

Effect of Electric Stimulation on Penetration of Molecules into Agarose Gel

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ABSTRACT

The effect of electric stimulation on the penetration of molecules into biological gel has been studied in phantom experiments. A phantom was made with agarose gel. Three kinds of electric stimulation were applied with electrodes of an aluminum film: direct current, sinusoidal current and pulses. Electric pulses (five volts amplitude, one millisecond pulse width) were generated with a function generator. Variation was made on frequency: 1 Hz, 1500 Hz and 5000 Hz. The penetration depth of three chemical molecules (phenol red, Brilliant Blue FCF, and trypan blue) was measured with time for one hour. In direct current, the phantom was concaved at the cathode, and chemicals penetrated faster at the cathode than at the anode. Penetration speed was higher in small molecular weight. Penetration was faster with pulses of a shorter interval. The experimental results show that electric stimulation accelerates penetration of molecules into biological gel.

Keywords: Biomedical Engineering, Electric Stimulation, Pulse, Agarose Gel and Penetration

1. INTRODUCTION

Drug delivery technology has been studied for targeted medical treatment. Several poultices have been applied to the skin as low invasive medical treatments. Sometimes electric stimulation has been applied with a drug delivery system to enhance penetration of a drug into biological tissue [1].

Agarose gel has often been used for phantom studies for biological tissue.

In the present study, the effect of electric stimulation on penetration of molecules into biological gel has been studied in the phantom experiments.

2. MATERIALS AND METHODS

A phantom was made with agarose gel. A powder agar (Kitahara Industry) of 4.0 g was dissolved in a saline solution (0.9 weight percent of sodium chloride aqueous solution) of 500 mL. The solution was pored into a mold and preserved at 13 degrees Celsius for three hours to make a rectangular phantom of 70 mm × 70 mm × 85 mm (Fig. 1).

A couple of electrodes were manufactured with an aluminum film (20 mm square, 0.015 mm thick) attached onto a non-woven cloth (36 mm square).

Three kinds of electric stimulation were applied with electrodes: direct current, sinusoidal current and pulses. Variation was made on frequency of the sinusoidal current of 1 Hz, 1500 Hz and 5000 Hz. Electric pulses (five volts amplitude, one millisecond pulse width; Fig. 2) were generated with a function generator (DF1906, NF). Variation was also made on the period of the pulse: 1 s, 0.0007 s, 0.0002 s. They are indicated as the frequency of 1 Hz, 1.5 kHz and 5 kHz in Figs. 3-10.

Three chemical molecules were used in the experiment: phenol red, Brilliant Blue FCF, and trypan blue. The average molecular weights of the three chemicals were 354.38, 792.86, and 960.8, respectively. Two milliliters of the solution of each chemical was dripped into the cloth of the electrode at the beginning of the test.

The colored penetration depth of the three chemical molecules was measured through the lateral surface every ten minutes for

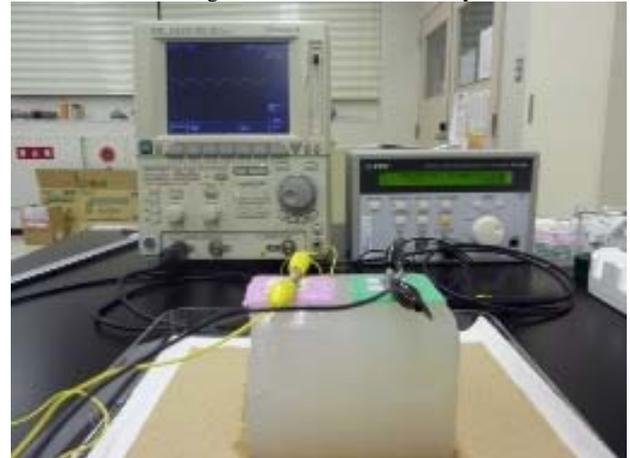


Fig. 1: Phantom and function generator. Electrodes are attached on the top of the phantom.

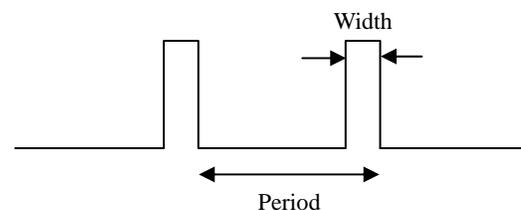


Fig. 2: Pulse.

one hour. The phantom was cut to confirm the penetration depth at the cross section at the end of each experiment.

3. RESULTS

Fig. 3 exemplifies the colored area of penetration of the three chemical molecules. Fig. 4 exemplifies the tracing of penetration of phenol red with pulse of 5000 Hz (period of 0.2 millisecond). The figure shows that penetration depth



Fig. 3: Penetration from top to bottom: upper, phenol red; middle, brilliant blue FCF; lower, trypan blue. (Pulse of 5000 Hz, 60 min)

increases linearly. The penetration rate was calculated with the slope of approximate line of each tracing. Figs. 5-7 show the penetration depth in one hour for each experimental condition. Figs. 8-10 show the penetration rate during one hour for each experimental condition.

The results on direct current of five volts show that the phantom is concaved at the cathode and the chemicals penetrated faster at the cathode than at the anode. The experimental results show that the penetration speed is higher in phenol red than in Brilliant Blue FCF, and that the speed is slowest in trypan blue. The results show that penetration is faster with pulses of shorter intervals (high frequency in Figs. 8-10). The experimental results show that electric pulses accelerate penetration of molecules into the biological gel.

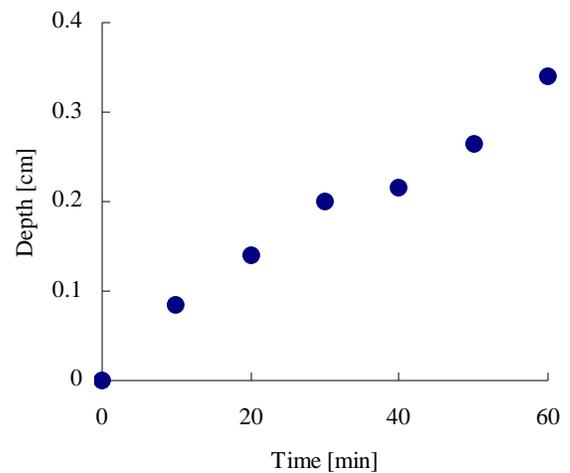


Fig. 4: Penetration depth tracings of phenol red, pulse 5000 Hz.

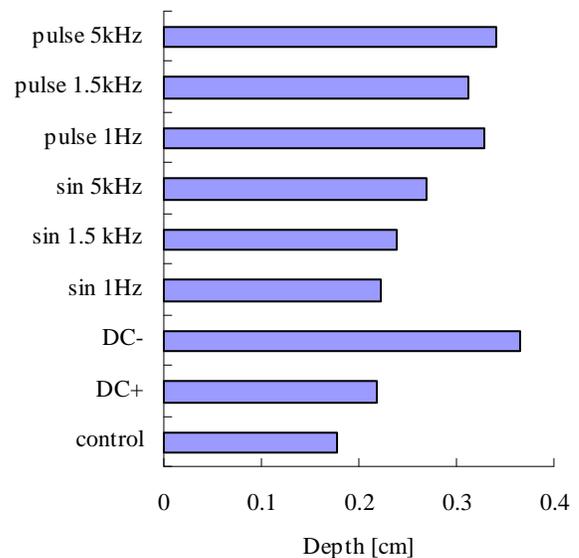


Fig. 5: Phenol red. 60 min.

4. DISCUSSION

A biological system generates electric pulses along the membrane with movements of ions. Those pulses convey not only signals but also chemicals through the biological systems. Pulses might be effective to be transmitted through membranes, which acts as an electric capacitance.

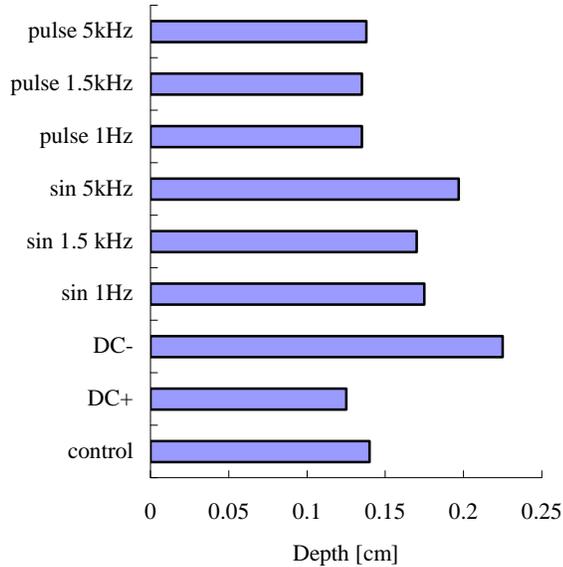


Fig. 6: Brilliant blue FCF. 60 min.

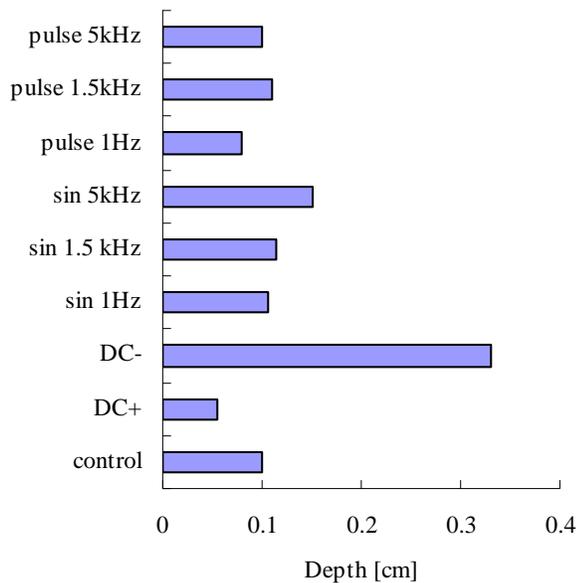


Fig. 7: Trypan blue. 60 min.

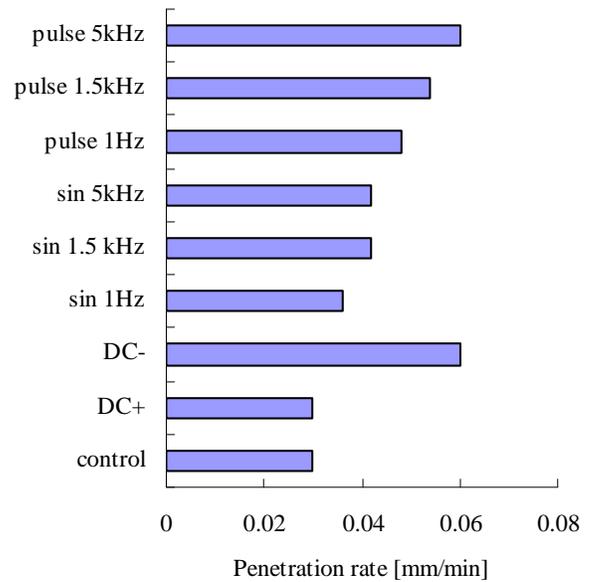


Fig. 8: Penetration rate, phenol red.

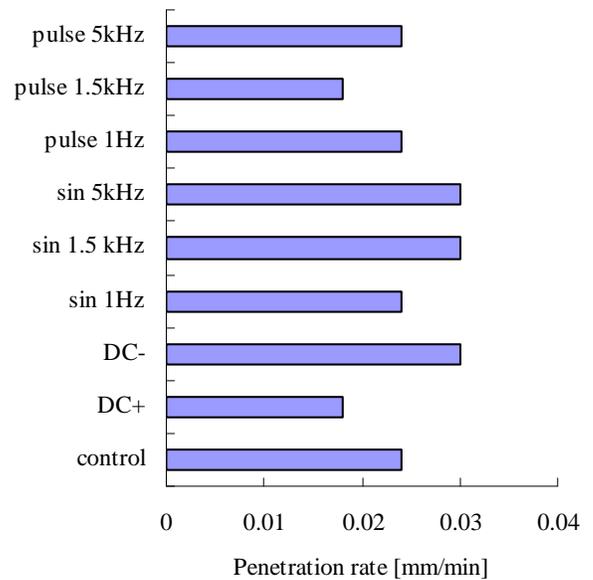


Fig. 9: Penetration rate, brilliant blue FCF.

Electric stimulation has been applied, on the other hand, to biological systems in some medical treatments such as iontophoresis. The electric field affects conformation of biological molecules [2, 3]. The electronic field is also applied in electrophoresis to analyze biological chemicals *in vitro*.

Previous studies show that electric pulses affect proliferation in the cell culture. Electric pulses also generate repetitive contraction in myotubes *in vitro* [4].

The basic idea of the present study is to design penetration through skin. That is the reason why the electrodes are located

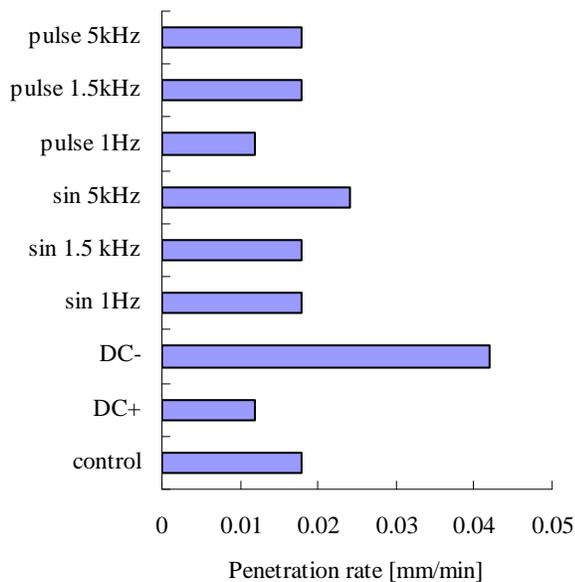


Fig. 10: Penetration rate, trypan blue.

not in the counter position, but at the same side (the upper surface in Fig. 1) in the present experimental model.

The transparency of the phantom was enough to measure the penetration depth through the lateral surface. The experimental results show that penetration speed is higher in chemicals of small molecular weight.

5. CONCLUSION

The experimental results with the phantom show that the phantom is concaved at the cathode and chemicals penetrate faster at the cathode than at the anode. The results also show that penetration speed is higher on chemicals of small molecular weight, and that penetration is faster with pulses of shorter intervals. The phantom study shows that electric stimulation accelerates the penetration of molecules into a biological gel.

6. ACKNOWLEDGMENT

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