International Journal of Electrical, Electronic and Communication Sciences
ISSN: 2517-9438
Vol:3, No:10, 2009

Temporal analysis of magnetic nerve stimulation—towards enhanced systems via virtualisation

Stefan M. Goetz, Thomas Weyh, and Hans-Georg Herzog

Abstract—The triumph of inductive neuro-stimulation since its rediscovery in the 1980s has been quite spectacular. In lots of branches ranging from clinical applications to basic research this system is absolutely indispensable. Nevertheless, the basic knowledge about the processes underlying the stimulation effect is still very rough and rarely refined in a quantitative way. This seems to be not only an inexcusable blank spot in biophysics and for stimulation prediction, but also a fundamental hindrance for technological progress. The already very sophisticated devices have reached a stage where further optimization requires better strategies than provided by simple linear membrane models of integrate-and-fire style. Addressing this problem for the first time, we suggest in the following text a way for virtual quantitative analysis of a stimulation system. Concomitantly, this ansatz seems to provide a route towards a better understanding by using nonlinear signal processing and taking the nerve as a filter that is adapted for neuronal magnetic stimulation. The model is compact and easy to adjust. The whole setup behaved very robustly during all performed tests. Exemplarily a recent innovative stimulator design known as cTMS is analyzed and dimensioned with this approach in the following. The results show hitherto unforeseen potentials.

Keywords—Theory of magnetic stimulation, inversion, optimization, high voltage oscillator, TMS, cTMS.

I. Introduction

About twenty years ago inductive nerve stimulation started as a for the patient nearly painless alternative to classical electric approaches for evoking action potentials. Its strong point is especially the capability to induce currents of defined focus without any contact to the body even in the brain. Today this method is widely known for lots of routine diagnostic procedures including cortical mapping, neuronal conduction velocity measurements and even first therapeutic approaches in psychopathology and metabolic disorders [1], [2], [3]. The invincable advantage of magnetic stimulation over the alternatives for these applications is mostly the absence of pain. Beside brain stimulation the usage in rehabilitation, especially for hemiplegia, spastic or other types of partial paralysis, seems to become the second main pillar for this powerful instrument within the next few years [4], [5], [6], [7].

But for these indubitable rewards one has to pay dearly. The technologic efforts are relatively high compared to electrical stimulation devices and the main drawback for users of magnetic stimulation apart from the head. The respective physical problem is the rather bad energetical coupling of the tissue and the nerves therein to the stimulation coil.

SM Goetz, Th Weyh and HG Herzog are with the Department of Electrical and Computer Engineering, TU München, D-80333 Munich, Germany; phone: +49 89 289-28429, fax: +49 89 289-28335 e-mail: sgoetz@tum.de

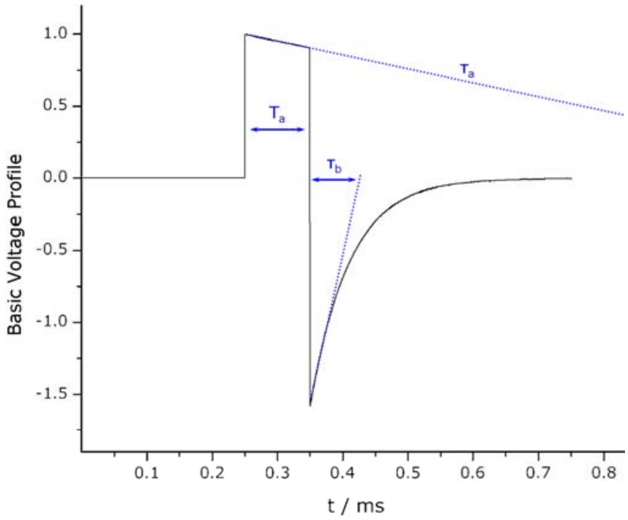

Fig. 1. Exemplary voltage shape of the analysed stimulation setup with $T_a = 100\ \mu s$, $\tau_a = 1\ ms$, $\tau_b = 75\ \mu s$. The positive rectangular shape is generated by switched loading of the coil from a buffered source, the negative fin is the return branch in the circuitry formed by a resistor R and a diode.

The biophysical and technological research concerning the system has mainly concentrated on the territory of magnetic coils and the special field design. The development of the devices was basically limited to pure technical evolution independent from more sophisticated views onto the stimulation effect itself. Nevertheless the systems are still extremely cumbersome, inefficient in respect to energy dissipation and expensive. Recently A. Peterchev et al. presented an experimental setup with the aim of lowering the extremely high voltage levels inside the stimulation oscillator with a novel circuit design [8]. Besides he introduced another degree of freedom for the user as will be seen in the following paragraphs.

II. Underlying System Design

All optimization approaches of inductive stimulation systems are up to now based on experimental setups and oversimplified linear neuron models. The former cause enormous expenses even in the case of rather primitive experimental high voltage stimulation circuits with minimum measures for patient safety. Due to the required high pulse powers magnetic stimulation devices are known to be rather costly.

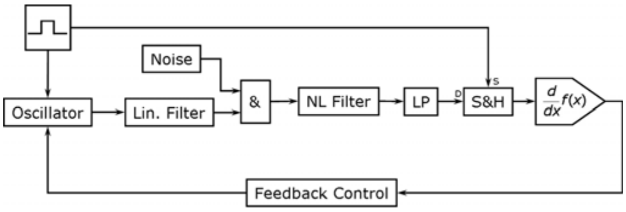

Fig. 2. Simplified flowchart of the modeled feedback control system. The linear filter designs the induction of the coil current generated by the oscillator of the stimulation device into the tissue that leads to an electric field. The time shape of the latter with some noise stimulates the neuron that can be found in the nonlinear filter block. The low-pass filter, the sample-and-hold-block as well as the differentiator just feed the control system. The clock initiates a new pulse of the oscillator and synchronizes the S&H to the same.

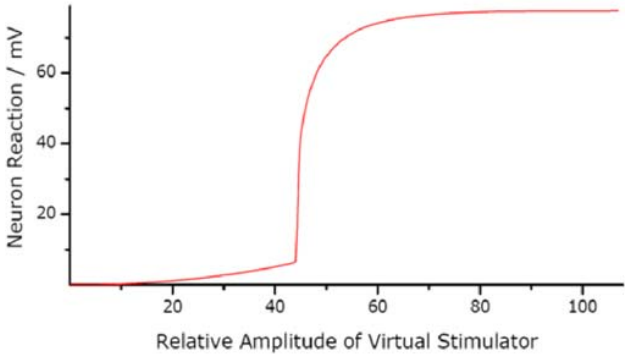

Fig. 3. Noise-free Transfer curve of the virtual stimulator exciting a single neuron with a typical all-or-none behavior for an exemplary pulse configuration.

We adapted a highly nonlinear neuron model for a closed loop control system that includes a stimulation oscillator, which reflects a whole physical device, and tested the robustness of this approach.

The simulated device was the oscillator design suggested by A. Peterchev in a recent article [8]. For a detailed description of the exact implementation and circuitry diagrams we refer to the original text. This setup comprises two innovative features. The basic waveform, also shown in figure I, is characterized by a nearly rectangular first part of the voltage shape and forced by the inductance of the stimulation coil to be dc-free in toto. The common and established devices in contrast have employed mostly sinusoidal oscillations (damped to a greater or lesser extent) ever since. The coil current of this novel concept, approximately proportional to the integrated voltage, shows accordingly a switch-on-switch-off profile with exponential onset defined by the time constant τ_a of the duration T_a and decays with τ_b towards zero thereafter.

The second feature is provided by the possibility for the user to control the pulse duration T_a arbitrarily within a certain range at the front panel of the device. The time constants τ_a and τ_b on the other hand are given by the hardware design of the system and are "hard-wired" accordingly. The latter for instance—the damping of the compensating negative spike τ_b—can be adjusted with the aid of a resistor in series to the diode in the return branch in the circuitry (with $\tau_b = L_{coil}/R$ simply).

This leads to at least two degrees of freedom that cannot be analyzed experimentally any longer and seems to be an excellent prime example for our research therefore.

III. Control System

When one tries to optimize magnetic stimulation in theory, a problem one has to face is that in general more realistic dynamic neuron descriptions cannot be inverted. Simple alternative reverse methods have been developed (see for example [9]), but seem unsatisfying for the current purpose. We therefore made use of a stratagem to deal with this missing inversion capability and generated the desired input parameters for certain output properties with a control loop.

The present approach is based on a (virtual) experimental setup with a control system that could be also used with a physical apparatus for in-vivo-studies. For the analysis we chose a dynamic neuronal model based on separate statistical description of voltage-gated proteins. We implemented the during an action potential dominating ion current types with their dynamical nonlinear behavior and a temperature correction for mammalian nerves, as can be found for instance in [10], [11]. The central issue was the implementation of this neuron model as a filtering stage in a feedback control system and modeling the whole setup in a numerical computing environment (see figure II).

The controlled system was the reaction of the axon. This was actuated by an oscillator which drives a linear filter with the coil current waveform. This filter with a differentiating behavior describes the induction within the tissue and provides the shape of the electric field over time. The latter excites, after adding Gaussian noise (for further reading see [12]), the axon that is constituted by a nonlinear filter. The output is fed into a (first order) low-pass system with a time constant that is long compared to the clock period. This clock initiates a new pulse of the oscillator circuit quite similar to a real device in repetition mode and actuates the sample and hold block simultaneously for a quantitative comparison of succeeding action potentials. The effect of a change of the input parameters is therefore diretly translated into a differential change of the response amplitude.

The whole virtual system was set up to lock in at the threshold of the neuron. This was defined at the inflection point, where minimal parameter adjustments lead to highest output change (very similar to other dynamic systems with a propensity for chaotic behavior). This corresponded quite well with the 50 % spiking probability in the presence of strong Gaussian noise. Dependent on the controller and the initial conditions less than 200 periods elapsed in most tests before the closed loop reached its locking state and provided the desired input parameter set.

IV. Results

The described control loop was diverted exemplary for studying and optimizing a new and auspicious stimulator design. The degrees of freedom for this semi-automatic analysis

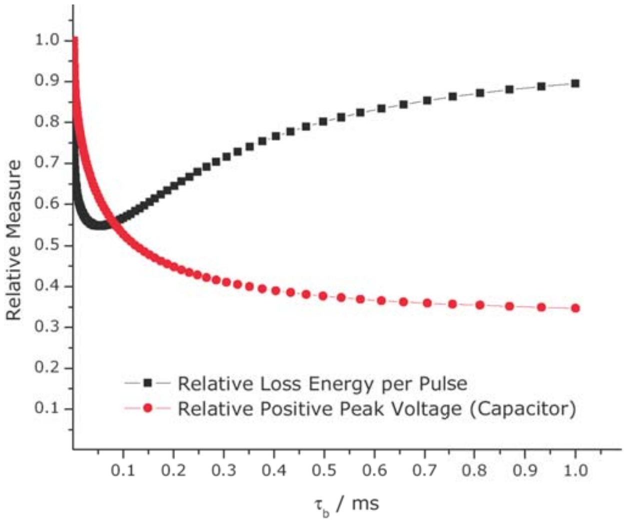

Fig. 4. Threshold loss energy (black, rectangular) and pulse capacitor voltage (red, circle) for evoking action potentials in neuron membranes for different values of the decay rate τ_b, $T_a = 50\ \mu s = const.$

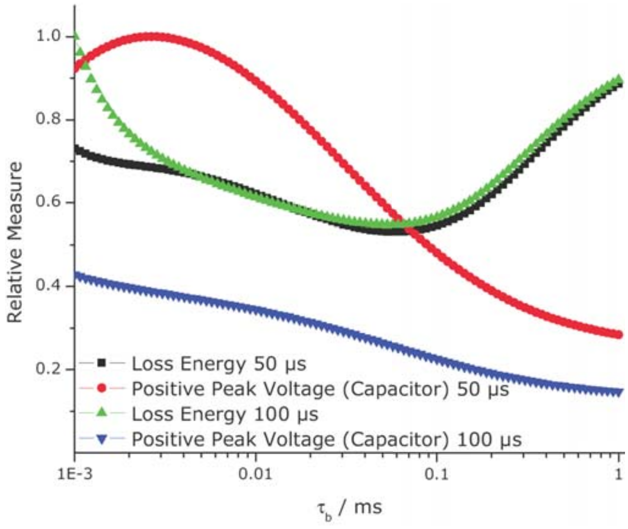

Fig. 5. Loss energy in the magnetic coil and pulse capacitor voltage level at the threshold for evoking action potentials for $T_a = 50\ \mu s$ and $T_a = 100\ \mu s$ in logarithmic scale displaying distinct minima—at different values of τ_b. All depicted curves of the same species, but different Ta have the same normalization and are, by implication, commensurable with one another.

have been the time length of the rectangular first part of the waveform, T_a, and the decay rate of the compensating negative spike after the latter, τ_b, as shown in figure I. The onset speed τ_a was kept constant at a rather high value (one millisecond) as this quantity can be changed also in the cited physical setup [8] only with some difficulties.

The virtual stimulator exhibited a surprisingly realistic transfer curve for a single neuron that is stimulated with the cTMS device, as can be seen in figure III. The sharp edge of the graph represents the empirical all-or-none law of electrophysiology. The superposition of several representatives of these functions with a random distributed shift along the x-axis (modeling parameter differences like the fiber diameter and channel surface density fluctuations within the cord [14], [15], [16], [17], [18], [19]) provides for instance already typical recruiting curves of a nerve fiber with their markedly less abrupt transition below saturation.

The results for a positive pulse length of 50 μs can be found in figure IV. Therein the required voltage level of the capacitor at the beginning of a new pulse for evoking an action potential with a probability of 50 % is represented by one curve (circle), the later discussed heating power at this threshold by the second (rectangular boxes). For a low voltage level of the capacitor an as long as possible second fin of the voltage shape is required.

This and especially the nonlinear progression with falling τ_b are not obvious when one thinks of the underlying mechanism. The (effective part of the) waveform is—for induction—of course dc-free, hence the area of the two fins with the zero line is exactly equal. A short severe onset of the second part of the pulse with negative polarity seems to counteract the generation of an action potential in the first crucial moment disproportionally. A linear model does not display this characteristics. This finding plays an important and also fiscal role for the selection of the rather expensive power switches inside the system.

Whereas a reduction of the required voltage level in such systems is patently obvious and, because of the nearly monotonic relationship, relatively easy to check experimentally, another important factor are losses in the magnetic coil [4], [8], [20]. Statutory provisions regarding medical devices of a lot of nations restrict of course the maximum temperature of parts that touch a patient for safety reasons to a relatively low value (for example 42 $°C$). But the high ohmic losses in such devices in the range of kilowatts additionally limits the operation time of the devices to only some minutes. When the coil reaches this critical temperature value, a typical stimulator stops operation. Accordingly figure IV depicts the normalized losses in the coil at the 50 %-threshold for several values of τ_b. The heat load was calculated via simply integrating the square of the coil current needed for evoking an action potential at the already mentioned 50 % probability. The results uncover for both shown values of T_a a distinct minimum of the heating losses (for τ_b just below 100 μs here), nearly halfing the power dissipation in the magnetic coil.

V. Conclusion and Further Steps

Beneath the rather prosaic ability to optimize an inductive stimulation device, another highly interesting facet presents the chance to get a deeper insight into the basic principles of magnetic stimulation. The mechanisms concerning this technology are only roughly understood at present. On one hand inexplicable effects have been discovered experimentally [21], [22], on the other simple linear models are still the main tool to study the effect of induced current pulses in cells [23].

The results presented here could, in the case of further experimental confirmation, turn over a new leaf in the field of inductive neuronal stimulation devices. A selective test of the presented model at characteristic points of the presented curves will additionally provide data to calibrate the underlying differential equations.

REFERENCES

[1] T.N. Schriefer, K.R. Mills, N.M. Murray, and C.W. Hess. Evaluation of proximal facial nerve conduction by transcranial magnetic stimulation. *Journal of Neurology, and Psychiatry*, vol. 51, pp. 60–66, 1988.

[2] J.L.R. Martin, M.J. Barbanoj, T.E. Schlaepfer, E. Thompson, V. Perez, and J. Kulisevsky. Repetitive transcranial magnetic stimulation for the treatment of depression. *British Journal of Psychiatry*, vol. 182, pp. 480–491, 2003.

[3] E.M. Wassermann, and S.H. Lisanby. Therapeutic application of repetitive transcranial magnetic stimulation: a review. *Clinical Neurophysiology*, vol. 112, pp. 1367–1377, 2001.

[4] S. M. Goetz et al. Peripheral Inductive Stimulation: Physical Issues and Advanced Technological Solutions. *WC IFMBE*, vol. 25, pp. 72–75 2009.

[5] W.D-C. Man, J. Moxham, and M. I. Polkey Magnetic stimulation for the measurement of respiratory and skeletal muscle function. *European Respiratory Journal*, vol. 24, no. 5, pp. 846–860, 2004.

[6] T.-R. Han, H.-I. Shin, and I.-S. Kim Magnetic Stimulation of the Quadriceps Femoris Muscle: Comparison of Pain with Electrical Stimulation. *American Journal of Physical Medicine & Rehabilitation*, vol. 85, no. 7, pp. 593–599, 2006.

[7] L. G. Cohen, S. Bandinelli, T. W. Findley, and M. Hallett Motor reorganization after upper limb amputation in man. A Study with focal magnetic stimulation. *European Respiratory Journal*, vol. 114, pp. 615–627, 1991.

[8] A.V. Peterchev, R. Jalinous, and S.H. Lisanby. A Transcranial Magnetic Stimulator Inducing Near-Rectangular Pulses with Controllable Pulse Width (cTMS). *IEEE Transactions on Biomedical Engineering*, vol. 55, no. 1, pp.257–266, 2007.

[9] B. A. Arcas, and A. L. Fairhall. Computation in a Single Neuron: Hodgkin and Huxley Revisited. *Neural Computation*, vol. 15, pp. 1715–1749, 2003.

[10] F. Rattay, R.J. Greenberg, and S. Resatz. Neuron modeling. In Handbook of Neuroprothetic Methods, CRC Press, Boca Raton, 2003.

[11] F. Rattay. The basic mechanism for the electrical stimulation of the nervous system. *Neuroscience*, vol. 89, no. 2, pp. 335–346, 1999.

[12] J.A. White, J.T. Rubinstein, and A.R. Kay. Channel noise in neurons. *Trends in Neuroscience*, vol. 23, pp. 131–137, 2000.

[13] E.M. Wassermann. Risk and safety of repetitive transcranial magnetic stimulation: report and suggested guidelines from the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation. *Electroencephalography and Clinical Neurophysiology*, vol. 108, no. 1, pp. 1–16, 1998.

[14] P. Koole, J. Holsheimer, J.J. Struijk, A.J. Verloop. Recruitment Characteristics of Nerve Fascicles Stimulated by a Multigroove Electrode. *IEEE Transactions on Rehabilitation Engineering*, vol. 5, no. 1, pp. 40–50, 1997.

[15] P.H. Veltnik, J.A. van Alste, and H.B.K. Boom. Simulation of intrafascicular and extraneural nerve stimulation. *IEEE Transactions on Biomedical Engineering*, vol. 35, no. 1, pp. 69–75, 1988.

[16] L.J. Dorfman. The distribution of conduction velocities (DCV) in peripheral nerves: a review. *Muscle & Nerve*, vol. 7, pp. 2–11, 1984.

[17] J.J. Rydzewski, and M.H. Evans. Diameter distribution spectra of myelinated axons in the median and ulnar nerves of the Soay sheep. *Journal of Anatomy*, vol. 123, no. 3, pp. 813–818, 1977.

[18] I. A. Boyd, and M. R. Davey. *Composition of Peripheral Nerves.* E.& S. Livinstone, Edinburgh and London, 1968.

[19] J. P. Reilly. *Applied Bioelectricity: From Electrical Stimulation to Electropathology.* Springer, New York, 1998.

[20] Th. Weyh, K. Wendicke, C. Mentschel, H. Zantow, and H.R. Siebner. Marked differences in the thermal characteristics of figure-of-eight shaped coils used for repetitive transcranial magnetic stimulation. *Clinical Neurophysiology*, vol. 116, pp. 1477–1486, 2005.

[21] L. Niehaus, B.-U. Meyer, and Th. Weyh. Influence of pulse configuration and direction of coil current on excitatory effects of magnetic motor cortex and nerve stimulation. *Clinical Neurophysiology*, vol. 111, no. 1, pp. 75–80, 2001.

[22] Th. Kammer, S. Beck, A. Thielscher, U. Laubis-Herrmann, and H. Topka. Motor thresholds in humans: a transcra-nial magnetic stimulation study comparing different pulse waveforms, current directions and stimulator types. *Clinical Neurophysiology*, vol. 112, no. 2, pp. 250–258, 2001.

[23] E. Corthout, A. T. Barker, and A. Cowey. Transcranial magnetic stimulation: Which part of the current waveform causes the stimulation? *Experimental Brain Research*, vol. 141, pp. 128–132, 2001.