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

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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 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 invincible 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.

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.
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 directly 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...
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, $\tau_b$, as shown in figure I. The onset speed $\tau_a$ 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 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 $\mu$s 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 $\tau_b$ 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 disproportionately. 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 $\tau_b$. 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 $\tau_b$ just below 100 $\mu$s here), nearly halving 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


