KIM R. FOWLER and RICHARD B. NORTH

COMPUTER–OPTIMIZED NEUROSTIMULATION

An implantable device called a neurostimulator alleviates chronic pain by delivering electrical pulses to the nervous system of a patient. The Applied Physics Laboratory, in collaboration with the Department of Neurosurgery at the Johns Hopkins Hospital, has developed software and a computer interface for patients to adjust and test their neurostimulators. The computer and interface extend the capabilities of the neurostimulators in both research and clinical practice.

INTRODUCTION

For the past two decades, electrical stimulation has been used to manage chronic, intractable pain. Stimulation of nervous tissue can evoke a sensation—paresthesia—while producing relief from pain—analgesia. Empirically, the paresthesia must correspond closely to the area of the pain within the body for therapeutic and analgesic effects to occur.

Permanently implanted devices generate and deliver the stimulation to the nervous system via electrodes. The most common site to implant the electrodes has been over the spinal cord in the dorsal spinal epidural space.[1] Stimulating nerves in the spinal cord can alleviate pain following lower back surgery and pain from injury to the lower extremities.

Figure 1 illustrates the general configuration for delivering electrical stimulation to nervous tissue. The transmitter and implanted receiver are RF coupled. The transmitter, worn externally by the patient, encodes the stimulation parameters and the electrode selections, which are then transmitted to the implanted receiver. The implant decodes the transmitted information and generates the desired electrical impulses for stimulation. The implant derives power for stimulation by rectification of RF energy generated by the transmitter; a typical implant generally has no other source of power.

Historically, the first stimulation devices were single-channel systems that drove monopolar or fixed bipolar electrodes. Because the position of the electrodes near the spinal cord proved critical to the analgesic effect, arrays of electrodes were developed that could be introduced and positioned through a needle.[2] At first, percutaneous (i.e, through-the-skin) test leads were used to determine the hard-wired configuration of an array of electrodes connected to a single-channel implant. For the past several years, programmable, multichannel implants have permitted the noninvasive selection of anodes and cathodes from arrays of electrodes. By permitting postoperative selection of electrodes, multichannel implants expedite surgical implantation and minimize the need for subsequent surgical revision of electrode position.

LIMITATIONS

Adjustments of multichannel implants pose considerable challenge, however, particularly if all combinations of anodes and cathodes are to be studied exhaustively. With four-electrode systems, fifty electrode combinations are possible; for newer systems incorporating additional electrodes, the number increases disproportionately. In general, for an array of n electrodes, the aggregate number of unique combinations of anodes and cathodes (including at least one of each polarity) is given by
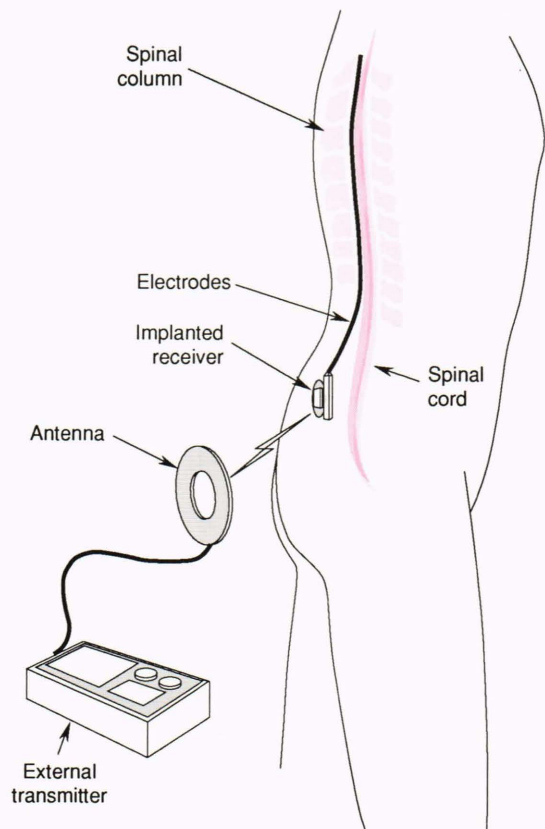

Figure 1. Schema for neurological stimulation.

$$\sum_{m=2}^{n} [n!(2^m - 2)] / [(n - m)! \, m!].$$

For example, eight-electrode systems have 6050 possible combinations.

Clearly, more electrodes tax the capabilities of the physician and medical staff to inventory the available electrode combinations in a reasonable time. Adjustments to the stimulation's pulse width or frequency compound the problem. Further difficulties arise with operator bias and with data acquisition and reduction.

COMPUTER INTERFACE

Optimizing stimulation for pain relief requires a large number of rather trivial, repetitive, and time-consuming tasks. Obviously, automating the process would save time for health professionals and would improve the acquisition and analysis of data. Therefore, we have developed an interface from an IBM personal computer to three commercially available RF transmitters (the Neuromed MNT-4, and the Medtronic SE4 and 3522). The computer, interface, and transmitters are collectively called the Neurological Stimulation System (NSS).

The NSS controls the associated implanted receivers and electrodes through antennas and RF coupling to stimulate the nervous system. The transmitters are housed in a peripheral enclosure and are connected by a cable to the computer. The enclosure also incorporates potentiometer and push-button controls for patient use. Figure 2 shows the first version of the NSS.
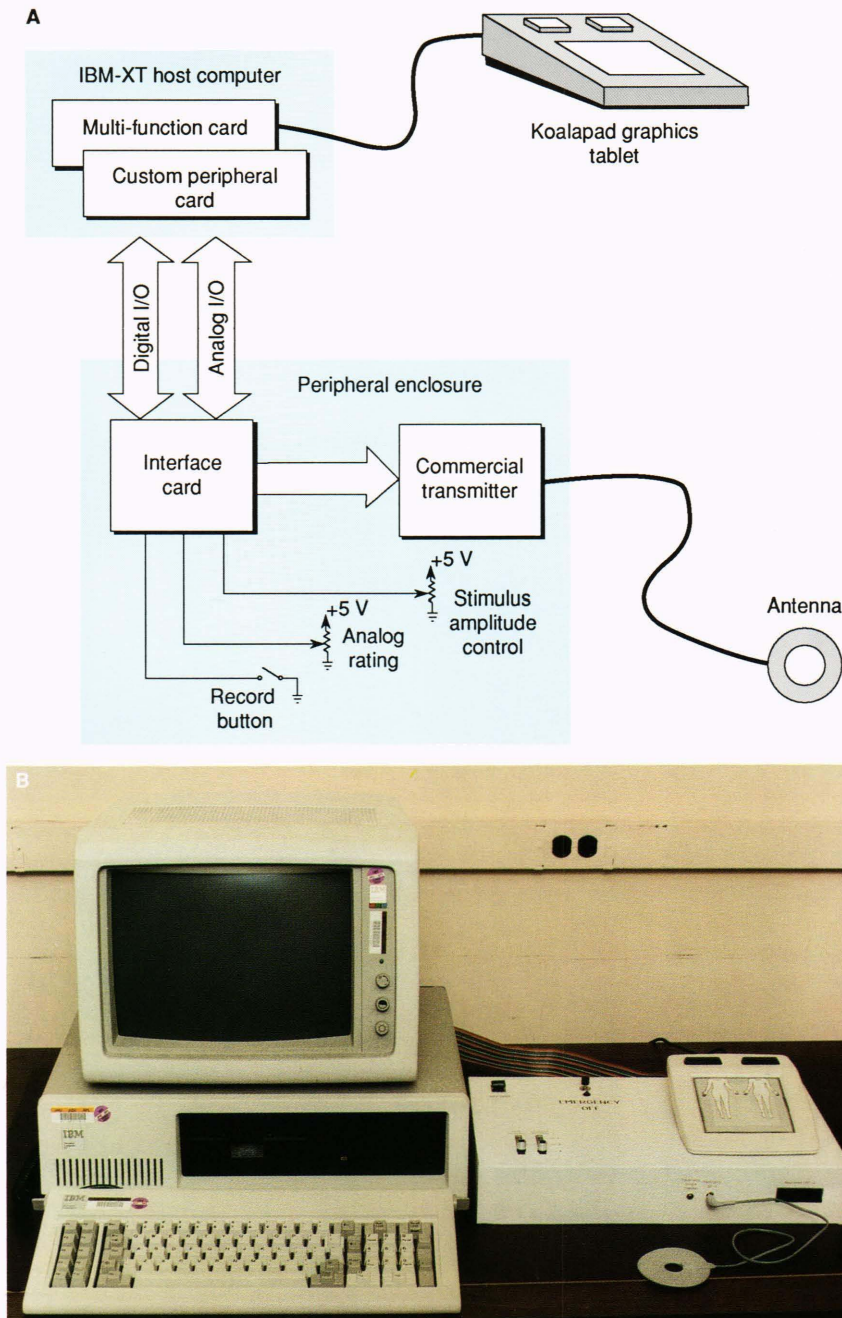

Figure 2. Neurological Stimulation System (NSS) currently in clinical use. **A.** Block diagram of the first version of the NSS. **B.** General configuration of the NSS.

The patient interacts with the NSS without direct supervision from the physician. The controls are both easier for the patient to operate and fewer in number than those of a standard commercial transmitter. A Koalapad graphics tablet permits the patient to enter outlines of his painful areas and of the stimulation paresthesias. Visual feedback and instructions are presented to the patient via the computer. The keyboard is required only by the system operator for program initialization and data analysis.

In routine clinical use, the NSS automatically presents a pseudorandom sequence of two-, three-, or four-electrode combinations. In addition, the NSS presents the stimulation with the pulse width and interpulse intervals defined by the physician or operator. The patient responds to the stimulation by controlling the amplitude of the stimulation and recording its effects. The patient then outlines the areas of paresthesia on sketches of the body on the tablet and subjectively rates the effect of the stimulation by adjusting a potentiometer. In this manner, the NSS records the optimal settings for the patient's transmitter. Figure 3 shows the graphical interface of the NSS.
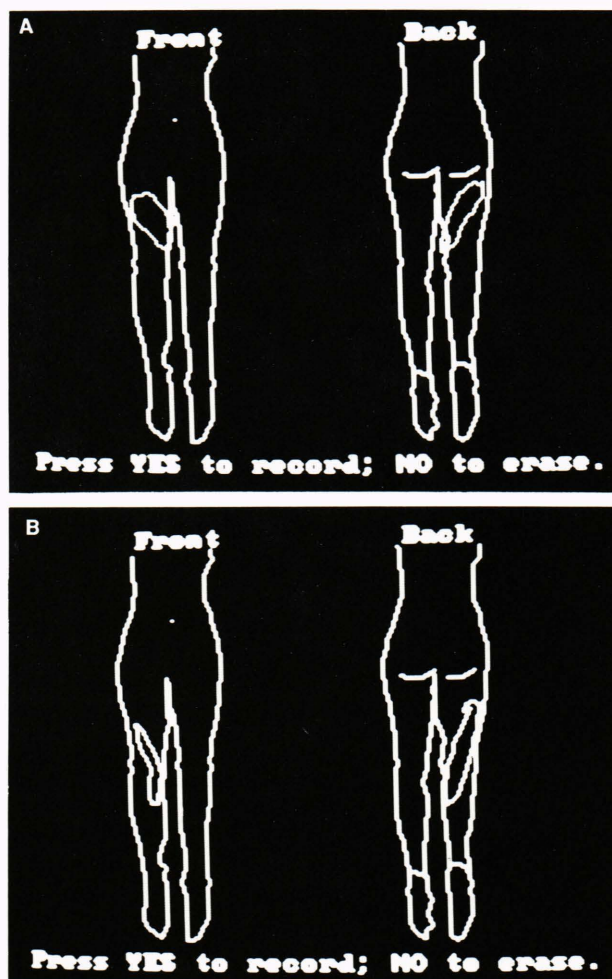
GRAPHICAL DATA ANALYSIS

After recording graphical data from the patient, the NSS quantitatively analyzes it. The software anneals the raw data that represent outlines around painful areas and stimulation paresthesias by closing the open contours and then by filling the interior of each outline. The software identifies the intersection of each outline with the interior of the body outline, compares the resulting pain and stimulation maps, and identifies the areas of overlap. Overlap is quantified as the ratio of intersection of pain and stimulation maps to the total area of the pain map, and is then tabulated with corresponding amplitude settings and patient estimations of pain relief.

Figure 4 illustrates the analysis that calculates overlap between areas of pain and stimulation. The calculated overlap, shown as "pain cover" in Figure 4, is 32%. The patient's rating of pain relief, shown as "pt. cover" in Figure 4, is 45%. The amplitude of stimulation at the usage level (Fig. 4) is 32% of full scale. The usage level is one of three levels of instruction given to the patient to indicate the amplitude of the self-administered stimulation. The combination of electrode polarities used in this session is "– off + off."

INITIAL CLINICAL APPLICATIONS

The goals of the stimulator adjustment were to maximize the overlap of stimulation paresthesia with the topography of pain, to minimize extraneous paresthesia
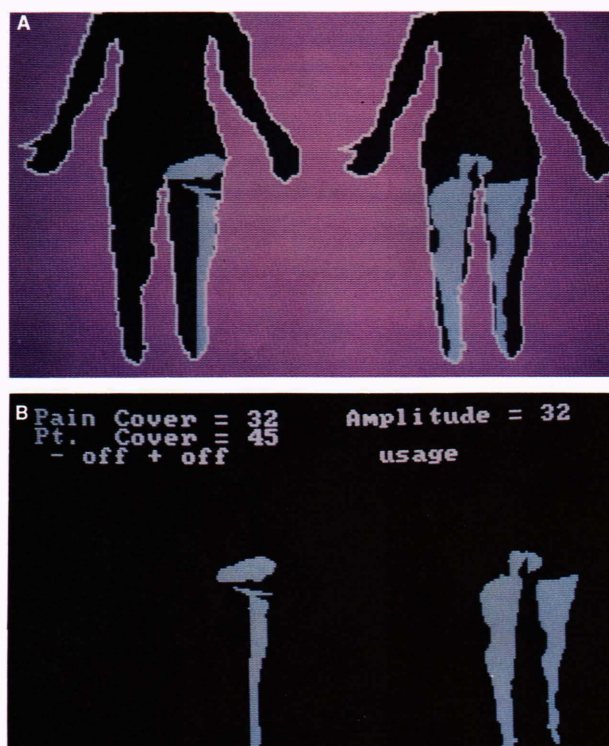

Figure 3. Graphical displays of data entered by a patient. **A.** Outlines of painful areas as entered by the patient. **B.** Outlines of stimulation paresthesias as entered by the patient.

Figure 4. Analysis of the overlap between painful areas and stimulation paresthesias. **A.** Outlines filled with blue color indicate areas of stimulation paresthesias. **B.** Results of calculating overlap for one combination of electrode polarities at one stimulation level.

outside the topography of pain, and to minimize the associated uncomfortable muscle cramping. Two experiments examined and optimized the overlap of the painful areas with stimulation. In the first experiment, the operation of the NSS and the manual operation of a transmitter were compared to determine the utility of the NSS. The metrics of comparison were the time duration of testing and the number of combinations of electrode polarities that the patient used for pain relief. In the second experiment, the computer-calculated overlap between the stimulation paresthesias and painful areas was correlated to the patient's estimate of overlap.

The NSS optimized stimulation for each patient through a series of steps. First, each patient ran a tutorial program for instruction in operating the controls and graphics tablet. The NSS then prompted the patient to draw outlines on the graphics tablet to indicate the areas of pain on the sketches of the body. The NSS selected, in random sequence, a combination of polarities for the four electrodes and then generated stimulation at fixed parameters (e.g., pulse widths of 200 ms and repetition rates of 60 pulses/s) while the patient controlled the amplitude. For each combination, the NSS prompted the patient to adjust the amplitude incrementally upward to one of three levels. At each amplitude and for each electrode combination, the patient recorded both an outline of the topography of the paresthesia and a magnitude estimation of the paresthesia's overlap with the topography of the pain. Patients were selected randomly from an ongoing clinical series regardless of prior exposure to computers or perceived aptitude.

To compare patient operation of the NSS, each patient manually adjusted the transmitter under supervised instruction. First, each patient received instructions in using the standard transmitter from a physician's assistant. Then the patient was assisted in testing the stimulation parameters. For each combination of electrode polarities, the assistant recorded verbal descriptions of both the stimulation coverage and the magnitude estimations of the overlap between paresthesia and pain. Following discharge from the hospital, each patient continued to test stimulation parameters so as to optimize pain relief.

RESULTS

Twenty-five patients with spinal cord stimulators implanted for the relief of chronic, intractable pain used the NSS, and their results demonstrated its utility.

The NSS eliminated the time required by a health professional to supervise the adjustment of a transmitter, while slightly increasing the time for adjustment by a patient. In addition, the NSS yielded useful combinations of electrode polarities for the patient in the same proportion as those found from supervised adjustment by a physician's assistant. In contrast, unsupervised testing by patients outside the clinic resulted in significantly fewer useful combinations being found in comparison with testing with the NSS or a physician's assistant.[3]

Pain relief is associated with the overlap of painful areas by stimulation paresthesias. Analysis of the clinical data strongly correlated the overlap of stimulation paresthesias and pain topographies with magnitude estima-

tions of pain relief by the patients. Figure 5 is a graph of the correlation between the overlap and pain relief for patients six weeks after the initial adjustment of the stimulators. Multivariate analysis of the relationship between stimulation performance and electrode geometry revealed that "guarded dipole" configurations (central cathodes flanked by anodes) enjoyed a significant performance advantage. Furthermore, cathode and anode positions, dipole lengths, and dipole orientations were not statistically significant predictors of overlap of stimulation paresthesias and pain.[4]

DISCUSSION

The great majority of our patients have adapted readily to the NSS—interacting with the computer and peripherals directly, running the tutorial program quickly, and requiring no ongoing supervision. By comparison, routine patient instruction in the use of the standard commercial transmitter is more time-consuming for health professionals.

For many patients, the NSS has become the primary method of optimizing the adjustment of stimulators, at considerable savings in professional time. In practice, the NSS has not replaced, but rather has supplemented, patient education in the manual adjustment of the standard device. Psychophysical data collected by the system have shown a close correspondence between graphical data (that indicate the topographies of pain and stimulation paresthesias) and patient ratings of pain relief. For typical topographies of lower back and lower extremity pain, overlap was significantly better for guarded dipole configurations.

ONGOING DEVELOPMENT

For future research purposes, we are redesigning the NSS so that it may reprogram all electrode combinations and stimulation pulse parameters in less than 1 ms from one pulse to the next. The redesigned NSS will confer virtual multichannel capabilities on neurostimulation de-
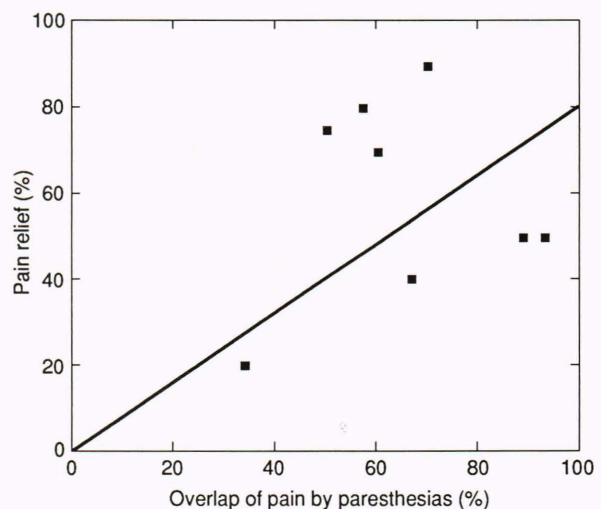

Figure 5. Pain relief compared with the amount of overlap between stimulation paresthesias and painful areas.

vices, which technically are single-channel systems gated to multiple outputs. Various pulse-modulation algorithms that cannot be achieved with standard commercial hardware will be generated by the redesigned interface and studied for therapeutic effect.

Figure 6 shows the components of the redesigned system. The interface replaces the manual adjustment knobs and switches of a commercial transmitter with a graphics tablet. The microcontroller within the interface accurately times the pulse width and frequency of the stimulation produced by the transmitter. The redesigned NSS will have a new graphics tablet that is easier to use and has much greater resolution. All input from the patient will be accepted through the graphics tablet, including the outlines of pain and stimulation paresthesia, analog rating scale, and stimulus amplitude control.

The redesigned interface will free the host computer from the mundane task of real-time control of the transmitters and will provide independence from the host computer architecture and software. Therefore, the host computer may perform real-time analysis or other tasks while the interface controls the transmitters. Also, the interface will allow a variety of computers to fill the role of host for the NSS.
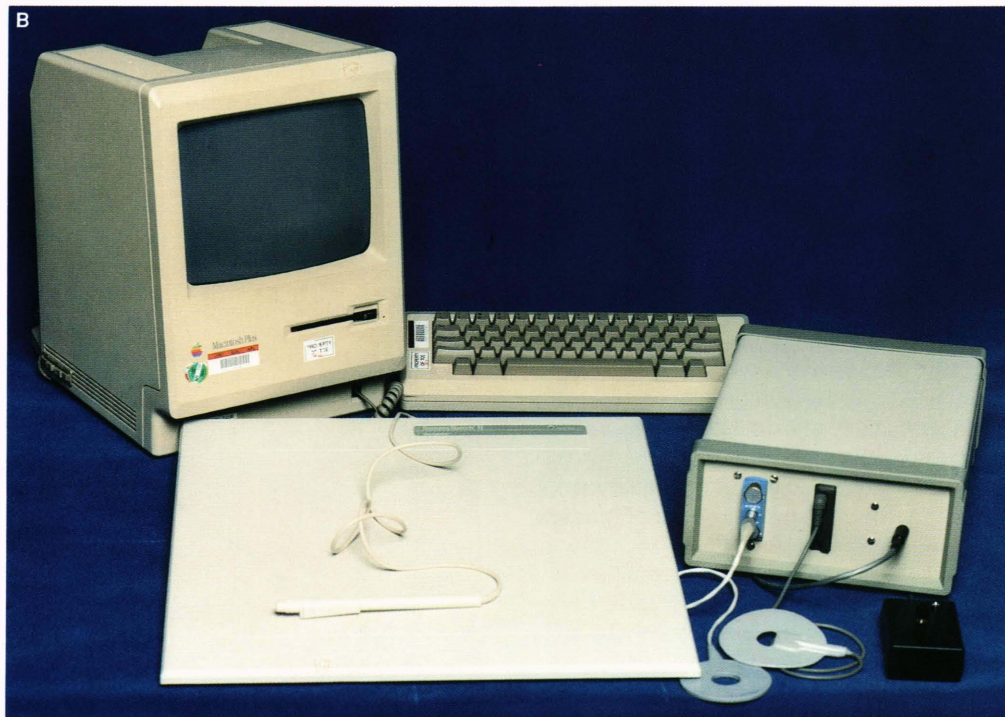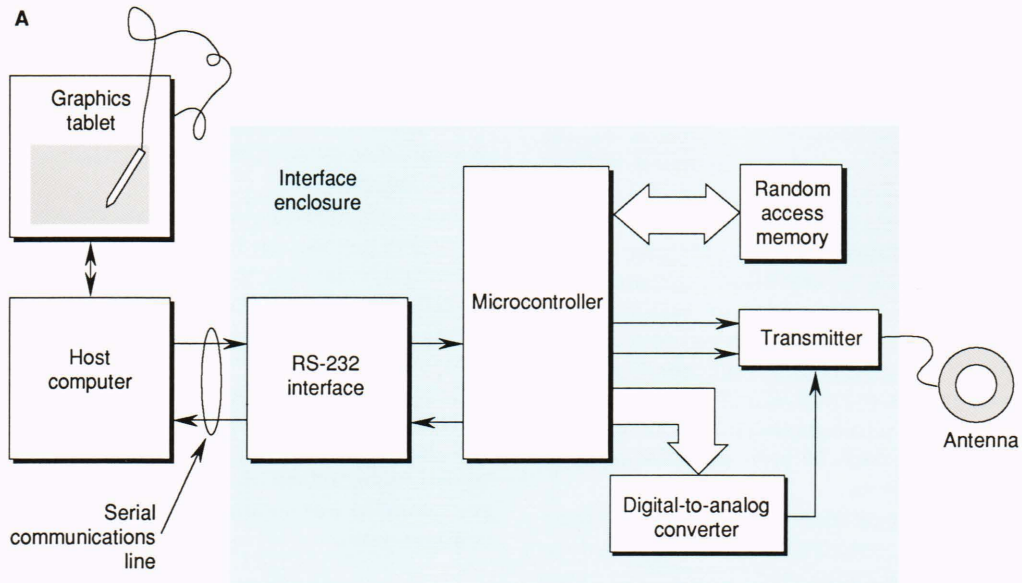

Figure 6. Components of the redesigned neurological stimulation system. **A.** Block diagram of the redesigned interface. **B.** Components of the system.

CONCLUSION

Computer-controlled, patient-interactive adjustment of implanted stimulators has proven clinically useful. Psychophysical data collected by the NSS have been consistent with clinical observations, indicating performance advantages for particular electrode geometries. Ongoing development of the NSS will accommodate the increasing number of electrodes provided by new generations of neurostimulation devices and will permit the delivery of novel stimulation sequences.

REFERENCES

[1] Long, D., Erickson, D., Campbell, J., and North, R., "Electrical Stimulation of the Spinal Cord and Peripheral Nerves for Pain Control: A 10-year Experience," *Appl. Neurophys.* **44**, 207–207 (1981).

[2] North, R. B., Fischell, T. A., and Long, D. M., "Chronic Stimulation via Percutaneously Inserted Epidural Electrodes," *Neurosurgery* **1**, 215–218 (1977).

[3] North, R. B., Nigrin, D. J., Szymanski, R., and Fowler, K. R., "Computer-Controlled, Multichannel, Implanted Neurological Stimulation System: Clinical Assessment," in *Pain,* Supplement 5, Elsevier Science Publishers, Amsterdam, p. S83 (1990).

[4] North, R. B., Nigrin, D. J., Fowler, K. R., Szymanski, R., Reagan, B., et al., "Pain Drawing Analysis by Computerized, Patient-Interactive Spinal Cord Stimulation System," Poster 33, The 7th Annual Meeting: Joint Section on Disorders of the Spine and Peripheral Nerves, Rancho Mirage, Calif. (13–17 Feb 1991).

THE AUTHORS
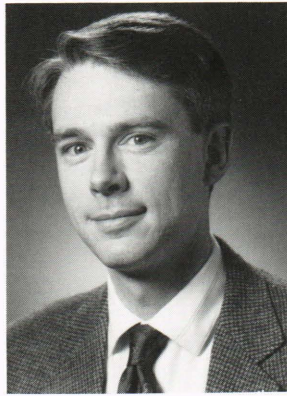
KIM R. FOWLER graduated from the University of Missouri—Rolla with a B.S.E.E. in 1978. He studied biomedical engineering at The Johns Hopkins University School of Medicine and received an M.S. in 1982. Mr. Fowler has worked at APL since 1982 in the Technical Services Department's Computer Engineering Group. He has been involved in a variety of projects such as arc fault detection, EF-111A electronic warfare development, SDIO (Delta 180, 181, and 183), and several medical devices.

RICHARD B. NORTH was educated at Harvard and The Johns Hopkins University School of Medicine. While on an APL postdoctoral fellowship in biomedical engineering, he worked on prototype implantable stimulation devices and drug-delivery systems. Following a surgical internship at Duke University, he returned to Johns Hopkins for training in neurosurgery; he has remained on the full-time School of Medicine faculty ever since. His major areas of clinical activity and research are in functional and spinal neurosurgery, and in particular the management of pain.