Closed Loop Optogenetic Stimulation for Position Control of Murine Limb

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***Abstract*— Functional electrical stimulation (FES) is currently the standard clinical modality used for restoration of function and therapy for neuromuscular disorders. While the methodology has been applied in humans for over four decades, FES has inherent limitations and disadvantages [1]. In this paper, we establish the ability of optogenetic peripheral nerve stimulation to be used in a closed-loop method, developing it a functional tool for neuromuscular control and therapy paradigms. The characteristics of functional optogenetic stimulation (FOS) are explored a rat model expressing ChR2 in the peroneal and tibial nerves. Through various control tests, we demonstrate the ability of the system to reach desired angles and move through sinusoidal patterns, mimicking the gait cycle. The system was optimized to perform with a steady state root mean square error < 10%.**

I. Introduction

Electrical stimulation has been historically used for the activation of muscle and nervous tissues and is the current clinical modality for various neuromuscular applications. However, FES may inappropriately activate vibration, pain, and touch fibers, co-localized within the nerve segment, which may interfere with central processing. Further, reverse order recruitment and quick fatigue can lead to a lack of long-term stable position/force feedback signal. Recent advances in opsin engineering, including transdermal approaches [2] and tissue-selective induction [3], have made optogenetic stimulation (OS) possible for control applications in the peripheral nervous system. Unlike FES, OS can perform anatomically targeted, end organ-specific stimulation with an orderly recruitment paradigm. [4]. Here, we develop a closed loop optogenetic stimulation system to control the hind limb position of a rat.

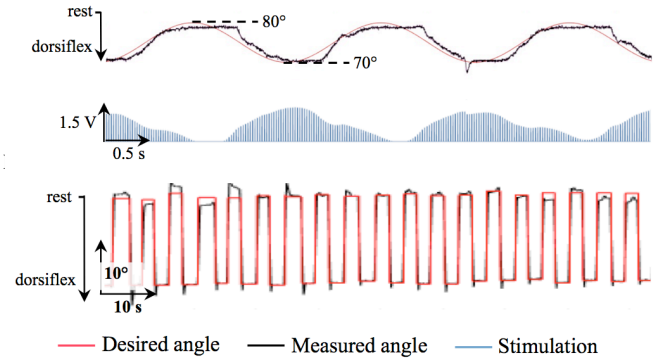

Figure 1. Closed loop optogenetic stimulation system yielding desired angles in sinusoidal/square wave patterns of the right hind limb of the rat

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II. METHODS

The AAV6-hSyn-ChR2(H134R)-EYFP viral vector was injected into the right hindlimb of Fischer 344 P2 neonates to induce expression of ChR2 in the peroneal and tibial nerves. 8 weeks later, the nerves were transdermally stimulated with 473 nm illumination (40 Hz, 0.6 W skin surface power, 5% DC), eliciting movement of the ankle joint. Ankle position was measured using a distance sensor and fed into a closed loop PID controller, which modulated the illumination amplitude to bring the limb to the desired angle/position.

III. RESULTS

Transdermal, closed loop OS yielded robust position control in both dorsiflexion and plantarflexion. In one set of trials, the joint angle was cycled in a sinusoidal pattern, mimicking the gait cycle (Fig 1 top). Additionally, the joint was controlled to reach and hold various degrees of dorsiflexion repeatedly. Full dorsiflexion is shown in the bottom of figure 1. Various system characteristics were measured including rise time = 29.7 +/- 9.4 (n=62) using OS. With the OS controller, finely tuned gains and stimulation parameters (to optimize joint stability, rise time, ringing, and opsin fatigue) enabled the ankle was able to reach the desired angles with a steady state root mean square error < 10%.

III. CONCLUSIONS

This study demonstrated the ability of OS to be conducted for the closed-loop control of joint angle. While currently a pre-clinical modality, we envision translation of optogenetic stimulation to be used for prosthetic devices and rehabilitation therapies through the use of LED stimulators and wearable sensors. This would confer the benefits of non-invasive and subtype-specific stimulation, increasing the functionality and convenience of stimulation-based applications.

References

[1] P. H. Peckham and J. S. Knutson, "Functional Electrical Stimulation for Neuromuscular Applications," *Annu. Rev. Biomed. Eng.*, vol. 7, no. 1, pp. 327–360, 2005.

[2] B. E. Maimon *et al.*, "Transdermal optogenetic peripheral nerve stimulation," *J. Neural Eng.*, vol. 14, no. 3, p. 034002, Jun. 2017.

[3] N. C. Klapoetke *et al.*, "Independent optical excitation of distinct neural populations.," *Nat. Methods*, vol. 11, no. 3, pp. 338–46, Mar. 2014.

[4] M. E. Llewellyn, K. R. Thompson, K. Deisseroth, and S. L. Delp, "Orderly recruitment of motor units under optical control in vivo," *Nat. Med.*, vol. 16, no. 10, pp. 1161–1165, Sep. 2010.