Distributed Live Muscle Actuators Controlled by Optical Stimuli

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INTRODUCTION

A multi degree of freedom skeletal muscle system stimulated via optical control is presented. These millimeter-scale, optically excitable 3D skeletal muscle bio-actuators are created by culturing genetically modified precursory muscle cells that are activated with light: optogenetics. These muscle bio-actuators are networked together to create a distributed muscle system. Muscle systems can manipulate loads having no fixed joint. These types of loads include shoulders, the mouth, and the jaw.

The building block tissue constructs we have developed are similar to the fascicle structural level of natural hierarchical muscle. Muscle is primarily composed of bundles of muscle. A muscle fascicle is a bundle of individual muscle cells that contract together. The form factor of a fascicle is significantly influenced by diffusion transport of chemicals. Essentially, it is an optimized building block that is robust against individual cell failure, and can be combined with others in a parallel and networked arrangements allowing for scalability.

The optogenetic approach offers high spatiotemporal resolution for precise control of muscle activation, and opens up the possibility to activate hundreds of interconnected muscles in a spatiotemporally coordinated manner. The temporal as well as spatial resolution of optical stimuli is significantly high, achieving millisecond-order temporal precision and 10 µm of spatial resolution. This spatial resolution is much more precise than electrical stimulation, as no parasitic stimulation field is generated with optical control. It is also less invasive than electric stimulation. Recently, we have applied this optogenetic control technology to 3D engineered skeletal muscles microtissues [1]. Simply projecting a light beam on a muscle construct causes contraction of the muscle. No mechanical contact is involved allowing for wireless control of each individual muscle cell.

METHODS

Cell/gel suspension is molded such that a uniform cylinder of controlled dimensions is suspended in medium anchored at both ends to either the walls of a well or a floating node. The cell/gel suspension contains GM with C2C12 cells at a concentration of 20e6 cells/ml, fibrinogen (Sigma-Aldrich) at a concentration of 5 mg/ml, and 6-aminocaproic acid (Sigma-Aldrich) at a concentration of 1 mg/ml. The initial fluid surrounding the construct contains thrombin (Sigma-Aldrich) at a concentration of 1 U/ml. The wells are 5 mm in diameter, with walls and floating nodes made of polydimethylsiloxane (PDMS, Dow Corning). The PDMS wells are plasma bonded to a glass coverslip (VWR) which constitutes the bottom of the well. The length of the molded gels are nominally 5 mm, and the initial nominal diameters of the molded gels range from 250 µm to 500 µm.

CONCEPT

The initial step towards producing a large scale muscle system is to show proof of concept of scalability. To do this we have designed and grown a system containing both parallel and serial muscle constructs as diagramed in Figure 1. There are 4 controllable tissue constructs in the system. The central floating node has 2 controlled degrees of freedom; one translational, and one rotational. When 2 parallel muscle strips are contracted, the floating node translates as (Fig. 1 (b)). When a pair of muscle strips located at diagonal positions is contracted, the floating node rotates (Fig. 4 (c)). From the redundancy of 4 muscle constructs controlling just 2 degrees of freedom, the system achieves robustness against individual unit failure (Fig. 1 (d)). Additionally, the nonlinear stiffness characteristics of muscle allow the redundant actuators to potentially be used to control stiffness (Fig. 1 (e))
RESULTS

A. Single Building-Block Muscle Actuator

Within a single muscle strip, multinucleated contractile muscle cells form in parallel with others suspended in fibrin gel. Each muscle cell extends ~1 mm in length along the axis of the strip. These cells populate the full length of the fascicle-like muscle construct and have generated 4.3% strain of the full tissue construct (Fig. 2).

B. Serial and Parallel Prototypes

Multiple building block actuators have been combined in series and parallel. Parallel muscle strips behave identically to individual muscle strips (Fig. 3(a)).

A serial connection between multiple muscle strips has been demonstrated in functional prototypes such as the one shown in Fig. 3 (b). In this figure, muscle actuators are anchored to a PDMS block that functions as a floating series node. Fibrin gel and non-functional cells occupy and anchor to the hollow cylinder in the center of the PDMS block. Light stimulation of the left or right muscle actuators has been shown to move the floating series node left or right, respectively.

C. Multi-Unit Actuator System Prototypes

We have produced functional serial/parallel systems using our building block actuators as components (Fig. 9). The unforced system in Fig. 4 contains four muscle actuators anchored by two hollow cylinders in a transparent PDMS block.

The un-acted young’s modulus has been measured using our custom-built force probe to be 210 kPa. In the loaded configuration, the geometric structure is bipennate further showing the potential concentration of generated forces.

CONCLUSION

In this work, we explore the design and initial results of muscle systems composed of multiple light-activated live muscular tissue constructs. We describe and compare massively parallel and highly serial/networked distributions of these building-block fascicle-like muscle units. We have produced functional fundamental prototypes and present experimental results to demonstrate the feasibility of the construction of larger scale muscle systems.

REFERENCES