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Direct current contamination of kilohertz frequency alternating current waveforms

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HIGHLIGHTS

- Unintentional DC contamination can be a problem in KHFAC waveforms used for nerve block applications.
- Current- and voltage controlled systems cause different amounts of unintended DC.
- DC-blocking inline-capacitors are not always sufficient to eliminate the resulting offset voltages.
- Large value inductors as DC-shunts can reduce DC offset to less than 1 μA.

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ABSTRACT

Kilohertz frequency alternating current (KHFAC) waveforms are being evaluated in a variety of physiological settings because of their potential to modulate neural activity uniquely when compared to frequencies in the sub-kilohertz range. However, the use of waveforms in this frequency range presents some unique challenges regarding the generator output. In this study we explored the possibility of undesirable contamination of the KHFAC waveforms by direct current (DC). We evaluated current- and voltage-controlled KHFAC waveform generators in configurations that included a capacitive coupling between generator and electrode, a resistive coupling and combinations of capacitive with inductive coupling. Our results demonstrate that both voltage- and current-controlled signal generators can unintentionally add DC-contamination to a KHFAC signal, and that capacitive coupling is not always sufficient to eliminate this contamination. We furthermore demonstrated that high value inductors, placed in parallel with the electrode, can be effective in eliminating DC-contamination irrespective of the type of stimulator, reducing the DC contamination to less than 1 μA. This study highlights the importance of carefully designing the electronic setup used in KHFAC studies and suggests specific testing that should be performed and reported in all studies that assess the neural response to KHFAC waveforms.

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1. Introduction

The use of charge-balancing in electrical stimulation has been well-established as a means of significantly increasing the charge per phase that can safely be delivered to living tissue (Agnew et al., 1989; Shannon, 1992; Shepherd et al., 1999). Typical off-the-shelf neural stimulators generate charge-balanced waveforms and often rely on capacitors in series with the electrode to filter out DC components (Huang et al., 1999). Any current passing to the capacitors passes as a displacement current causing the build-up of an electric field inside the capacitor. Ideally, in order for signals to be charge balanced, every electric pulse in one direction (e.g. cathodic) through the load (e.g. electrode) is followed by a pulse of equal amplitude and opposite charge (e.g. anodic). The second pulse is often referred to as the "recharge pulse" and is only used to establish safety of the stimulation. However, capacitors are not perfect charge storage elements, and this can produce a slight imbalance in charge between the two phases of the stimulus. The resulting differential charge causes small residual electric fields after each pulse pair inside the dielectric of the DC-blocking capacitors (Maxwell, 1881; Huang et al., 1999). In conventional neural stimulation, these fields remain practically unnoticed as the residual charge can dissipate through the capacitor's internal impedance or is shorted out by the signal generator during the interval following the current

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pulses. This is because stimulation waveforms typically have a relatively long "off" period between each stimulus pulse. For example, a motor neuroprosthesis using a 200 μs balanced biphasic pulse delivered at 20 Hz (typical parameters) will have a 400 μs "on" period (two balanced 200 μs phases) followed by 49.8 ms of "off" time, for an on:off ration of 0.008 (Chae et al., 2000). The "off" period allows time for any small charge imbalance between the two stimulus phases to dissipate before the next stimulus pulse is delivered, preventing any significant accumulation of charge. In general, the use of a capacitively coupled stimulus output stage reduces the charge imbalance to negligible levels (Huang et al., 1999). However, recent discoveries in the field of neuromodulation have resulted in the use of progressively higher frequencies of stimulation, such as deep brain stimulation (~130–300 Hz) (Jensen and Durand, 2009), spinal cord stimulation (600 Hz to 10 kHz) (Tiede et al., 2013), and peripheral nerve block (1–50 kHz) (Joseph and Butera, 2011; Bowman and McNeal, 1986; Boger et al., 2008; Kilgore and Bhadra, 2013). Of particular interest is the kilohertz frequency range, where the biphasic pulses are often delivered continuously, i.e. there is no "off" time during delivery of the stimulus. In this manuscript, we evaluate whether a small charge imbalance in the output of these continuous waveforms might accumulate on the electrode (or charge-balancing capacitors) and possibly result in unintended electrical, electrochemical, and physiological effects.

Most reports in the literature regarding the use of continuous waveforms in the kilohertz range do not provide a detailed description of the hardware used to produce the waveform (Joseph and Butera, 2011; Tiede et al., 2013; Tai et al., 2004; Dowden et al., 2010; Waataja et al., 2011). In particular, there have been no reports of direct measures of the magnitude of the DC offset during delivery of these waveforms, except when used in cochlear stimulator applications (Huang et al., 1999). A significant DC offset in the signal could produce unexpected or unwanted effects in neural tissue, including nerve conduction block (Bhadra and Kilgore, 2004), and neural damage (Huang et al., 1999), both of which can occur below 10 μA. Therefore, it is important to make direct and accurate measurements of the magnitude of the DC offset during continuous waveforms at kilohertz frequencies. In this manuscript we present methods for measuring the DC offset and demonstrate that any offset can be significantly reduced in an experimental setting with the use of high value inductors.

2. Methods

Calibration and verification of the output of electrical stimulation generators is generally accomplished by substituting a fixed value resistor (commonly 1 or 10 kΩ) for the electrode and measuring the voltage across the resistor. However, in the case of continuous waveforms, we considered that it was important to evaluate the effect of charge imbalance using real electrodes in saline. Our evaluation proceeded in two stages, using two different experimental configurations, as detailed below. The **first stage** involved measuring the voltage directly across the electrode during delivery of 1 kHz continuous waveforms. This stage utilized a relatively simple measurement technique, and could be used for screening a variety of waveform generators, including those with voltage-controlled and current-controlled outputs. We also used this measurement technique to evaluate one current-controlled generator at 10 kHz and 40 kHz (both continuous waveforms) to determine if there were significant differences in the electrode voltage and voltage offset as a function of frequency. The **second stage** involved measuring the electrode potential of each contact against a standard reference electrode (Ag/AgCl) to evaluate whether the voltage offsets observed in the first stage were sufficient to reach or exceed the water electrolysis window for the electrode under test. Current flow through the electrodes during, and immediately after, delivery of the continuous high frequency waveforms was also measured in this second stage. The electrode contact potential and current flow through the electrode were measured using one representative current-controlled and one voltage-controlled waveform generator, first testing the generator directly connected to the electrode and then testing the generator with additional capacitive coupling to the electrode.

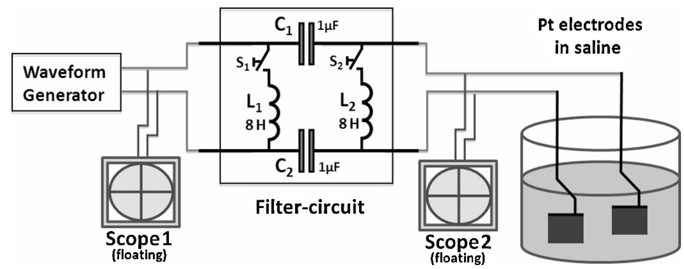

Fig. 1. Electronic setup for Stage 1, used to measure DC-offset voltages caused by KHFAC waveforms. Switches S_1 and S_2 allowed to selectively add DC-shunting inductors L_1 and L_2 to the filter circuit. Offset was first determined with electrically floating Agilent TDS2004c oscilloscopes 1 and 2, then acquired using a Solartron SI1280B (electrode side) and NI DAQ USB-6258 substituting the oscilloscopes.

In both stages of our assessment, high value inductors, placed in parallel with the electrodes and/or the stimulator, were used as a final comparison to the results obtained with standard high frequency generator configurations. High value inductors serve to shunt direct current (DC) in parallel to the electrode, thereby preventing the accumulation of any significant charge-imbalance across the electrodes, while simultaneously providing a large impedance (>200 kΩ) to alternating currents in the kilohertz range, essentially forcing the kilohertz-waveform through the electrode. To our knowledge, inductors have not been commonly utilized in this manner with high frequency waveform generators when used for physiological purposes. We evaluated whether our circuit configuration with inductors included could be used to accurately assess essentially "DC-free" high frequency waveforms for future physiological experimentation.

2.1. *Stage 1: determining unintentional DC voltage offset: experimental setup*

Two current- and two voltage-controlled waveform generator configurations, listed in Table 1, were tested using the experimental setup shown in Fig. 1. A 1 kHz sinusoidal signal, generated by the stimulator being tested, was applied across a bipolar spiral cuff electrode (Naples et al., 1988) suspended in 0.9% NaCl saline. The platinum contacts each had a 1 mm^2 surface area. The impedance of the electrode (Z_E) was 1.28 kΩ at 1 kHz for sinusoidal signals, measured with an impedance metre (Protek Z580; Protek Test, Englewood, NJ). Two inline-capacitors C_1 and C_2 of 1 μF each were placed between the generator and the electrode. Two inductors (with switches) of 8.2 H at 1 kHz were placed on both the stimulator and the electrode side of the capacitors. The high value inductors were achieved using the primary side of signal transformers with an open secondary side. These offered a frequency dependent impedance of $Z_{1\,\mathrm{kHz}}$ = 241 kΩ for KHFAC signals and a low DC-impedance (Z_{DC} = 418 Ω), effectively acting as a shunt for DC-currents. Four capacitor/inductor combinations were evaluated for their ability to minimize offset voltages across the electrodes. Data were sampled at 20 kHz. On the electrode side, a Solartron SI1280B (input impedance Z_{in} > 10 GΩ) was used to measure the voltage between the two electrodes in saline, and on the stimulator side one channel of a USB DAQ-6258 (National Instruments, Austin, TX), captured the Solartron output on a second channel with both