Muscle mechanics outline

- Types of muscle
- Muscle anatomy
- Function: macro, micro
- Motor unit
- Applications
  - Tissue engineering
  - Basic studies
  - Drug screening
  - Biobots
- Other motile systems

Types of muscle:
Skeletal (striated) and smooth muscle

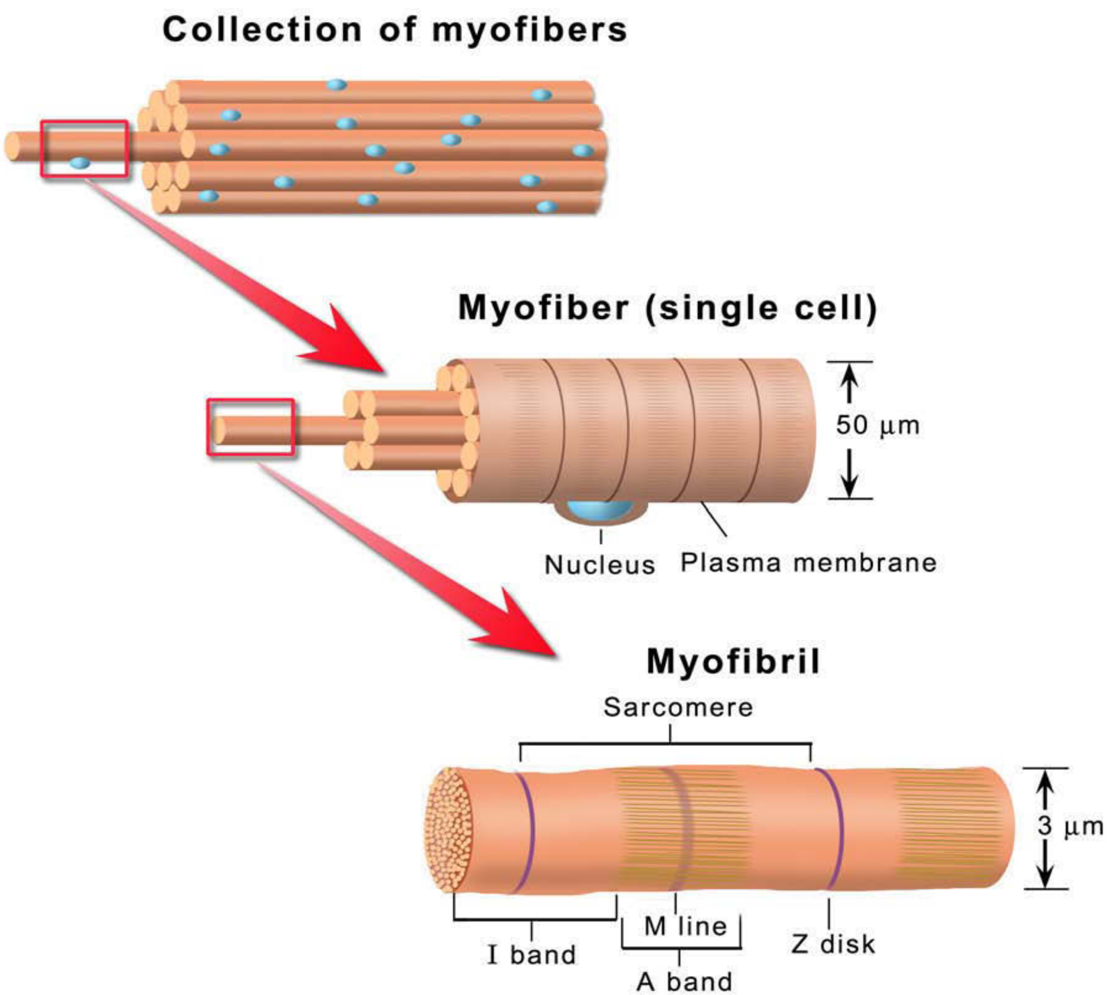

Image by MIT OpenCourseWare.

Gut, arterioles, sphincters

Cardiomyocytes

Courtesy of Jan Lammerding, Harvard Medical School.

Jan Lammerding

Dimensions ~ 30x10 μm; Cross-sectional area ~ 300 μm^2

Total force = ??

Skeletal muscle

Figure of the structure of a skeletal muscle removed due to copyright restrictions.

Detailed structure of a single skeletal muscle cell

Figure of the detailed structure of a single skeletal muscle cell removed due to copyright restrictions.

Macro behavior: Temporal patterns of muscle contraction

- Single twitch
- Periodic sequence of excitations
- Fused tetanus (F_{max})

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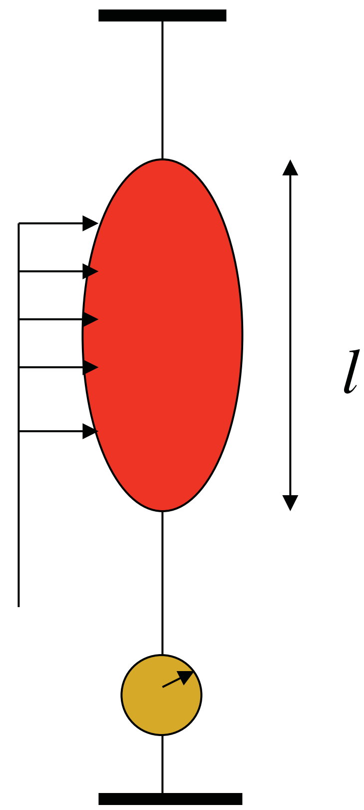

Tension-length curves for a muscle fiber (relaxed and maximally stimulated)

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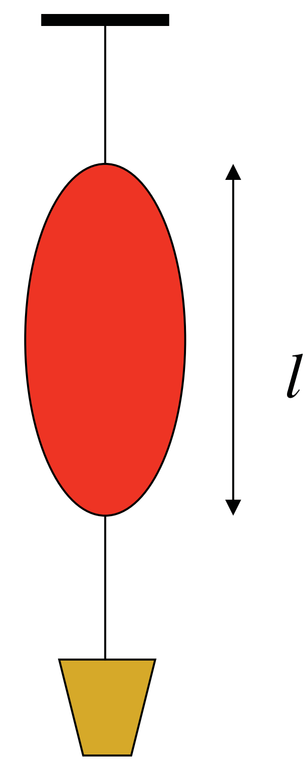
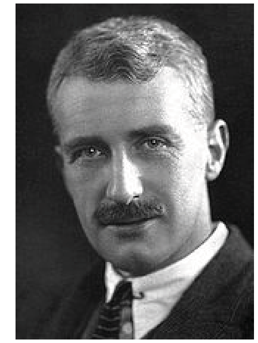
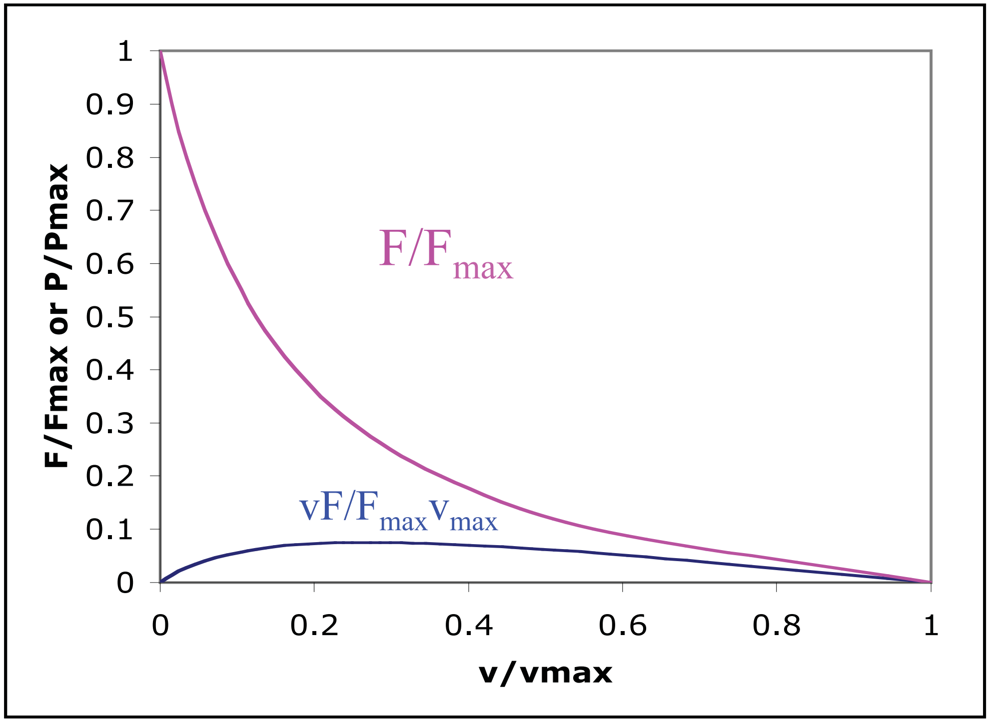


Dynamic: Hill’s equation

Empirically determined force-velocity relationship obtained from macroscopic measurements



Archibald Hill, Nobel Prize in Physiol, 1922.



$$\frac{v}{v_{\max}} = \frac{1-(F/F_{\max})}{1+C(F/F_{\max})}$$

$$\frac{vF}{v_{\max}F_{\max}} = \frac{1-(F/F_{\max})}{(F_{\max}/F)+C}$$

$\sigma_{max} \sim 2 \text{ x } 10^5$ *Pa*

v = velocity of shortening

~ 30 cm/s

Figure removed due to copyright restrictions.

Micro: The sliding filament model

in separate, back-to-back papers by *A. Huxley & Niedergerke* and *H. Huxley & Hanson*, *Nature*, 1954

No. 4412 May 22, 1954 NATURE

STRUCTURAL CHANGES IN MUSCLE DURING CONTRACTION

Interference Microscopy of Living Muscle Fibres

By A. F. HUXLEY and Dr. R. NIEDERGERKE*
Physiological Laboratory, University of Cambridge

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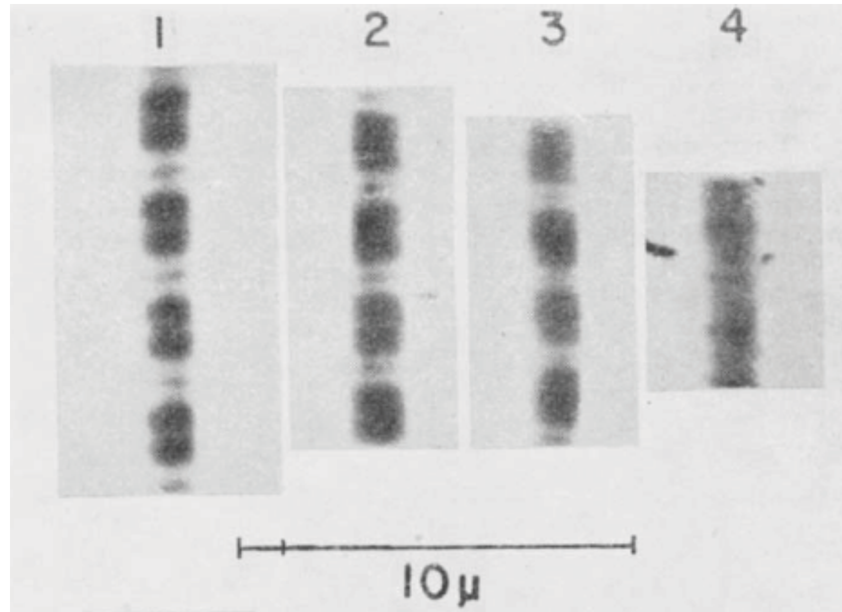
Changes in the Cross-Striations of Muscle during Contraction and Stretch and their Structural Interpretation

By Dr. HUGH HUXLEY* and Dr. JEAN HANSON
Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts



Phase contrast images of myobrils

Source: Huxley, Hugh, and Jean Hanson. "Changes in the Cross-striations of Muscle during Contraction and Stretch and their Structural Interpretation." *Nature* 173 (1954): 973-6.

Thick and thin filaments slide past one another during contraction

Figure of relaxed and contracted muscle removed due to copyright restrictions. See a similar image on wikipedia.

Skeletal muscle contains a regular array of actin and myosin

Figure removed due to copyright restrictions.

Videomicrograph of contracting muscle

Figure removed due to copyright restrictions.

Motor Speeds (assemblies)

Motor type	***speed in vivo (nm/s)***	***in vitro(nm/s)***	***in vitro ATPase (s^{-1})***
Myosin II (skeletal muscle)	*6000*	*8000*	*20*
Myosin II (smooth muscle)	*200*	*250*	*1.2*
Myosin V (vesicle transport)	*200*	*350*	*5*
Conv. Kinesin (axonal transp)	*1800*	*840*	*44*
Nkin (sec. Vesicle transp.)	*800*	*1800*	*78*
BimC/Eg5 (Mitosis/meisos)	*18*	*60*	*2*
Dyneins (cytoplasmic)	*-1100*	*-1250*	*2*

Speed in vivo = cell/extracts, motion of motor relative to filament w/o a load. Positive values indicate movement toward positive end of filament.

Speed in vitro = purified motors at high ATP concentrations.

ATPase = max rate of hydrolysis per head per sec, measured at high ATP, filament concentrations.

Forces generated by skeletal muscle

Figure of relaxed and contracted muscle removed due to copyright restrictions. See a similar image on wikipedia.

Striated skeletal muscle

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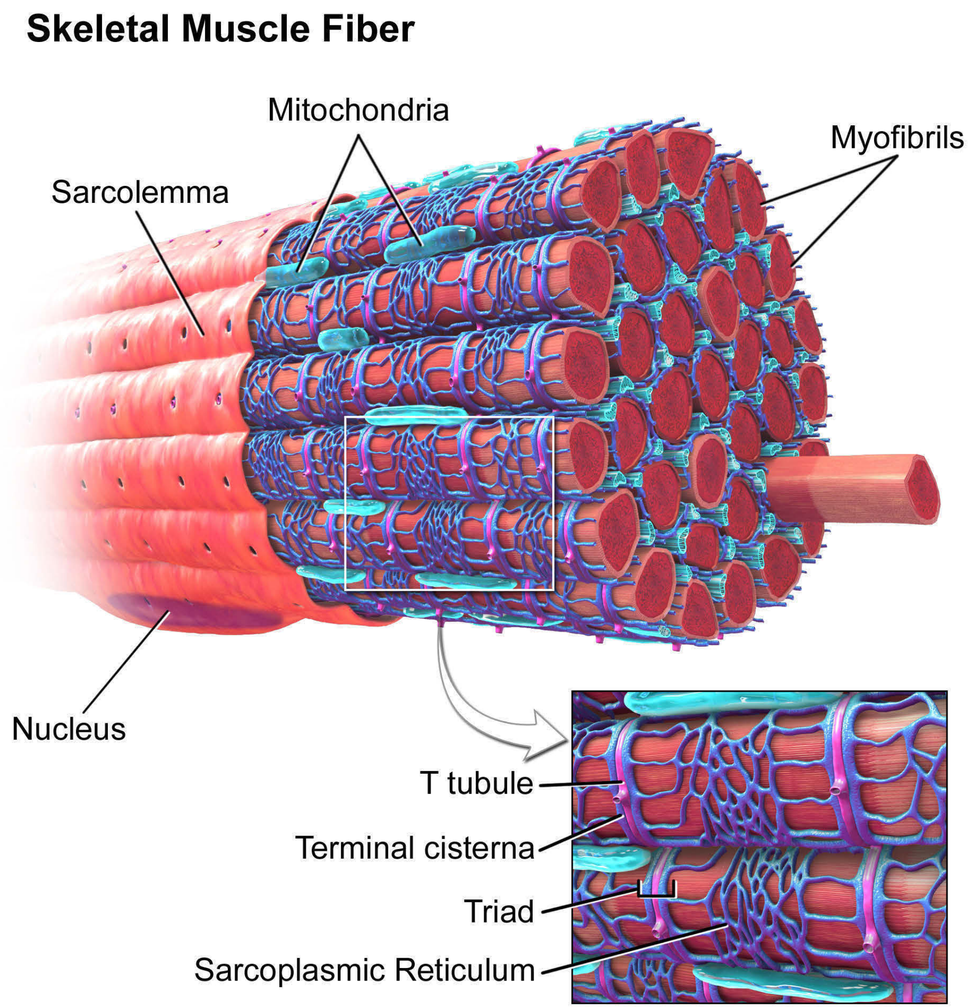
Structure of activating mechanism



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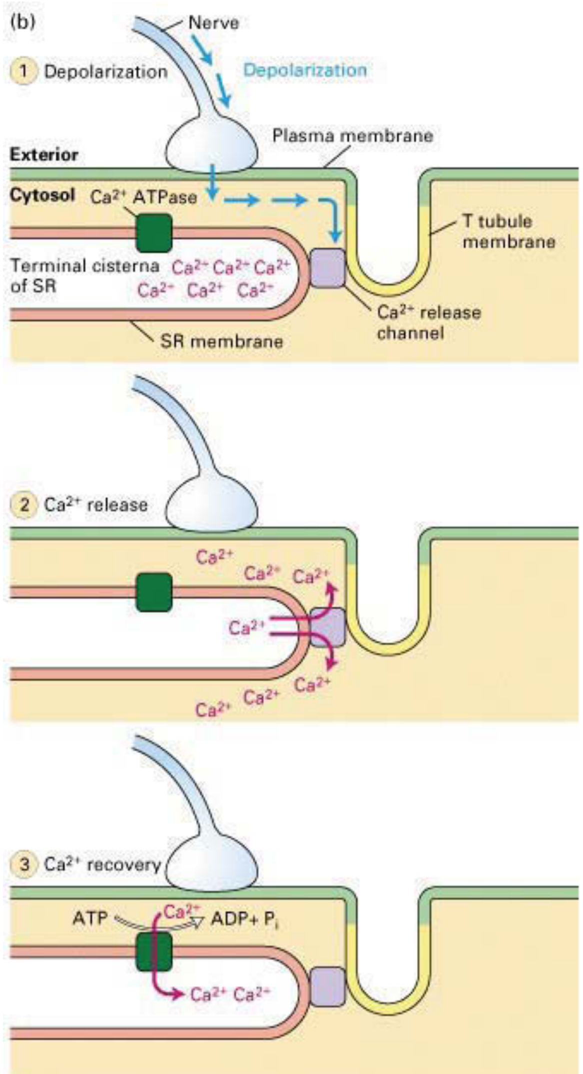
A rise in cytosolic Ca^{2+} triggers muscle contraction



Step 1: An excitation signal travels along the efferent nervous pathways towards the muscle.
Step 2: The excitation signal de-polarizes the cell membrane. This allows spread of the action potential along the sarcoplasmic reticulum.
Step 3: The potential triggers the release of calcium into the sarcoplasmic matrix surrounding the filaments of the motor unit.
Step 4: This removes the hindrance (tropomyosin) for interactions between actin and myosin filaments through chemical, mechanical, and electrostatic actions.
Step 5: The stepping action of myosin along the adjacent actin filament causes the two to slide relative to each other, reducing the length of the sarcomere, producing contraction.
Step 6: Sequestration of calcium ions in the sarcoplasmic reticulum (ATP-dependent) switches the contraction activity off.

Figure removed due to copyright restrictions.

Figures removed due to copyright restrictions.

http://www.sci.sdsu.edu/movies/actin_myosin.html

Living Machines: Simple Biobots

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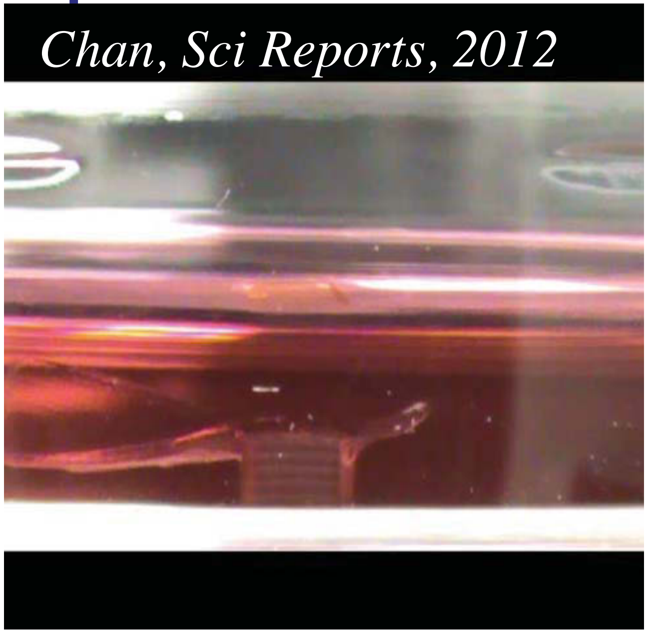
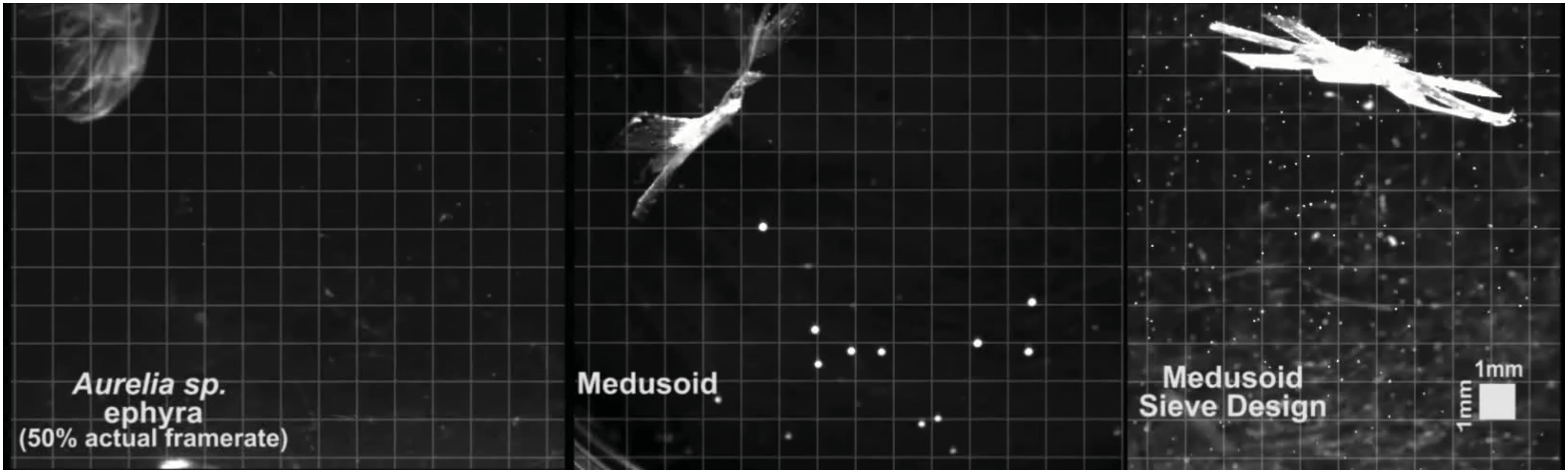
Williams et al.,
Nat Comm, 2014



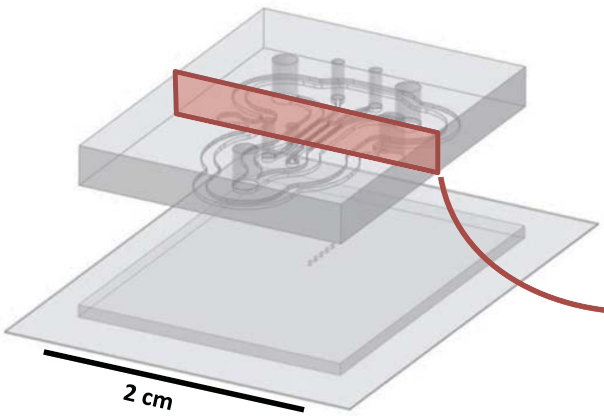
Source: Chan, Vincent, et al. "Development of Miniaturized Walking Biological Machines." *Scientific Reports* 2 (2012).

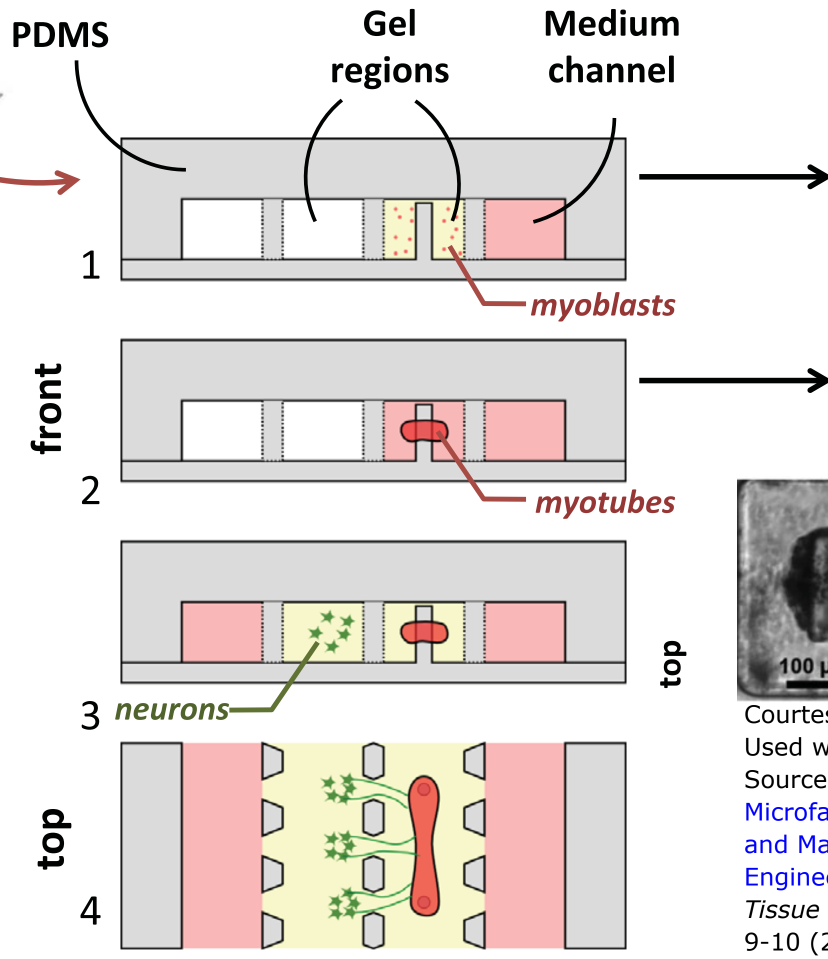


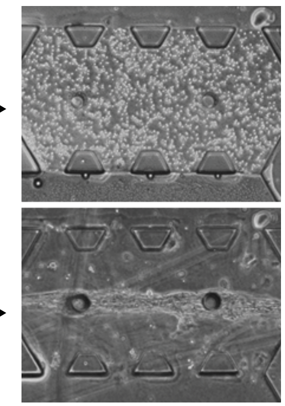
Source: Nawroth, Janna C., et al. "A Tissue-engineered Jellyfish with Biomimetic Propulsion." *Nature Biotechnology* 30, no. 8 (2012): 792-7.

Naworth et al., Nat Biotech, 2012

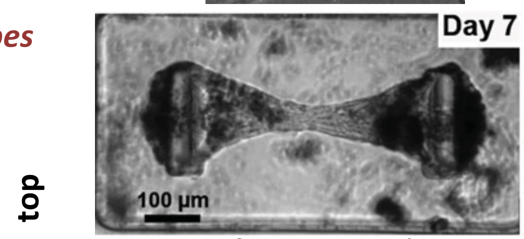
Muscle-on-a-chip systems



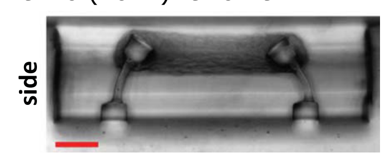




1. C2C12 cells suspended in a collagen-matrigel matrix are seeded in the right gel region, and the adjacent filled with medium
2. The myoblasts compact the gel and differentiate into multinucleated myotubes over ~10 days
3. A plain gel is injected around the myotubes and the adjacent gel region is filled with a gel containing motor neurons.
4. Finally, motor neurons extend axons toward the muscle construct

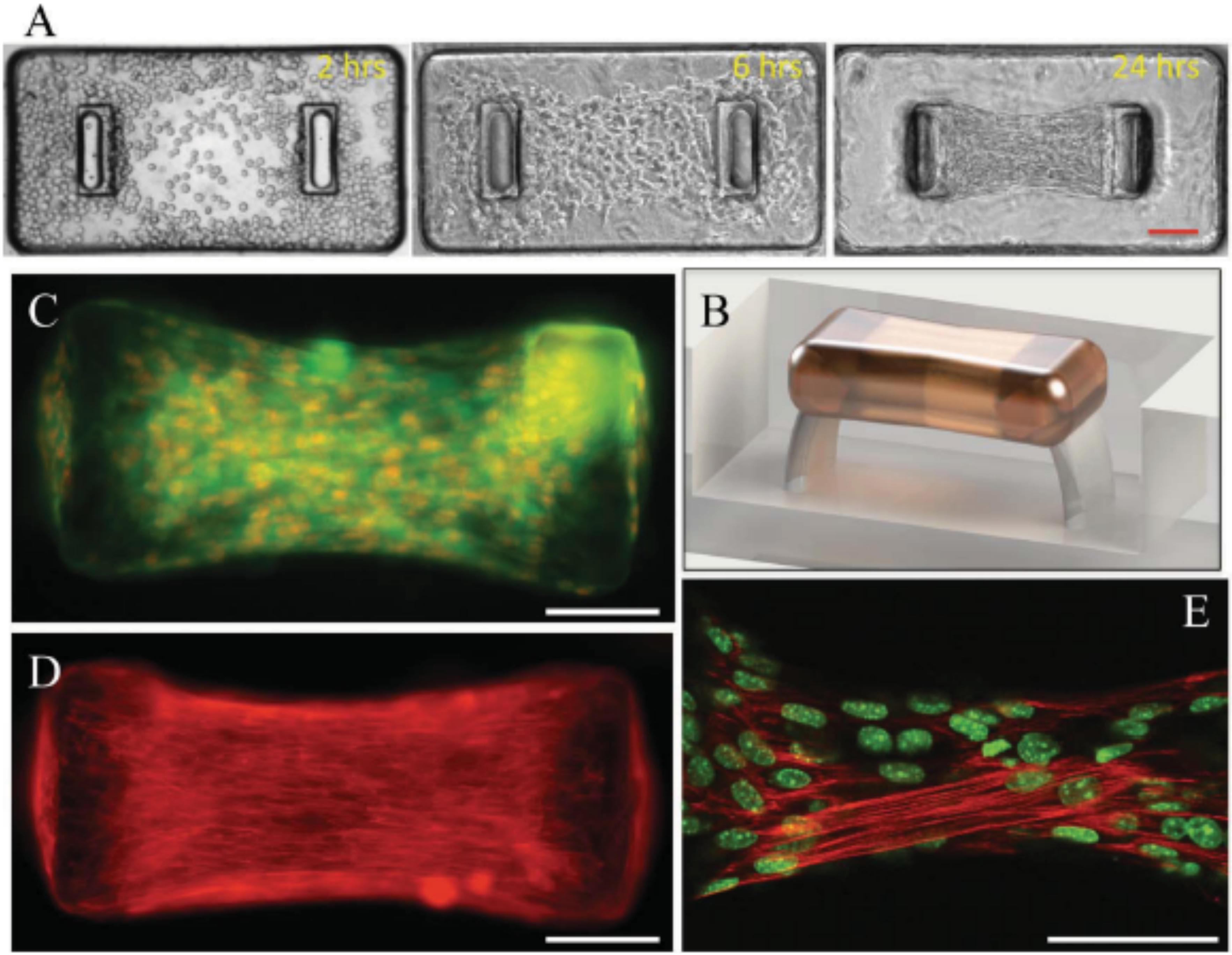


Source: Boudou, Thomas, et al. "A Microfabricated Platform to Measure and Manipulate the Mechanics of Engineered Cardiac Microtissues." *Tissue Engineering Part A 18*, no. 9-10 (2011): 910-19.



Legant, W. R. et al (2009). *PNAS*, *106*(25), 10097-102.

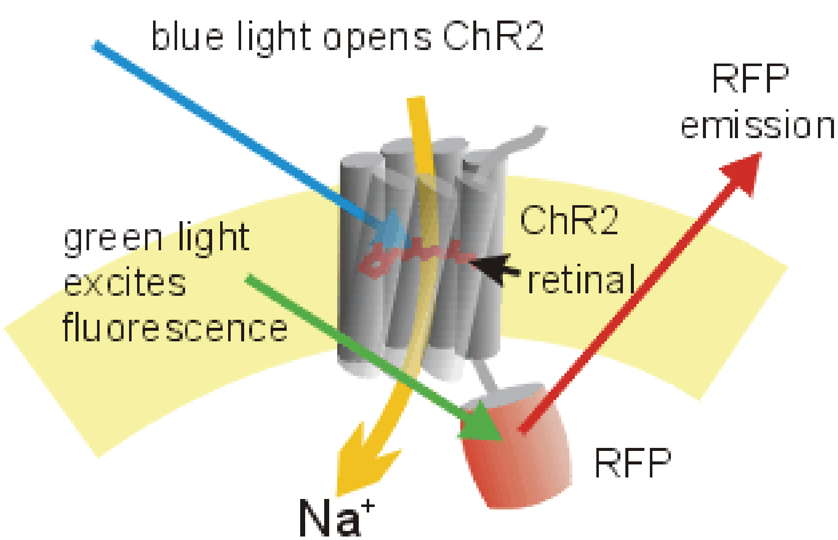
Source: Legant, Wesley R., et al. "Microfabricated Tissue Gauges to Measure and Manipulate Forces from 3D Microtissues." *Proceedings of the National Academy of Sciences* 106, no. 25 (2009): 10097-102.

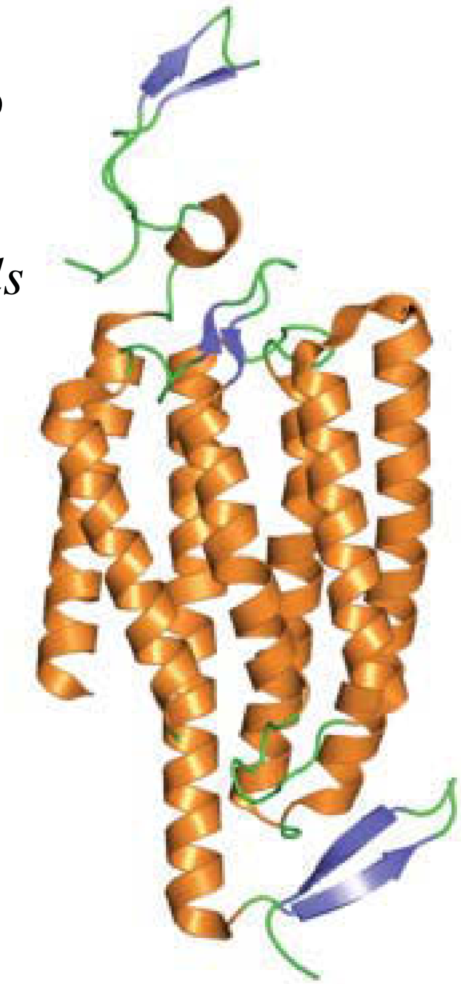


Source: Sakar, Mahmut Selman, et al. "Formation and Optogenetic Control of Engineered 3D Skeletal Muscle Bioactuators." *Lab Chip* 12, no. 23 (2012): 4976.

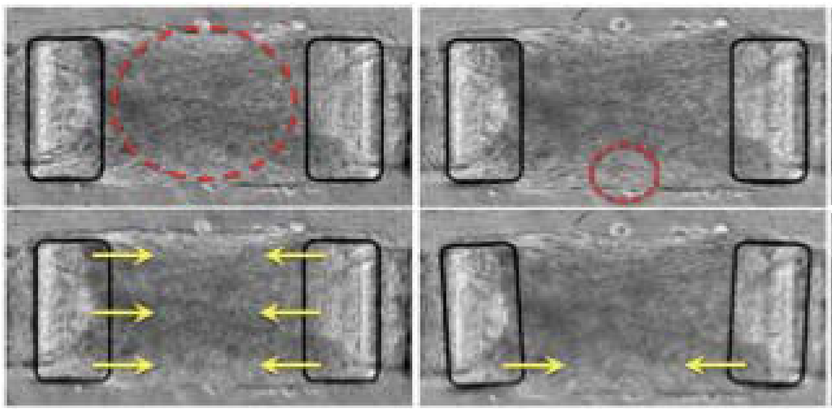
Optogenetics

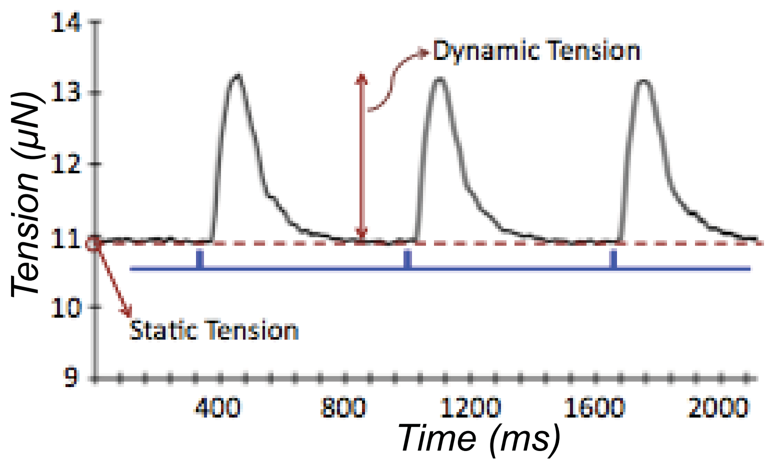
- *Channelrhodopsins are light-activated ion channels (discovered in green algae that respond to light).*
- *Can be used to activate neurons or muscle.*

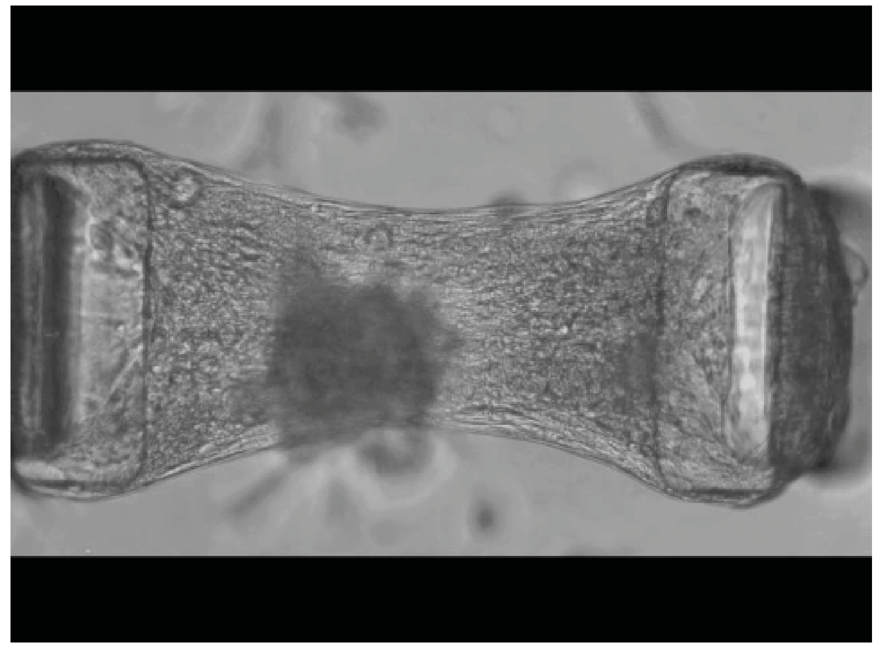


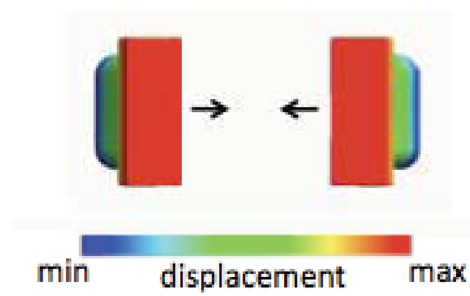


Light-sensitive cardiomyocytes demonstrate coordinated actuation





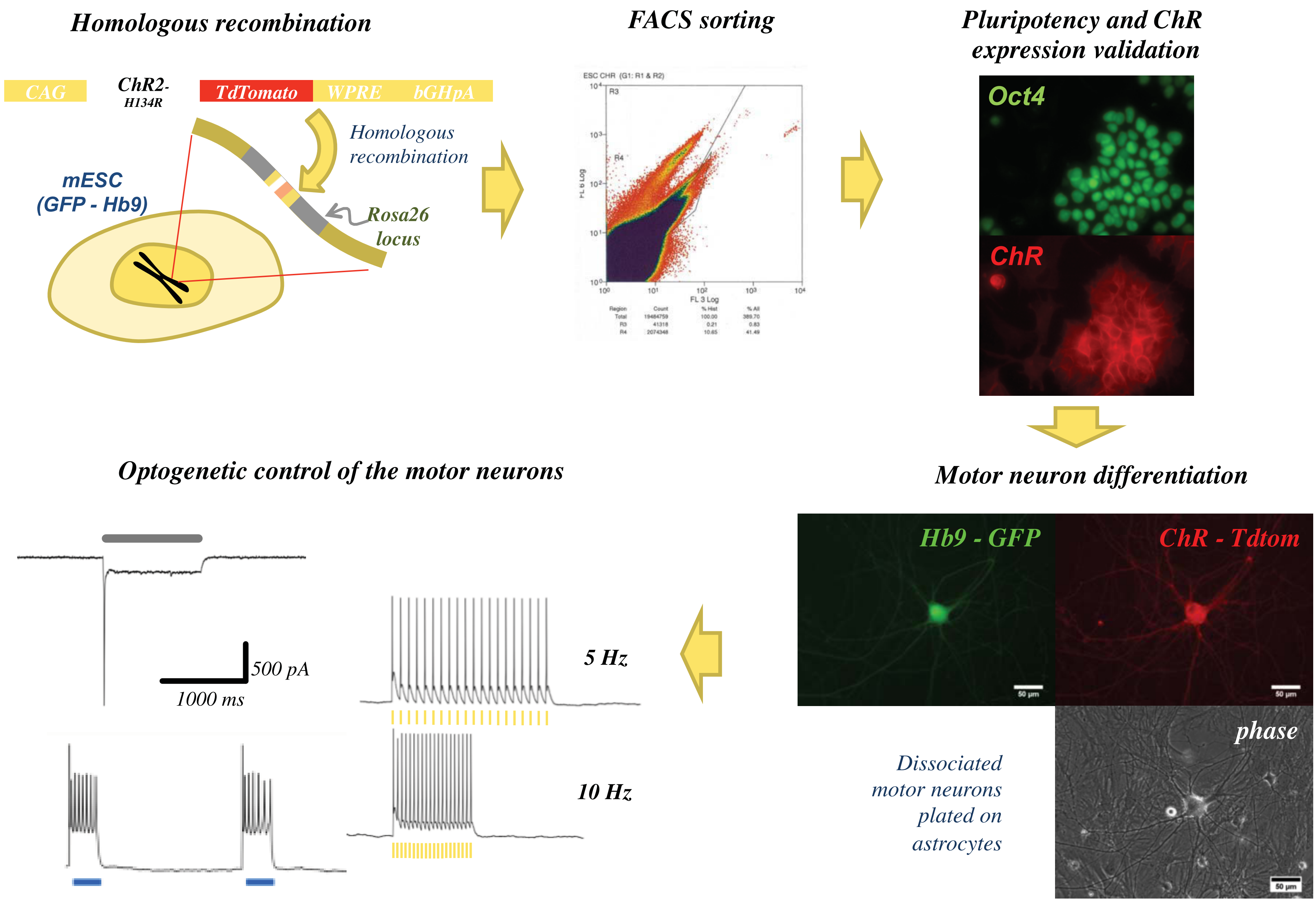




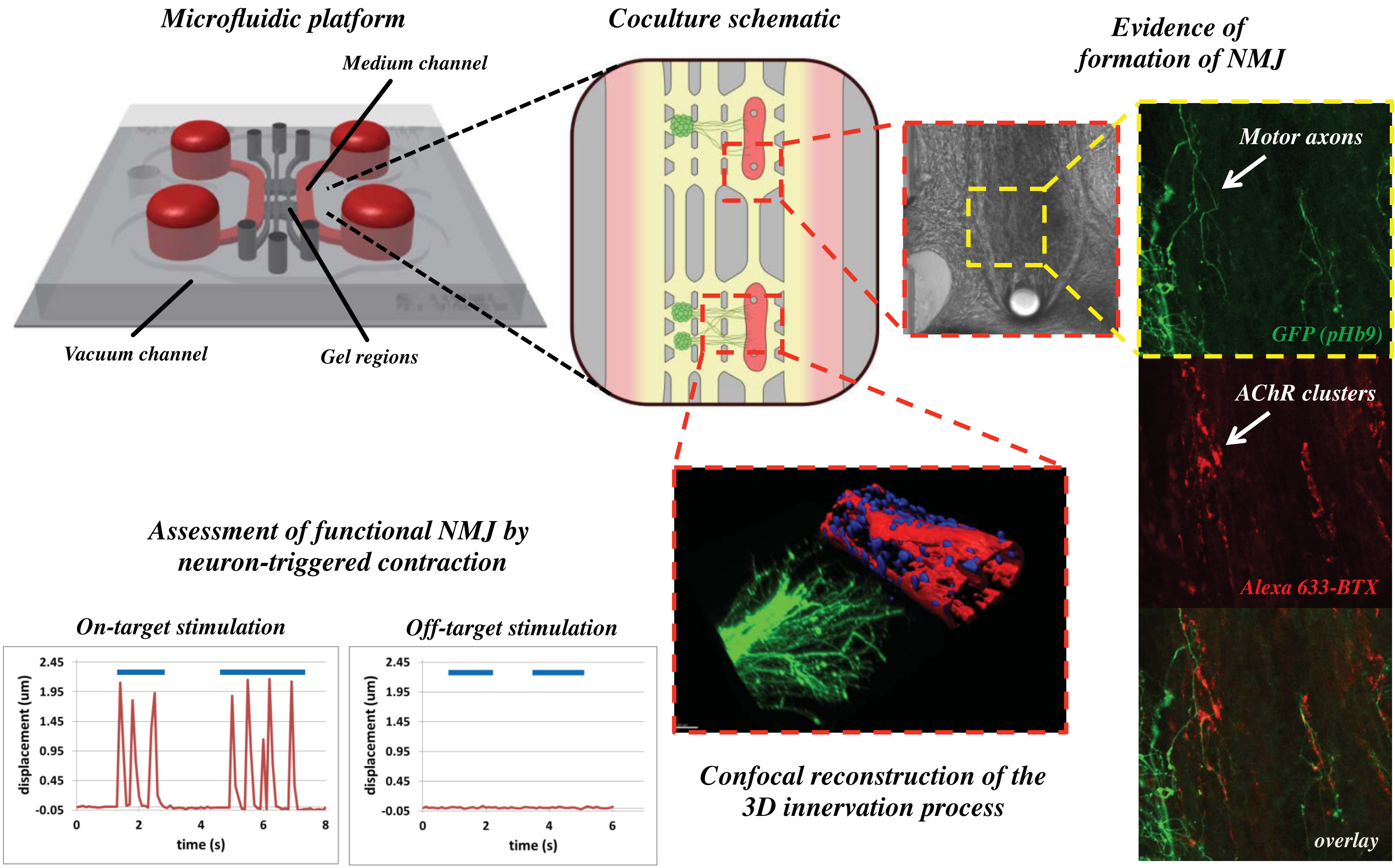
[Sakar et al. 2012]

Source: Sakar, Mahmut Selman, et al. "Formation and Optogenetic Control of Engineered 3D Skeletal Muscle Bioactuators." *Lab Chip* 12, no. 23 (2012): 4976.

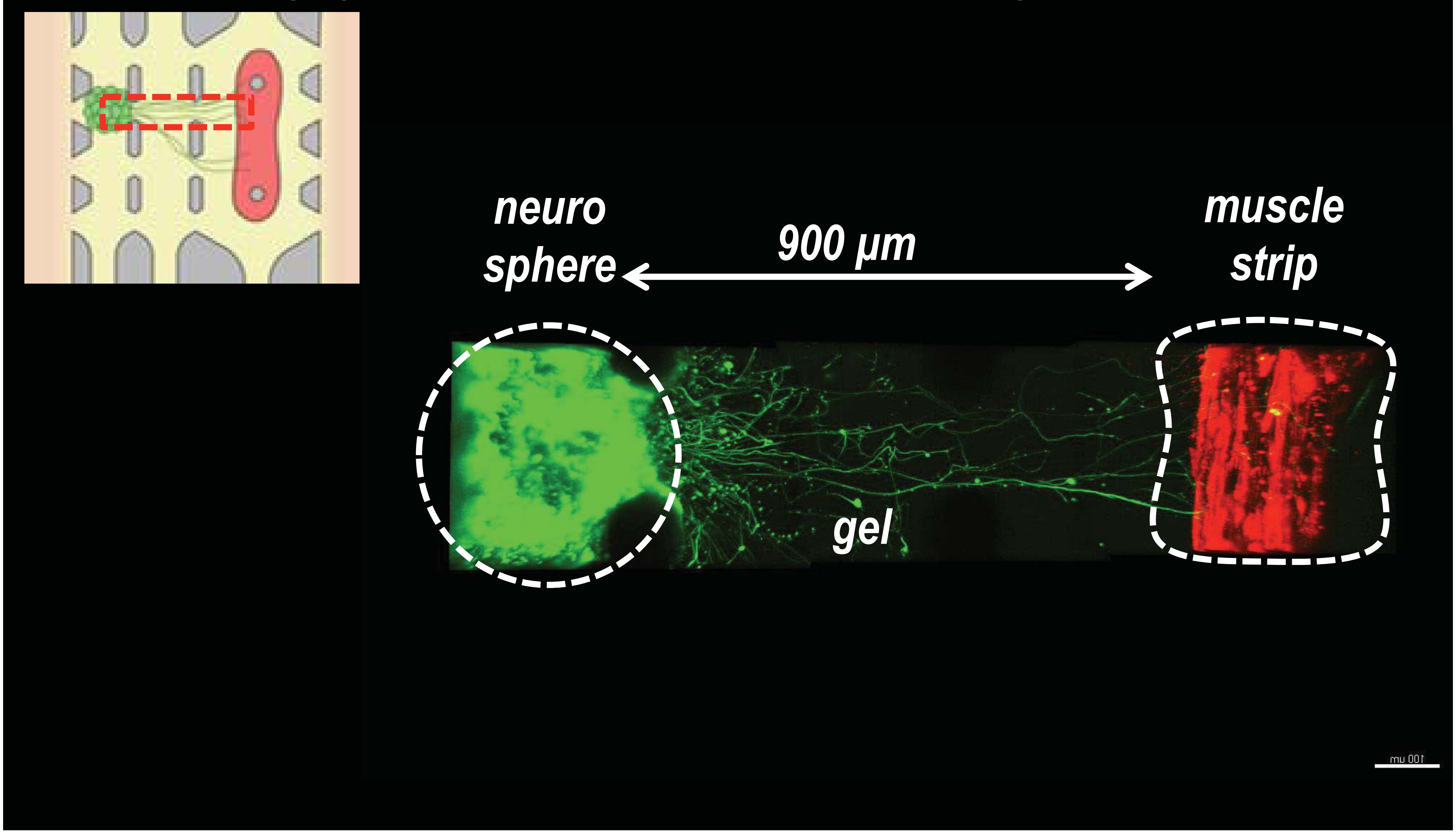
Optogenetic control of mESC-derived motor neurons



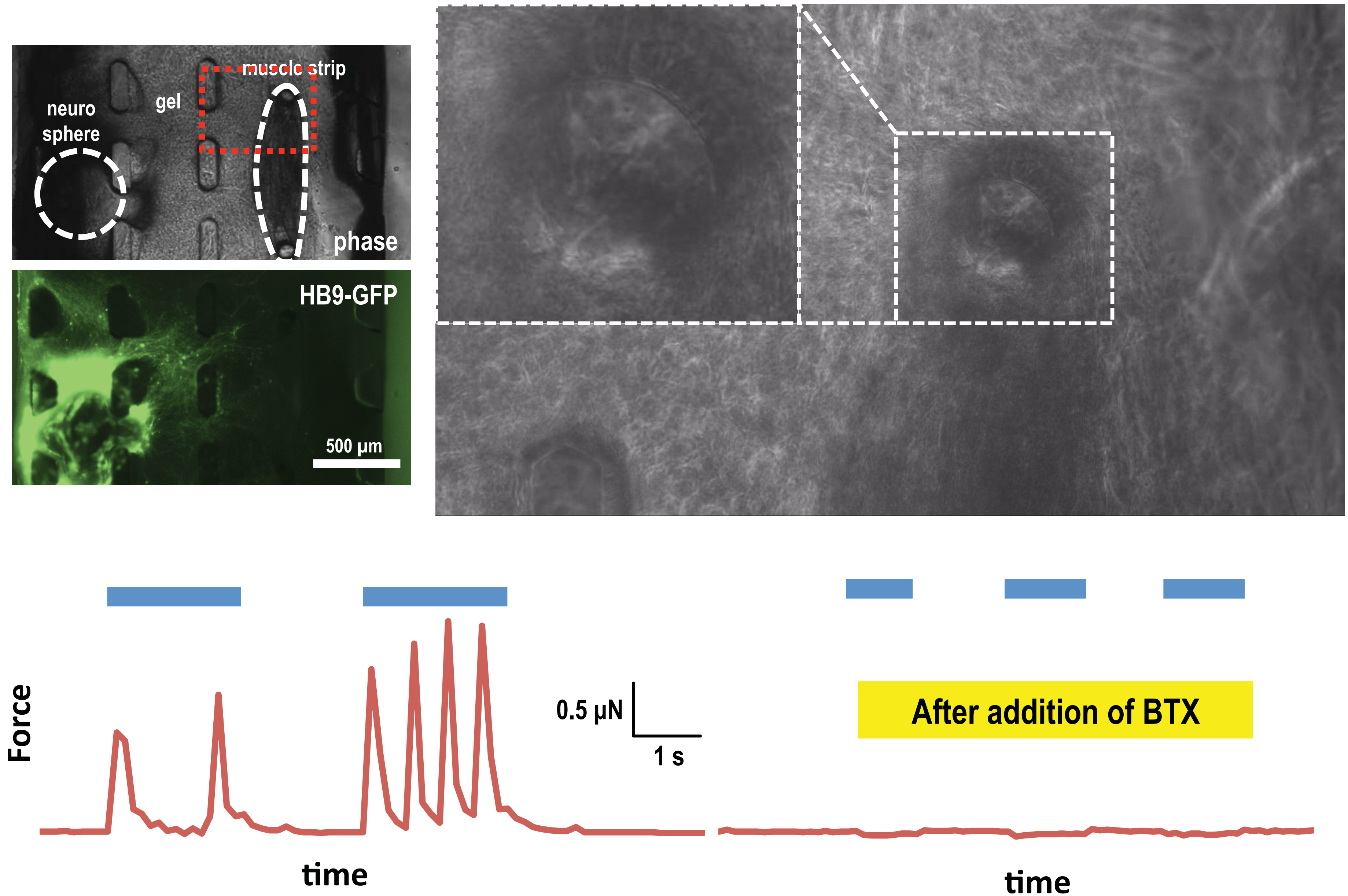
μFluidic device for neuromuscular co-culture



Confocal imaging allowed for the verification of the 3D outgrowth of the motor axons



Optogenetic control of the NMJ in 3D



What you should know

- Gross and microscopic structure of muscle
- Different types of muscle
- Twitch, summation and tetanus
- Sarcomeric structure and striations
- Sliding filament theory – basic concepts
- Forces generated
- Connecting micro and macro behavior
- Events during cross-bridge cycling
- Mechanisms of muscle activation and control

20.310J / 3.053J / 6.024J / 2.797J Molecular, Cellular, and Tissue Biomechanics
Spring 2015