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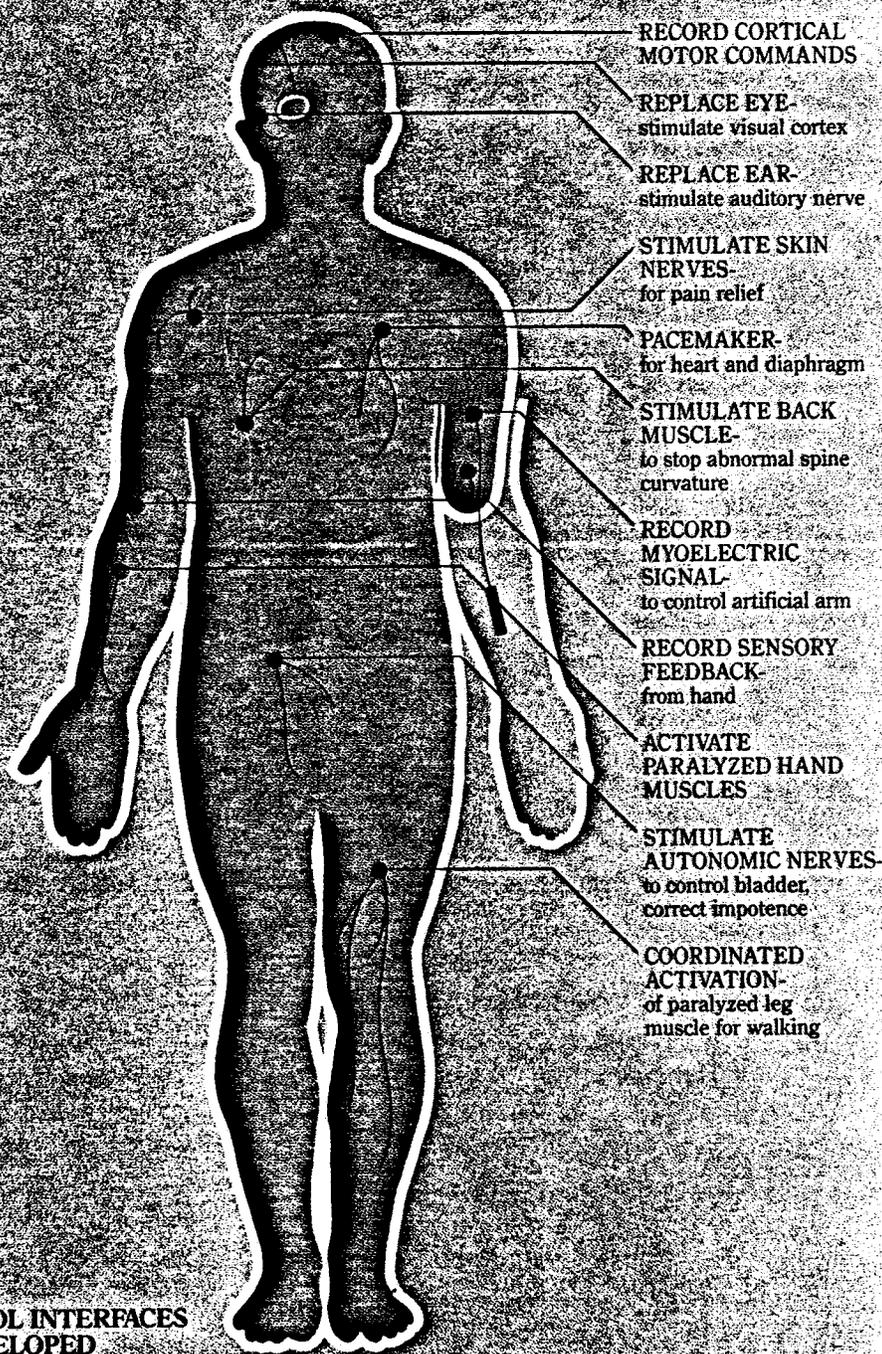
Routine pre-hysterectomy endometrial biopsy

Mesenchymal chondrosarcoma

Hypertensive encephalopathy

Corpus callosal lipoma

CME quiz



NEURAL CONTROL INTERFACES
NOW BEING DEVELOPED



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Keynote address: Neural control and prosthetics— Interfaces with the nervous system

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Imagine a complex manufacturing plant that has been completely automated. Everything is under the control of a central computer: the ordering of raw materials, the operation of machine tools, the maintenance and repair of capital equipment, the shipping of products, and the accounting of expenses and income. No matter how well the system was originally designed, problems are bound to arise: equipment breaks down, market demand changes, some assembly lines back up, while others lie idle. Now imagine that you are hired to get things working again. Your workshop has lots of mechanical and plumbing parts and tools, but you are told that you can't change the computer program or repair or modify any of the electrical circuits. I think most of us would quit in frustration rather quickly.

Yet that is approximately the situation in which medical practitioners work today. We have acquired amazing tools to diagnose, treat, and repair the mechanical, chemical, and plumbing functions of the body, but the central nervous system that controls it all has remained virtually untouchable. It has been estimated that 80 percent or more of the symptoms that cause patients to seek medical treatment arise through damage to or dysfunction of this global control system. People become patients when they cannot interact properly with the outside world: pain, paralysis, impotence, incontinence, deafness, and blindness.

There are two fundamental reasons why the treatment of neurological dysfunction lags so far behind other fields such as orthopedic and cardiovascular surgery. First, nervous tissue is not self-repairing. Bones and blood vessels have mechanisms for completing the functional repairs that are started by surgeons, but sense organs and central nervous system neurons neither regenerate nor reconnect. Second, the physical scale of function in the nervous system is much finer. The smallest ossicle or arteriole amenable to microsurgical repair is likely to perform a singular, easily identified function. A similarly sized nerve tract contains thousands of diverse and independent functional elements. And there may be a third, not so fundamental reason: the neurosciences seem to be the most isolated of medical specialties. A circulatory physiologist could probably give a passable lecture in renal physiology, but most wouldn't volunteer to explain the Hodgkin-Huxley equation

describing the neural action potential. A chest surgeon could certainly take out an appendix, but he wouldn't resect a brain tumor. However, as clinicians start to repair the control circuits as well as the mechanical equipment, we will need interdisciplinary specialists who know something about how nerves work as well as the functions they are supposed to control.

The concept of neural control

Some of the functions performed by our central nervous system have started to be duplicated using the artificial intelligence of computers. While still vastly inferior to our normal sense organs, computers can use video signals to "see" objects and microphone signals to "understand" human speech. Robotic controllers can organize the movement of motorized "arms" and "hands" to perform useful tasks. Given that both brains and computers operate via electrical impulses, it should be possible to interface the two by exchanging the necessary control signals and data. Neural control consists of development of such bidirectional interfaces.

The most common form of interface consists of an array of metal electrodes positioned close to nerve fibers whose activity must be recorded and/or stimulated. The objective may be functional restoration, basic neurophysiological research, or a combination of the two. The methodology involves a variety of physiological and engineering disciplines, but there are unifying principles that have facilitated recent, rapid progress across widely separated clinical fields: (1) Most neural circuits transmit information via large numbers of parallel channels, each of which uses pulse-rate coding to signal the amplitude of a single dimension of information (e.g., brightness, loudness, force, etc.); (2) the all-or-none impulses consist of fluxes of cations which are controlled by well-characterized membrane processes and which propagate through the volume-conductive body fluids in predictable ways; (3) electronic circuits carrying current in the form of electron motion in metal conductors can interact in both directions (recording and stimulating) with the biological ionic currents using safe, stable, easily controlled electrochemical reactions; and (4) the closer an electrode is to a given neural process, the better it is able to selectively record or evoke activity in that process.

As we learn to build and implant arrays

with larger numbers of smaller electrode contacts, we become able to interact functionally with more complex and less accessible parts of the central nervous system (Fig. 1). For some functions such as pain control, single channels for activating superficial nerves from outside of the body may suffice (e.g., transcutaneous electrical nerve stimulation). For others such as vision, hundreds of channels, each directly and locally activating only a few neurons directly in the cerebral cortex, will be required. In between, lies the present, rapidly expanding state of the art.

Auditory prosthetics

Perhaps the best-known and most successful clinical application of neural control is in the treatment of profound sensorineural hearing loss. There are hundreds of thousands of deaf patients with relatively intact auditory nerves and perceptual centers who derive no benefit from hearing aids because they have lost their cochlear hair cells, which normally transduce acoustic vibrations into neural impulses. Perhaps a dozen different functional cochlear prostheses are now commercially available or undergoing clinical testing. Although they are quite different in their electrode placements and signal processing, they all work by transforming the sounds picked up by a microphone into patterns of electrical stimulation directed toward the remaining auditory nerve fibers. Even a single channel of such stimulation can produce clinically useful auditory sensations via the temporal information content of common sounds. While far short of enabling speech comprehension, such devices aid in lipreading, permit identification of many ambient sounds (e.g., doorbells and car horns) and help the wearer control and modulate his own speech. Multichannel devices divide the stimulation among spatially localized subsets of tonotopically organized auditory nerve fibers, thereby replacing the tuned spatial filter of the basilar membrane as well as the transduction of the hair cells. Predictably, these devices provide much more information and are now verging on providing unaided speech recognition, at least in selected subjects under acoustically clean ambient conditions.

From these devices we have learned two important lessons. First, the empirical results have confirmed the applicability of theoretical biophysics to

electrically excitable processes. The actual and relative performance of these prostheses and the agreement among design predictions, animal testing, and clinical performance mandate that future work on even more ambitious neural control interfaces must be based on these principles, rather than the cut-and-try empiricism that was required of the pioneers in this field. Second, the clinical evaluation of these devices has provided an unparalleled opportunity to conduct psychophysical experiments regarding some of the least understood cognitive processes of the human brain. We have just begun to exploit this basic research aspect of neural control, but it seems likely that the iterative process of building well-characterized electrode arrays, testing the responses of human subjects to well-controlled patterns of electrical stimulation, and then redesigning the prostheses accordingly, will lead to rapid advances in both neuroscience and prosthetics.

Functional neuromuscular stimulation

This is another ambitious, active, and promising application of complex neural control interfaces, although clinical rehabilitation remains as yet somewhat elusive. Current research includes reanimation of the hand in quadriplegics, walking in paraplegics, and bladder control in a variety of spinal cord disorders. Patterned electrical stimulation of muscle nerves can provide tension and motion. As with sensory prostheses, the complexity and finesse of the possible motor activities so elicited depends on the number and selectivity of stimulation channels. However, there are several factors that further complicate clinical implementation:

(1) In addition to pure motor effects, electrical stimulation tends to activate

the complex reflex-control circuits which persist but tend to vary greatly in their functional state among patients.

(2) Most motor behaviors require detailed and rapid command signals from the patient to be executed safely and efficiently. These must be obtained from the limited set of motor functions still under voluntary control by the patient or by direct recording from motor cortical centers where they presumably originate.

(3) Most motor behaviors are regulated both consciously and unconsciously by multimodal somatosensory feedback. These signals must either be recorded and decoded from afferent nerves or replicated via electromechanical transducers and then reintroduced to both the patient and the stimulation control circuitry.

(4) Sensory prostheses rely on the brain to perform the computational chores of perception, so the designer only needs to know the form of the required input signal, not the perceptual algorithms. The controller for a functional neuromuscular stimulation prosthesis must embody the control algorithms of such poorly understood central nervous system centers as the cerebellum and spinal cord.

Nevertheless, primitive but useful motor control has been achieved in clinical trials of functional neuromuscular stimulation controllers of the hand, legs, and bladder. For determined patients and practitioners trying to cope with problems of living for which no alternative is available, the limited performance and surgical intervention will be deemed acceptable, providing researchers with continuing opportunities to refine their understanding of motor control and the capabilities of the prostheses.

The future

The past decade has been spent building the tools, both technical and conceptual,

that space constrains me from detailing here (see references for further reading). We are now beginning to build the prostheses. Even with these sophisticated tools, progress will come by evolution rather than revolution, moving cautiously through the cycles of design, fabrication, animal and clinical testing, and then redesign and retesting. Yet each time around each loop, we will learn important things about our science and our technology that will have implications for many other applications of neural control.

This synergism will be exploited best by multidisciplinary teams with larger perspectives than a single device or disorder. We need imaginatively led teams in which the very different expertise and personalities of clinicians, engineers, and basic scientists can work together smoothly on a variety of projects. We need administrative and funding mechanisms that permit assembling a critical mass of technology, science, and rehabilitation services. But above all, we need persons who know enough about enough different aspects of these problems to be able to find, understand, and implement the solutions that are starting to emerge.

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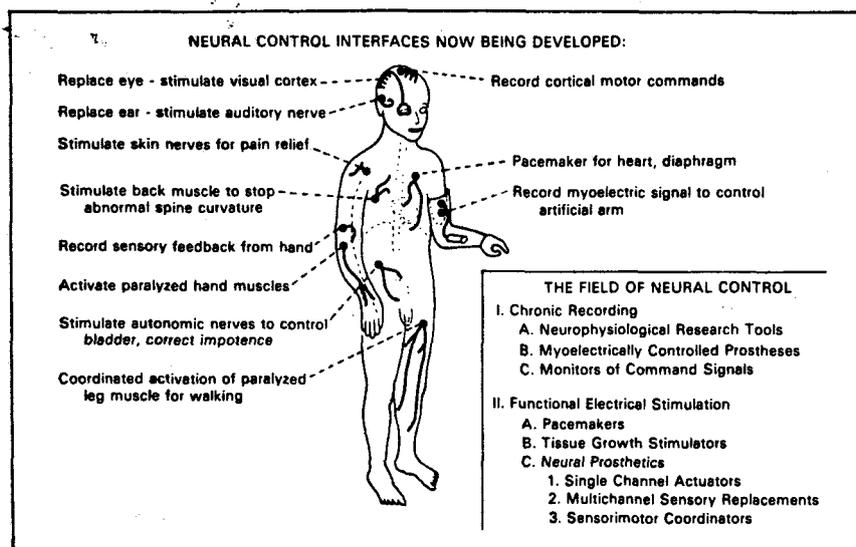


Fig. 1.