

# BION™ system for distributed neural prosthetic interfaces

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## Abstract

We have developed the first in a planned series of neural prosthetic interfaces that allow multichannel systems to be assembled from single-channel micromodules called BIONs (BIOnic Neurons). Multiple BION implants can be injected directly into the sites requiring stimulating or sensing channels, where they receive power and digital commands by inductive coupling to an externally generated radio-frequency magnetic field. This article describes some of the novel technology required to achieve the required microminiaturization, hermeticity, power efficiency and clinical performance. The BION1 implants are now being used to electrically exercise paralyzed and weak muscles to prevent or reverse disuse atrophy. This modular, wireless approach to interfacing with the peripheral nervous system should facilitate the development of progressively more complex systems required to address a growing range of clinical applications, leading ultimately to synthesizing complete voluntary functions such as reach and grasp. © 2001 IPEM. Published by Elsevier Science Ltd. All rights reserved.

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## 1. Rationale and objectives

The functional reanimation of paralyzed limbs has long been a goal of neural prosthetics research, but the scientific, technical and clinical problems are formidable (reviewed in [1]). The BION (BIOnic Neuron) technology described in this paper was originally intended to provide a reliable and convenient means to achieve such functional electrical stimulation (FES). In order to be clinically useful, however, FES usually requires more sophisticated command, feedback and control signals than can be provided by any currently available technology. Therefore, our research has been directed toward three different fronts:

1. understanding the sensorimotor control problem for various voluntary behaviors in order to determine the requirements for sensing and control technologies;
2. extending the capabilities of the BION technology to support the required sensing modalities; and

3. applying the currently available BIONs in therapeutic electrical stimulation (TES) to prevent secondary complications related to disuse atrophy, which appears to offer immediately feasible and commercially viable opportunities [2].

Voluntary exercise is the main mechanism on which most animals, including humans, rely to maintain muscle strength. The field of exercise and sport science has made great strides in identifying exercise regimes to increase the strength, bulk and fatigue resistance of normal muscles. Such regimes are often impossible for individuals with clinical problems such as stroke, cerebral palsy, spinal cord injury and chronic arthritis. Their muscles become atrophic from disuse, resulting in a wide range of pathological sequelae, including contractures, joint trauma, osteoporosis, venous stasis, decubitus ulcers, and cardiorespiratory problems.

In the clinical setting, atrophic muscles have usually been stimulated transcutaneously by using large electrodes mounted temporarily on the skin [3]. This approach has several undesirable features. High stimulus voltages and currents are required to overcome the high resistance of the skin and the long distance to the muscles. The contractions elicited by the stimulation are

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generally confined to superficial muscles, which tend to contain fast twitch, glycolytic and fatigable fiber types. The stimulation often produces unpleasant skin sensations and can cause skin irritation. The technology is tolerated by highly motivated adult patients or athletes who can understand its usefulness; it is often rejected by less compliant or less motivated patients.

Intramuscular electrodes permit more targeted stimulation of selected muscles but the long leads may break and are difficult to repair. Semi-implanted percutaneous systems suffer problems associated with maintaining delicate wires passing through a chronic opening in the skin. Fully implantable multichannel systems are bulky, expensive and difficult to implant if deep or widely separated sites of stimulation are required [4]. They are gaining acceptance for certain FES applications [5], but the expense and morbidity of the surgery itself may be difficult to justify for many therapeutic applications. Various implantable single-channel stimulators powered by radio-frequency (RF) fields have been developed for foot drop following stroke [6–9] but they are not suitable for more general therapeutic use, which often requires separate control of several different muscles.

We have developed a new class of generic wireless devices that can be injected into muscles and near nerves to deliver precisely metered stimulation pulses. Development is underway on a second generation of similar devices that will include sensing and back-telemetry functions to obtain sensory feedback and voluntary command signals required for functional reanimation of paralyzed limbs. This paper describes the functional requirements and technological strategies for this class of devices.

## 2. System specification

Each BION™ (BIONic Neuron) microstimulator consists of a tiny, cylindrical glass capsule whose internal components are connected to electrodes sealed hermetically into its ends (Fig. 1) [10,11]. BIONs receive power and digital data from an amplitude-modulated RF field via inductive coupling described below. The field controlling the devices is produced by using an external coil that can be configured physically in a variety of ways, so that it can be contained inconspicuously in a garment, a seat cushion or a mattress cover. One such transmitting coil can power and control up to 256 individually digitally addressable implants.

BIONs avoid the donning, stimulus adjustment and doffing procedures required with temporary, skin-surface electrodes. BION implants generate digitally controlled, current-regulated pulses (Table 1) [11]. They have been shown to be located permanently and stably in the target muscles [12], resulting in consistent thresholds and muscle responses over extended periods of time [13]. If

additional channels of stimulation are required to treat the patient's condition, they are easily added.

BIONs are small enough to implant by injection in an outpatient procedure that can be performed by any physician. They can be placed in small, deep or hard-to-reach muscles that have been impossible to stimulate selectively from the skin surface. They minimize the threat of infection, skin breakdown or tissue damage, which are important concerns if many long leads and electrodes must be placed in multiple deep sites in patients with circulatory or neurological problems. Further, electrical stimuli are delivered deep to the skin, so that the uncomfortable sensations associated with skin-surface stimulation are avoided.

Eliminating the expense and morbidity of surgery reduces total clinical costs, an important factor for the ultimate commercialization and reimbursement potential of this treatment [2]. None of the external or internal components is intrinsically expensive to manufacture, so economies of scale will eventually make BIONs highly cost-effective for rehabilitation of a wide range of neuromuscular dysfunctions.

## 3. System design

Each patient is provided with an external control box and transmission coil that generates the 2 MHz magnetic field that powers and commands the implant functions (see system block diagram in Fig. 2; external components are illustrated in Fig. 4 below). The present system for exercising muscles is called a Personal Trainer™. As described below, the clinician uses a personal computer to load exercise programs into the Personal Trainer, which converts those programs into sequences of amplitude modulation of the 2 MHz carrier. Each operation of each implant is initiated by a command consisting of 3 data bytes and various formatting and parity bits, requiring a total of 288  $\mu$ s for transmission. The electronic circuitry in each implant consists of a self-resonant receiving coil, a custom integrated circuit (IC) chip, a Schottky diode, and two electrodes. The IC derives direct-current (DC) power by rectifying and filtering the carrier energy picked up by the coil. The carrier itself provides a synchronous clock and its amplitude modulations encode a serial bit stream, which is decoded by a state machine in the IC. The first data byte specifies an address, which is compared with the address specified by a hardwired read-only memory (ROM) in each IC. If they match, the subsequent data bytes are decoded to specify the desired operation. Stimulation operations require a pulse width and a pulse amplitude specification.

The power delivered during a maximal stimulation pulse (30 mA $\times$ 17 V=0.51 W) is about 100 times higher than the power that can be delivered by the inductive

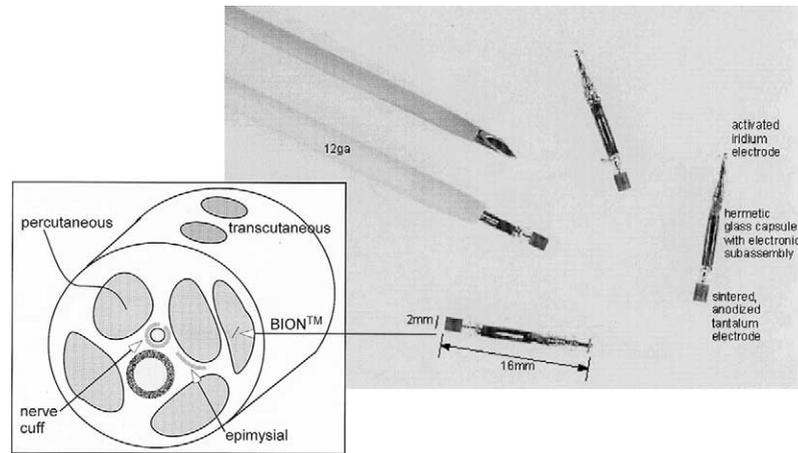


Fig. 1. Neuromuscular interface options shown in an idealized limb with cross-sectional view. Conventional stimulation interfaces include transcutaneous electrodes affixed to the surface of the skin, percutaneous wires inserted into muscles, and surgically implanted multichannel stimulators with leads to electrodes wrapped around nerves as cuff electrodes or sutured epimysially where each muscle nerve enters the muscle. Detail: BION1™ implants shown as they would be injected individually into muscles through the sheath of the insertion tool.

Table 1

BION1 specifications	Values and ranges (decimal)
Address	0–255
Stimulus pulse width	4–512 $\mu$ s in 256 steps of 2 $\mu$ s
Stimulus pulse current	0–30 mA in two ranges of 16 linear steps (0–3 mA, 0–30 mA)
Recharge current	0, 10, 100 and 500 $\mu$ A
Continuous maximal rated output	50 pps (at 10 mA $\times$ 250 $\mu$ s)
Command transmission time	320 $\mu$ s
Dimensions	2 mm o.d. $\times$ 16 mm long

link. This problem can be overcome because the stimulation typically required to activate a muscle consists of relatively brief pulses ( $\sim$ 0.2 ms) at low frequencies ( $<$ 20 pulses per second). During the interpulse period (typically  $>$ 50 ms), energy is stored on an electrolytic capacitor consisting of the tantalum electrode and the body fluids. The Ta electrode is made of sintered Ta powder and is anodized to +70 V DC, providing a large surface area of metal covered with a very high quality, biocompatible dielectric layer of tantalum pentoxide [14]. This results in about 5  $\mu$ F capacitance with less than 1  $\mu$ A DC leakage at the +17 V DC compliance voltage of the BION. The counter-electrode is activated iridium [15], which forms a metal–electrolyte interface that resists polarization under any achievable sequence of charging and discharging of the capacitor electrode [10]. When the carrier is on but the implant is idling, the capacitor electrode can be charged at one of four selectable rates (0, 10, 100 and 500  $\mu$ A) until it becomes fully polarized to the +17 V DC compliance voltage.

Sensing functions require a back-telemetry link that operates during pauses in the external carrier, during which the external coil acts as a receiving antenna. The self-resonant coil in the implant acts as the tank circuit

for an oscillator that is amplitude-modulated to transmit digitized data obtained from a previously commanded sensing operation. The sensing modalities now under development are described later.

### 3.1. Implant packaging

The packaging provides the required injectable form factor, hermetic encapsulation to protect the electronic circuitry from body fluids, and a biocompatible external surface. As shown in Fig. 3, the BION implants are assembled from three principle subassemblies.

- The capsule subassembly provides the bulk of the packaging plus the hermetic feedthrough to the tantalum capacitor electrode. It is formed by melting a borosilicate glass bead on to the Ta wire stem of the sintered Ta slug and melting a short length of glass capillary tubing to the bead to create an open-ended capsule. Both glass-melting steps are accomplished by rotating the parts under an infrared CO<sub>2</sub> laser beam. The internal end of the Ta wire is welded to a small Pt–10% Ir washer to provide a noble metal electromechanical contact with the electronic subassembly.
- The feedthrough subassembly provides the other end of the glass capsule and a hollow feedthrough for testing the glass-to-metal hermetic seals, which are the most critical. It is formed by melting a glass bead on to a Ta tube. The capsule is closed after sliding the electronic subassembly inside, by melting the open end of the glass capillary to the glass bead on the feedthrough tube. A small spring welded previously to the inside end of the Ta tube makes electromechanical contact with the electronic subassembly.
- The electronic subassembly is built like a sandwich



in order to maximize the surface area available for the IC chip and maximize the volume occupied by the ferrite and antenna coil. A ceramic two-sided microprinted circuit board ( $\mu$ PCB) provides the mechanical platform for the inside of the sandwich and makes all of the electrical interconnections on both surfaces and ends. On one side, the  $\mu$ PCB carries the custom IC chip, a discrete Schottky diode chip and their conventional gold wirebonds to the substrate. Two hemicylindrical ferrites are glued to the top and bottom surfaces of the subassembly. The self-resonant coil is wound over the ferrites and solder-terminated to the back of the  $\mu$ PCB.

The unusually small size of the implant (less than 1% of the volume of conventional electronic implants such as cardiac pacemakers and cochlear prostheses) creates unusual demands on the hermetic seals and their testing. The open-ended Ta tube can be attached to a helium leak tester that detects trace amounts of helium applied to the outside of the capsule that might leak through the glass seals down to  $2 \times 10^{-11}$  cm<sup>3</sup> atm/s. However, any leaks just below that level could result in entry of sufficient water vapor over a period of months to reach the dew point at body temperature, whereupon the electronic circuitry would be at risk from various failure mechanisms [16]. The water getter is a machinable composite material consisting of crystalline aluminum silicate in a polymeric binder (this replaces the molded silicone with magnesium sulfate illustrated in Figs. 1 and 3). This desiccant can absorb 16% of its weight in water vapor, which translates into a 5000-fold increase in the total amount of water that can be present in the capsule without risking condensation. In fact, long-term accelerated life testing without getters and monitoring of test packages with sensitive moisture detectors suggest that, when properly made, these hermetic seals are functioning reliably far beyond their production test limits. Important design factors include a good match between the thermal coefficient of expansion of the metal and glass, a well-polished metal surface free of longitudinal scratches, and vacuum annealing to eliminate absorbed gases in the metal that may interfere with the formation of a stable oxide bond to the glass.

The final packaging step consists of welding shut the Ta tube and attaching the Ir electrode. The Ta electrode is then anodized in a 1% phosphoric acid bath. The completed BION implant is characterized electronically in a wetwell test in which non-contacting electrodes suspended in saline around the implant are used to monitor the electrical fields created by the stimulation and recharge currents produced by the implant. They are then packaged in individual polyethylene vials and sterilized by conventional steam autoclaving.

A wide range of tests have been performed to demonstrate that the BIONs provide a stable, biocompatible

interface when implanted passively in or used actively to stimulate muscles in cats [13] and rats [17]. They are mechanically rugged under conditions including repeated autoclaving and temperature cycling, axial and transverse loading, and shocks from dropping on to surfaces in various orientations [18]. When the glass capsule is embedded in muscle tissue, the maximal impact force that can be transmitted through the surrounding tissue is limited by the viscosity and yield strength of active muscle. Capsule strain during potentially lethal impacts (up to 14 J) under laboratory conditions has been measured at less than 25% of the breaking point for the capsule.

### 3.2. RF power and communications

The implants draw very little power but they must do so by inductive coupling between two coils that have a very low coupling coefficient (<3%) because of their physical separation and mismatch in size. This requires an intense RF magnetic field, up to 1 A at 500 V peak in a wearable coil consisting of 4–6 turns of stranded wire (18 American Wire Gauge). In order to generate this field strength efficiently, we use a class E amplifier to exploit a very high  $Q$  tank circuit consisting of the coil and a small tuning capacitor ( $Q \sim 100$ ). The class E amplifier injects a brief current pulse into the tank circuit only at the time when the current through the primary coil is passing through zero and the voltage across the driving transistor is at its negative peak, which is ground in the circuit. A feedback circuit consisting of an adjustable phase shift and zero-crossing detector compensates for propagation delays in the drive circuitry and shifts in resonant frequency that may result from deformation of the coil (introduced by Troyk and Schwan [19]; new circuit shown in Fig. 4). All reactive components must be selected to minimize dissipation (e.g., silver mica capacitors, highly stranded antenna wire, very fast transistors).

The highly resonant tank circuit makes it difficult to modulate the carrier rapidly by the usual methods. The Manchester-encoded digital commands are transmitted to the BION1 by a weak modulation every 8 or 16 carrier cycles. The modulation circuit (Fig. 4) adds a second parallel reactance (C3) to the drive circuit to change the power in the tank circuit. An alternative scheme is under development in which the carrier is 100% modulated by opening a switch in the tank circuit at the instant when all the power is stored across the tuning capacitor [20]. This allows data to be sent more rapidly in terms of carrier cycles per bit, but it requires a lower transmitter frequency to minimize the effects of gate capacitance in the high current transistor. It also facilitates the abrupt extinguishing of the external power oscillator and the use of its transmission coil as a receiving antenna during the outgoing telemetry of sensor data.

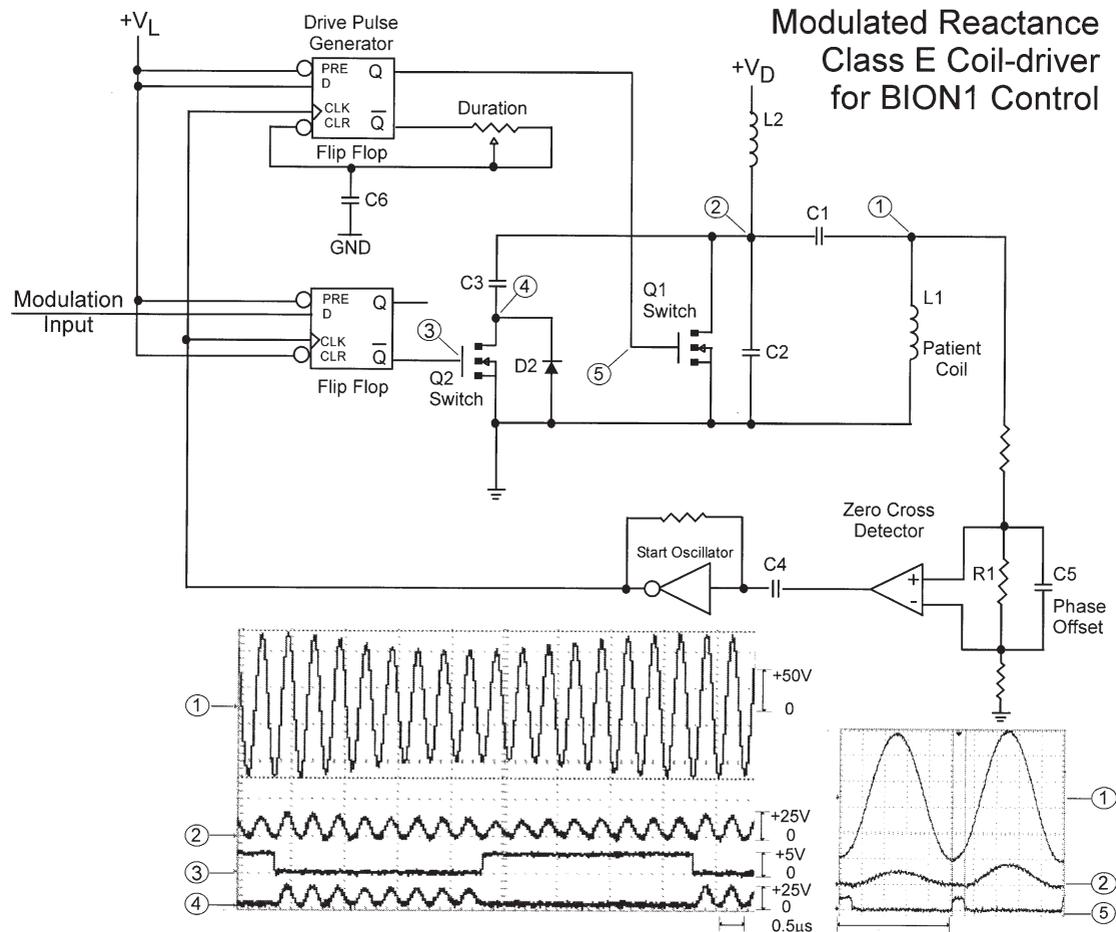


Fig. 4. Class E modulated power oscillator. The resonant frequency of the tank circuit is set by L1, the transmission coil on the patient, and C1. The zero-crossing of the current on the inductor is detected across R1–C4, whose phase can be adjusted to ensure that the Drive Pulse Generator fires for a preset duration that straddles the time when the voltage across the MOSFET Q1 is minimal and power injection is most efficient. Modulation is accomplished by switching in parallel capacitor C3, which increases the current drawn into the tank circuit through choke L2, in turn increasing the amplitude of the oscillations to a new steady state over about four carrier cycles.

### 3.3. Patient interface for therapeutic stimulation

The Personal Trainer contains a 68HC11 microcontroller with battery-backed random access memory (RAM), powered by a conventional alternating current (AC) to DC converter that plugs into an AC power outlet. It functions like a very large, externally synchronized shift register to produce previously stored sequences of carrier modulations that activate the patient's various BION implants (developed and manufactured under contract to Aztech Associates, Inc., Kingston, Ontario, Canada). The transmission coil is sized and shaped for the body part to be stimulated and has an integral small enclosure for its tuned RF power circuitry that connects to and is controlled by the Personal Trainer. As shown in Fig. 5, the Personal Trainer has been designed to provide a relatively large, mechanically stable and simply operated interface for patients and caregivers to use for TES sessions while the patient is seated or reclining, e.g., reading, watching television or even sleeping. The

Personal Trainer can be programmed with up to three different stimulation programs, whose prescribed usage is written on a slip of paper that slides into a pocket on the faceplate. The internal microcontroller monitors, timestamps and records all usage of these programs by the patient. These data are uploaded to the ClinFit system when the patient returns with the Personal Trainer for follow-up and adjustment of the stimulation parameters. Power consumption and electronic functions in the Personal Trainer are compatible with eventual miniaturization into a wearable, battery-powered configuration as required for many FES applications.

### 3.4. Clinical tools

BION implantation is performed in an examination room using aseptic techniques and local anesthesia with lidocaine at the site of insertion. Each BION is presterilized by autoclaving and can be tested while still in its sterile package using an accessory drywell to the exter-

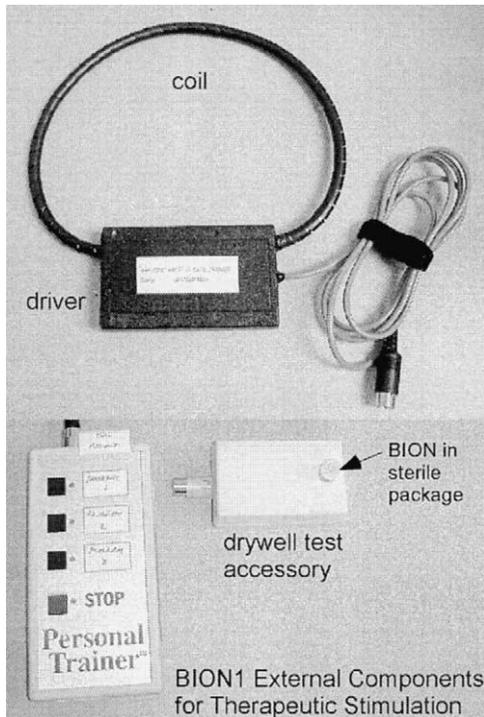


Fig. 5. External components of the BION1 system: 2 MHz RF transmission coil and class E driver electronics (top), which are driven by the Personal Trainer™ during use by the patient. An accessory drywell can be plugged into the Personal Trainer to test BION implants in their sterile package prior to implantation in the body. The Personal Trainer sends commands to activate all 256 possible addresses, recording which address generated a response. This is detected by capacitive coupling to ring electrodes that surround the sterile package in the drywell. Testing and programming are performed with the Personal Trainer connected via a serial RS232 port to a portable personal computer.

nal hardware (Fig. 5). The insertion tool is a modified 12 gauge Angiocath™ (visible in Fig. 1) in which the back end of the stainless steel trochar has been equipped with a connector. Electrical stimulation is delivered through the trochar tip from a conventional clinical stimulator to find the location where a strong twitch of the target muscle can be achieved with a low stimulus current (the technique is similar to that used for botulinum toxin injections to paralyze excessively active muscles). The trochar is then removed and the BION is slid down the lumen of the plastic sheath and expelled by a plunger into this site as the sheath is withdrawn. At the conclusion of the insertion procedures, weak stimulation is applied through each BION to confirm its placement and functionality, and to record threshold for producing a palpable twitch. Threshold is remeasured and tracked at each subsequent programming session, beginning 4–6 days after implantation and at gradually lengthening intervals thereafter.

All of the implantation, fitting and monitoring procedures are performed by the clinician through a portable personal computer running ClinFit™ software developed

specifically for BION therapeutic applications. The software was written in Visual Basic 5 and runs in the Windows™ operating system. It uses an Access™ relational database to maintain complete records on the implant sites, threshold tests, exercise programs prescribed and actual use of the Personal Trainer by the patients.

One important objective was to make the ClinFit interface intuitively clear to clinicians. While electrophysiologists generally think about stimulation in terms of milliamperes of current and microseconds of pulse width, clinicians are more comfortable thinking in terms of strength relative to the threshold for muscle contraction. Similarly, temporal sequences of activation in one or more muscles are more easily appreciated in a graphical display of stimulus envelopes than by lists of numbers specifying durations, ramp times, delays and pauses. Fig. 6 shows the main screen for creating or editing a stimulation program. Stimulation pulses are converted to a single strength value (in units of charge) by multiplying current times duration. Stimulus efficacy can be modulated by either of the two control variables, which are linearly interchangeable for a range of at least 0.5 to 2.0 times the chronaxie for myelinated axons (about 50–200  $\mu$ s). The threshold charge is shown as a dashed line across the graph for each implanted BION. The clinician uses click-and-drag handles on the trapezoidal icons to set the strength and timing of the desired exercise pattern. An algorithm in the ClinFit software simultaneously adjusts the relatively coarse current steps and the fine pulse width steps to achieve the desired stimulus strength, expressed as a multiple of the threshold charge for each channel. The repetition rate for stimulus pulses in each train is selected from a color-coded palette. One feature of this system is that any changes in threshold can be converted immediately into new versions of the same exercise program that preserve the desired level of recruitment relative to threshold.

#### 4. Current status

In order to establish the clinical safety and efficacy of BIONs, a “first in man” pilot study was initiated at Queen’s University in 1999, where the BION system was originally developed. This study seeks to use TES to prevent disuse atrophy and chronically painful shoulder subluxation in patients with flaccid hemiparalysis following a stroke. The first patient (BT1-001, November 1999) was implanted with two BIONs, one each in middle deltoid and supraspinatus muscles. The muscles already had visible atrophy and the shoulder was clinically subluxed but not painful after five weeks of flaccid hemiparalysis. The prescribed exercise program was increased gradually in strength and duration over six weeks up to eight times threshold, 5 pps, 10 s on and 5

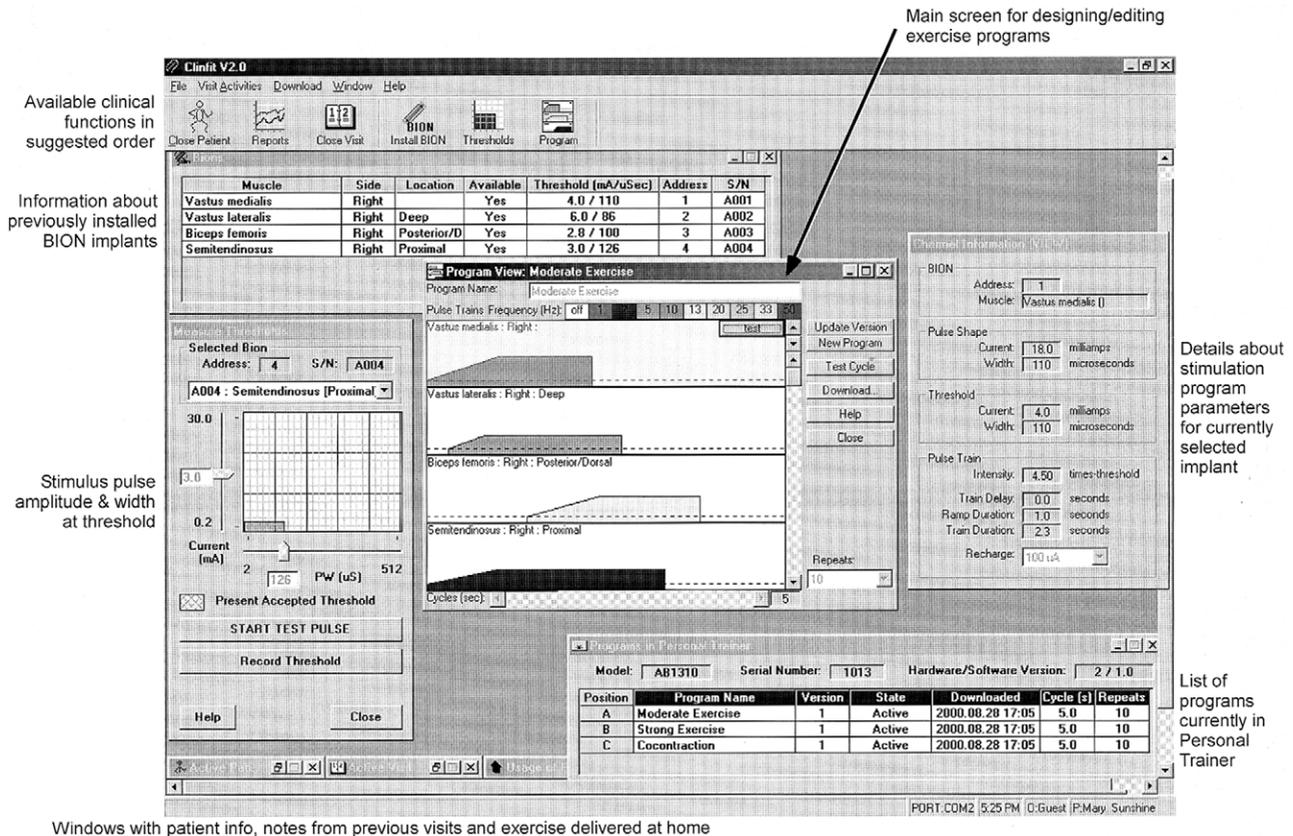


Fig. 6. ClinFit™ exercise programming screen as it would appear on the physician's portable personal computer while setting the parameters of a stimulation program.

s off for 25 min, three times a day. Thresholds were stable over time (8–12 mA at 200  $\mu$ s in both sites) and there were no adverse reactions. The patient self-administered the treatment and found the sensations generally pleasant and easily ignored. The exercise was effective in reducing the subluxation as seen on X-rays and in building muscle thickness as seen on ultrasound [21]. There was also an unexpectedly large return of functional movement specific to shoulder abduction and elevation, which may reflect the increased ability and motivation of the patient to recruit and obtain functionally useful contractions from the chronically exercised muscles.

As of this writing, five patients have been implanted in the shoulder study, which calls for a total of 30 patients to be implanted in a randomized, prospective cross-over design. Half of the patients receive six weeks of BION treatment and then six weeks without stimulation to see if their symptoms recur. The other half are followed without stimulation for the first six weeks and then offered implantation and stimulation if their condition warrants. All patients can elect to continue stimulation indefinitely after the initial 12 week study period. Plans are underway to expand this study to include stimulation of wrist and finger extensors to prevent

flexion contractures often caused by spasticity following stroke.

A second clinical trial began in June 2000, with Dr Carlo Romano at the Pini Orthopedics Institute in Milan, Italy. BIONs have been implanted to exercise the quadriceps muscles in three patients with chronic, stable osteoarthritis of the knee; preliminary results are encouraging. It is known that strengthening of these muscles tends to reduce pain and progression of the arthritis by protecting the joint [22], but compliance with voluntary exercise and surface electrical stimulation programs tends to be poor. Other clinical trials in the planning phase for the BION1 technology include incorporation of BIONs into the WalkAide stimulator to correct foot drop in stroke patients [23], use of BIONs to reduce hemostasis [24], and use of BIONs to reduce equinus deformities of the ankle in patients with cerebral palsy and traumatic brain injury.

## 5. Development underway

Sensing and back-telemetry functions under development for the BION2 system are required to provide command and feedback signals for FES applications. Unfor-

tunately, it is not clear which sensors are required, what their specifications should be or how their signals will be integrated into a portable control system for a particular clinical requirement. FES applications differ greatly in the nature of their command and control problems, and individual patients differ in the details of their sensorimotor pathology and their musculoskeletal mechanics. A parallel effort is underway to develop a general computer modeling environment in which it will be feasible to create accurate models of specific musculoskeletal systems and FES interfaces and control systems in order to understand these requirements [25]. Meanwhile, we have begun work on the following three modalities of sensors, which appear to be technically feasible and likely to be useful for command and control.

- *Bioelectrical recording*: voltages present on the electrodes can be amplified, integrated and digitized according to gain and timing programmed by the command that initiates the sensing operation. Thus, the data might represent the impedance of the tissue through which a current pulse is being delivered simultaneously, the electrical field created in the tissue by a stimulus pulse from another implant, or a bioelectrical signal such as electromyographical activity.
- *Acceleration*: microelectromechanical silicon systems (MEMS) can be incorporated into the BION package to sense acceleration of the implant or inclination with respect to the gravitational field.
- *Relative position*: when one BION is transmitting an RF signal, other BIONs in the vicinity can record the strength of the detected signal, which depends on the distance and relative orientation between the emitting and detecting implants. Changes in limb posture produce relative motion of the BIONs located in various muscles, permitting limb posture and motion to be inferred from a sufficiently rich set of coupling strengths among several BIONs. This is similar to the normal extraction of kinesthetic information from the naturally occurring muscle spindle receptors [26].

One convenient technique for digitizing all of these signals is a voltage-controlled oscillator and counter. The signals to be sensed require only modest resolution but they tend to have substantial noise and a large dynamic range that changes relatively slowly depending on the ongoing motor behavior. Integration helps to overcome the noise, and the duration of the integration period can be digitally controlled to adjust the dynamic range on the basis of the previously received data.

It is unclear whether some or all of these sensing modalities can be combined with each other or with stimulation functions in a single injectable module. One advantage of the BION system design for packaging and communications is that it facilitates development of a

family of individual devices that can be combined ad hoc to meet the needs of each individual patient.

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