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**An Investigation of Neural Stimulation Efficiency With Gaussian Waveforms**

# An Investigation of Neural Stimulation Efficiency with Gaussian Waveforms

Steffen Eickhoff, and Jonathan C. Jarvis

*Abstract*—***Objective:*** **Previous computational studies predict that Gaussian shaped waveforms use the least energy to activate nerves. The primary goal of this study was to examine the claimed potential of up to 60% energy savings with these waveforms over a range of phase widths (50-200µs) in an animal model.** ***Methods:*** **The common peroneal nerve of anaesthetized rats was stimulated via monopolar and bipolar electrodes with single stimuli. The isometric peak twitch force of the extensor digitorum longus muscle was recorded to indicate the extent of neural activation. The energy consumption, charge injection and maximum instantaneous power values required to reach 50% neural activation were compared between Gaussian pulses and standard rectangular stimuli.** ***Results:*** **Energy savings in the 50-200µs range of phase widths did not exceed 17% and were accompanied by significant increases in maximum instantaneous power of 110-200%. Charge efficiency was found to be increased over the whole range of tested phase widths with Gaussian compared to rectangular pulses and reached up to 55% at 1ms phase width.** ***Conclusion:*** **These findings challenge the claims of up to 60% energy savings with Gaussian like stimulation waveforms. The moderate energy savings achieved with the novel waveform are accompanied with considerable increases in maximal instantaneous power. Larger power sources would therefore be required, and this opposes the trend for implant miniaturization.** ***Significance:*** **This is the first study to comprehensively investigate stimulation efficiency of Gaussian waveforms. It sheds new light on the practical potential of such stimulation waveforms.**

*Index Terms*—**Electrical stimulation, Gaussian waveform, Energy efficiency, Charge efficiency, Power efficiency**

## I. Introduction

ELECTRICAL stimulation (ES) of excitable tissues successfully finds application in a number of therapeutic systems and medical devices such as the cochlear implant, the cardiac pacemaker, deep brain and spinal cord stimulators. Electrical impulses are used to activate or inhibit activation in a target excitable structure, which might be a block of cardiac tissue, a region of the brain, or a peripheral nerve. This can be achieved using voltage- or current-controlled stimulation waveforms: the latter has the benefit of eliminating threshold variations that result from changes in electrode-tissue impedance and is therefore commonly used today.

While the basic requirement of a stimulation waveform is to activate (or block) the target structure, energy efficiency as well as stimulation selectivity and safety are of high importance [1]. In view of the many implantable ES devices and the trend towards miniaturized applications such as so-called electroceutical systems for stimulation of the autonomic nervous system [2], energy efficient stimulation is important to the whole field as it enables increased battery lifetime or the use of smaller batteries. There are recent early successes in wireless power delivery, for example to a passive miniature radio-frequency identification (RFID) tag placed inside a central organ of pigs [3]. However, the higher amounts of electrical energy required by active implants such as neural stimulators as well as the safety limits of human exposure to radio frequency electromagnetic fields [4] indicate that the need to optimize stimulation efficiency remains. Superficially placed implants, such as cochlear implants, that use transcutaneous power transmission can also benefit from increased energy efficiency. Although not as critical as for devices with implanted batteries, a more economical use of energy allows reduction in size and fewer recharge cycles from an external power source. Although it is not often mentioned as a key parameter of electrical stimulation, charge efficiency is also an important cofactor as it can influence both selectivity and safety. An increased charge efficiency, that is, a reduction of the charge injection required to activate a nerve, can increase the stimulation safety due to reduced charge density at the electrode-tissue interface and/or increase selectivity because electrode size may be reduced without exceeding safe limits for charge density. Furthermore, the maximum instantaneous electrical power delivered via the stimulation electrodes is an important criterion for implantable stimulators. Battery size scales directly proportionally with maximum power since the specific power (W/kg) is constant for any specific battery technology.

In many cases, rectangular current waveforms are used in electrical nerve stimulation, not least because of the ease of generating them with simple electronic circuits. They are often

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biphasic so that the overall net charge injection is near zero. Many studies have been conducted to investigate variations of the rectangular biphasic waveform such as interphase gaps (IPG), asymmetric pulses [5]–[7] and pre pulses [8]–[11]. Some of these studies sought to discover whether non-rectangular stimulation waveforms might have an advantage in terms of efficiency or selectivity. Several programmes also incorporated computational simulations. Employing the Hodgkin-Huxley nerve membrane model [12], [13] Jezernik and Morari predicted that an exponentially rising stimulation waveform would provide the best energy efficiency [14]. Comparing this and other non-rectangular waveforms to standard rectangular stimuli applied to a computational model of a single mammalian axon [15], exponentially rising and decaying waveforms were found to be most charge efficient across the whole range of phase widths. When the threshold charge was expressed as a fraction of the charge injection capacity with practical titanium nitride microelectrodes, exponential and linearly decreasing (i.e. reverse ramp) waveforms were most charge efficient. Both exponential waveforms were most energy efficient at long phase durations (>250µs). Gaussian shaped stimuli achieved the best energy efficiency at shorter phase widths [16]. Using a more sophisticated computational simulation of a population of mammalian myelinated axons [17] as well as in vivo experiments, the apparent superiority of exponential waveforms in terms of charge and energy efficiency at long phase widths was shown to be misleading and therefore over-estimated because the waveform shape became insensitive to the phase duration since only the low amplitude ‘tail’ of the computed current waveform grew with increasing phase width. Furthermore, exponential waveforms had significantly lower power efficiency than rectangular stimuli and triangular pulses were most charge efficient for phase widths ≤ 200µs. It was shown that none of the tested rectangular, exponential or ramp waveforms was simultaneously most efficient in terms of energy, charge and power [18].

Promisingly, three recent studies independently found a Gaussian shaped stimulation waveform to be optimal in terms of minimized energy consumption using model-based approaches probed by a genetic algorithm [19], the calculus of variation [20] and the least action principle [21]. While these studies agree that a Gaussian stimulation waveform shows increased energy efficiency over rectangular stimuli, there are considerable differences in the claimed potential to save energy by replacing simple rectangular waveforms with modified pulses. The largest claim of 5-60% increased energy efficiency over a clinically relevant range of phase widths (~ 50-200µs) can be found in the genetic algorithm study of Wongsarnpigoon and Grill, based on the outcome of their computational and in vivo work [19]. However, these studies on Gaussian shaped stimulation waveforms recognize that the energy costs of generating such complex waveforms may decrease the achievable benefit in energy efficiency of neuro stimulators and conclude that more practical investigations of the incorporation of Gaussian waveforms are warranted. We here respond to this challenge.

To the best of our knowledge, the practical implementation of the Gaussian stimulation waveform has not been studied further till now. The primary goal of our study was to explore the findings of these recent computational studies in an animal model. Single electrical stimuli were used to activate the common peroneal nerve (CPN) of anaesthetized rats via monopolar or bipolar electrodes. The isometric peak twitch force of the extensor digitorum longus muscle (EDL) was recorded to indicate the extent of neural activation. To bring the detailed computational findings closer to practical application, we reduced the phase-width-dependent variation of the optimal waveforms. Only one fixed Gaussian waveform, which was chosen to closely resemble the waveforms used by Wongsarnpigoon and Grill [19] in the range of 50-200µs phase widths, was compared to rectangular stimulation. Since charge balance is a key requirement of most electrical stimulation applications, only biphasic stimuli were incorporated in this study. As well as a comparison of energy efficiency between Gaussian and rectangular stimuli, charge and power efficiency of stimulation with these waveforms were also investigated, as these are important parameters of stimulation for the design of implantable devices.

## II. Materials and Methods

### A. Surgical procedure

All experiments were carried out in strict accordance with the Animals (Scientific Procedures) Act of 1986 which regulates the use of experimental animals in the UK. The procedures in this study were approved by the Home Office (PPL 40/3743) and were conducted in terminal experiments in seven adult, male Wistar rats.

The animals were anaesthetized using a gaseous mixture of Isoflurane and oxygen. An initial Isoflurane concentration of 3% was used to induce anaesthesia, then lowered to 2% for the surgical procedures. To maintain a stable, deep level of anaesthesia, during the measurements, the respiration rate of the animals was monitored and the isoflurane concentration adjusted accordingly between 1% and 2%. For analgesia, Buprenorphine (Temgesic, Indivior, Slough, UK) was administered intra muscularly at a dose of 0.05 mg $kg^{-1}$ body mass. To control the body temperature and keep it at 37-38°C, the animals were placed on a heat pad (E-Z Systems Corporation, Palmer, Pennsylvania, USA) and core temperature was monitored using a rectal temperature probe.

Loop electrodes with an inner diameter of approximately 1mm and a surface area of 0.025$cm^2$ were made from PVC-insulated stainless steel wires (Electrode wire AS634, Cooner Sales Company, Chatsworth, California, U.S.A.). Two electrodes were placed under the common peroneal nerve (CPN) one at the border of the lateral gastrocnemius muscle and one approximately 3mm proximal (Fig. 1). In 3 animals a third electrode was placed 1cm away from the long axis of the nerve, a distance sufficient to exclude the possibility of any additional activation at this electrode. The more distal electrode at the nerve was used as active electrode. For bipolar stimulation (in 7 animals) the proximal electrode under the nerve served as

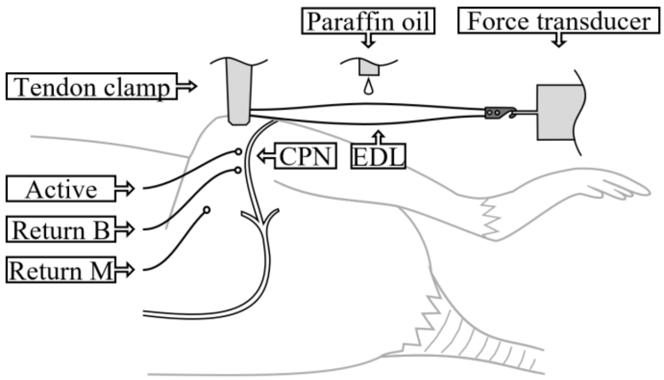


Fig. 1. Experimental model: Nerve-muscle-preparation with Common Peroneal Nerve (CPN) and Extensor Digitorum Longus (EDL). Electrodes: The active electrode was placed most distal at the CPN. For bipolar stimulation "Return B" was used, for monopolar stimulation "Return M" served as return electrode.

return, while for monopolar stimulation (in 3 animals) the third electrode was used as return electrode.

In order to gain access to the extensor digitorum longus (EDL), the distal tendon of the tibialis anterior (TA) as well as the fascial tissue connecting the TA with peroneus longus and lateral gastrocnemius muscles was dissected. After freeing both tendons of the EDL from connective tissue, the proximal EDL tendon at the knee joint was clamped with a sturdy artery forceps fixed to the steel table. The distal EDL tendon was dissected and clamped in a miniature titanium-alloy hook by which the muscle was connected to a force transducer (Gould Inc, Statham Instrument Division, Oxnard, California, U.S.A.), also mounted on the experimental steel table. Thereby the EDL muscle was mechanically isolated and held in an isometric condition, while retaining its blood supply and innervation. The muscle was set to optimal length by increasing in 0.5mm increments from a slack length to the length for which single stimuli resulted in the highest isometric developed force, that is peak-active minus passive force, while the passive muscle force was not yet exponentially increasing [22]. The EDL muscle was prevented from drying and maintained at a physiological temperature of 37-38°C by dripping heated liquid paraffin oil over it. A peristaltic pump (Watson-Marlow Ltd., Falmouth, Cornwall, UK) delivered the oil with a flow rate of 0.1ml $min^{-1}$ to a local miniature heater with temperature control (Fluke 54II Thermometer with k-type thermocouple, Fluke Corporation, Everett, Washington, U.S.A.), from where it was applied to the muscle surface. Since this surgical preparation took about one hour, a volume of 1 - 1.5ml sterilized saline solution (OXOID Ltd., Basingstoke, Hampshire, UK) was administered subcutaneously to replace normal fluid loss during the time under anaesthesia.

### *B. Stimulation*

The stimulation impulses were generated in LabVIEW™ 2016 (National Instruments Corporation, Austin, Texas, U.S.A.) and delivered via the analog output of a NI PCIe 6351 Data Acquisition Card (National Instruments Corporation, Austin, Texas, U.S.A.) with a sampling rate of 1MS/sec to a galvanically isolated voltage-to-current converter, which then delivered current controlled stimuli to the electrodes. Stimuli were presented at a rate of one pulse every 3 seconds to allow sufficient recovery between twitches and thus minimise muscle fatigue. To achieve charge balanced stimulation, all impulses were biphasic with the cathodic phase first. The kurtosis of the Gaussian waveform is described by

$$I(t) = e^{-\frac{\left(\frac{t}{PhW}-0.5\right)^2}{0.045}}, \tag{1}$$

as this current profile was a close match to the waveforms used by Wongsarnpigoon and Grill in what they called the clinically relevant range of phase widths [19]. Recruitment curves (that is peak muscle force plotted against pulse amplitude, see Fig. 2.a) for phase widths of 40,60,80,100, 120, 140, 160, 180, 200, 250, 325, 425, 550, 775 and 1000µs were recorded with 100µA amplitude increments for biphasic Gaussian and rectangular pulses. For both waveforms and both electrode configurations, the different combinations of stimulation parameters, that is,

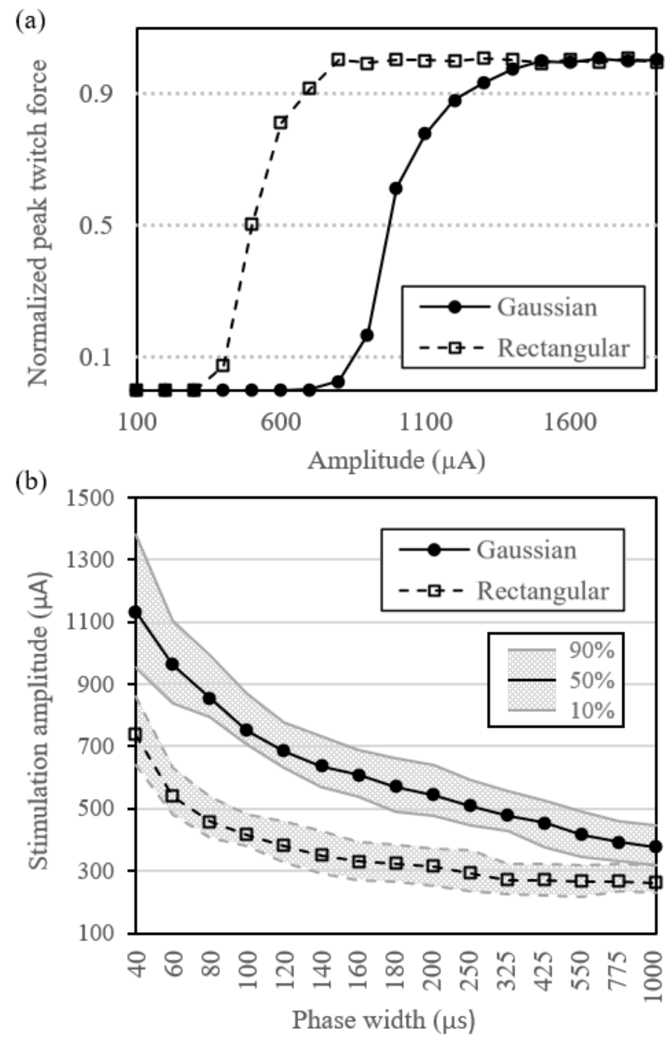


Fig. 2. Exemplary recruitment data for Gaussian and rectangular pulses with bipolar electrodes. a) Normalized recruitment curves for PhW=60µs. 10%, 50%, and 90% of maximum isometric twitch force were determined by linear interpolation of experimental measurement points. b) Strength-duration curves for 50% activation (black traces) and dynamic ranges (gray area) between 10% (lower traces) and 90% (upper traces) activation levels. Data are means of n=7.

amplitudes and phase widths, were applied in randomized order. Every 20 test stimulations a standard control stimulation pulse (biphasic rectangular, 200µs PhW), with an amplitude set for each subject to elicit supramaximal nerve recruitment (typically 1mA) was delivered and the resultant force recorded.

### *C. Recording*

Isometric twitch forces were recorded using a PowerLab 16/35 (ADInstruments Pty Ltd, Bella Vista, New South Wales, Australia) with a sampling rate of 100kS/sec. ADInstruments LabChart 7 Pro (ADInstruments Pty Ltd, Bella Vista, New South Wales, Australia) was used to store, pre-process and export the force data. We wished to record the electrode current at a higher sample rate, so stimulation current through a resistor in series and stimulation voltage across the electrodes, were recorded separately at 500kS/sec with an NI PCIe 6351 Data Acquisition Card, which was also used for stimulation.

### *D. Data analysis and statistics*

The isometric peak twitch force values elicited by the randomly applied test stimulations were normalized to the force response of the nearest control pulse. The normalized peak force values were then sorted by pulse shape, phase width and stimulation amplitudes, to reveal the normalized recruitment data. Thus, the final recruitment curves were assembled from test pulses that were placed randomly from start to end of the respective recording period, and therefore are not affected by variations of temperature, level of anaesthesia or fatigue. Linear interpolation between data points was used to determine the 50% activation thresholds of all recruitment curves (Fig. 2.a). The energy consumption (2) and charge injection (3) values for all applied stimuli were attained by integration of the electrical stimulation recordings:

$$E = \int_0^{2PhW} V(t)I(t)dt, \tag{2}$$

$$Q = \int_0^{2PhW} |I(t)|dt. \tag{3}$$

Energy and charge values at 50% activation level were scaled according to the threshold interpolation. Furthermore, the percentage differences in energy consumption (4) and charge injection (5) with Gaussian pulses compared to rectangular stimuli at 50% activation threshold were calculated:

$$\text{Difference in energy} = \left(1 - \frac{E_{gaus}}{E_{rect}}\right) * 100\%, \tag{4}$$

$$\text{Difference in charge} = \left(1 - \frac{Q_{gaus}}{Q_{rect}}\right) * 100\%. \tag{5}$$

In addition to these integrated measures of stimulation efficiency, the maximum instantaneous power across the electrodes was also calculated

$$P(t) = V(t) * I(t) \tag{6}$$

for both tested waveforms and expressed as a percentage difference between the response to rectangular and Gaussian pulses:

$$\text{Diff. in max. inst. power} = \left(1 - \frac{P_{gaus}}{P_{rect}}\right) * 100\%. \tag{7}$$

Fig. 3 shows an example of the electrical recordings (stimulation current and voltage) as well as of the computed efficiency measures (energy, charge, and maximum instantaneous power) with rectangular and gaussian pulses of 100µs PhW near 50% activation level.

A two-way repeated measures analysis of variance (ANOVA) was performed for each measure of stimulation efficiency separately. The dependent variable was the normalized charge, energy or maximum instantaneous power value at 50% activation level. The independent variables were waveform (rectangular or Gaussian), PhW, and rat (subject). Where the effect of the waveform was found to be significant ($p<0.05$), Sidak's multiple comparisons were conducted post hoc for the means of the respective efficiency measure (charge, energy or power) of Gaussian and rectangular stimuli at each PhW separately.

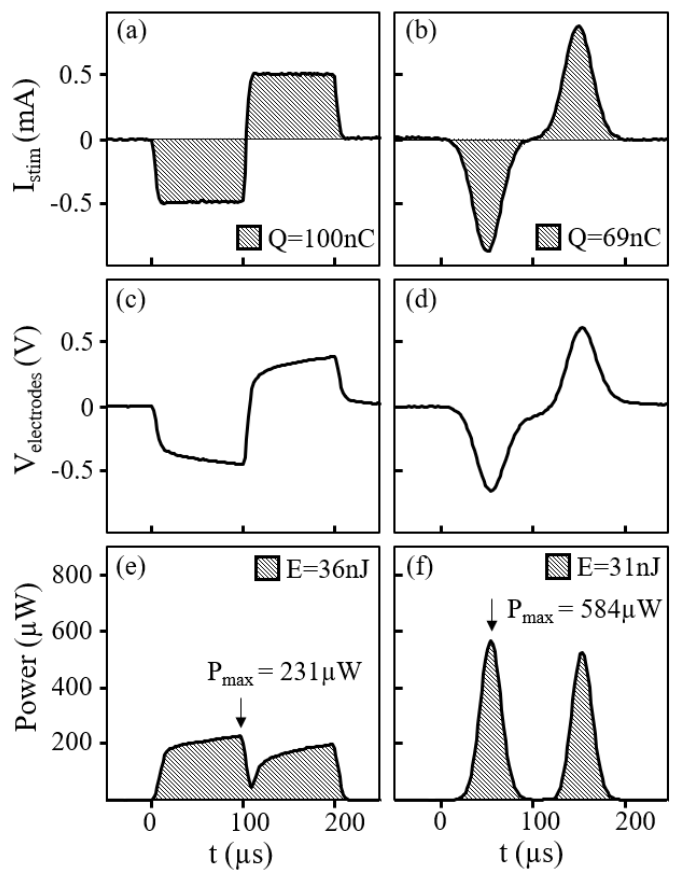


Fig. 3. Electrical recordings of rectangular (left column: a, c, e) and Gaussian (right column: b, d, f) stimulation (PhW=100µs) near 50% activation threshold. Stimulation current and charge: a) Rectangular stimulus with 500µA amplitude and 100nC overall charge injection; b) Gaussian pulse with 900µA amplitude and 69nC (31% reduction) charge injection. Stimulation voltage across electrodes during rectangular c) and Gaussian d) stimulation. Instantaneous power and energy consumption: e) Rectangular pulse consumes 36nJ energy and has a max. inst. power of 231µW; f) Gaussian pulse consumes 31nJ energy (14% reduction) and has a max inst. power of 584µW (153% increase).

## III. Results

The recruitment data underlying the calculations of the efficiency measures are well behaved. Fig. 2.a shows examples of typical recruitment curves with their characteristic sigmoidal shape. Strength-duration curves at 50% activation level as well as the dynamic ranges (10% to 90% activation) exhibit the characteristic hyperbolic shapes (Fig. 2.b).

### A. Energy efficiency

*Bipolar case:* The energy-duration curves for 50% activation with Gaussian and rectangular stimuli applied via bipolar electrodes (in n=7 animals) intersect at a phase width between 60 and 80µs (Fig. 4.a). After this intersection the energy consumption values of Gaussian stimuli increase less with increasing PhWs than for rectangular stimulation. This implies an increasing energy efficiency of Gaussian compared to rectangular pulses with increasing PhW (Fig. 4.c). The effect of waveform on energy efficiency was significant ($P<0.001$). However, stimulation with Gaussian pulses of the shortest tested phase width of 40µs required on average 17.7% (±4.8% SEM) more energy than rectangular stimuli of the same PhW. In the range of 50-200µs PhWs the differences in mean energy efficiency of Gaussian compared to rectangular pulses ranged from -5.8% (±1.4% SEM) at 60µs to +17.1% (±2.4% SEM) at 200µs. At the longest tested PhW of 1000µs, excitation with Gaussian pulses was achieved with 46.7% (±5.9% SEM) less energy than with rectangular impulses (Fig. 4.c).

*Monopolar case:* Energy duration curves for stimulation via a monopolar electrode configuration (in n=3 animals) intersect at a phase width of 100µs; for shorter pulses rectangular stimulation appear to require less energy while Gaussian stimuli are more energy efficient at PhWs over 100µs (Fig. 4.b), although ANOVA revealed no significant effect of waveform ($P=0.11$). At 40µs PhW stimulation with Gaussian pulses was on average 17.6% (±4.7% SEM) less energy efficient than stimulation with rectangular pulses. As the energy duration curves intersect within the range of 50-200µs PhWs, the energy efficiency of Gaussian compared to rectangular pulses ranged from -7.5% (±4.9% SEM) at 60µs to +17.5% (±5.9% SEM) at 140µs. The highest difference in energy efficiency of 61.6% (±3.9% SEM) was observed at 1000µs (Fig. 4.d).

### B. Charge efficiency

For both electrode configurations the charge injection values required to elicit 50% of the maximum isometric twitch force are remarkably linear functions of the stimulation phase width (Bipolar: Fig. 5.a, Monopolar: Fig. 5.b). In both electrode setups and throughout the whole range of tested phase widths (40-1000µs), Gaussian stimulation required less charge injection than standard rectangular pulses to activate the target nerve. Absolute charge injection values never exceeded 0.5µC per phase, so the charge density per phase was always below 20µC/cm2. This means the stainless steel stimulation electrodes were operated within the limits of their specific charge injection capacity [23] and within the safe operating range [24].

*Bipolar case:* The superiority of Gaussian pulses in terms of lower charge injection requirements compared to rectangular stimuli (in n=7 animals) was highly significant ($P<0.001$). Gaussian stimulation with the shortest tested phase width of 40µs required on average 20.9% (±1.6% SEM) less charge than rectangular pulses of the same duration. In the range of 50-200µs PhWs, the reduction in charge injection with Gaussian pulses ranges from 25.1% (±0.5% SEM) at 60µs to 33.7% (±0.9% SEM) at 200µs. In stimulation with the longest tested phase width of 1000µs Gaussian pulses needed on average 47.4% (±3.1% SEM) less charge than rectangular stimuli (Fig. 5.c).

*Monopolar case:* The reduction of charge injection with Gaussian pulses in monopolar stimulation (in n=3 animals) was significant ($P=0.013$). At 40µs phase width Gaussian pulses needed 21.0% (±1.6% SEM) less charge than rectangular stimuli to elicit the same force response. The average charge reduction achieved within the range of 50-200µs PhWs ranged from 24.5% (±1.8% SEM) at 60µs to 33.9% (±2.3% SEM) at 140µs. Stimulation with 1000µs phase width was on average 54.9% (±2.3% SEM) more charge efficient with Gaussian pulses (Fig. 5.d).

### C. Power efficiency

Throughout all tested phase widths and in both electrode configurations, the Gaussian stimulation waveforms were less power efficient, i.e. they required a higher maximal instantaneous power than the rectangular stimuli. ANOVA revealed the effect of waveform to be significant in both electrode configurations (bipolar: $P<0.001$, monopolar: $P=0.017$). The difference in maximum power between the compared waveforms decreased with increasing phase duration from approximately 230% at 40µs to 31.1% (±14.7% SEM, bipolar in n=7 animals) or 7.5% (±10.9% SEM, monopolar in n=3 animals) at 1000µs (Fig. 6).

These substantially increased values of maximal instantaneous power are due to the higher stimulation amplitudes required with Gaussian pulses. The exemplar recordings in Fig. 3 show two pulses (phase width 100µs) near the 50% threshold. The rectangular pulse has a stimulation amplitude of 500µA (Fig. 3.a), whereas the Gaussian pulse needed 900µA to elicit the same level of neural activation (Fig. 3.b). The increased current is associated with a higher voltage across the electrodes for the Gaussian (Fig. 3.d) than for the rectangular pulse (Fig. 3.c). As the instantaneous power across the electrodes is the product of stimulation current and voltage (see Equation 6), it scales approximately quadratically with the current. In the exemplary data of Fig. 3, the higher stimulation amplitude led to a 153% increase in maximum instantaneous power. It increased from 231µW with the rectangular pulse (Fig. 3.e) to 584µW with the Gaussian pulse (Fig. 3.f).

## IV. Discussion

Following the findings of recent computational studies on energy optimal stimulation waveforms [19]–[21], Gaussian shaped stimuli were compared against standard rectangular stimulation in a nerve-muscle preparation in anaesthetized rats in terms of energy, charge and power efficiency. In order to attain results that can be applied for practical applications such

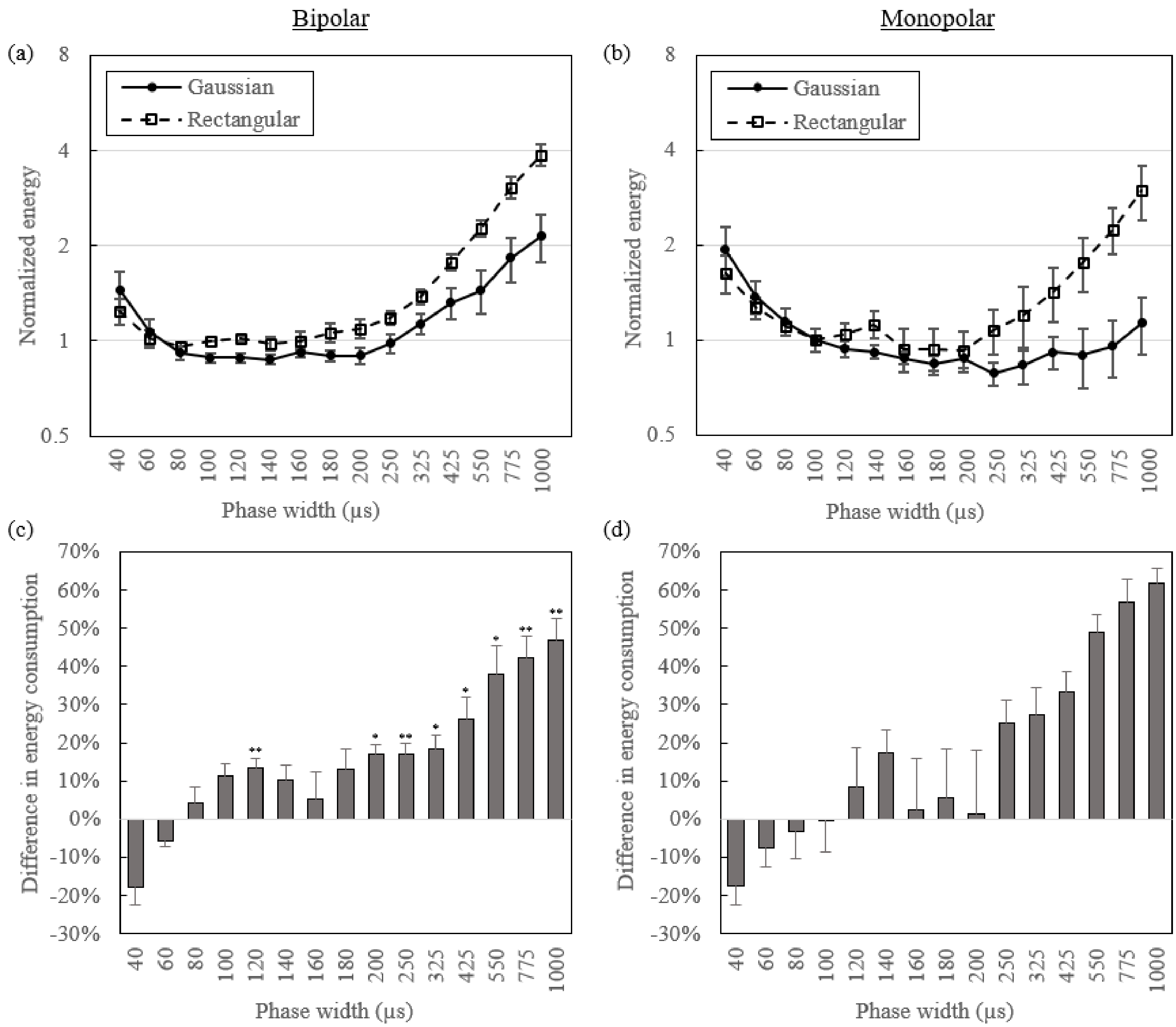


Fig. 4 Energy efficiency of biphasic Gaussian waveform compared to biphasic rectangular stimuli. Data for 50% of maximal isometric twitch force with bipolar (left column: a, c) and monopolar electrodes (right column: b, d), mean +/- SEM (bipolar n=7, monopolar n=3). a), b) Energy-duration curves normalized to energy consumption with rectangular pulses of PhW=100µs. c), d) Energy consumption of Gaussian waveform compared with rectangular; positive values of "Difference in energy consumption" indicate that Gaussian pulses were more energy efficient.

as cochlear implants or neuromuscular prosthetics, both commonly-used electrode configurations, monopolar and bipolar stimulation, were tested. To further bring this investigation closer to practical implementation, instead of duration-dependent pulse shapes only one fixed Gaussian waveform was used for all phase widths and all tested stimuli were biphasic and charge balanced. In both electrode configurations, Gaussian stimulation was found to be less energy efficient than rectangular pulses at short phase widths. However, at phase durations above approximately 80µs the Gaussian waveform becomes more energy efficient than the traditionally used rectangular stimulus. This superiority of the Gaussian pulse in terms of energy efficiency increases with increasing stimulation phase width up to 46.7% in bipolar and 61.6% in monopolar stimulation at the upper end of tested phase durations of 1ms. Energy savings in the so-called clinically relevant range of phase width (50-200µs) were less than the claims made in previous papers and did not exceed 17%. Furthermore, these energy savings did not take the additional energy requirement to generate such gaussian waveforms into account, so the realistically achievable savings might be even lower. We found that charge efficiency of Gaussian shaped stimuli was significantly greater than that for standard rectangular pulses with both electrode configurations. Neuronal activation was achieved with 21-55% less charge injection with the Gaussian waveform. In the range of 50-200µs PhWs a 25-33% reduction of charge injection was realised. However, the maximum instantaneous power was greater for Gaussian than rectangular stimuli over the whole range of phase widths. This disadvantage in power efficiency, which ranged from

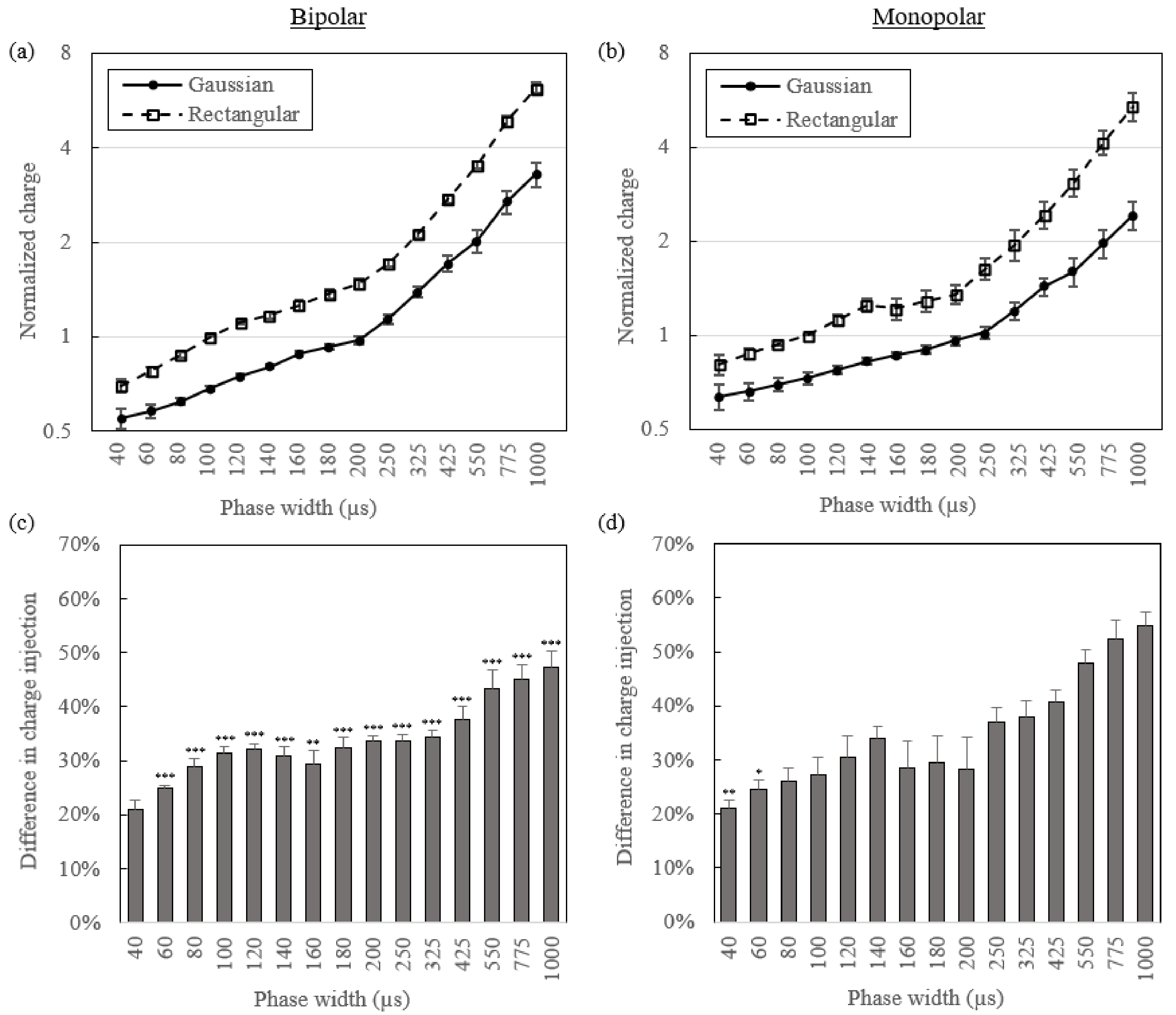


Fig. 5. Charge efficiency of biphasic Gaussian waveform compared to biphasic rectangular stimuli. Data for 50% of maximal isometric twitch force with bipolar (left column: a, c) and monopolar electrodes (right column: b, d), mean +/- SEM (bipolar n=7, monopolar n=3). a), b) Charge-duration curves normalized to charge injection with rectangular pulses of PhW=100µs. c), d) Charge injection of Gaussian waveform compared with rectangular; positive values of "Difference in charge injection" indicate that Gaussian pulses were more charge efficient.

approximately -200% to -110% in the range of 50-200µs PhWs, decreased with increasing phase duration (Fig. 6).

The general finding of increased energy and charge efficiency with Gaussian compared to rectangular stimuli fits well with the data from single axon models, which predicted Gaussian stimuli to be more charge efficient throughout all phase widths and more energy efficient at phase durations over approximately 60µs [16]. However, the observed extent of energy savings in the range of 50-200µs PhWs of only up to 17% challenges the predicted energy benefit of up to 60% with Gaussian stimulation waveforms, in this so-called clinically relevant range [19]. The lower energy savings described in the present study might have partially originated from differences in the fixed Gaussian waveform used here (1) with the PhW dependent waveforms used by Wongsarnpigoon et al. Since we chose our Gaussian waveform to best match the average pulse shape used by Wongsarnpigoon et al. in the range of 50-200µs PhW, we expect little influence of PhW depend shape variations with our results in this range. However, the biphasic pulses generated by their genetic algorithm were not perfectly symmetrical, but the peak of the cathodic phase was shifted further away from the anodic phase [19], which was not the case in the pulses used here (1). The asymmetrical shifting of the peak effectively introduces a greater interphase gap (IPG) than a symmetric Gaussian pulse would have. It is known that the anodic phase of a biphasic pulse can abolish action potentials in near threshold scenarios at short PhWs [5], [7]. Thus, the introduction of a (greater) IPG might lead to greater stimulation efficiency. It might be argued that the (limited) energy savings with biphasic Gaussian pulses at short PhWs are also a result of

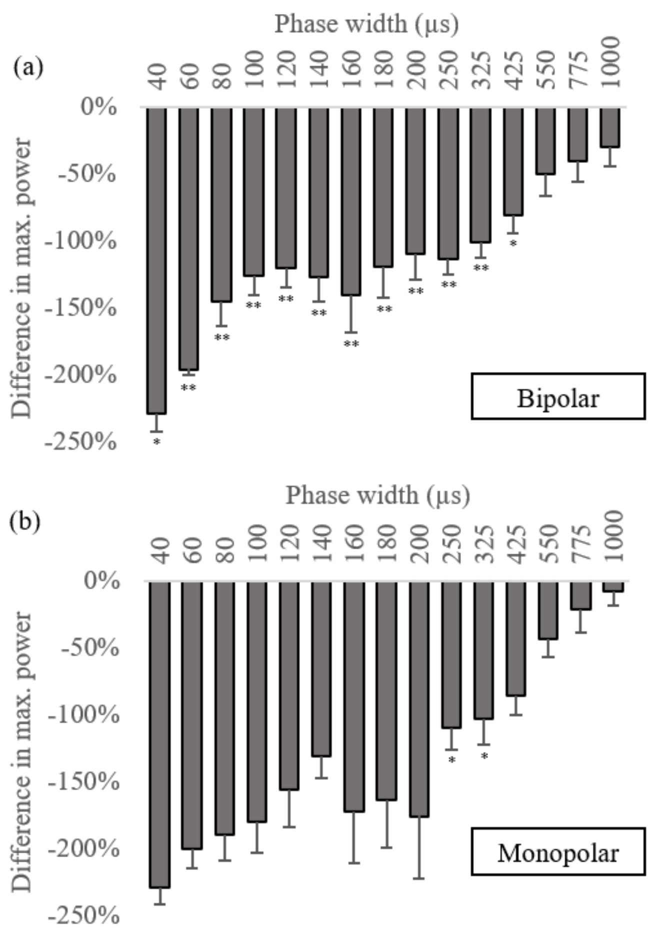


Fig. 6. Difference in maximum instantaneous power of Gaussian waveform compared to rectangular in a) bipolar (n=7 animals) and b) monopolar stimulation (n=3 animals). Negative values of "Difference in max. power" indicate that Gaussian pulses had higher values of max instantaneous power.

the separation of the stimulation phases compared to a biphasic rectangular pulse without IPG (compare Fig. 3.a and 3.b). Investigations of this hypothesis would require new experiments.

We found that the increase in energy and charge efficiency was accompanied by a decreased power efficiency, which extends the finding of Wongsarnpigoon et al. that no rectangular, exponential or ramp waveform was at the same time most efficient for energy, charge and power [18]. The benefits in charge efficiency in the range of 50-200µs PhWs with the Gaussian waveform were greater than those reported by Wongsarnpigoon et al., who found ramp pulses to be most charge efficient for 20-200µs phase duration with 5-18% less charge injection than required with standard rectangular pulses. Energy savings at long phase widths were similar to those reported for exponential waveforms based on a population model and in vivo work [18]. However, due to certain constraints in pulse shaping the effective part of the exponential pulses used in that study did not change as the phase width increased over approximately 0.3ms. The results were therefore misleading for longer phase durations as the authors conceded. By contrast, the Gaussian waveform used in the present study was scaled to fill the whole phase duration (compare Fig. 3.b).

## V. Conclusion

The results of this study in terms of improved energy efficiency with Gaussian stimulation waveforms challenge the predicted range of up to 60% energy savings in a so-called clinically relevant range of phase widths (50-200µs) [19] since only moderate savings of up to 17% were observed. Furthermore, the comparison of maximum instantaneous power required with Gaussian and rectangular stimuli revealed that in the range of 50-200µs PhWs, these moderate energy savings were accompanied with profound losses in power efficiency. While the energy savings could (if the additional instrumentational energy consumption is neglected) increase the number of pulses that a given battery can deliver by up to 17%, the 110% to 200% higher maximum power requirements would necessarily lead to an undesired increase in battery size. Thus, the tested Gaussian waveform is not advantageous to improve performance of implanted stimulation devices that operate at the range of 50-200µs phase widths. The need for a larger energy source clearly opposes the ambition for device miniaturization.

As all three measures of stimulation efficiency improved with increasing phase duration (in the case of power efficiency, a decrease in the disadvantage) we conclude that the implementation of the Gaussian stimulation waveform may have great potential especially for applications with long phase widths such as stimulation of denervated or partially denervated muscle [25], [26]. And for stationary therapeutic devices, where energy efficiency might not be as crucial as it is for battery powered devices, the significant increase of charge efficiency could increase stimulation selectivity by allowing electrode size to be reduced without exceeding safe limits of charge density. The significant improvement in charge efficiency of over 50% which we observed at 1ms phase width would allow the safe use of electrodes only half the size of those required with conventional stimuli. Such a reduction in electrode size would enable major improvements in applications like laryngeal [27] or facial stimulation [28], where space is highly limited and coactivation of nearby innervated structures is undesired and may be painful.

This study provides promising results and limitations related to the practical implementation of Gaussian stimulation waveforms.

## VI. References

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