Neuromuscular Bioengineering

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What is a neuron?

Neurons conduct electrical signals that allow our brains to function and our muscles to twitch.
Intracellular processes facilitate electrical activity in the neuron

Neurons are also highly polarized cells that require protein production and degradation, and cargo transport to function.

Protein production and packaging by nucleus, Golgi, and ER

Degradation by lysosomes, autophagosomes, proteasomes, and secretion

Synaptic vesicles, mitochondria, organelles, cytoskeleton, mRNA...

Cell Body  \[\rightarrow\]  AnteroGraDe  \[\rightarrow\]  Synapse

Neurotrophic factors, endosomes, injury signals, recycled cell components, viruses...
Neurons also interact with their environment

- Myelin
- Muscle
- Mechanical Loading
- Blood-Brain Barrier
- Vasculature
Transport mutants display axonal damage and paralysis

Axons of fruit fly transport mutants display organelle-filled clogs...
These then result in paralysis ("tail-flip") phenotypes
Defects in protein clearance also induce axonal defects

Increase in autophagic activity in cells expressing “stickier” mutant amyloid
Aggregates are similar to those seen in disease pathology

Conspicuously similar accumulations are observed in neurodegenerative diseases

Transport mutants in fly and mouse

Lewy-body disorders, (e.g., Parkinson’s)

Poly-Q disorders, (e.g., Huntington’s)

Spongiform encephalopathies, (e.g., Mad Cow (Prion) Disease)

Dementia (e.g., Alzheimer’s)

Motor neuron diseases (e.g., ALS)
What types of neuroscience problems need bioengineering solutions?

**NORMAL NEURONAL FUNCTION**
(Understanding basic processes involved in the regulation of transport)

**NERVE PLASTICITY AND DISEASE**
(Determining mechanisms of neurodegeneration and neuronal adaptation)

**TARGETED DELIVERY OF THERAPEUTIC CARGOES**
(Designing approaches to prevent neurodegeneration or modulate neuronal function)
Imaging individual cargoes allows analysis of traffic patterns

- We can image the transport of specific fluorescently-tagged proteins
- We can quantify traffic patterns using a custom particle-tracking software

Courtesy of Richard Brusch
Neuronal plasticity: Mechanical loading of neurons

- Mechanical loading (chronic stretch, cyclic loading, exercise)

- Cell and tissue level studies of strain-mediated adaptations in neurons
Your toolbox: approaches to attacking these problems

- **Fluorescence Microscopy**
  - Fixed cells/tissue
  - Live-cells
  - In vivo imaging

- **Biomechanics/Physiology**
  - Animal Models
  - Tissue
  - Single-cell
  - Organelles

- **Biochemistry**
  - Purification of organelles from tissue
  - *In vitro* motility assays
  - Development of synthetic/hybrid cargoes

- **Cell/Molecular Biology**
  - Cell culture
  - Basic cloning

- **Theoretical modeling**
  - Finite-element analysis
  - Transport modeling

- Kinesin
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