

## Block of Mammalian Motor Nerve Conduction Using High Frequency Alternating Current

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### Abstract

The conduction of action potentials in nerves can be blocked through the application of high frequency alternating current near the nerve. This type of nerve block has a rapid onset and is quickly reversible. Acute in-vivo experiments were carried out in a rat model to determine the effect of frequency, amplitude and electrode geometry on the nerve block characteristics. A blocking electrode was placed on the sciatic nerve and motor nerve block was quantified by measuring force output of the gastrocnemius muscle. Continuous sinusoidal waveforms in the range of 10 KHz to 30 KHz were tested. The results indicate that a 100% nerve block of motor activity can be accomplished at all the frequencies tested. The block is complete but can be reversed within 1 second after the cessation of the high frequency waveform. Block thresholds (peak to peak voltage of the waveform) were measured and demonstrated a linear relationship to frequency. The lowest voltage necessary for block was obtained at 10 KHz. Depending on the specific parameters for block, there is an onset response when the block is first initiated that produces significant activity in the muscle. Methods for reducing this onset response are currently being examined. By proper selection of waveform parameters and electrode geometries, this type of nerve block could have multiple applications in the treatment of spasticity and pain.

### 1. INTRODUCTION

Pathological hyper-activity of neuronal signals, with resulting hyper-activity of muscles or sensory inputs is the hallmark of numerous disease conditions. In many of these conditions, arresting the conduction of these nerve signals could alleviate the disease effect. Therefore, an

effective and reversible means of blocking nerve conduction could have many clinical applications, such as blocking chronic peripheral pain or stopping unwanted motor impulses. Existing methods for surgically or pharmacologically blocking nerve impulses have significant disadvantages, including non-specificity, serious side-effects, low success rates, and nerve destruction.

The use of high frequency alternating currents (HFAC), applied directly to the nerve, has been previously shown to have the potential to produce a quick-acting, quick reversing nerve block with a minimum of side effects [Tanner 1962; Woo and Campbell 1964; Bowman and McNeal 1986; Sawan, et al. 1996; Kilgore and Bhadra 2004; Tai et al., 2004]. A detailed review of this literature has been recently published [Kilgore and Bhadra 2004].

In this present study, we sought to analyze the influence of frequency and amplitude on the effectiveness of the nerve block in mammalian nerves. We identified differences between the mammalian and amphibian results in our preliminary rat studies. Specifically, the mammalian nerve responds with high rate continuous firing when the high frequency stimulation is first applied. This firing subsides after a period of seconds, and subsequently the block is effective with similar characteristics to the amphibian results. The nature of this "onset" response varies considerably with experiment time, electrode position on the nerve and the waveform parameters. Therefore, it was necessary to design a randomized set of experiments to determine the influence of frequency and amplitude on the nerve response and block effect. The randomization provided the analytical means to separate the effects of frequency, amplitude, experiment time and surgical preparation.

## 2. METHODS

Acute experiments were conducted on adult rats. Animals were anaesthetized with intraperitoneal injections of Phenobarbital Sodium (Nembutal). The gastrocnemius-soleus muscle was exposed and the Achilles tendon divided. A suture was inserted into the tendon and the distal portion of the muscle was freed from the tibia. The sciatic nerve was carefully exposed from one cm lateral to the spine to the terminal branching into tibial and peroneal nerves. The nerve was protected with a layer of mineral oil. The animal's leg was stabilized in a fixture with a clamp on the ipsilateral tibia. The tendon suture was connected to an in-line force transducer to measure isometric muscle force.

Electrodes were placed on the sciatic-tibial nerve, as shown in Figure 1. One electrode was placed on the proximal end of the nerve and was used to generate an electrically stimulated muscle response. The second electrode was placed between the stimulating electrode and the muscle, and was used to generate the high frequency conduction block. The distance between these two electrodes was approximately 5 mm. In some experiments, a third electrode was placed between the blocking electrode and the muscle. The stimulating electrodes consisted of a tripolar hook with a central cathode and flanking anodes. The blocking electrode was of a tripolar configuration consisting of three U shaped platinum rectangles in a split silastic cuff.

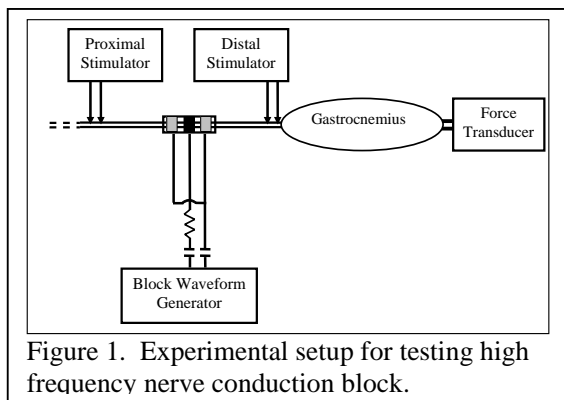


Figure 1. Experimental setup for testing high frequency nerve conduction block.

A single-channel current-controlled battery-powered stimulator was used to deliver the stimulating pulses. The high frequency blocking stimulus was delivered by a waveform generator with a 3 $\mu$ F capacitor was placed in series in each output line of the waveform generator to minimize DC leakage currents.

A standardized series of randomized trials was conducted with six rats. Each trial consisted of a period of proximal stimulation alone, followed by a period of proximal stimulation plus block, and concluding with another period of proximal stimulation alone. The conduction block was initiated after 5 seconds of proximal stimulation and typically maintained for 60 to 90 seconds. The block was then stopped and the recovery response of the nerve to the continuing proximal stimulation pulses was recorded for at least ten seconds after the cessation of block.

Charge-balanced sinusoidal waveforms between 10 KHz to 30 KHz were tested. Two types of trials were carried out. In one type, frequency and amplitude pairs were tested. The frequencies were 10, 14, 18, 22, 26 and 30 KHz and the amplitudes were 4, 6, 8 and 10 Vpp at each frequency. In the other type of trial, the block was initiated at 10 Vpp, complete block was obtained, and then the amplitude was reduced in one Vpp steps until block was detected to be incomplete. The lowest voltage at which complete block persisted was identified as the block threshold at each frequency.

## 3. RESULTS

A complete and reversible conduction block was achieved in all six animals at all six frequencies tested. A typical trial showing block and distal electrode stimulation is shown in Figure 2. The voltage range for complete block across all frequencies was 2 to 10 Vpp. The electrode impedance range was 730 Ohms to 1.8 K Ohms. The corresponding current range was 1 mA to 12 mA (peak to peak). There was a linear relationship between threshold amplitude (in voltage) and frequency ( $R^2=0.7$ ); higher frequencies required higher amplitudes to achieve complete block. In all cases where a 100% block was achieved, the block was maintained at higher amplitudes, up to the highest amplitude tested (10 Vpp).

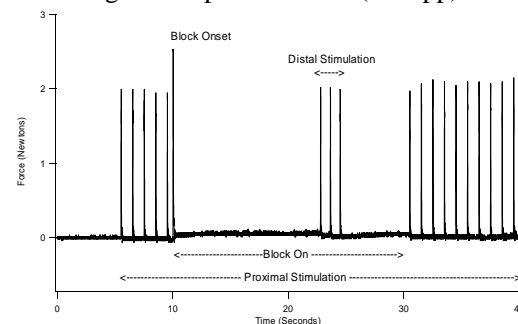


Figure 2. HFAC nerve block trial.

The high frequency block resulted in a typical response pattern marked by three phases. The initial phase was an “onset” response occurring as the block waveform was turned on. The second phase, which was not always present, was a period of recurrent firing of the nerve which produced tetanic contractions or fibrillations of the muscle. The third phase was the block, which could either be complete or partial. The characteristics of each phase depended on the block parameters. The first phase, the “onset” response, occurred as soon as the blocking waveform was turned on. This response could vary from a single twitch response to a summated twitch response which varied in peak height and duration, as shown in Figure 3. The range for the ratio of block onset peak height to the preceding normal unblocked twitch height, over all experiments, varied from 1 to 8. The shortest block onset response had a duration equal to a single muscle twitch, which was ~ 100 ms.

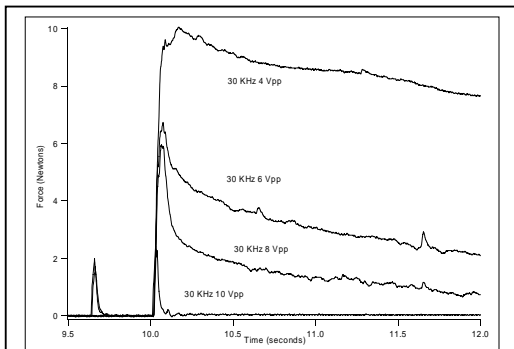


Figure 3. Response due to the initiation of the high frequency block. The high frequency is turned on at 10 seconds in each trial. At low amplitudes, the initial response to the high frequency is very large and includes an “onset” response (first 100ms) and significant recurrent firing lasting for many seconds. At high amplitudes (10Vpp), only the onset response is present, with no recurrent firing. In all cases, complete conduction block is obtained once the initiation response is complete.

The second phase, recurrent firing, followed the block onset response in most trials. This recurrent firing diminished over time and blended into the third phase of partial or complete block. The area under the force-time integral curve was used to measure the magnitude of recurrent firing. The amplitude and duration of the recurrent firing phase was related to both the frequency and the amplitude of the HFAC. Recurrent firing was inversely related to frequency, being least at 30 KHz. Recurrent firing varied inversely with

amplitude, being least at 10 Vpp. Therefore, the fastest blocks with the smaller block onset height and minimal recurrent firing occurred at the higher frequencies and higher amplitudes.

#### 4. DISCUSSION AND CONCLUSIONS

HFAC waveforms can be used to produce effective and reversible nerve conduction block in both amphibians and mammals. The results of this study show the relationship of frequency and amplitude to the nerve block threshold. Nerve block was obtained at the lowest amplitudes for the lowest frequency tested (10 KHz). The block thresholds are repeatable in each preparation over the time course of the experiment (two hours). The block onset is often marked by a large “on” response which can be minimized by the proper selection of parameters. At frequencies below 10KHz, the onset response was often prolonged and produced rapid fatigue of the muscle.

Experiments are ongoing to determine the specific parameters that will be necessary for human use. It will also be necessary to demonstrate the safety of chronic block of nerve using these waveforms. We are in the process of preparing for these chronic studies.

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