 8 shows photomicrographs of single- and double-electrode probes before the final attachment of output leads.

In addition to using such multielectrode arrays only for biopotential recording, it should also be possible to use some of the electrodes for stimulation while recording with the rest. The effects of very localized potential fields on single cells and small populations of cells might then be monitored.

Electrical Characterization

A. The Metal–Electrolyte Interface

It is well known that when two dissimilar metals are immersed in an ionic electrolyte, a potential difference will be developed between them. This potential difference is a function of the metals and electrolyte used, and the potential drop across each metal–electrolyte

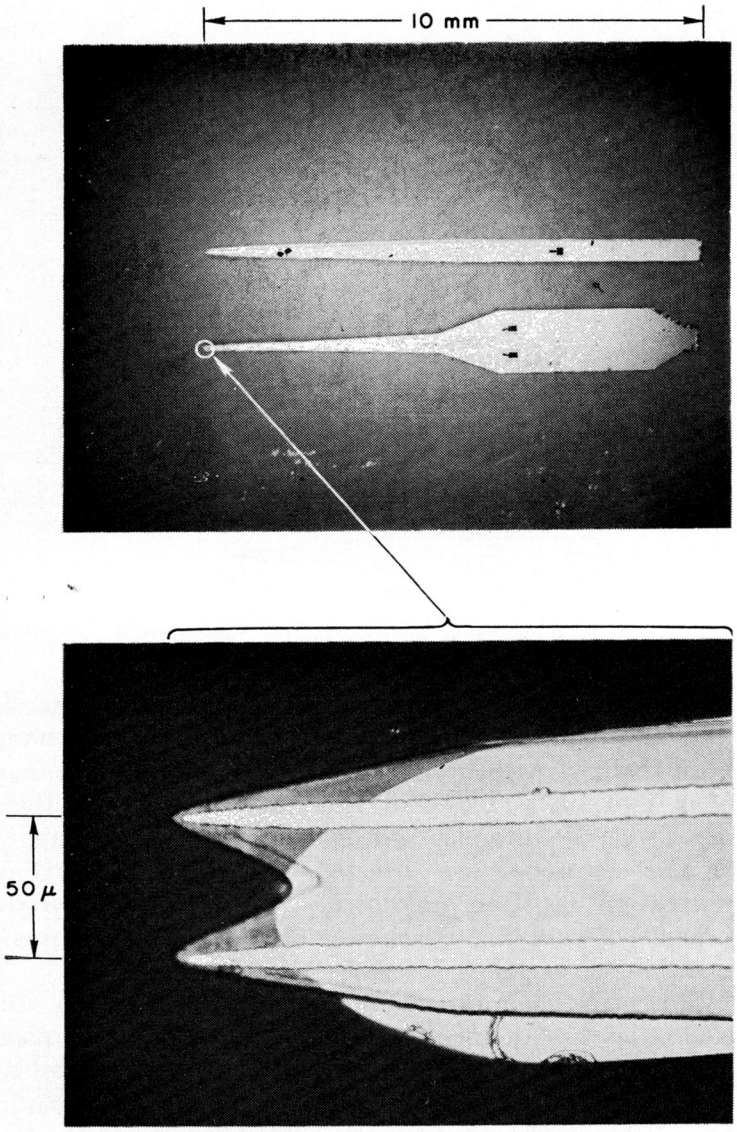

Fig. 8. Photomicrographs of a double-electrode probe.

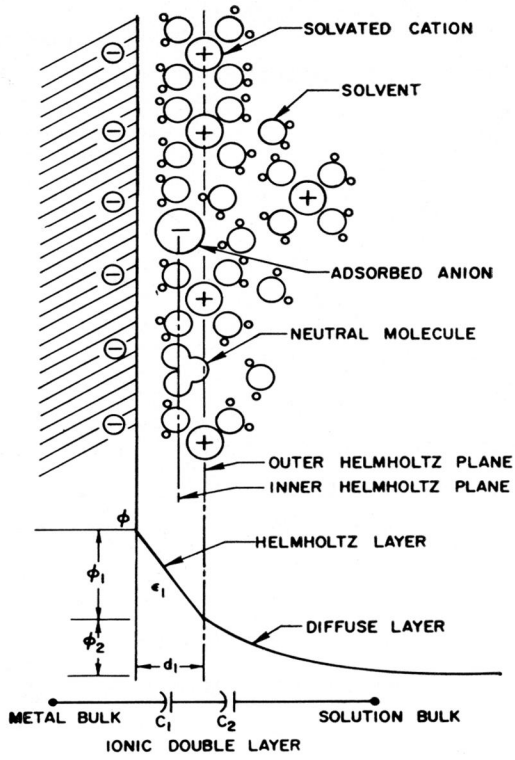

Fig. 9. The electrical double layer at an electrode surface.

interface is typically several tenths of a volt. If current is now drawn from this electrochemical cell, the potential of the microelectrode with respect to a larger area reference electrode will be a function of that current. The change in electrode potential due to current flow is defined to be the electrode polarization η.

The relationship between i, the electrode current, and η is often of the form [9]

$$i = i_0 \left[\exp\left(\frac{\alpha e\eta}{kT}\right) - \exp\left(-\frac{(1-\alpha)e\eta}{kT}\right)\right]$$

where $kT/e = 26$ mV at $T = 300°\text{K}$, α is a symmetry factor, and i_0 is the exchange current. For gold in a buffered saline electrolyte[3] which closely approximates extracellular fluid, this relationship holds anodically with $\alpha \approx 0.5$ for $\eta < 100$ mV, while cathodically it is still obeyed at $\eta = -200$ mV with $\alpha \approx 0.2$. The measured exchange-current density is about 10^{-9} A/cm^2, which for a recording area of 100 μ^2 would represent a current of only 10^{-15} amperes. All metal microelectrodes, and especially those of the noble metals, polarize at extremely low currents so that even if the open-circuit electrode potential did not drift with time, this polarization would make these metals unsuitable for dc bipotential recording.

The exchange-current density is also important in another regard. The measured exchange-current densities for different metals in buffered saline correlate well with the results of reported histological studies [10], [11] on the effects of metals chronically implanted in the brain. Gold and stainless steel are known to produce the least tissue response while platinum, tungsten, copper, and silver produce progressively more. The corresponding values of i_0 fall in the same order, and the measured exchange-current density on silver is greater than 10^{-5} A/cm^2.

The ac impedance of the metal–electrolyte interface is dominated by the electrical double layer formed by electrons in the metal and ions close to its surface as shown in Fig. 9. For the concentrated solutions found in the body, the diffuse layer is less than 50 Å thick, while the thickness of the Helmholtz layer, d_1, is of the order of an ionic radius, i.e., 2 to 4 Å. The important point here is that the factors responsible for the electrode impedance are highly localized spatially even relative to an electrode whose dimensions are in microns. As a result, microscopic surface roughness on the metal plays a large part in determining the electrode impedance, and platinizing can be used to lower this impedance without greatly affecting electrode size.

The metal–electrolyte interface impedance is very nearly equal to that of the Helmholtz capacitance, $C_1 = \epsilon_1 A/d_1$, where A is the recording area and ϵ_1 is the effective dielectric constant in the Helmholtz layer,

[3] The electrolyte consists of 6.75 gm NaCl and 2.25 gm $NaHCO_3$ in 1 liter of water.

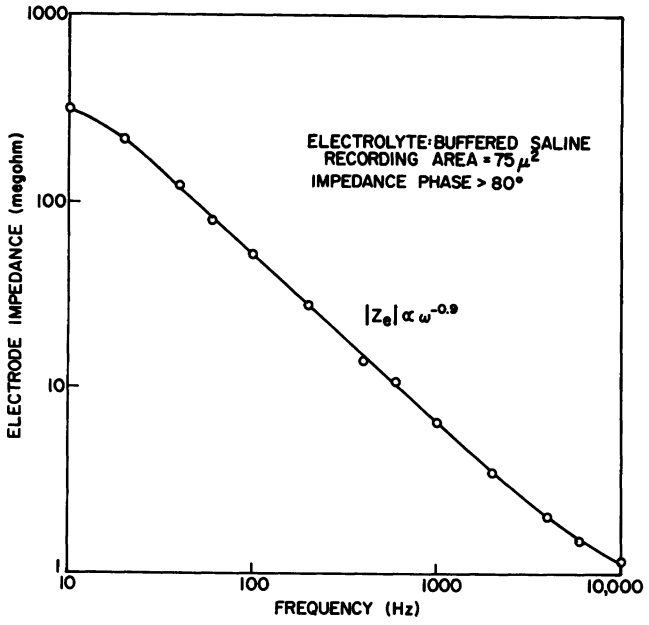

Fig. 10. Electrode-impedance magnitude versus frequency for a gold microprobe.

With the relative dielectric constant taken as 10, the calculated capacitance is about 0.2 pF/μ^2.

The impedance of a single-electrode microprobe measured in buffered saline is shown in Fig. 10 as a function of frequency. This electrode is typical of the semibright gold electrodes fabricated. The recording area here was about 75 μ^2 so that at 100 Hz the impedance per unit area is equivalent to a series capacitance of 0.4 pF/μ^2. For optically rough electrodes, the capacitance per unit geometrical area can exceed 1 pF/μ^2.

B. Signal Attenuation

The electrical equivalent circuit for the microprobe structure is identical in form with that for a conventional metal electrode and consists of a series capacitance, corresponding to the impedance of the metal–electrolyte interface (Fig. 10) followed by a shunt capacitance to ground. Comparing a probe electrode with a conventional metal electrode having a conical recording area of equivalent linear dimensions, the recording-area sizes and hence series electrode impedances are found to be similar. There are important differences, however, in the amounts of shunt capacitance present for the two structures. Robinson [12] has estimated that for conventional electrodes this shunt coupling from the electrode metal through the insulation to the electrically neutral electrolyte varies between 1 and 5 pF/mm of electrode insertion into the brain, depending on the insulating material used.

Because so little metal is used in the microprobe structure, coupling through the deposited glass insulation to the electrolyte is quite small and can be made negligible by coating the upper surface of the probe with an insulating lacquer film. Since in a typical recording situation the silicon carrier is a virtual ground with respect to the surrounding electrolyte (as compared with the impedance level of the electrode), the major contribution to shunt loading for the probe structure comes from the MOS electrode-to-carrier capacitance. For the 20-μ-wide 7.5-mm-long electrodes now used, this coupling amounts to a shunt capacitance of about 4 pF. For 10-μ-wide electrodes of the same length, also easily fabricated, the coupling is only 2 pF. Furthermore, this capacitance is well controlled and independent of the recording depth in tissue.

For both electrode structures there are additional contributions to shunt loading from the leads as well as from the amplifier itself. These contributions can easily amount to several picofarads. For a recording area of 50 μ^2 ($\sim$20 pF series capacitance) the signal attenuation can therefore be significant for the microprobe structure and can be severe for a conventional electrode, especially if the recording site is more than a few millimeters below the surface of the brain. Capacitance neutralization [13] can minimize this attenuation but often increases system noise.

The ability to integrate source-follower preamplifiers on the microprobe carrier makes the elimination of the effects of stray lead capacitance a very real possibility. If this integration can be accomplished, the resulting signal attenuation for the probe structure will not only be very small but will be predictable and constant from electrode to electrode in an array having constant recording-area sizes as well. As a result of this integration, the necessity of using capacitance neutralization will therefore also be avoided.

C. Recording Bandwidth

The recording bandwidth of a metal microelectrode is usually well beyond the frequency range for extracellular bipotential recording, and in practice the upper half-power frequencies of gold microprobes have been found to exceed 10 kHz. The lower half-power frequencies are less than 10 Hz, the lowest frequency at which electrode impedance was measured. Satisfactory recording bandwidth should not be viewed as an indication of negligible signal attenuation, however, since significant attenuation can occur at a nearly constant level over the entire frequency range for these structures.

D. Interelectrode Coupling

For the microprobe structure, the interelectrode coupling is quite low. It can occur via coupling through the substrate, in which case it amounts to half the electrode-to-substrate coupling, or from 1 to 2 pF for the present electrode configurations. However, in the usual case where the substrate is virtually grounded, this component is largely removed.[4] Interelectrode coupling on the probe itself is then well under 1 pF so that the

[4] The presence of the silicon ground plane greatly reduces the interelectrode coupling below what it would be if the carrier were a pure insulating dielectric. For example, consider two parallel electrodes, 20 μ wide by 7.5 mm long, separated by 50 μ on a 50-μ thick carrier. The calculated coupling capacitance is 0.15 pF when the substrate is pure SiO_2. In contrast, for the SiO_2–Si carrier employed in the microprobe structure, the calculated coupling is primarily dependent on the impedance of the carrier with respect to ground and is less than 0.001 pF for the present design.

major contribution to interelectrode coupling is crosstalk between output leads. Thus lead positioning becomes quite important. If this lead coupling could be eliminated, e.g., through the integration of buffer amplifiers on the carrier, then the interelectrode crosstalk would truly be negligible.

E. Electrode Noise

Three types of noise will be considered here: thermal noise at the metal–electrolyte interface, neural noise coupling of bipotentials through the deposited insulation to the electrode, and photopotentials induced by the generation of carriers by light within the silicon space-charge region. For the probe structure, the thermal noise [14] should be comparable to that of a conventional electrode having the same electrode impedance, and qualitative observations in recording situations support this conclusion. Wolbarsht and Spekreyse [15] have, in fact, observed gold and platinum to be somewhat less noisy in biopotential recording than other less noble metals.

To minimize neural noise, the impedance across the insulating film covering the electrodes must be high compared with the electrode impedance to ground. As a worst case, we assume that the unwanted noise voltage at the surface of the insulation (directly over the electrode) is 100 times the biopotential of interest, and that the effective contact area is 1000 μ^2. This situation corresponds to that of an active neuron lying very close to the probe surface somewhere removed from the recording area. In this worst case the calculated ratio of signal-to-neural noise on the electrode is about 3 for the deposited SiO_2 films now used (3000 Å thick). The application of an insulating lacquer over the deposited glass insulation, however, allows this noise to be reduced to negligible values. The importance of the lacquer film in the present application is evident.

The last source of noise is light. When light strikes the semiconductor surface, carriers are generated in the silicon space-charge region, and the surface potential is decreased. The change in surface potential on illumination is known as the photopotential. Under fluorescent room light (120 Hz), the measured photopotential on silicon[5] has been observed to vary from nearly 100 mV for 3 Ω·cm n-type silicon to a weak 2 mV for 6 Ω·cm p-type silicon. The choice of substrate resistivity and type is therefore important in minimizing this source of noise, which couples to the electrode via the MOS electrode-to-substrate capacitance. Often it is not inconvenient to position the electrode via a hydraulically driven micropositioner controlled from a remote location, and in these cases the electrode environment can be dark. In other cases steady illumination could be used. Only when light flashes are used to stimulate evoked responses visually is this noise especially troublesome, and in these cases the problem can be eliminated by proper choice of carrier resistivity and by shielding the electrode from the light source.

[5] A saturated calomel reference electrode and buffered saline electrolyte were used to complete the electrochemical cell.

Physiological Evaluation

Preliminary tests have been conducted to evaluate the performance of the microprobe structure in the brain. Although statistical information relating the number and types of units[6] encountered to the characteristics of the microprobe structure has not yet been gathered, we would like to discuss some of our preliminary results concerning the microprobe structure and the feasibility of single-unit recording. A more extensive program of physiological evaluation is now underway.

A. Methods

A total of five adult cats have been used thus far in the evaluation of probe performance. The animals were anesthetized with sodium pentobarbitol and placed in a stereotaxic apparatus. An opening approximately 1 cm in diameter was made in the skull (anterior 5, lateral 8: Horsley–Clark coordinates), and the dura was removed to expose the brain. The probes to be evaluated had previously been characterized electrically in terms of their impedance and had been inspected under a microscope to determine recording-area size, carrier width, and the distance which the electrode projected beyond the carrier. The probes were mounted in a holder on the stereotaxic frame and were advanced by a hydraulically driven micropositioner. Electrical activity was amplified by a unity-gain source follower in series with a Grass model P511 amplifier (35 Hz to 10 kHz) and was then displayed on an oscilloscope.

A total of 40 probes have been evaluated in the brain, and of these electrodes, 18 recorded the activity of populations of cells and 7 were successful in recording from individual units. The electrical and geometrical characteristics of these probes varied (by design) over the following ranges: electrode impedance levels at 60 Hz, 1 MΩ to 110 MΩ; carrier widths,[7] 50 μ to 120 μ; and electrode projections beyond the carrier, 0 μ to 100 μ.

B. Experimental Results

The mechanical strength of the microprobe structure is adequate for biopotential recording in the brain provided that the distance which the electrodes project beyond the carrier does not exceed 50 μ. Only five instances of broken tips have been encountered in over sixty passes through the brain with such probes. The silicon carrier itself is strong enough to pass through intact dura; however, in their present form the projecting electrodes are not. The possibility of retaining a few microns of silicon under the projecting electrodes for increased strength is being investigated, and if this can

[6] "Unit" is interpreted to mean a single, electrically active neuron.

[7] Carrier width is specified at a distance of 50 μ behind the record site.

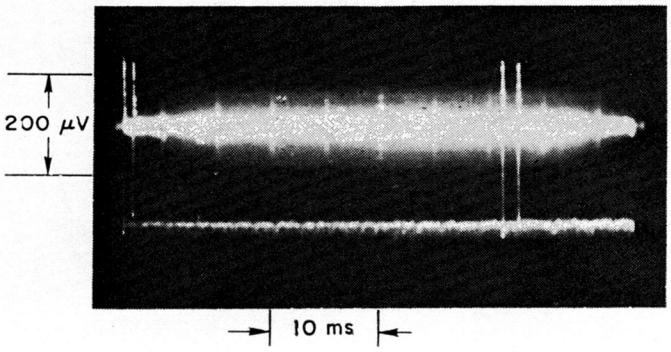

Fig. 11. Single-cell discharges recorded from cat cortex using a single-electrode microprobe.

be accomplished, the necessity of removing the dura prior to insertion of the probe can be avoided.

Where electrodes have projected at least 10 μ beyond the carrier and where carrier tip diameters have been less than 80 μ, these microprobes have generally performed well as population electrodes—recording from several cells simultaneously. For single-cell recording, however, the electrode must be able to approach an individual neuron closely and must be specific enough in its spatial recording sensitivity to isolate and record from only that one cell. Steady improvement in probe performance in this application has been noted as the carrier size has been reduced and the distance which the electrode projects beyond the carrier has been increased. The best results achieved thus far were with two probes having carrier widths of 60 μ and electrode projections of 50 μ. The tip diameters of these electrodes were 3 μ. These two probes were comparable to conventional metal electrodes in recording from single units, and discharges recorded from a cell[8] in cat cortex are shown in Fig. 11. The activity of single cells has been maintained for as long as twenty minutes.

Most of the recordings obtained thus far from single isolated cells have been of spontaneous activity. With some cells, especially when first encountered, this activity has occurred at a high rate (injury potentials), probably due to the disturbance produced near the cell membrane by the probe. No histology has yet been performed to determine the tissue damage produced by these probes. It is not surprising, however, that for the measurement of evoked responses from single isolated cells it will be necessary to decrease the size of the supporting carrier still further. Using the mesa technique summarized in Fig. 2, carrier-tip diameters have recently been fabricated as small as 25 μ. In terms of volume of tissue displaced, these probes are as small as conventional metal microelectrodes and have the advantage of being well controlled. As these probes are tested and the techniques for shaping the silicon carrier are improved still further, probe performance is expected to improve correspondingly. We believe that microprobes which equal and exceed the performance of conventional metal microelectrodes in their ability to isolate and record from single units without tissue damage are feasible using present techniques.

[8] There has been no evidence to suggest that these probes will record from the more ocalized potential fields of single nerve fibers.

Discussion

The construction and electrical characterization of both metal and glass micropipette electrodes have recently been reviewed by a number of authors [2], [4], [10], [12], [16]. Glass pipettes are well suited to intracellular biopotential recording and are usually used in these applications. Their design makes it possible to record dc and low-frequency potentials with good accuracy, and the fabrication techniques used in their construction permit the realization of the very small tip sizes needed for membrane penetration. The frequency response of the micropipette is limited to a few kilohertz by the high series resistance of the pipette coupled with the shunt capacitance from electrode to ground, however, and the pipette structure is therefore less well suited for recording fast biopotentials.

Although metal microelectrodes can not be used for dc recording due to the polarization problems mentioned earlier, they are well suited for recording fast extracellular activity. Their impedance levels are usually lower than those of pipettes, and because here the electrode impedance is largely capacitive, metal microelectrodes escape the high-frequency limitations associated with glass pipettes. The choice of the metal electrode over the pipette sacrifices dc and very low-frequency response for good low-noise performance, and metal and glass electrodes are accordingly used in extra- and intracellular applications, respectively.

The advantages of the microprobes described in this paper over conventional metal electrodes include a high degree of dimensional control and reproducibility, the ability to fabricate arrays of closely spaced electrodes, and the potential ability to fabricate buffer amplifiers as an integral part of the probe structure. The most important advantage, however, is probably the ability to design the electrode for a particular experiment. Although many questions remain to be answered concerning just what the proper electrode design is for a given application, the ability to choose the recording-area size, number of electrodes, and carrier shape, and then reproduce this structure may make such questions answerable.

The microprobe structure was designed for extracellular recording, and this constitutes its first limitation. It can not be used in its present form for dc or intracellular recording. Gold is far too inert to be used as a dc microelectrode, and it is doubtful that even a more active metal (e.g., silver–silver chloride) could escape the polarization problems accompanying such small recording areas. The minimum tip diameters now technologically possible (2 to 3 μ) are still too large for most intracellular applications although, as the fabrication techniques improve, this situation might change. Submicron

geometries have been realized in several industrial integrated-circuit laboratories.

A second disadvantage of the probe structure is that its realization requires skills and technology not usually available to neurophysiologists. This disadvantage could be overcome if the probes were to be made commercially available by a firm having an integrated-circuit facility. Although the cost of such probes does not appear prohibitive, only further development, including a detailed program of physiological evaluation, can determine if the probes are sufficiently useful to merit commercial production. The advantages obtained through the use of integrated-circuit technology and the preliminary physiological data appear to more than justify continued development of this approach to extracellular microelectrodes.

Conclusions

This paper has described the design, fabrication, and characterization of a new multielectrode microprobe for biopotential recording. On the basis of the results achieved, the following conclusions can be drawn.

1) Using microelectronic fabrication techniques and materials which are suitable for use in the body, it is possible to realize single- and multiple-electrode probes which are capable of recording single-cell discharges in the central nervous system. In their present form these electrodes are well suited for recording from small populations of neurons and have successfully isolated single cells in cat cortex.

2) The fabrication techniques used permit the geometrical characteristics of the probe structure to be controlled to within a few microns, and therefore permit the microprobes to be designed for a given experiment. As these techniques are refined still further, additional improvements in the probe characteristics are expected.

3) The characterization of the various materials and interfaces present in the probe structure has permitted the development of an equivalent circuit which allows the electrical characteristics of the probe to be determined. In comparison with a conventional metal microelectrode, the microprobe structure possesses less parasitic capacitance from electrode to ground (hence less signal attenuation), and that shunt capacitance which is present is predictable and independent of the recording depth in the brain. Interelectrode coupling is limited to coupling between output leads, while the probe bandwidth and noise characteristics are comparable to those of a conventional microelectrode.

The present study has proven the feasibility of a new approach to extracellular microelectrodes. Many questions remain unanswered, however, and there are a number of areas for additional work. To minimize tissue damage and increase the strength of the structure, more work is needed on the technology for shaping the silicon carrier to still smaller dimensions. Certainly more physiological tests need to be conducted to determine optimum geometries for electrode–cell coupling. Finally, source-follower preamplifiers need to be integrated on the carriers to eliminate the undesirable effects of stray lead capacitance, and one proposed structure is shown in Fig. 12. Here, the integrated buffer amplifiers eliminate the effects of this stray lead capacitance, and an auxiliary carrier is used to facilitate the connection of output leads. On single-electrode probes this integration should allow signal attenuation to be minimized. On multielectrode structures the presence of integrated source followers is even more important if interelectrode crosstalk is to be eliminated. The problems of device fabrication and surface passivation associated with this integration are formidable; however, the need for intissue signal processing justifies the effort required.

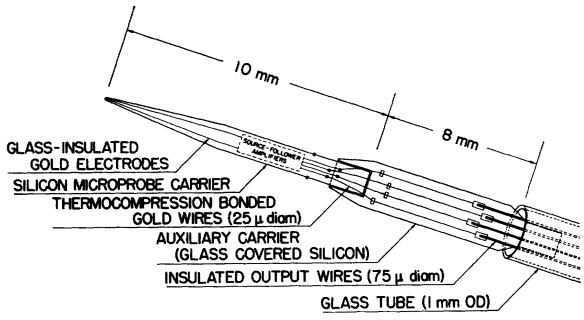

Fig. 12. A proposed multielectrode microprobe with integrated buffer amplifiers.

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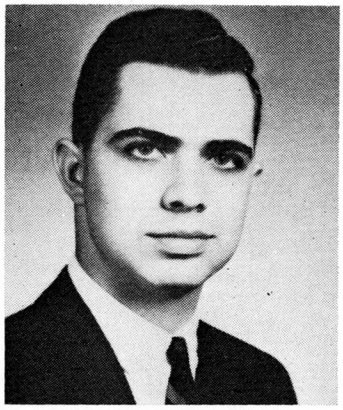
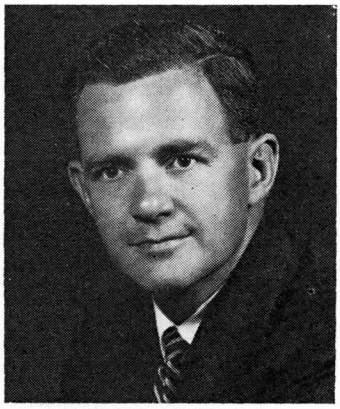


Kensall D. Wise (S'61–M'69) was born in Muncie, Ind., on August 1, 1941. He received the B.S.E.E. degree from Purdue University, Lafayette, Ind., in 1963 and the M.S. and Ph.D. degrees in electrical engineering from Stanford University, Stanford, Calif., in 1964 and 1969, respectively.

From 1964 to 1965 he was a Member of the Technical Staff in the Digital Device Integration Department at Bell Telephone Laboratories, Murray Hill, N. J., where his work was concerned with the design, integration, and testing of high-speed digit-detection circuitry for digital memory stores. From 1965 to 1969 he was a Research Assistant in electrical engineering at Stanford University, involved with the design, fabrication, and characterization of multielectrode microprobes for biopotential recording. He is now a Research Associate in the Department of Electrical Engineering at Stanford where his work is concerned with the application of integrated-circuit technology to biomedical sensors.

Dr. Wise is a member of Tau Beta Pi, Eta Kappa Nu, Sigma Xi, and the Electrochemical Society.



James B. Angell (S'45–M'47–SM'57–F'66) was born in Staten Island, N. Y., on December 25, 1924. He received the S.B. and S.M. degrees in 1946 and the Sc.D. degree in 1952, all in electrical engineering, from the Massachusetts Institute of Technology, Cambridge.

From 1946 to 1951 he was a Research Assistant in the Research Laboratory of Electronics at M.I.T., studying noise in tracking radars. From 1951 to 1960 he was with the Research Division of Philco Corporation, Philadelphia, Pa., where he was manager of solid-state circuit research and led a group studying the principles of evaluating and applying transistors and other solid-state devices, particularly for computers and high-frequency functions. He joined the faculty of Stanford University, Stanford, Calif., in September, 1960, and was promoted to Professor of Electrical Engineering in 1962. He became Director of the Solid-State Electronics Laboratory at Stanford in 1964 and was appointed Associate Chairman of the Electrical Engineering Department in 1969. His current research is concerned with techniques for testing large-scale integrated circuits and the application of integrated-circuit technology to biomedical instrumentation. He has consulted for Fairchild Semiconductor, Dana Laboratories, Philco Corporation, the U.S. Army Electronics Command, and the U.S. Army Scientific Advisory Panel. He is a member of the Electronics Advisory Group of the U.S. Army Electronics Command.

Dr. Angell was chairman of the 1965 International Solid-State Circuits Conference of the IEEE. He organized and was first chairman of the IRE–AIEE Technical Subcommittee on Masers and Reactance Amplifiers. He served on the IRE and AIEE Solid-State Devices Committee and the Joint Semiconductor Devices Subcommittee from 1954 to 1964. He is presently Vice Chairman of the Solid-State Devices Technical Committee. In addition, he is a member of Tau Beta Pi, Eta Kappa Nu, Sigma Xi, and the AAAS.

Arnold Starr was born in New York, N. Y., on August 5, 1932. He received the A.B. degree from Kenyon College, Gambier, Ohio, in 1953 and the M.D. degree from New York University, New York, in 1957. He completed his internship at Beth Israel Hospital, Boston, Mass., in 1957 and 1958 and his residency in neurology at Boston City Hospital from 1958 to 1960.

He was a Research Associate in Neurobiology at the National Institute of Health from 1960 to 1962. From 1962 to 1964 he was at the Neurophysiology Institute in Copenhagen, Denmark, the Sechenov Institute of Physiology in Moscow, USSR, and was an NIH Fellow in Neurophysiology at the Centre of Recherches Neurophysiologque in Paris, France. Since 1964 he has been Assistant Professor of Neurology at Stanford University, Stanford, Calif., and the V.A. Hospital, Palo Alto, Calif., where his primary research interests have been concerned with the physiological processes related to hearing.