Subnanosecond Pulses for Electrostimulation

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***Abstract*—S u b nanosecond pulses can be delivered with impulse antennas, offering the potential for noninvasive treatment of subcutaneous tissue. The pulse duration, 100–200 ps, makes it possible to focus the radiation on the target efficiently and produces a focal spot of 1-cm^3 in the tissue. We found that very intense electric fields are needed to cause significant cell death, making it difficult to use antennas. Other effects, such as membrane permeabilization or stimulation of action potentials, however require lower electric fields, which makes the approach of pulse delivery with antennas more practical. This paper presents the typical pulse parameters for electrostimulation and discusses possible pulse delivery methods for *in vitro* and *in vivo* models.**

Keywords- subnanosecond pulses, electrostimulation

I. INTRODUCTION

A previous study [1] showed that for the 800-ps pulses and an electric field of 150 kV/cm, approximately 18,000 pulses were required in order to cause 50% B-16 cell death. For a moderate field intensity of 20 kV/cm [2], increasing the pulse repetition rate caused an increase of cell killing partially due to the increase in temperature. A recent experiment on liver cancer cells [3] also confirmed the role of temperature elevation in facilitating cell death.

While cell death may require a large number of high intensity subnanosecond pulses, moderate or mild effects, such as the increase of cell membrane conductance, can be induced with much fewer pulses. In neuroblastoma cells (NG-108) for example [2], after exposure to 1000-2000 pulses, the inflow of current was measured, an indication of increased membrane conductance. The modification of membrane transport processes by subnanosecond pulses suggests the feasibility of stimulating excitable cells.

A whole-cell current clamp recording configuration was used to measure the membrane voltage of the neurons [4]. The selected neurons were patched before subnanosecond pulses were applied. The current varying in a stepwise fashion was injected to the neurons and subsequently subnanosecond pulses were applied (100 pulses within 200 ms) in the course of the constant current.

II. RESULTS

Shown in Fig.1 is a neuron stimulated by subnanosecond pulses. An immediate increase of the membrane potential (depolarization) was observed (Fig.1a), regardless of whether the cell was hyperpolarized or depolarized by the injection current. The increased potential stayed as long as the pulses were applied. But it was within the rising phase, i.e., in the first 30 ms, that the firing of an action potential was recorded. The time it took was somewhat correlated with the membrane potential at the instant of the pulse application. For instance, when the injection current was held steady (-100 pA), the action potential was recorded after 20 pulses. But fewer pulses were needed to induce the action potential if the injection current had already caused depolarization. The neurons may not fire an action potential at all if the cells were hyperpolarized. We note that stimulating with subnanosecond pulses will not cause any damage to the neurons, evidenced by their capability to fire the action potentials repeatedly. Shown in Fig.1b is a neuron stimulated 20 times at 1 Hz under the same pulse conditions, indicating that this method is safe and reliable.

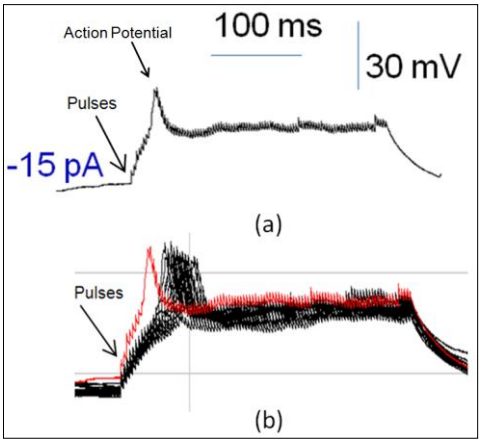

Figure 1. A neuron was stimulated by subnanosecond pulses *in vitro*. a) The neuron was clamped by a constant current (-15 pA) and subnanosecond pulses were applied to induce the depolarization. An action potential was fired approximately 30 ms after applying the subnanosecond pulses; b) Repeated firing of the action potentials at 1 Hz by the same neuron for 20 stimulations in a row.

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