

Preface

Electrical neural stimulation is an established treatment methodology for an increasing number of neural pathologies, while its application is under consideration for an even larger number of diseases. In line with this development, there is a need for neural stimulator devices that are safe and reliable and have a small form factor. The design of such devices requires a multidisciplinary approach, combining the needs from neurological, physiological, electrochemical, and electrical perspectives.

The concept of electrical stimulation is typically approached from two distinct directions. One way starts at the neuron and asks the question: what kind of signals are needed to achieve the desired neural modulation? This approach typically calculates the neural response based on the electrode configuration, the applied electrical field, and the physical properties of the neurons under consideration. The other approach starts at the stimulator and asks the question: what kind of circuit techniques can be used to implement the stimulation signals? Typical characteristics addressed are power efficiency, safety aspects (such as charge cancelation), and scalability (such as number of outputs).

Both approaches seem to operate rather isolated from each other. The first approach is typically unaware of how a certain optimal waveform can be translated into electrical circuitry. Similarly, the second approach is often not aware how alternative circuit topologies will influence the neural activation mechanism.

It would be much better to combine both approaches: what kind of signals allow for both efficient activation and efficient circuits? This book aims to assist neural stimulator circuit designers in taking such an approach by presenting the complete stimulation sequence: from the neural stimulator down to the neuronal membrane where the activation (or inhibition) takes place. By understanding this complete chain, it is possible to devise novel stimulator architectures while understanding the safety aspects that are important for neural stimulation. Some examples of novel approaches are given throughout the book. These include considerations about safety, electrochemical stability, and stimulator architectures.

One of the drawbacks of taking a fundamentally different approach is that it is generally much harder to get the work recognized in the scientific community. The following story illustrates this point well and is therefore worth sharing. In 1892

the scientist Jan Leendert Hoorweg from Utrecht, the Netherlands, published a bold article in the journal *Archiv für die gesamte Physiologie des Menschen und der Tiere* (the contemporary *Pflügers Archiv*) [1]. He had studied the conditions under which a charged capacitor could excite muscle contractions in human subjects. He found that the relationship as proposed by the famous founding father of electrophysiology, Emil du Bois-Reymond, seemed invalid. In 1845 E. du Bois-Reymond had formulated a relationship [2] in which the momentary muscle movement $\epsilon(t)$ was hypothesized to depend on the momentary change in stimulation current: $\epsilon(t) = F[di(t)/dt]$.

Hoorweg, not being satisfied with the empirical “evidence” from [2], conducted a series of systematic experiments and found a relationship independent on $di(t)/dt$, but on the stimulation circuit parameters used such as capacitance, resistance, and voltage. His fundamentally different point of view caused big consternation, and many famous scientists, such as Eduard Pflüger, were quick to reject his idea in a single-sentence publication without any further proof [3].

It took another 9 years until, in 1901, Georges Weiss established a relationship between stimulation charge and duration [4] and showed that the measurements from Hoorweg were actually correct. In 1909 Louis Lapicque reformulated [10] (Chap. 2) the results into the famous strength-duration curve, which is now one of the fundamental principles of neural stimulation.

Discovering Hoorweg’s story gave me an odd sense of satisfaction, not only because it turned out that his ideas were correct but mainly because it showed me that convincing the scientific community to consider alternative approaches was as difficult as it is today. During my years of research, I also experienced that it is not always easy to convince the society to at least allow alternative ideas as an input to the field.

It is thanks to the people around me that I was able to push on to continue and prove the validity and usefulness of the ideas and concepts that are presented in this book. In this aspect I would like to thank the section Bioelectronics of the Delft University of Technology: it was a privilege to be part of this group of people. Furthermore, I enjoyed great cooperation with several other research groups as part of the SINS consortium in which I experienced the multidisciplinary character of this research field. Here I would like to mention the Neuroscience Department of Erasmus University Rotterdam and the Neurosurgery Department of the University of Otago and the University of Antwerp.

Finally, I would like to thank the most important people in my life: my wife Lin and daughter Danya. It is you who gave me the strength and support needed to finish my work and this book.

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