Zero Mean Waveforms for Neural Stimulation

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***Abstract*—Biphasic charge balanced waveforms do not minimise faradaic processes at the electrode-electrolyte boundary and do not leave electrodes neutral with respect to the tissue. Superior waveforms for electrode health (and consequently tissue safety) exist and may also offer better performance in terms of power consumption and stimulation effectiveness within charge injection limits. This paper aims to provide intuitive insight into the limitations of biphasic waveforms and presents a simple method for assessing how well other waveforms will perform, as well as methods for designing waveforms to theoretically give zero residual voltage and zero net faradaic charge transfer.**

***Index Terms*—Neural stimulation, biphasic waveforms, High frequency AC block, triphasic waveforms, zero mean waveforms, neuromodulation**

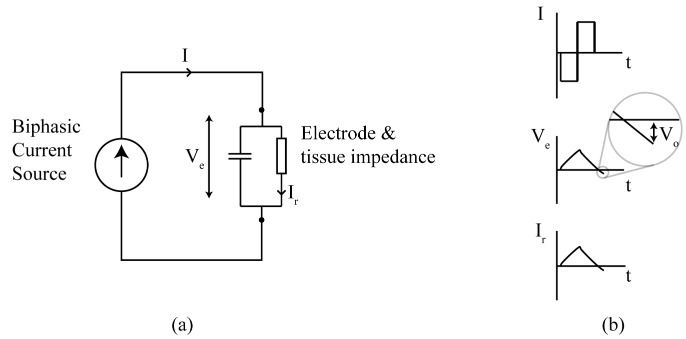

Fig. 1. (a) Simplified model of electrode impedance. (b) From top: input biphasic current waveform; voltage across the electrode; and faradaic leakage current through the parallel resistance.

I. Introduction

It has been known for decades that DC current flow through electrodes in an electrolyte solution leads to faradaic processes at the electrode-electrolyte boundary. This DC flow causes unreversed reactions that can degrade the electrodes and, in biological systems, the products of these reactions can cause tissue damage.

Since Lilly et Al. published their paper [1] describing short biphasic current pulses just over 60 years ago, biphasic current pulses that are charge balanced (i.e. having zero net charge) have been the default for neural stimulation. Indeed compared to the monophasic or voltage pulses that preceded them, these waveforms represented a giant leap forward in neural stimulation safety. However, over the years the concept of zero net charge has been often conflated with no net DC current flow across the electrode-electrolyte boundary and also with the idea that there will be zero residual voltage on the electrodes following this biphasic waveform. Unfortunately as nicely explained in section 2.4 of a paper by Merrill et Al. [2] neither of these things is true in practice. Indeed, if a train of charge balanced stimulation pulses is applied, a ratcheting effect is observed where the residual voltage accumulates (due to net faradaic current flow) until a steady state is achieved with zero average faradaic current flows. Unfortunately, this steady state is dependent on the pulse train parameters remaining constant and any interruptions of the train or changes in frequency, duration or amplitude of the pulses will disturb the achieved equilibrium and again lead to net faradaic current flow.

This paper presents an illustrative analysis of this fundamental problem as well as a new method for assessing a waveforms susceptibility to this problem and leads to an intuitive understanding of the proposed solution - a class of waveforms that do not suffer from this ratcheting effect and methods for designing these waveforms.

II. Analysis

Intuitively this residual voltage can be understood with a simplified version of the standard lumped element model [2] of the electrode-electrolyte interface impedance. This simplified model is shown in Figure 1(a) and consists of a single parallel capacitor and resistor representing an aggregation of the two electrode-electrolyte boundary impedances (series resistances are ignored as it is current pulses that are applied). Assuming a starting point of zero voltage across the electrode, the biphasic current waveform simply charges the double layer capacitance up and then discharges it. However, the parallel resistance represents the faradaic processes at the boundary (i.e. leakage of the capacitor) and the average voltage across the resistor is positive, giving a positive average current during the period of the stimulation (see Figure 1(b)). This results in an offset voltage (V_0) at the end of the stimulation and the subsequent slow discharge of this capacitive charge through the faradaic resistance (not shown).

In the literature this voltage offset has often been attributed to non-charge balanced pulses rather than the intrinsic leakage across the electrodes. As a result ever increasing effort has been focused on achieving charge balance by precisely matching the charges delivered, or by applying active charge balancing – e.g. measuring V_0 and adapting the stimulation waveform to remove it or by shorting the electrodes together. It is important to note that V_0 is present even with a perfectly charge balanced waveform and that active charge balancing would therefore actually degrade the charge balance of the waveform. It is also important to note that V_0 works to oppose this DC faradaic current, i.e. if the charge balanced stimulation in Figure 1 were repeated thousands of times back-to-back (as is the case in High Frequency nerve block) the accumulated offset would shift V_e such that its mean ($\overline{V_e}$) would asymptotically tend to zero (and the mean faradaic current $\overline{I_r}$ would likewise tend to zero). Active charge balancing works to

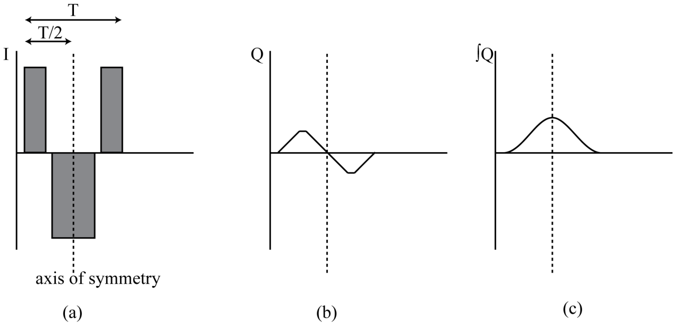

Fig. 2. (a) Triphasic symmetrical charge balanced waveform. (b) Resulting charge on the electrodes (proportional to the voltage across the electrodes Ve and leakage current Ir). (c) Resulting integrated charge on the electrodes.

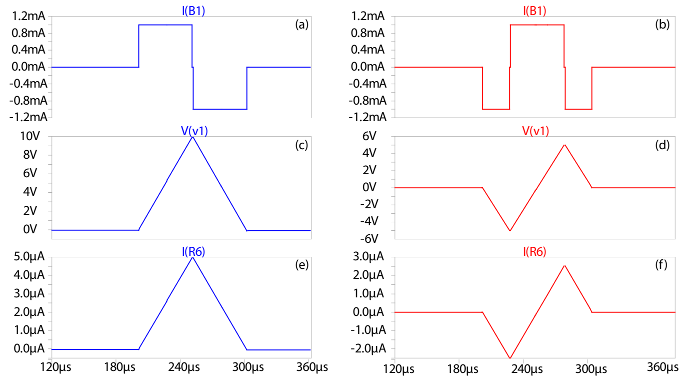

Fig. 3. Simulation waveforms: (a) biphasic current waveform; (b) triphasic current waveform; (c) voltage across the electrodes for biphasic stimulation; (d) voltage across electrodes for triphasic stimulation; (e) current through the faradaic resistance for biphasic stimulation; (f) current through the faradaic resistance for triphasic stimulation.

oppose this drift and depending on the application may cause more harm than good.

The offset voltage resulting from a biphasic charge balanced pulse is determined by the impedance of the electrodes and the average voltage across the electrode-electrolyte boundary. This latter factor cannot be directly measured, but can be estimated from the average charge on the electrodes, this average is affected by the shape and interphase intervals of the chosen waveform and as such these factors can have previously unforeseen implications for electrode and tissue health. The situation is further complicated in highly flexible systems employing multi-channel bipolar or multipolar stimulation as the electrode offsets that will accumulate will be essentially uncontrolled.

The conclusion of this analysis is that biphasic charge balanced waveforms cannot minimise faradaic DC current flow and cannot leave a pair of electrodes neutral with the tissue.

III. Proposal

To address this issue a charge balanced waveform not limited to two phases and which meets an additional criterion is required: namely that the mean of the charge on the electrodes is zero (or equivalently the second integral of current with respect to time is zero over the duration of the waveform (T)).

$$\iint_0^T I.dt = 0 \qquad (1)$$

A more intuitive description of this criteria is that the average voltage across the electrodes and the net current through the electrodes should be zero.

The simplest waveform (and one that could be implemented easily on many existing systems) is the use of a charge balanced triphasic waveform (duration T) that is symmetric about its midpoint (T/2) – see Figure 2. An alternative method of finding a suitable waveform is to take any n-phase charge balanced stimulation and repeat it in reverse (i.e. creating a function that is even around its midpoint). It should be noted that symmetry is not a requirement for meeting the criterion, but is just the simplest method.

Triphasic waveforms have been used experimentally for over 30 years (as it has been noted that they reduce the residual voltage and improve electrophysiological recording shortly after stimulation), but they have never found widespread favour. This is likely because they require higher stimulation currents (Bahmer and Baumann 2013 [3]) – which at first glance is associated with increased power consumption and risk of electrode damage. However, a closer look shows that neither of these are necessarily true. Power consumption is a factor of the stimulation compliance voltage as well as the current, and for a given current and pulse duration a triphasic waveform causes can be as little as half of the voltage swing of a biphasic waveform (for electrodes and stimulations where the voltage developed is primarily a result of charging and discharging the double layer capacitance) implying that the break even point for power consumption is when the current necessary for triphasic stimulation may be up to 2 times that of a biphasic waveform as the voltage is approximately proportional to the current. Similarly the key parameter for electrode degradation is the overpotential on the electrode and in terms of electrode potential the equivalent overpotential for a simple triphasic waveform occurs at up to 2 times the charge per phase of a biphasic waveform (because the initial half phase is negative) . Adding in the improved performance of a charge balanced waveform meeting the criterion described here and it is possible that even at 2 times the charge per phase, the resulting electrode degradation will be decreased.

IV. Initial Results

A. Simulated Results

A current based stimulator was modelled in freely available (SPICE based) circuit simulation software (to support verification the author has made a model available at https://github.com/williamsi350/ZeroMeanWaveforms). Figure 3 shows the simulated stimulation waveforms for a single stimulation cycle with biphasic and triphasic current waveforms with key stimulation parameters of 1mA current, 100μs duration and electrode parameters of 10nF capacitance, 1MΩ faradaic resistance.

To model the accumulation of residual voltage (and subsequent discharge through the faradaic resistance) a pulse train of 100 rapid repetitions was simulated (Figure 4). These

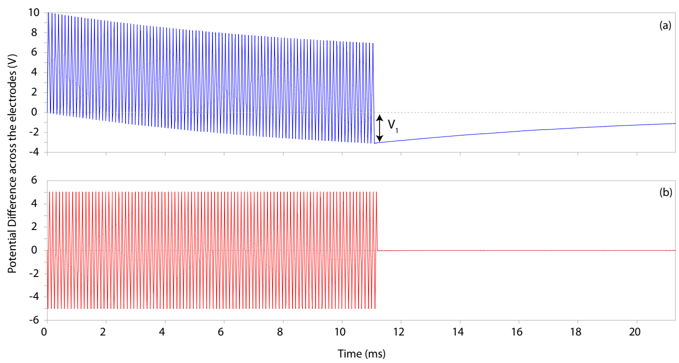

Fig. 4. Simulated voltage across the electrodes for 100 rapid repetitions of (a) the biphasic waveform and (b) the triphasic waveform. (Electrode capacitance 10nF, faradaic resistance 1MΩ, stimulation duration 100μs, stimulation amplitude 1mA)

results show how a biphasic waveform (Figure 4a) causes accumulation of residual voltage (asymptotically tending to shift the mean of the waveform to average around zero), ultimately resulting in an offset V_1 that discharges through the faradaic resistance once the pulse train is stopped. For the selected stimulation parameters and electrode parameters this led to net faradaic currents of 15nC for biphasic stimulation and 19pC for triphasic stimulation – an approximately 3 orders of magnitude improvement.

B. Measured Results

The effect of pulse trains of biphasic and zero mean (triphasic) stimulations are currently being tested with platinum electrodes in saline to investigate long term changes and any damage that results. An initial recording from the electrodes is shown in Figure 5 and appears to corroborate all the features observed in the theoretical analysis and simulations. One slight deviation from expectation is that the electrodes' equilibrium voltage isn't quite zero (approximately 0.1V for the biphasic electrodes and 0.2V for the triphasic ones). It isn't yet clear what the cause of this is.

V. Discussion

Fundamentally the premise presented here is simple and should be uncontroversial - biphasic stimulation necessarily causes an average DC voltage across the electrodes (leaving them no longer in equilibrium) and since the electrode-electrolyte interface is not purely capacitive then DC current will flow.

However, if there is disagreement about the above statement or the proposed solution then it is likely that a key concern will be the appropriateness of the simple R||C electrode model and this concern is discussed here from 2 perspectives: 1) whether the effect is still present and consistent with more complicated lumped element models of the electrodes (e.g. including 2 electrodes, constant phase elements or Warburg impedances; and 2) whether using a lumped element circuit model is appropriate to represent the non-linear electrochemical processes occurring at the electrode-electrolyte boundary.

1) The first is readily testable with the aforementioned circuit simulator. Tests to-date indicate that the model chosen does not have a substantial impact on the described problem and solution.
2) The second aspect is more challenging. Lumped element models do not adequately capture effects associated with reaction kinetics and mass transport or longer term effects such as depletion of reactants or accumulation of products. They will not identify whether reversible or irreversible reactions are occurring. However, they are widely used for analysing faradaic current flow and, given the very rapid timescales associated with neural stimulation pulses, they should be an appropriate tool for this kind of analysis.

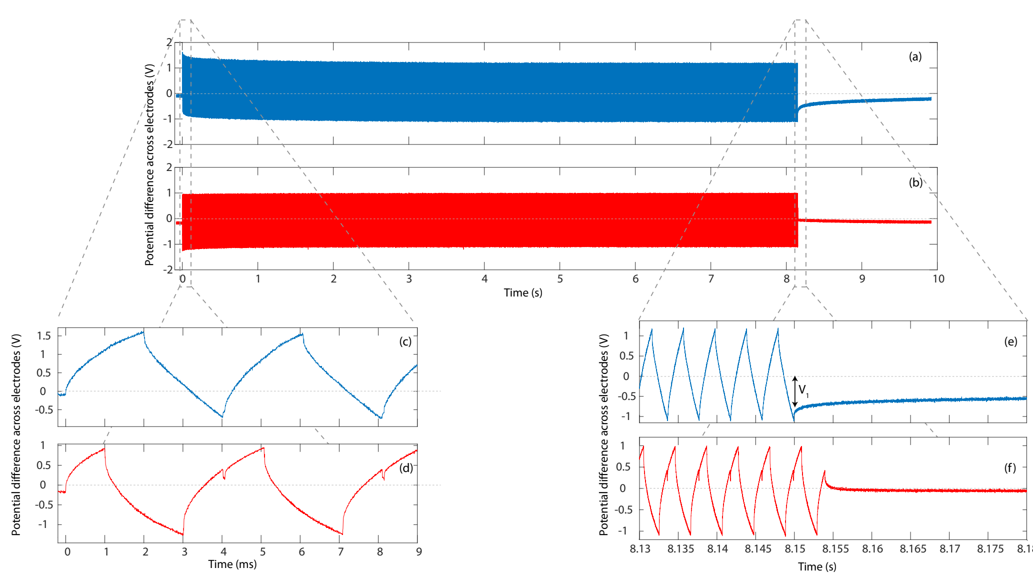

Fig. 5. Measured voltage across the electrodes for 2000 rapid repetitions of biphasic or triphasic stimulations. (a) and (b) The full pulse train for biphasic and triphasic stimulation respectively. (c) and (d) zoom in of the first couple of stimulation cycles for the biphasic and triphasic stimulations respectively. (e) and (f) zoom in on the final stimulation cycles of the pulse train showing the accumulated charge for biphasic and triphasic stimulations respectively.

VI. Conclusion

The conflation of charge balance with zero residual voltage and minimised DC faradaic current flow is an oversight with potential safety implications. The severity of the problem is dependent on the electrode impedances, stimulation amplitudes, frequency of stimulation, waveforms chosen, interphase intervals and whether active charge balancing is employed. It should be noted that DC blocking capacitors do not address the problem, but equally do not appear to exacerbate it.

The observation that charge balance is not synonymous with zero residual voltage has been discussed before in academic publications, but it is clear from recent patent literature and academic publications that this has not been sufficiently widely known or understood. Indeed it seems necessary to state the problem clearly and re-examine the conclusions and claims in various literature.

This paper presented a criteria and method for assessing waveforms to theoretically give zero residual voltage and outlines some simple waveform design techniques for optimal waveforms.

References

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