Microelectrodes, Microelectronics, and Implantable Neural Microsystems

Progress in development of tiny electrodes, cables, circuitry, signal processors and wireless interfaces promises to advance understanding of the human nervous system and its disorders.

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ABSTRACT | Lithographically defined microelectrode arrays now permit high-density recording and stimulation in the brain and are facilitating new insights into the organization and function of the central nervous system. They will soon allow more detailed mapping of neural structures than has ever before been possible, and capabilities for highly localized drug-delivery are being added for treating disorders such as severe epilepsy. For chronic neuroscience and neuroprosthesis applications, the arrays are being used in implantable microsystems that provide embedded signal processing and wireless data transmission to the outside world. A 64-channel microsystem amplifies the neural signals by 60 dB with a user-programmable bandwidth and an input-referred noise level of 8 \( \mu \text{V}_{\text{rms}} \) before processing the signals digitally. The channels can be scanned at a rate of 62.5 ks/s, and signals above a user-specified biphasic threshold are transmitted wirelessly to the external world at 2 Mbps. Individual channels can also be digitized and viewed externally at high resolution to examine spike waveforms. The microsystem dissipates 14.14 mW from 1.8 V and measures 1.4 \( \times \) 1.55 cm\(^2\).

KEYWORDS | BioMEMS; implant; microelectrodes; microstimulation; microsystems; neural probes; neural recording

I. INTRODUCTION

Of all the parts that make up the human body, the nervous system is by far the least understood and its disorders are the most difficult to treat. Research on the use of electrical stimulation to restore movement to paralyzed limbs goes back at least 250 years to the work of Franklin [1] and others, but it was midway through the last century that physiologists began to use electrical recording to try to understand the nervous system at the cellular level [2]. Electrolytically sharpened metal wire electrodes [3] were used for extracellular recording, while glass micropipettes [4] were used to probe individual cells. Significant progress was made in understanding the behavior of single neurons and some sensory areas of the brain, but it became increasingly clear that understanding the organization and signal-processing techniques used at the system level would require simultaneous recording and stimulation from many sites having known spatial locations in tissue—something that existing technology did not then permit.

From the 1950s onward, there was also growing interest in developing electronic interfaces to the brain for use in prosthetic devices for treating various disorders. Work on visual prostheses began with Brindley’s early efforts [5], but by the late 1960s, a program to develop a cortical prosthesis for the blind was also under way under Dobelle at the University of Utah [6], [7]. Initial work on cochlear prostheses for the deaf began about the same time [8]–[10]. Most early work involved experiments using wire-based stimulating electrode arrays, but it was quickly recognized that better technology was needed, not only for
forming the arrays themselves but also for the implanted microsystems that would be required for any practical device. In addition to chronically implanted electrodes, reliable leads, signal-processing circuitry, telemetry interfaces, and power sources would be needed. The required technology did not exist at that time, but it was coming.

Microelectronics had taken a significant step forward in 1959 with the invention of the lithographically based planar process for integrated circuit fabrication, and by the mid-1960s, the use of this process for fabricating extracellular microelectrode arrays for neurophysiology was under way [11]–[13]. This work drew on the selective silicon etching technology being developed at Bell Telephone Laboratories [14] and established the basis for subsequent work on micromachined integrated sensors, microelectromechanical systems (MEMS), and the microsystems of today. After 40 years, most of the technology needed for the realization of chronically implantable neuroelectronic microsystems is now in place [15]. Advanced electrode design and wireless implantable microsystems are hot topics today [16], with entire conferences and journals devoted to them. Optimism is being fueled by the spectacular successes achieved by cochlear implants for the deaf and by deep brain stimulation (DBS) in the subthalamic nucleus for Parkinson’s Disease. Over 125 000 cochlear microsystems have now been implanted worldwide, allowing profoundly deaf patients to function normally in a hearing world, and the use of DBS for the suppression of Parkinson’s tremor has been remarkably successful, with very few side effects when the electrodes are positioned correctly. Improved prostheses for deafness and Parkinson’s Disease are being developed [17]–[19], along with new devices aimed at treating blindness [20], [21], paralysis [22], [23], epilepsy [24], and other disorders. Extracellular microelectrodes, which provide the critical interface between the nervous system and microelectronics, are discussed first below, followed by a look at the present state-of-the-art in implantable microsystems, including the interconnect cables, site-interface circuitry, embedded signal processor, and wireless link to the external world.

II. MICROELECTRODE TECHNOLOGY

Extracellular microelectrodes record the voltages produced by ionic current flow around neurons as their cell membranes depolarize as the result of inputs received from other cells. These neural spike potentials represent the electrical half of an electrochemical system, with amplitudes as high as several hundred microvolts and a frequency content extending up to perhaps 10 kHz. Almost 40 years ago, authors questioned whether this ionic current flow was effectively isotropic or whether it was constrained to flow only in narrow clefts between the surrounding nonneuronal cells [3], making the observation of a cell discharge (‘‘single unit’’) largely a matter of luck. This speculation was partly a result of the observation that in a single pass through tissue, an electrode typically ‘‘sees’’ only a few neurons, far fewer than the number known to exist anatomically. However, based on many years of recording with multisite probes, there is no evidence that electrode-cell coupling is anisotropic. Cortical neurons can typically

**Fig. 1. Basic structure of a micromachined multielectrode probe for recording or stimulation in the central nervous system.**
be seen electrically above background noise as far as 100 \( \mu m \) away, and in areas such as the cochlear nucleus, where cells are smaller, recording fields are 40–50 \( \mu m \) in extent. Thus, in order to record simultaneously from essentially all neurons within a single block of tissue, sites on 80–200 \( \mu m \) centers are required. This is possible today using the lithographic techniques developed for integrated circuits.

The use of integrated circuit technology to create dense arrays of thin-film electrodes for single-unit recording in the nervous system began at Stanford University in 1966. The resulting neural probes [11]–[13] had the general structure shown in Fig. 1, which is typical of virtually all lithographically defined electrode arrays reported since that time. The probe structure consists of a selectively etched (“micromachined”) substrate, with conducting leads insulated above and below by inorganic dielectrics and recording/stimulating sites formed by an area of exposed metal. In 1970, it was difficult to fabricate such devices reproducibly, but as MEMS technology developed in the 1970s and 1980s, diffused boron etch-stops, reactive ion etching (RIE), and silicon-on-insulator wafer technology allowed probes to be realized reproducibly with high yield using single-sided processing of wafers having normal thickness [25].

As electrode technology developed, a wide variety of materials were explored for use as the probe substrate [26]–[30], including silicon, metals, glass, sapphire, and polymers. While some of the resulting devices recorded from neurons acutely, shaping the substrate, the strength of that substrate [31], and the lack of suitable encapsulating dielectrics for chronic use were all important problems. Most present approaches to probe formation use silicon substrates [32]–[35]. Silicon can be shaped with a precision that probably exceeds that of any other material [36] and taps directly into a plethora of processing knowledge and equipment developed for the microelectronics industry. It is compatible with the use of high-quality silicon dioxide and silicon nitride dielectrics along with some polymers, as well as with the formation of on-chip circuitry [37]. It is also compatible with the realization of probe structures that are very small (a few micrometers or even submicrometers in width).

The probe substrate must be realizable in reasonable volumes with high yield, and that implies the ability to define it lithographically in a batch process. Since silicon wafers are typically 500–800 \( \mu m \) thick, it is important that the probe shanks be formed using some form of etch stop, either as a diffused-boron layer [25] or a buried-oxide layer [34], [35]. Either approach can be effective, although boron etch-stops permit the use of multiple substrate thicknesses and produce a smooth surface that is probably helpful in minimizing tissue damage (Fig. 2). The boron etch-stop also avoids any possibility of silicon substrate dissolution in-vivo. It should be noted that not all silicon electrode arrays are formed lithographically in a planar process. The two-dimensional silicon depth arrays developed at the University of Utah [38], [39] are based on glass reflow, sawing, and etching. They have produced some of the longest chronic implants reported to date.

Using silicon as the substrate and thermally grown silicon dioxide (fused quartz) and low-pressure chemical-vapor-deposited (LPCVD) silicon nitride as the insulating dielectrics, conductors from the sites to bonding pads, cables, or circuitry at the rear of the probe can be formed using refractory metals, metal silicides, or polysilicon. In spite of its relatively high resistance (10 \( \Omega /\text{square} \)), polysilicon is adequate for most recording electrodes. For stimulating probes, however, lower resistance materials are needed to reduce drive voltages and the resulting
voltage-stress on the encapsulating dielectrics. Typical cell thresholds for stimulation are 10–20 μA, but stimulating currents can reach 100 μA or more. Since the conducting substrate below the leads and the extracellular fluid above them both act as ground planes, interchannel crosstalk is virtually negligible on such probes, and the small area of the lithographically defined leads minimizes shunt capacitance so that signal attenuation is negligible as well. Site impedances are dominated by the series capacitance of the metal-electrolyte double layer. Recording sites are usually formed using gold or platinum, although anodically formed iridium oxide [40], [41] is increasingly used. It produces significantly lower recording impedances than other materials and is essential for stimulating sites, permitting more than 20 times the charge delivery to tissue than platinum or gold at the same voltage [15], [42].

Sites are thought to average the potential field seen in tissue over their area. For recording from small cells, site areas of 100 μm² have often been used, although larger areas of 300–400 μm² have been more typical recently to reduce thermal electrode noise, which is inversely related to area. For stimulating sites, 1000 μm² is suitable for current levels of about ±70 μA at supply voltages of ±5 V, limited by the spreading resistances in tissue near the site [43].

Fig. 3 shows several neural probes on the back of a U.S. penny. More than 7500 such devices have been supplied to the neuroscience community by the University of Michigan and have changed research directions in systems neurophysiology. One of the additional benefits of using silicon as the substrate material is that circuitry for site
selection, signal amplification, stimulus current generation, command decoding, and self-test can be integrated in the probe substrate itself. Fig. 4 shows a 64-site eight-channel recording probe on a U.S. postage stamp [44], [45], while Fig. 5 shows a 64-site four-channel stimulating array [46]. Several such probes can be microassembled [47] to form three-dimensional (3-D) electrode arrays, as in the 256-site four-probe 16-channel array also shown in Fig. 5. This array has sites on 400 μm centers in three dimensions. Three-dimensional arrays of recording and stimulating probes are poised to launch a revolution in our understanding of neural systems, allowing computer-controlled mapping of the connections between different areas of brain in a few minutes that would be impossible using discrete wire electrodes.

Lithographically defined probes can also support more localized studies at the cellular level. By omitting the boron diffusion in selected areas of the substrate, back-looking sites can be realized as well as top-looking sites and combinations of the two. Fig. 6 shows a diagram and photograph of an 18-μm-wide probe containing top, back, and double-sided sites separated in depth by 40 μm. The 5-μm-diameter back-looking sites are separated from the conducting substrate by less than 2 μm and yet record.

Fig. 5. A 64-site eight-channel stimulating probe with sites on 400 μm centers and with CMOS electronics for stimulus generation, recording, and self-test. Below, four such probes are mounted in a micromachined silicon platform to form a 256-site 32-channel array.
well, with the substrate appearing as an insulator to the extracellular current [48]. Fig. 7 shows recordings made with a 50-μm-wide probe having top-, double-, and back-sided sites on 20 μm centers as it advances in guinea pig inferior colliculus. Cells can clearly be handed off from one site to the next, but the substrate here is screening some cells from some sites. The double-sided sites average the potentials seen on their two surfaces, but as shank width

**Fig. 6.** Diagram and backside view of an 18-μm-wide probe shank having top-, double-, and back-looking sites. The sites are separated in depth by 40 μm.

**Fig. 7.** Recordings made with a 50-μm-wide neural probe having top-, double-, and back-sided sites on 20 μm centers as it advances in depth through guinea pig inferior colliculus.
decreases, screening becomes less pronounced. For exploring questions in neuroscience using acute extracellular recording and stimulation, the necessary electrode array technology is here now and is sufficient to allow rapid progress in our understanding of neural structures. The challenges are to provide high-density two-dimensional (2-D) and 3-D electrode arrays commercially and to develop ways of asking the right questions of the recorded data using appropriate algorithms embedded in smart multichannel data acquisition systems.

For studies of plasticity and learning and for practical neural prostheses based on recording, viable interfaces with tissue for months, years, or even decades will be required. Long-term (years) stimulation and shorter term (weeks) recording is possible now, but single-unit recording for years will require further progress at the probe–tissue interface. Probes implanted chronically are encapsulated by a layer of glia a few micrometers thick. Stimulating currents can penetrate this layer, but it can shield small recording sites from extracellular potentials that may be present. A variety of approaches are being explored to increase recording life in-vivo from weeks or months to years [49]. These include coating the sites with materials that prevent protein adsorption or attract neuronal growth along with forming projections on the sites that extend beyond the glial sheath.

Tresco [50] has also found that 100–150 μm-wide probe shanks produce a 30–40% cell loss within 100 μm of the shank (throughout the recording field of a typical site) and elevated levels of astrocytes considerably beyond this. One possible explanation for these far-field effects is mechanical motion of the probe in tissue, which is exacerbated by any tethering of the probe to the skull. Designing probes with shank widths that approach cellular dimensions and with back-ends that fold over flat on the cortical surface [51] to allow the dura to be replaced over the implant is one approach to reducing such motion. Ultimately, scaling probe size to smaller dimensions will be limited by strength rather than technology, especially if penetrating the pia arachnoid is required. Fig. 8 shows a probe whose shank consists of a 10-μm-wide lattice of supporting silicon but which is otherwise open, allowing cellular processes to regrow through the shank. Histological studies are now under way to determine the efficacy of such structures. The probes still have sufficient strength for cortical use.

![Fig. 8. Back side of a multisite lattice recording probe on a human hair, with an inset of the tip of the probe.](image)

![Fig. 9. Diagram of a probe containing devices for both electrical and chemical recording and stimulation.](image)
Fig. 10. View of a 50-μm-wide probe shank containing a microchannel and an integrated thermal flowmeter. Insets show two such probes on a U.S. penny and the cross-section of a channel before etch-back to form the channel wall [57].

Fig. 11. Neural spike counts in the presence of ten 100 ms injections of AMPA (an excitatory drug) delivered over a 10-s period [57].
Considerable progress has been made recently in addressing the chemical aspects of the electrochemical neural system, with the goal of realizing probes that, in addition to stimulating/recording electrodes, have a complete set of microfluidic components: drug delivery channels, flowmeters, valves, and chemical sensors. Fig. 9 shows the diagram of such a probe. Probes having fluidic drug-delivery channels [52], shutters [53], and flowmeters [54], [55] have been demonstrated, and integrated microvalves [56] are being developed. Fig. 10 shows probes having drug-delivery channels and integrated thermal flowmeters. Such probes can resolve flows below 200 pL/s, have thermal time constants of about 200 μs, and are vacuum-shielded to limit any temperature rise in tissue to less than 1 °C. Fig. 11 shows 10 μM AMPA, an excitatory neural agonist, being delivered in ten 100-ms-long pulses over a 10-s interval [57]. The neural spike rate increases after delivery, gradually returning to pre-AMPA levels. The use of voltammetry to measure in-vivo chemical concentrations (e.g., dopamine) has also been recently demonstrated [58]. By combining electrical recording and stimulation with chemical recording and stimulation, new windows are being opened in neuropharmacology, with new prospects for the treatment of disorders such as severe epilepsy by providing therapies at point of need.

Fig. 12. A neural microsystem consisting of 2-D and 3-D arrays of cortically implanted electrodes with ribbon cables connecting them to a subcutaneous electronics package containing circuitry for amplification, spike detection and encoding, and the wireless transmission of power and bidirectional data.

Fig. 13. Block diagram of a wireless implantable microsystem for cortical single-unit recording along with its external user interface.
III. FULLY IMPLANTABLE NEURAL MICROSYSTEMS

Chronic recording and/or stimulation in neuroscience and in neural prostheses requires more than electrodes. Electronic site selection, stimulus generation, signal amplification, spike detection and encoding, and the wireless transmission of power and bidirectional data are also required, in addition to any microfluidic functions needed. Fig. 12 shows one possible configuration for such a system, where two- and three-dimensional electrode arrays interface with the cortex and are connected to a subcutaneous electronics package using ultraflexible ribbon cables. Within this package, the neural signals are amplified, interpreted, and wirelessly interfaced to the outside world. The remote location of the electronics with respect to the cortex here allows more flexibility in power dissipation since, in cortex, any temperature rise must be less than 2 °C to avoid damage. It also allows better shielding of the front-end neural signals from the wireless power link and permits satellite platforms for antennas or fluidic reservoirs when needed. The tissue displaced by the electrode array must be small enough to avoid any significant disruption of the physiological system, and its vertical rise above the cortical surface should be less than 1 mm to allow the array to remain free of the skull and float in tissue. Based on this implant architecture, the various components of the microsystem will now be discussed.

A. Interconnect Cables and Site-Interface Circuitry

The recent integration of parylene films, deposited and patterned at wafer level prior to probe release, into the probe process [59] is important not only because it allows the use of parylene over the upper surface of the probe but also because it permits the fabrication of parylene ribbon cables as an integral part of the probe structure. Such cables are more robust than silicon alternatives [60] and potentially solve the mechanical interconnect problems between the electrodes and the electronics package. Accessing a few leads from an acute electrode array is relatively simple, but for more than 30–40 sites, the back-ends of such probes become prohibitively large. For chronic implants, the situation is even worse, and since the first silicon probes were produced in the 1960s, the integration of circuitry on the probe itself has been an important goal. The primary reason for on-chip circuitry is to reduce the number of external leads (through site selection and/or multiplexing) and permit the use of more sites, but other benefits are to reduce impedance levels, increase signal amplitudes, and decrease sensitivity to cable leakage.

The design of on-chip amplifiers for neural probes has progressed from open-loop designs [44], [61] to capacitively coupled closed-loop designs [62], [63]. Reported amplifiers provide closed-loop gains of 1000, equivalent input noise levels of 8 μVrms, an upper cutoff frequency of 10 kHz, and lower cutoffs below 100 Hz [62]. Programmable low-frequency cutoffs have recently been demonstrated [64] to include or reject slow-wave activity, depending on the application. State-of-the-art amplifiers [45] dissipate 75 μW from ±1.5 V and fit in an area of 0.07 mm² in 0.5 μm complementary metal–oxide–semiconductor (CMOS). Recognizing that most sites will not be near neurons of interest, a front-end site selector allows the user to choose from a large number of sites on
the probe (electronic site positioning). The external probe interface then typically requires seven leads (three power, data in, data out, clock, and strobe), independent of the number of sites. For a stimulating probe, the desired current amplitudes and site addresses are entered serially, and the generated currents are steered to the sites through
the site selector while providing recording access to any site [46], [65]. Microsystems using both active (multiplexed and nonmultiplexed) and passive electrode arrays have been reported, but as these systems evolve, more will likely incorporate on-chip circuitry to reduce lead counts and improve system reliability.

B. Neural Signal Processors

Fig. 13 shows a block diagram of the complete microsystem required for wireless cortical recording, either for neuroscience or for neuroprosthesis applications. After amplification of the neural signals, here using 16- or 64-channel amplifier chips housed in the electronics package, the signals are fed to a neural signal processor (NPU). In its simplest form, such a processor could be realized by a simple time-domain analog multiplexer as in Fig. 14. This approach keeps the system complexity low as long as the number of recording channels is small. For instance, the three-channel analog recording system reported in [66] easily fits on a 2.2 × 2.2 mm² chip in 1.5 μm CMOS technology. As soon as the number of channels grows, however, the amount of neural

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**Fig. 18.** (a) Time-domain data compression in an eight-channel spike detector module by using a local memory and (b) forming the outgoing data packets out of the neural activity retrieved from four such modules.
information to be wirelessly transmitted will increase to such an extent that it cannot be easily handled. Thus, the signal processor in Fig. 13 must take a more active role in processing and compressing the recorded data. Much of the emphasis in future generations of implantable microsystems will focus on improving both the quantity and quality of neural recordings. Work on the former will focus primarily on increasing the number of channels, while quality will focus on preserving as many features of the neural signal as possible, starting from the spike width above a user-supplied threshold and progressing to a high-resolution digital record of the spike waveform. In this evolution, tradeoffs among system capability, power, and size will be important. Sophisticated digital signal-processing (DSP) algorithms for spike detection and classification [67]–[73] require too much power and size at present, so reported spike detectors have used user-programmable thresholds to provide information on spike occurrence. This is adequate for some applications [74], [75] and significantly reduces the amount of transmitted data.

A simplified block diagram of a mixed-signal neural processor [76] is shown in Fig. 15. It receives four time-multiplexed analog signal channels, each containing the neural signals recorded on eight sites. After 5-bit analog-to-digital conversion, the resulting signal amplitudes are separated into 32 individual channels. A special-purpose digital spike processor then computes the signal averages and standard deviations for the individual channels and calculates appropriate biphasic thresholds based on a user-specified number of standard deviations. The amplitude of each channel is then compared to its threshold to detect neural spikes. If the channel is active (contains a spike), the sample is tagged with the associated channel address and put in a buffer to be transmitted wirelessly at 2.5 Mbps. This NPU provides full waveform information on neural spikes above threshold, ignores subthreshold noise, saves a factor of about 12 in output bandwidth, and increases the number of allowable channels from 25 to 312.

The 32-channel signal processor [77] shown in Fig. 16 supports two operational modes.

- **In Scan Mode**, all neural channels are scanned for the occurrence of neural spikes. The addresses of the active channels, i.e., channels with above-threshold neural activity, are sorted, packed, and sent to the outside world through a reverse (outgoing) telemetry link. The threshold polarity (positive, negative, or biphasic) and its level are set by the user for each channel individually.

- **In Monitor Mode**, a neural channel is selected, sampled at high resolution, and transmitted to the outside world.

This processor is equipped with additional circuitry that allows it to be used as a 32-channel module in a 64-channel neural processing architecture. **Intrachip modularity** (implemented by using eight-channel spike detector modules (SD-8) in parallel) helps achieve high channel scan rates. The number of channels handled by each module, the number of parallel modules, and the size of the local memory on each module are parameters that can be optimized according to the targeted recording

![Diagram](image)

**Fig. 19.** Data packaging [80]: (a) Incoming data packet, (b) outgoing data packet in Scan Mode, and (c) outgoing data packet in Monitor Mode.
capacity and speed. *Interchip modularity* allows expansion of the system by simply configuring one processor as the master and another one (or more) processor(s) as the slave(s).

C. Data Compression

Perhaps the simplest scheme for sending the detected neural activity to the outside world is to use time-division multiplexing, as illustrated in Fig. 17. The binary outputs of all the spike detectors are periodically scanned and sent to the external interface after data packet formation [78]. However, since the extracellularly recorded action potentials from cortical neurons have typical durations of approximately 1 ms with firing rates from < 1 to 150 spikes per second [79], the output of each spike detector contains useful information (neural activity) only a small fraction of the time. The binary transmissions can therefore be punctuated with longer pauses to reduce traffic on the external interface and extend the battery life of the system. As shown in Fig. 17(a), the binary outputs periodically scanned at a fixed rate are combined with the control and power signals in the Manchester encoding format and sent to the external interface through an OOK modulated wireless link.

**Fig. 20.** Wireless transfer of data packets along with a synchronized clock [80]: (a) functional block diagram and (b) actual operating waveforms.
portion of time. Hence, transmitting the outputs of all the spike detectors (independent of their contents) wastes significant recording bandwidth. A more efficient approach is to transmit only spike activity information from active channels [77]. Here, when a spike is detected on a given channel, the address of that channel is sent to the external host. As shown in Fig. 16, the local memory in each SD-8 module temporarily stores the active channel addresses. The memory space is shared among all eight channels. The data fusion core polls the four SD-8 modules to fetch the active channel addresses, completing the process of spike detection, channel-address tagging, spike sorting, and spike queuing. The addresses retrieved from the four parallel queues will then be used to make an outgoing data packet, as illustrated in Fig. 18.

D. Bidirectional Wireless Interfaces

Implantable recording microsystems need to be powered and programmed through a forward telemetry link in order to perform long-term wireless recording via a reverse wireless path, as shown in Fig. 13. To support these requirements, a major building block in such systems is a bidirectional wireless interface that contains at least two parts:

- a forward telemetry front-end that retrieves an incoming stream of data packets containing setup commands and data and provides the microsystem with regulated supply voltages derived from the modulated inductively coupled radio-frequency carrier.
- a reverse telemetry back-end that prepares the outgoing stream of neural data packets, and transmits the recorded information to the external world.

E. Data Transfer and Packaging

Wireless digital data transfer between the implantable microsystem and the external host is basically asynchronous, so to simplify detection and minimize power, a synchronized clock is embedded in the data stream. To facilitate recognition of a data packet and help the receiver separate it from the preceding one, a start pulse (usually a predefined pattern of 0s and 1s) is sent ahead of each packet, and parity bits are added to each packet to allow error detection. Fig. 19 shows incoming and outgoing data packets [80], designed to program the microsystem and transmit the recorded information, respectively. In the incoming data packet, B0 and B1 encode four commands, and B2–B9 carry the channel address of interest for either spike detection setting or for Monitor Mode operation, or to convey required settings to the channel of interest for operation in Scan Mode. The outgoing data packet format in Scan Mode reports the detected neural activity on one channel per each SD-8 using four bits. Every 8 bits are accompanied by a parity bit. In Monitor Mode, each data packet carries two consecutive 8-bit amplitude samples, along with two parity bits. The chip address bit (CAB), seen in the outgoing data packet in both modes, is used when two 32-channel neural processors of the same type (shown in Fig. 16) are connected in a master–slave configuration to realize a 64-channel processor. The CAB represents the chip that has
prepared the data packet ("1" for the master chip and "0" for the slave).

Fig. 20 presents the functional details of the reverse telemetry link. First, the data packets are Manchester encoded in order to incorporate the system clock. Then, the encoded bit stream is on-off key (OOK) modulated and is wirelessly transmitted to the external system. On the external receiver side, after amplification, the reverse process consisting of OOK demodulation and Manchester decoding is performed in order to retrieve the received data and a synchronized clock.

F. Wireless Recording

Wireless implantable recording microsystems have recently been demonstrated [78], [80]. Fig. 21 shows in-vivo recordings obtained in Monitor Mode from the guinea pig auditory cortex using one of these systems [80]. The “original signal” here is the amplified neural signal before analog-to-digital conversion on the microsystem side, and the “reconstructed signal” is the retrieved signal after passing through the wireless link, external receiver, and postprocessing software in the host computer (see Fig. 13). The signals shown in Fig. 21 are a small slice of a 30-s recording in which two separate units were identified based on postrecording analysis. For the first unit, the signal/noise ratio (SNR) decreased from 11.21 on the system side to 8.77 after recovery on the external side; the second unit experienced an SNR reduction from 4.56 to 3.35 in passing through the same path. This degradation in the signal quality comes from analog/digital conversion with 8-bit resolution. Wireless data transfer does not contribute to SNR reduction because digital data modulation/transfer is used. Averaged over 24 886 data packets, the packet error rate was 0.33%, which is excellent performance for wireless data transfer in this application. For a 2 MHz clock, the channel scan rate for spike detection in this system is 62.5 k/s and the total system power dissipation at 1.8 V is 14.4 mW. The implantable version of the microsystem measures 1.4 × 1.55 cm2, fitting on a U.S. penny.

IV. CONCLUSIONS

The technology for creating neural probes capable of acutely measuring the neuronal activity throughout a volume of tissue is now in place. Using three-dimensional arrays of stimulating and recording electrodes, detailed mapping of connections in the nervous system should soon be possible. Such studies will give important insights into the signal-processing techniques used in the nervous system and into the disorders that disrupt them. For chronic studies, further advances are needed in the electrode–tissue interface, and these needs are driving electrode size toward cellular dimensions and below. Beyond the electrodes themselves, substantial progress has been made in the cables, site-selection and amplification circuitry, embedded neural signal processors, and wireless interfaces needed for chronic investigations in neuroscience and for neural prostheses. The first completely implantable neural microsystems are now emerging and should stimulate substantial progress in both areas. The coming decade should see some dramatic breakthroughs in our understanding of the nervous system and in our ability to treat its disorders.

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