Commentary on Chapter 9: electronics

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Chapter 9.1

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Neuromodulation is a promising area in medicine that can markedly improve the quality of life. The last three decades also show an expanding variety of indications where implantable neurostimulators nowadays are used in therapies for chronic pain, movement disorders, psychiatric disorders, and urinary incontinence. This progress is connected in parallel with still evolving experience, scientific knowledge, refinement of the clinical applications, and progressing neurophysiological insights. These trends are bidirectional entangled with the developments of microelectronics, computer and communication technologies with their integration in portable devices. These technological developments are also reflected in the timeline of designs of implantable neuromodulation devices which can be considered as a special field of engineering.

The author Kerry Bradley witnessed the developments of IPG over a wide spectrum of applications. As a trained electrical engineer he worked in an R&D, clinical, and research capacity in IPGs over almost three decades. He joined several companies where he developed algorithms for pacemaker optimization, performed R&D on algorithms for precision SCS systems and was involved in small-scale clinical studies for technical and parameter optimization in SCS. Since 2013, he leads a research team on clinical and preclinical investigations into mechanisms of action of HF10 therapy. He holds many patents and collaborated in many publications.

The author gives a comprehensive overview of basic electronic concepts of neurostimulator devices as they have evolved in time to current IPGs.

Prior to a description of the architecture of present IPGs, an outline is given on the history of neurostimulators, their relation to cardiac pacemakers and how these interact act on the nervous system. This is followed by engineering aspects of electronic solutions for a safe delivery of stimulation pulses.

The chapter starts with a guiding design rationale. In a cable model, it describes how action potentials (AP) are generated in nodes of myelinated axons and how the generated intraaxonal currents distribute across subsequent nodes to finally reunite extracellularly back at the node of origin. From there it is explained how a negative potential of an external electrode generates APs in nodes. After assertion that narrow pulses of 100 μs can start the AP process, basic aspects of the electric-neurophysiological interface at the electrode are described. A neurostimulator converts a constant power source into a pulse series where at typical SCS frequencies from 50 to 100 Hz or higher each pulse generates a single AP. It should be remarked that axons with the largest diameters have the lowest thresholds and therefore recruited first and may cause paresthesia as a side effect. In adjunct to the chapter, newer stimulation paradigms use high-frequency stimulation (HFS) between 1 and 10 kHz and burst stimulation with repeated series of five 500 Hz HF pulses. These appear to give more efficient pain relief without paresthesia. In contrast to the preferential recruitment of thicker axons at lower frequencies, at clinical HFS frequencies and pulse widths larger-diameter fibers are blocked while medium and smaller fibers concomitantly are recruited. Since the repetition time of HFS pulses is markedly smaller than the refractory period after the AP generation, each pulse cannot generate a single AP [1−4].

The section on the neurostimulator design is a short portrayal of the development of electronic circuit designs. The history starts with implanted passive pulse generators consisting of a simple envelope demodulator that by transcutaneous electromagnetic coupling via wire coils was activated and powered by externally applied amplitude modulated radiofrequencies. The reader becomes gradually acquainted with evolving challenges for a designer toward current microprocessor-based IPGs that control complex multicontact electrode connections, generate pulse series, and enable the choice and selection of stimulation parameters and electrode configurations by the physician and patient.

Special attention is paid to electronics for pulse delivery and safety aspects regarding prevention of tissue damage at the electrode-electrolyte interface to the adjacent tissues. It is explained how capacitive coupling secures a net zero charge transfer according to a charge balancing principle. The least energy consumption is achieved by passive unloading of the capacitor after a monophasic pulse. The unloading time allows passive charge balancing in a low frequency range up to ~200 Hz. Higher frequencies require active charge balancing by a compensating pulse of opposite polarity, where the designer can choose longer pulse widths to reduce the energy drain.

In addition, it is remarked that passive charge balancing is also possible in high frequency stimulation, when instead of continuous pulse series, pulse series are given as bursts, for example, five pulses of 500 Hz and 1 ms width, which are repeatedly given with a frequency of 40 Hz as described by Ahmed et al. [4]. The idle time between the bursts is sufficient long enough for recovery of the applied charge.

The architecture of modern IPGs is outlined in a large section starting with a reflection at system level. The advent of wide range low power systems in portable consumer electronics also made their venue in IPGs and expanded the size of designer toolboxes markedly. The appearance of microcontrollers made software development a substantial part of the engineering and offered an unprecedented flexibility with a myriad of functions. The diversity of current IPG models consists of microcontrollers that are usually combined with custom chips. The microcontroller can be considered as the "brain" of the IPG handling duties as stimulation, external communication, power management, data capture, and logging. Originally, custom chips, known as ASICs (Application-Specific-Integrated-Circuits) consolidated the necessary functions in one chip. These required a lot of engineering time. Changes in the demand and a competitive market forced to mitigate these risks by making ASICs very flexible to be accessible by the software in microcontrollers, which reduced the development time. When such general IPG concepts are powered by rechargeable batteries, the lifetime of an implanted device is markedly expanded because upgrades of new designs can be accomplished in software upgrades. These can telemetrically be installed without the necessity of surgical IPG replacement.

The functional heart of the stimulator is categorized by the functional domain of analog and digital signals and is discussed in a subsection. The analog functions are usually embedded in an ASIC, whereas the pulse timing and sequencing is usually performed by the microcontroller. Sometimes, digital control functions consisting of a pulse/phase sequencer and control logic to drive the dedicated circuitry for the delivery of pulses is also embedded in ASICs. The section addresses analog functions of impedance measurements, pulse formation and delivery, radio communications, battery, and power management. Some design examples are presented.

Impedance measurements are intended to check intact electrode connections of the IPG, such as detection of broken or short-cut leads. An example describes the delivery of very short subthreshold current pulses of which the delivered voltage is measured by an amplifier and converted to a digital number representing the impedance. In electrode grids, impedance measurements can be implemented in a scanning procedure by subsequent activation of cmos switches to the specific contacts.

Pulses can be generated by turning switches to the electrodes on and off, while in the given example the output of a digital-to-analogue (DA) converter that via matrix switches connect to selected electrode contacts in a grid or array. The polarity of pulses is controlled by cmos-switches as well. An example of a constant current source illustrates how the current amplitude can be controlled by the DA voltage. Another example for a voltage stimulator illustrates a possibility how pulse voltages can be increased by a fast switching charge pump interposed after the DA output, where the microcontroller provides two fast switching pulses.

An active compensating charge balance pulse can be obtained reversing the polarity by cmos switches. The accuracy of the voltages or currents is optimized by voltage regulating circuits to suppress influences of varying temperatures and battery voltages.

The author states that neurostimulation outcomes depend upon consistency and controllability of recruited neurons. It is expected that this is best controlled by constant current stimulation. Constant voltage stimulation would yield less consistent effects since it will deliver more varying currents because of its dependence on varying impedances. A constant current stimulator is by definition independent the electrode load impedance.

The feature of constant current pulses applies only for single electrode contact selections. However, when more electrodes are connected in parallel, the current divides over the electrode contacts and is markedly decreased at each electrode contact and becomes less effective and may even operate below stimulation threshold. This problem can be avoided by constant voltage stimulators. The delivered voltages of constant voltage stimulators are by definition independent of load resistances and thus independent of the number of parallel connected electrode contacts. For flexibility in choices for electrode selections voltage stimulators would be in favor of constant current. It is important to note that some devices on the market solve this problem by using independent current sources for each electrode thus avoiding the current spread across multiple contacts.

A section entitled "Neurostimulation power" describes the timeline toward lithium ion batteries which are used in conjunction with rechargeable technologies embedded in the hardware and software of the current IPG circuits. The power management of the batteries is inherited from portable devices like smartphones.

Power management is a pivotal design topic in IPGs to face the power demand. At one hand, the limited charge capacity of rechargeable batteries of about 0.3 Ah should be able to bridge recharging intervals of at least several days for a practical comfortable use. On the other hand, the application of higher therapeutic pulse frequencies in latest clinical applications of HF10 requires more than a 1000-fold of pulse energy when compared to the $\sim$1 Hz frequencies of cardiac pacemakers. Moreover, additional energy is required for many other functions of the IPG which include monitoring of the energy status of the battery to alarm for near depletion conditions, telemetric interchange of data, microcontroller and ASICs, datalogging, detection of malfunctioning electrodes and connections, impedance measurements, and control of switches and supporting logic for active charge balancing.

Several power management strategies are discussed, which are based on the alternating use of sleep and awake states of the microcontroller. The power consumption of the microcontroller in sleep-state is low.

The challenge is to use awake states only when specific actions are required. Discussed are solutions at relative low pulse frequencies to use sleep-stages during the long idle time between pulses, while for higher pulse frequencies awake states are further restricted during start and cessation while sleep-states are also assigned to intrapulse time intervals. Another suggestion is to only use the microcontroller for the creation of templates with steering patterns of a pulse cycle that are translated from defined pulse parameters and storage into flash memory. These are cyclic replayed in sleep-state by using DMA for the control of ASICs and/or switches.

To-date similar appealing suggestions relating to power saving techniques are discussed for telemetric communication with an external programmer along a historic timeline from a transformer-like coupling to RF communications via a dedicated two-way communicating antenna where the Medical Implant Communications Service band (MICS) allows some standardization and improvement of performance. Current features support fast downloading and bidirectional external transfer of data, real-time parameter adjustment and sensing while the range to the programmer of about 2 m enables an intra-operative use outside the sterile field during surgical placement of electrodes. The advent of Bluetooth Low Energy (BLE) with its low energy demand and data security, are key to achieving this goal in current IPG developments.

Concluding remarks

When evaluating, the chapter gives an realistic impression of the engineering trends of IPG circuits where an increasing spectrum of medical applications go hand in hand with fast expanding technological possibilities of miniaturization with microcontrollers, interfaced with ASICs and other components, augmenting complexity of multicontact electrode grids, progressing techniques in telemetric communication, and evolving battery technologies. It is nearly impossible to cover the whole field in a short outline. The chapter gives a clear impression on the engineering aspects of IPGs of the wide field and clearly reflects the experience of the author.

References

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