

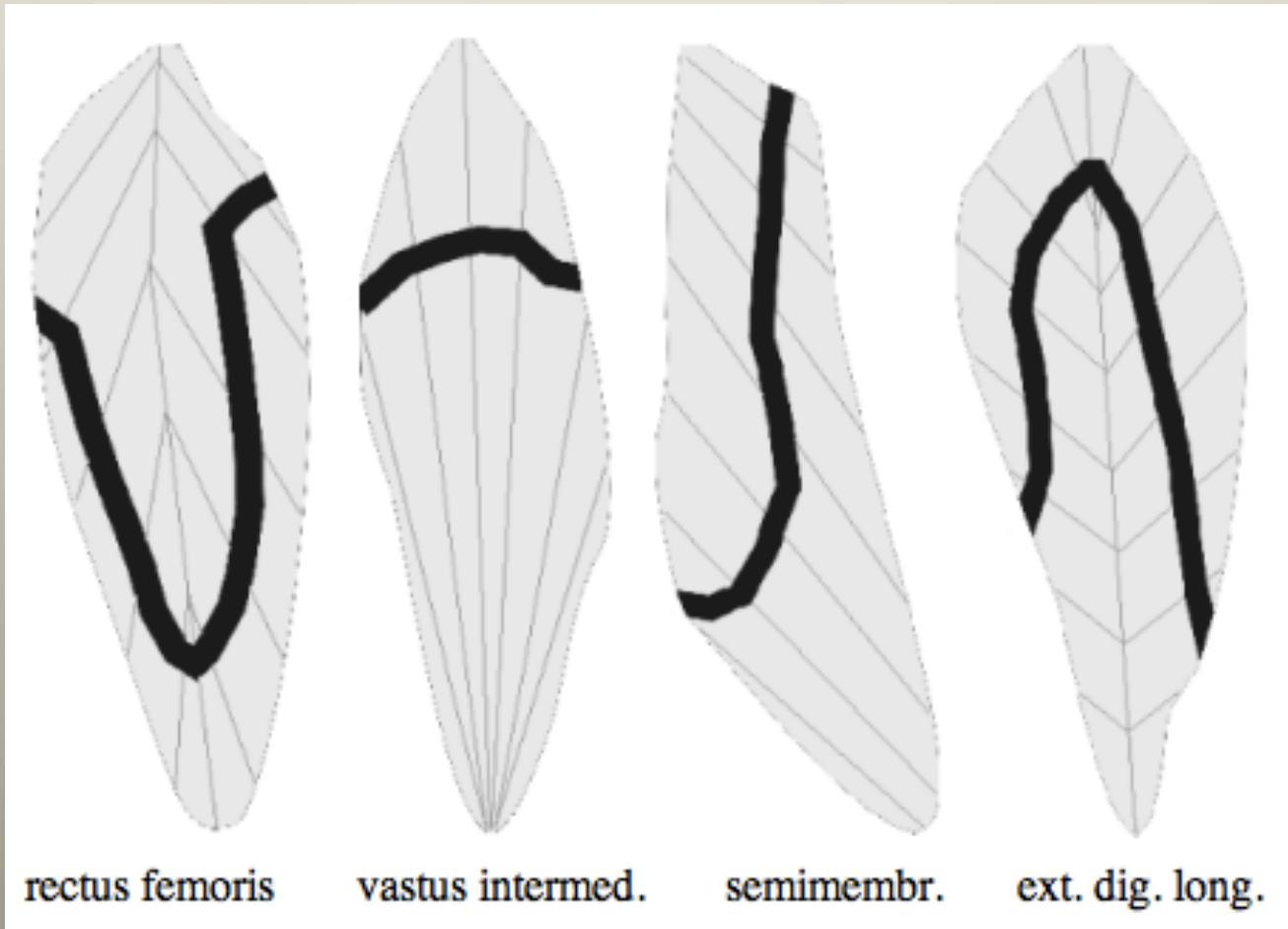
Structure of the Neuromuscular Junction

Introduction to physiology

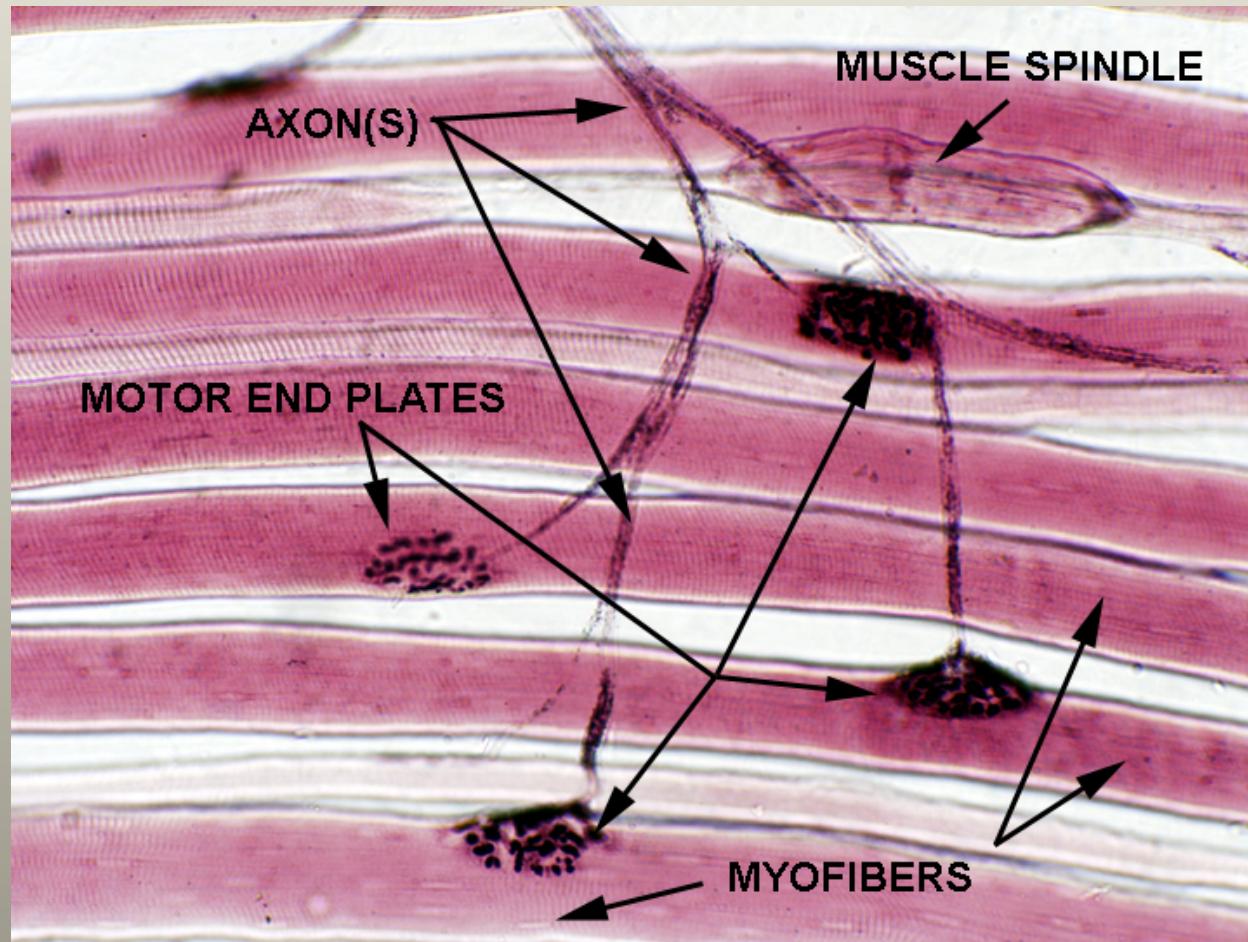


Dr. Thomas Caceci, Virginia Tech

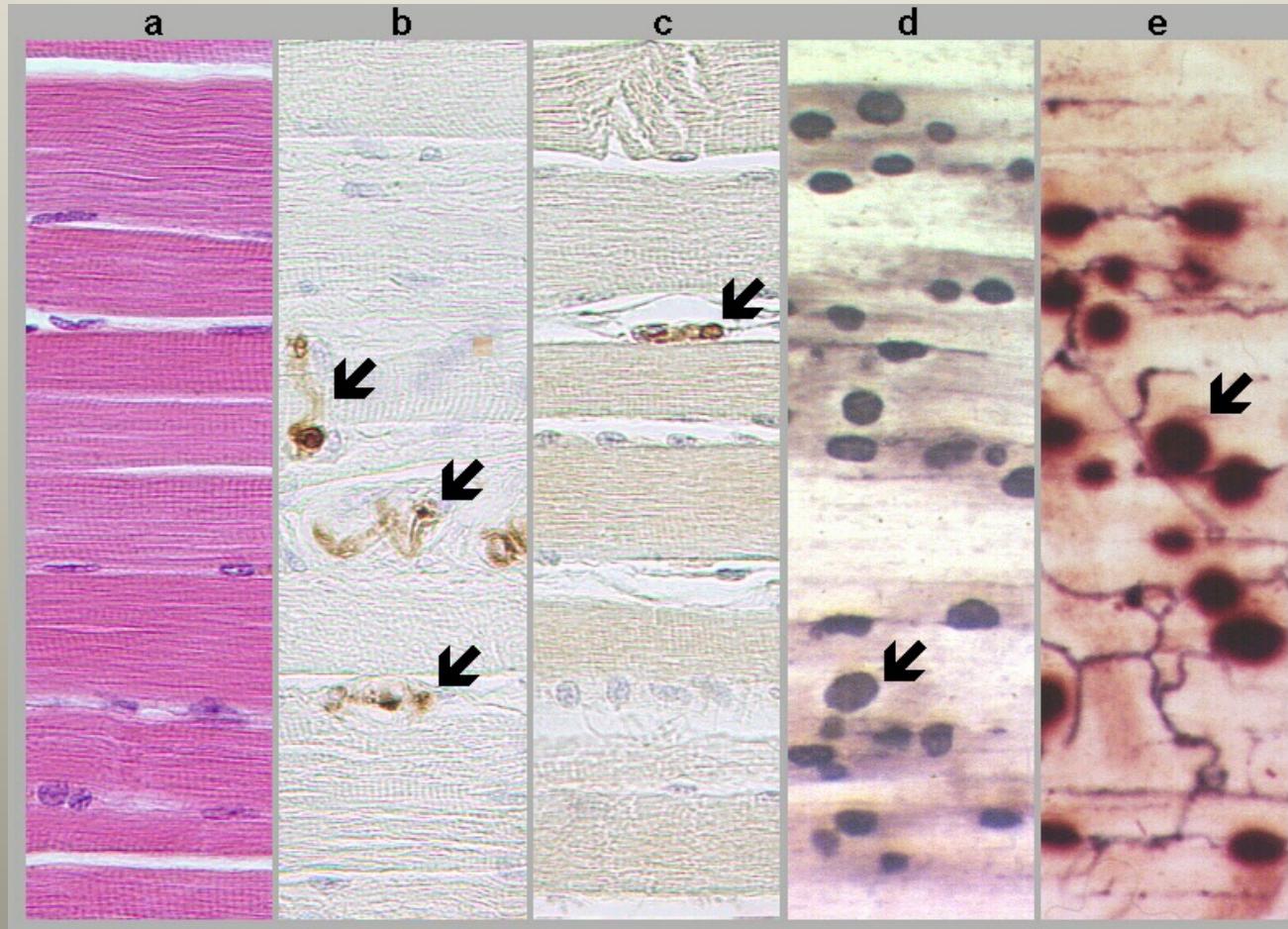
Motor endplates are distributed across striations



Light microscopy of NMJ



Light microscopy of NMJ

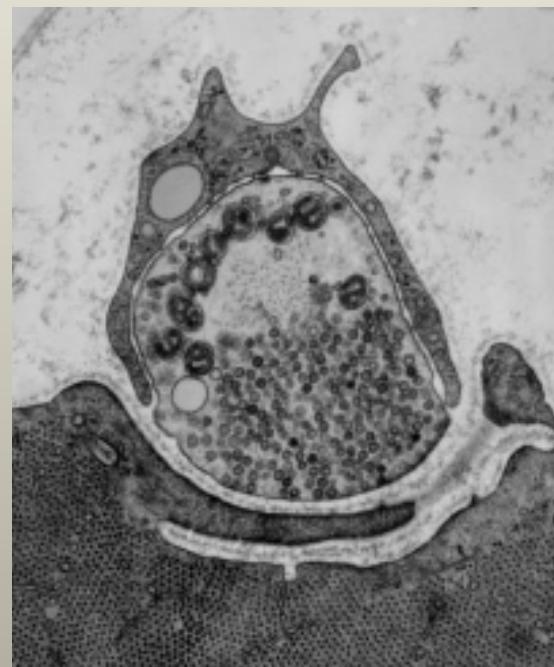


Electron micrographs of NMJ



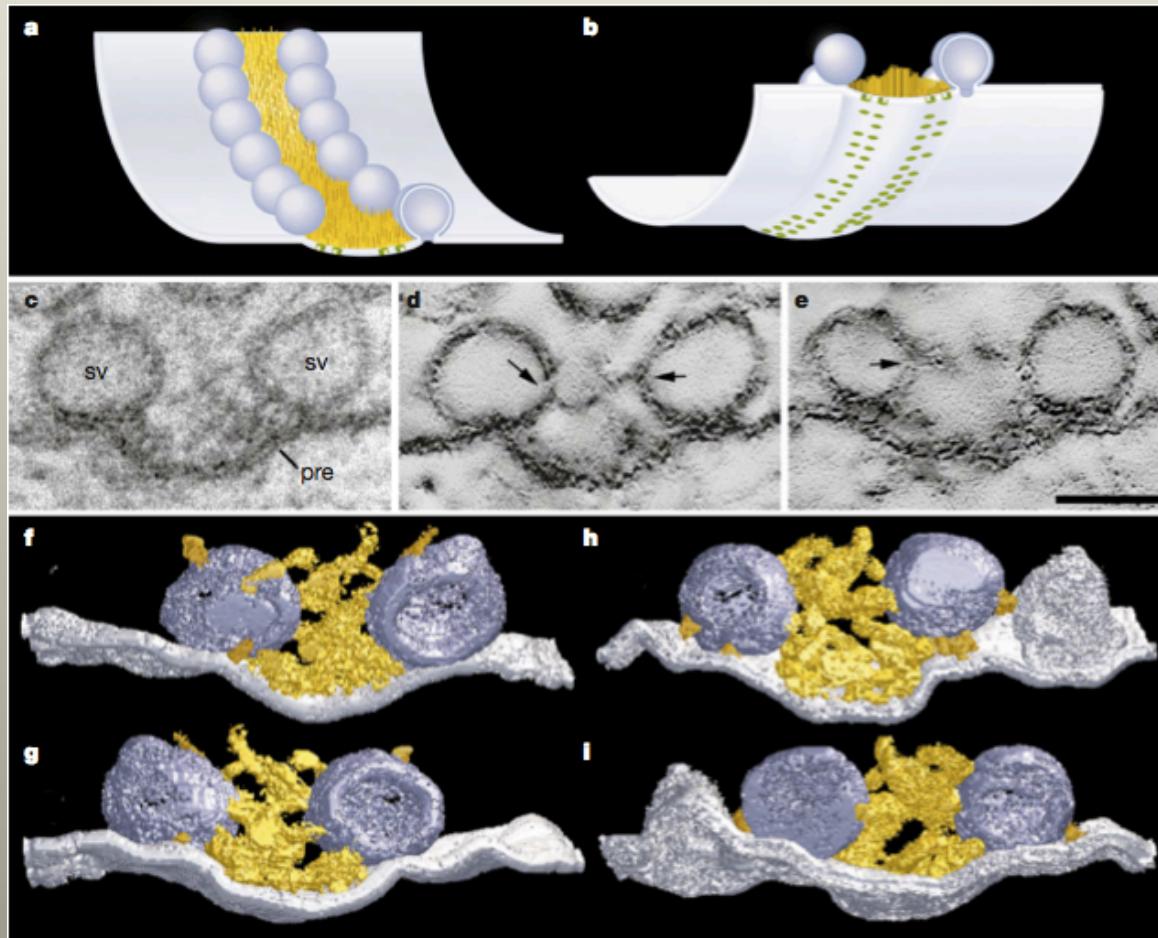
Scale bar = 0.3 microns

Electron micrographs of NMJ

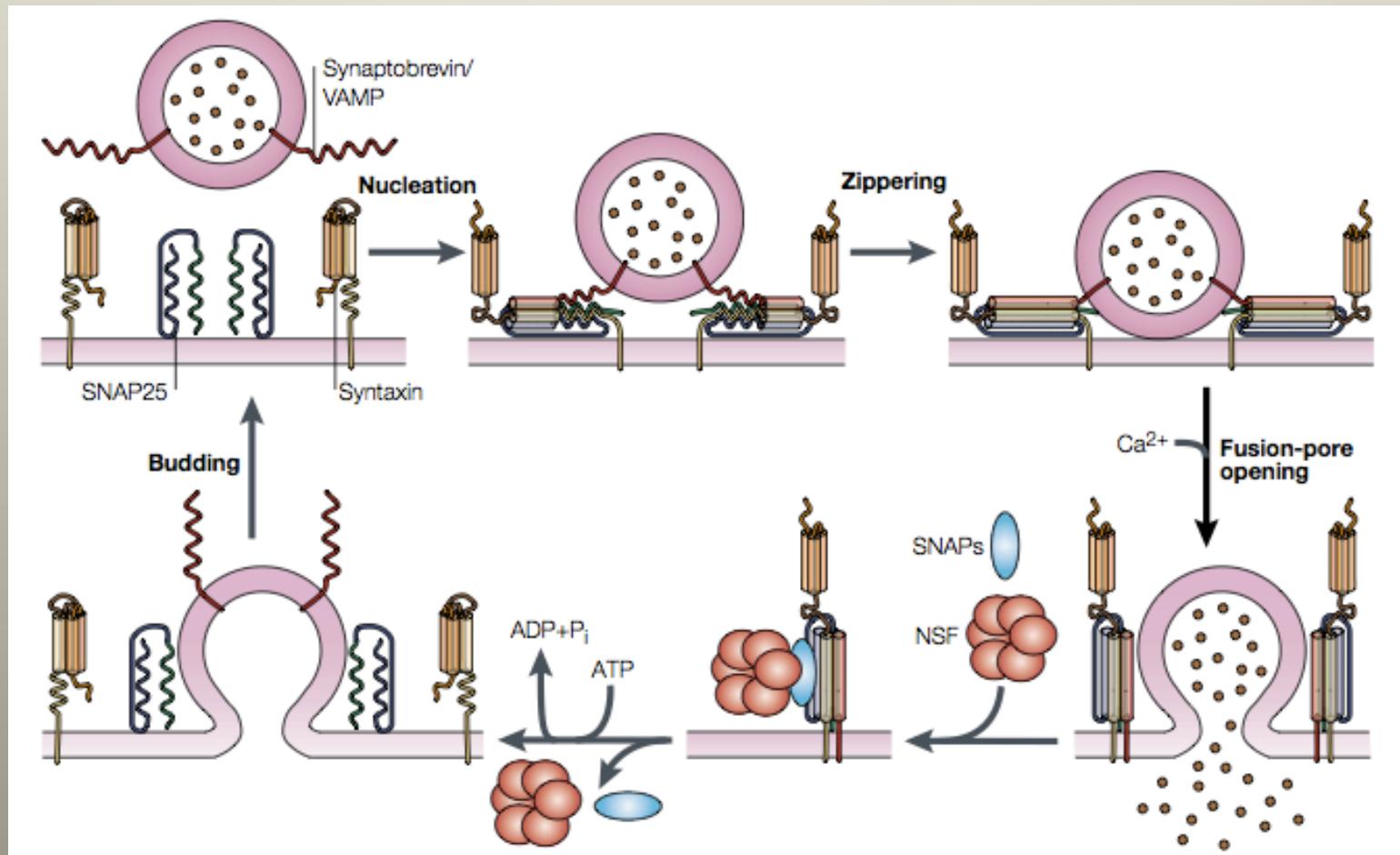


Dr. John Heuser of Wash. U.

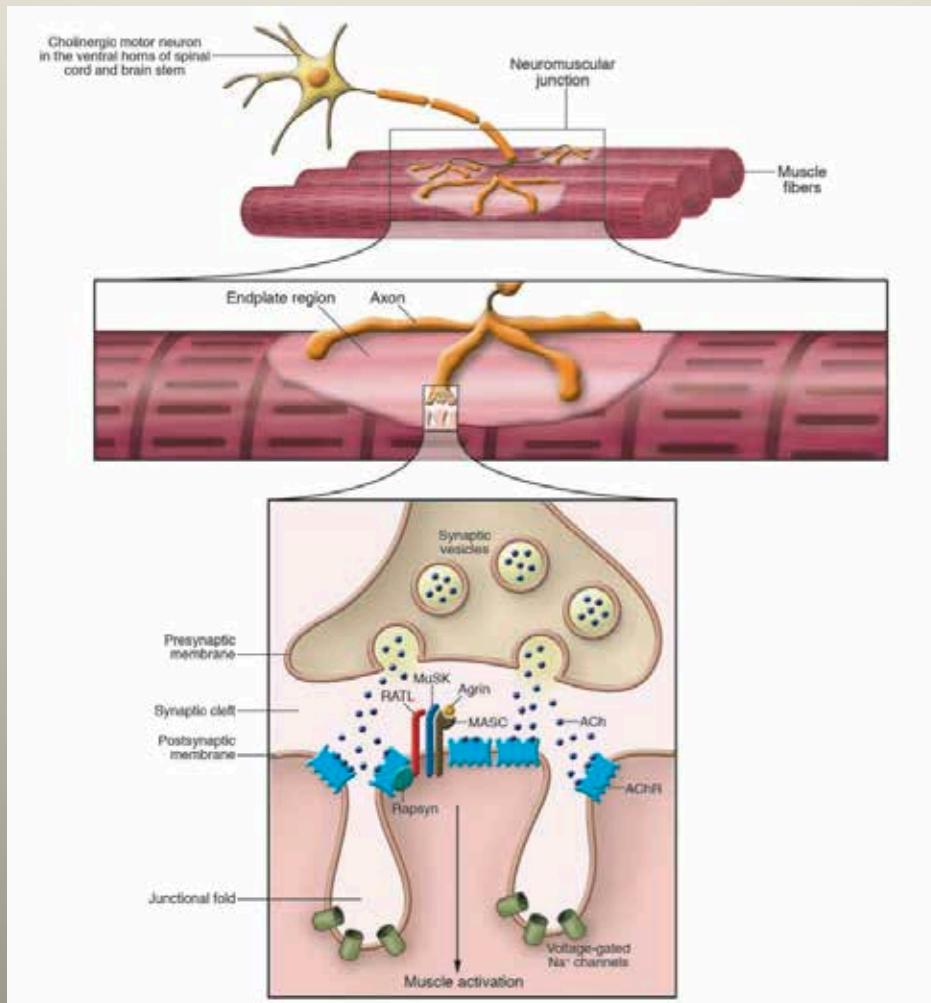
Active Zone Material in presynaptic terminal



Presynaptic SNARE complex



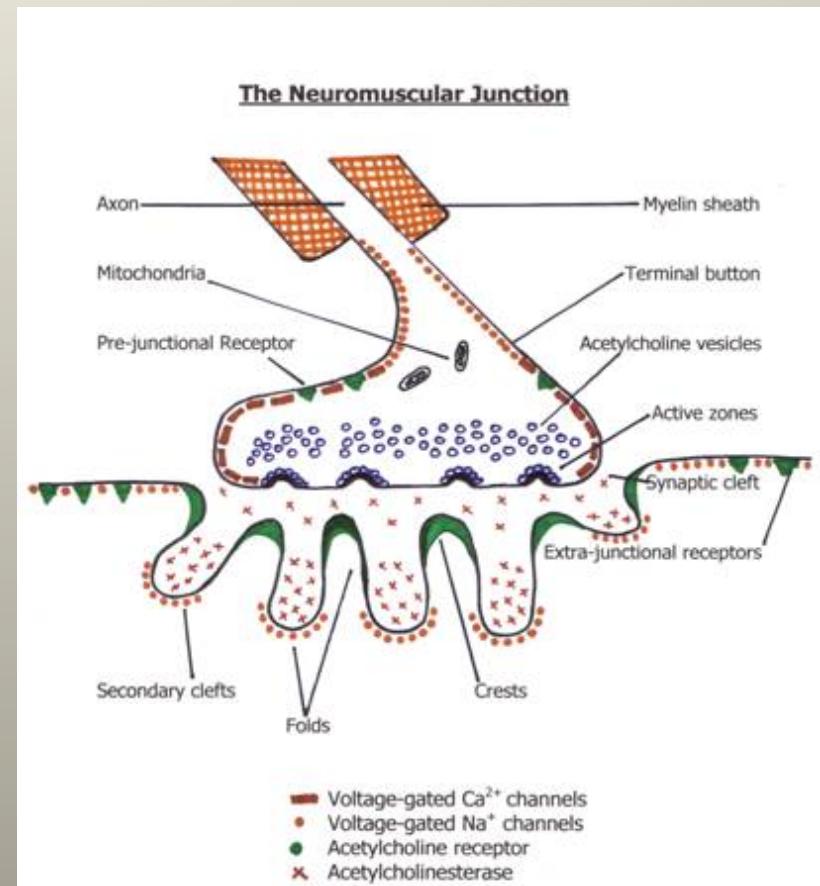
NMJ Structure



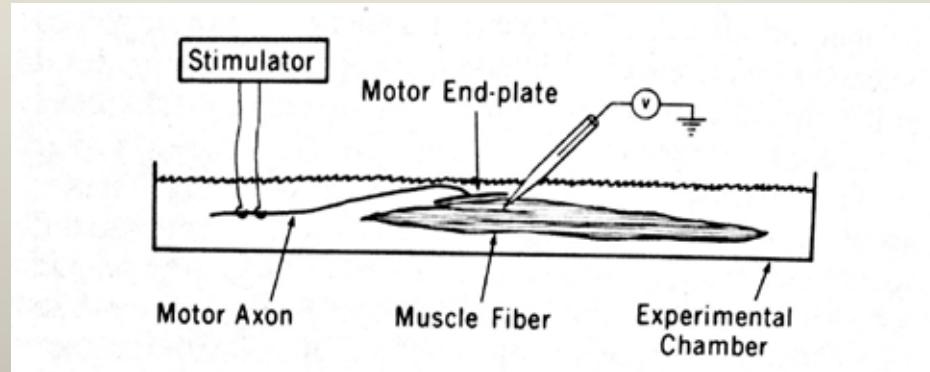
Conte-Fine, et al (2006) J. Clin. Invest.

NMJ Transmission Sequence

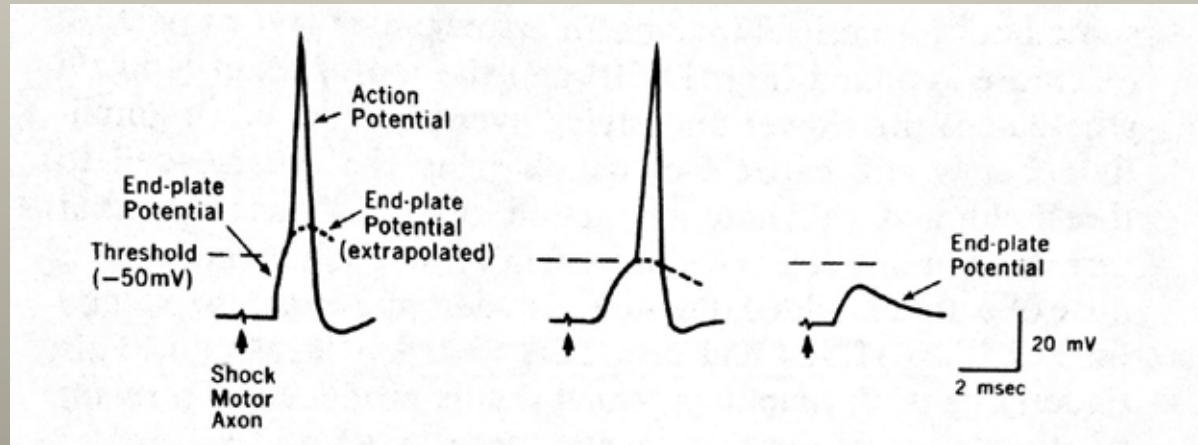
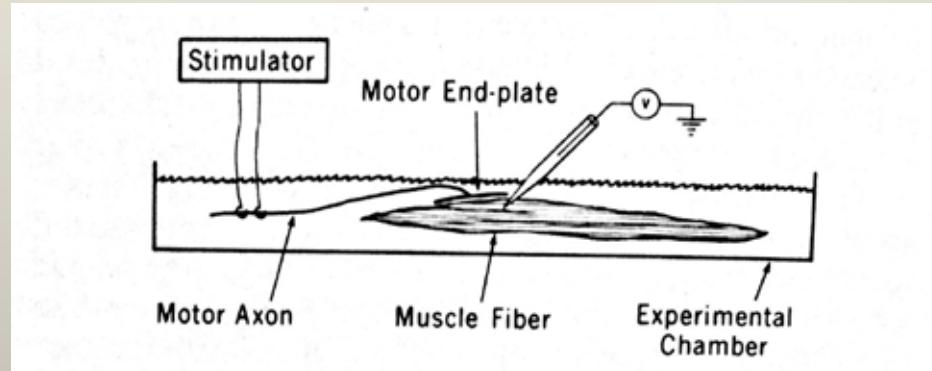
- Nerve action potential propagation to the pre-synaptic terminus opening voltage-gated calcium channels
- Calcium entry triggers acetylcholine vesicle release
- Acetylcholine binding to AChR opens cation channel for about 1 ms
- Post-synaptic membrane depolarization (Endplate potential) builds
- If sufficient to open voltage-gated sodium channels (depolarization threshold) muscle fiber action potential ensues.



End Plate Potential



End Plate Potential

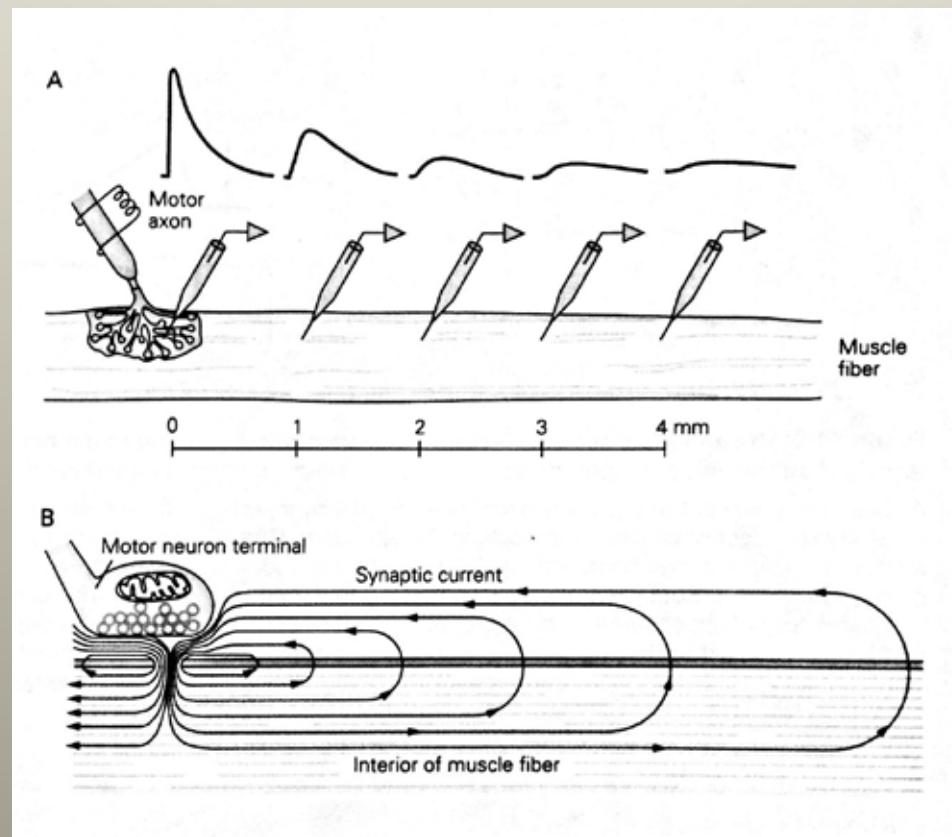


Normal

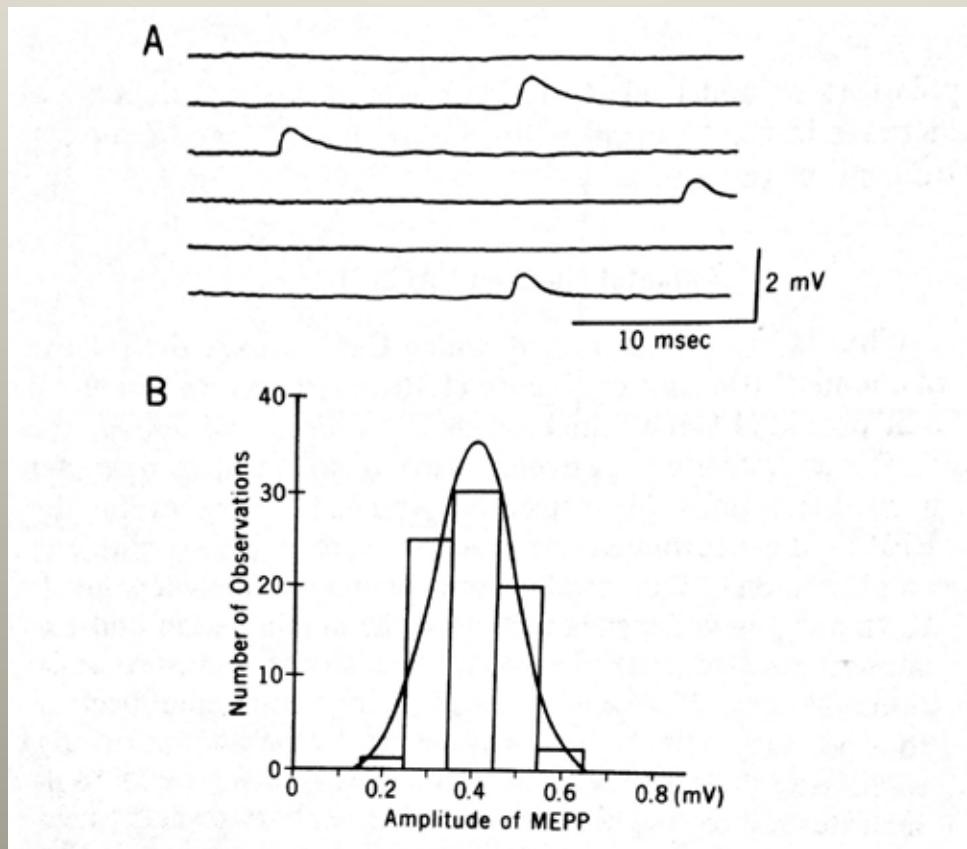
Low Dose
Curare

High Dose
Curare

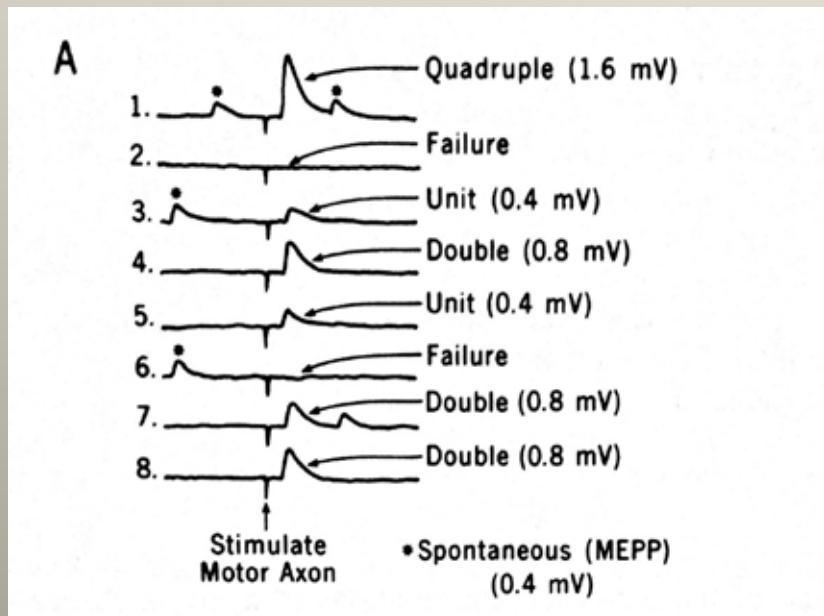
Synaptic Potential in Muscle



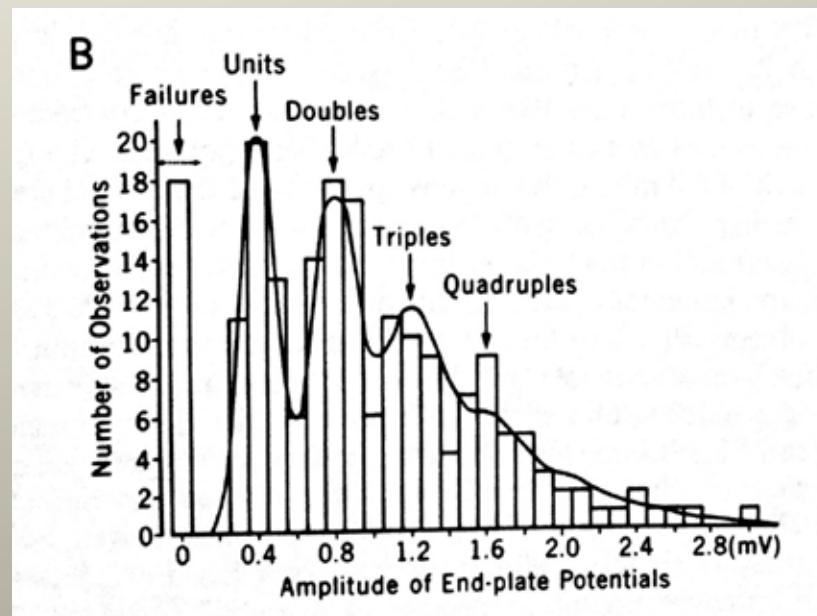
Miniature Endplate Potential



Quantal Release of Neurotransmitter



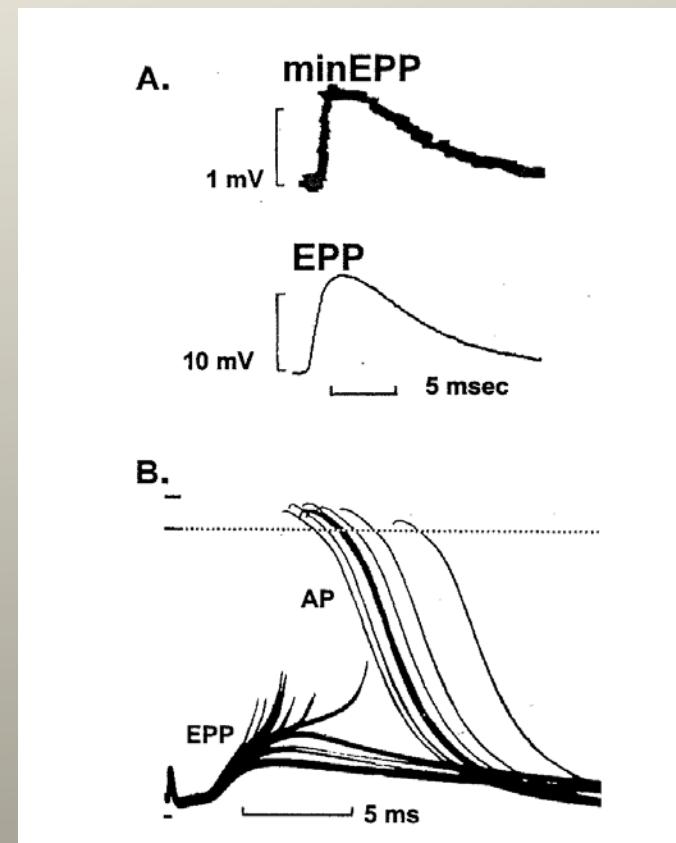
Liley (1956) J. Physiol.



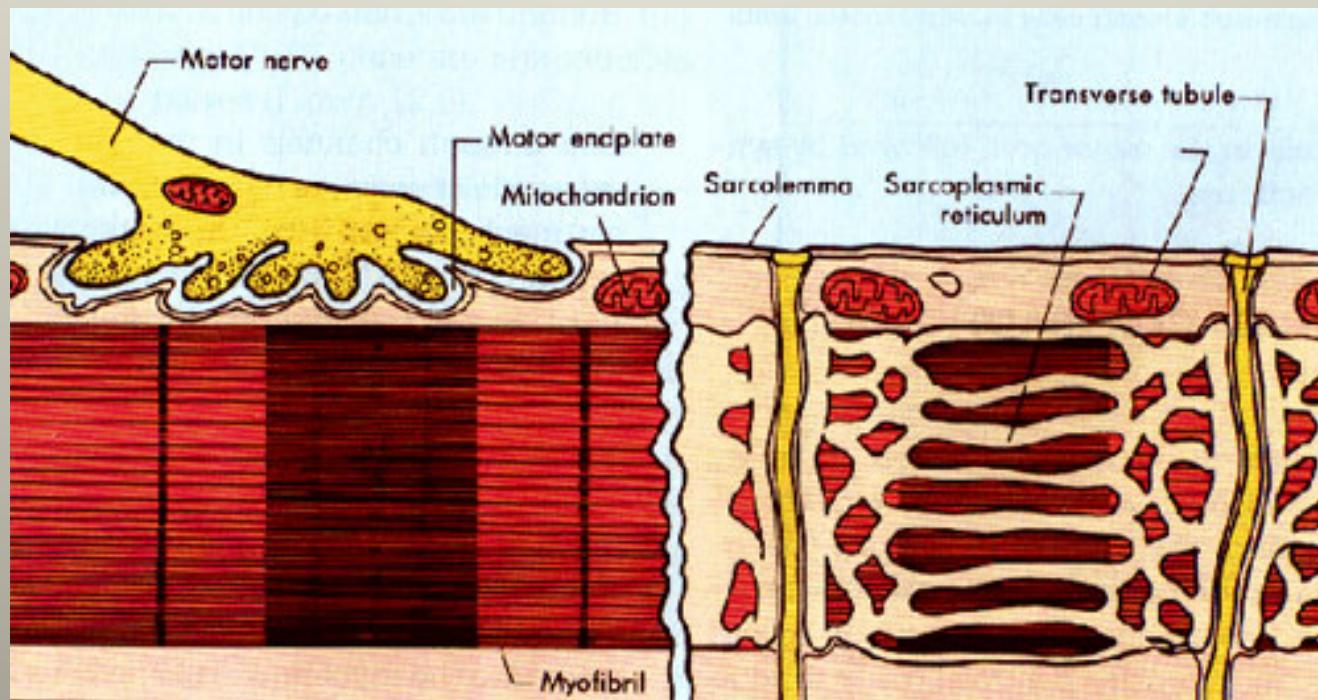
Boyd and Martin (1956) J. Physiol.

How many acetylcholine molecules to produce a MEPP?

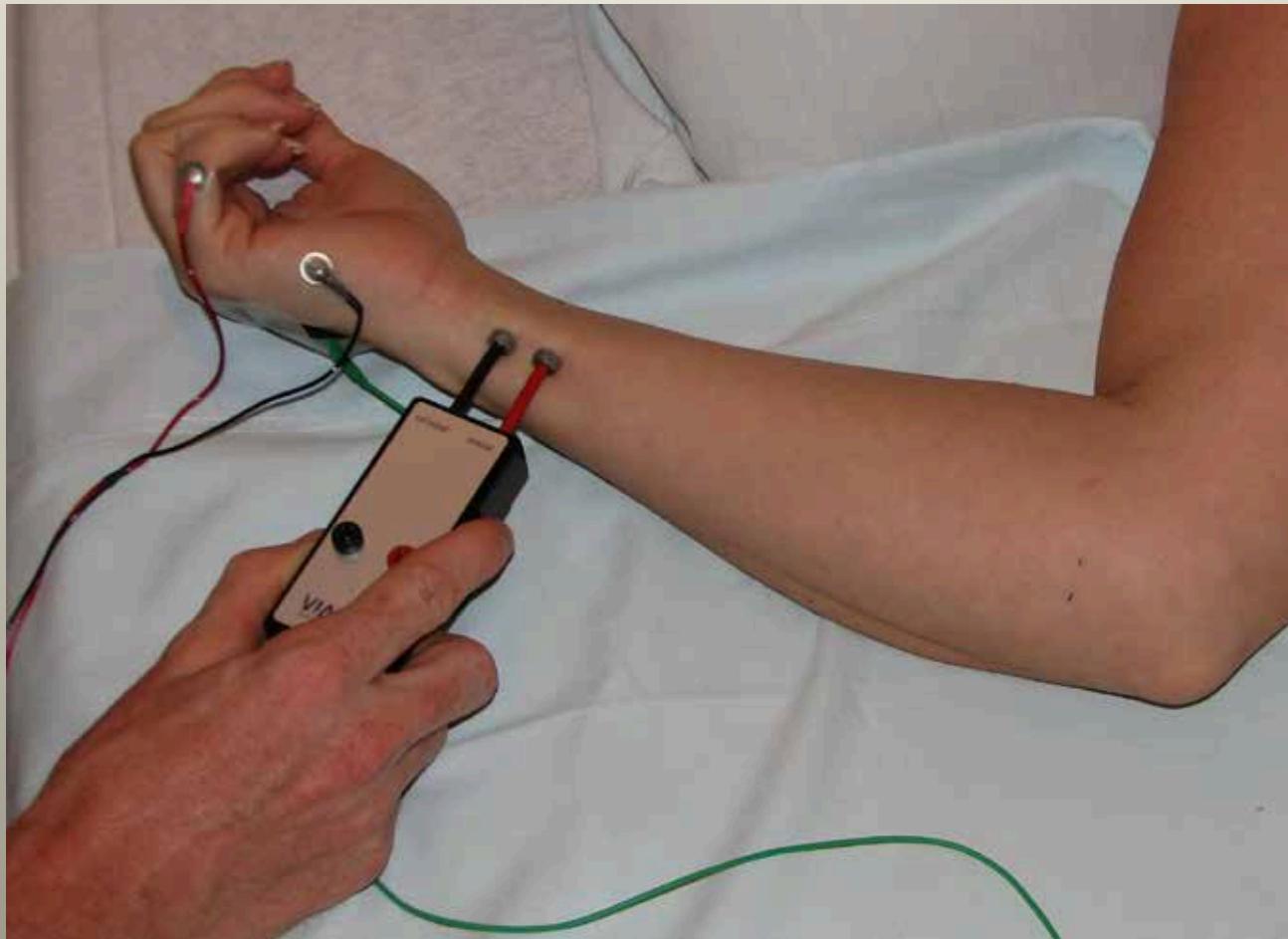
- Each Vesicle releases about 5000 molecules of ACh
- Each Quantum causes approx. 1 mV depolarization (miniature endplate potential, MEPP)
- About 17,000 ions move through receptor in 1 ms
- Each nerve impulse releases about 50 quanta
- Summated quanta leads to an endplate potential (non-linear)
- Muscle resting potential = -75mV
- VGNC threshold potential = -50mV
- Need around 15 vesicles to fire muscle
- $50 - 15 = 35$ vesicles = **SAFETY FACTOR**



Muscle Action Potential

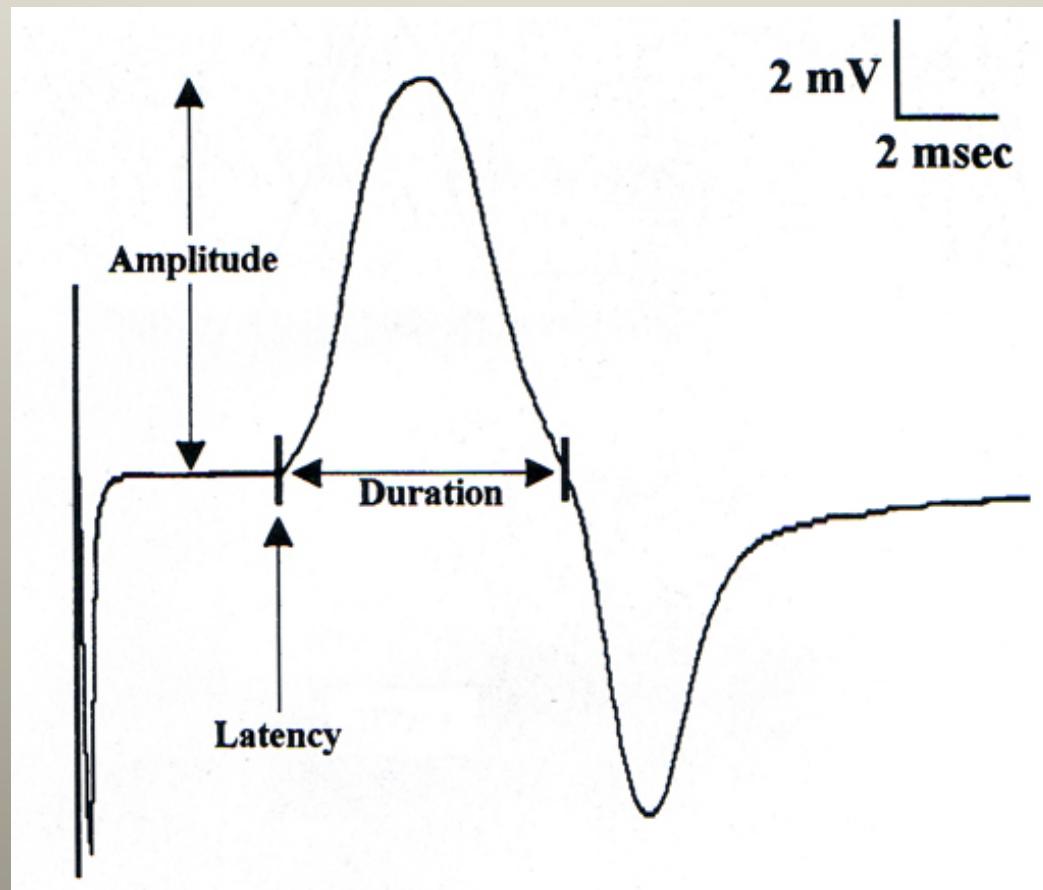


CMAP setup

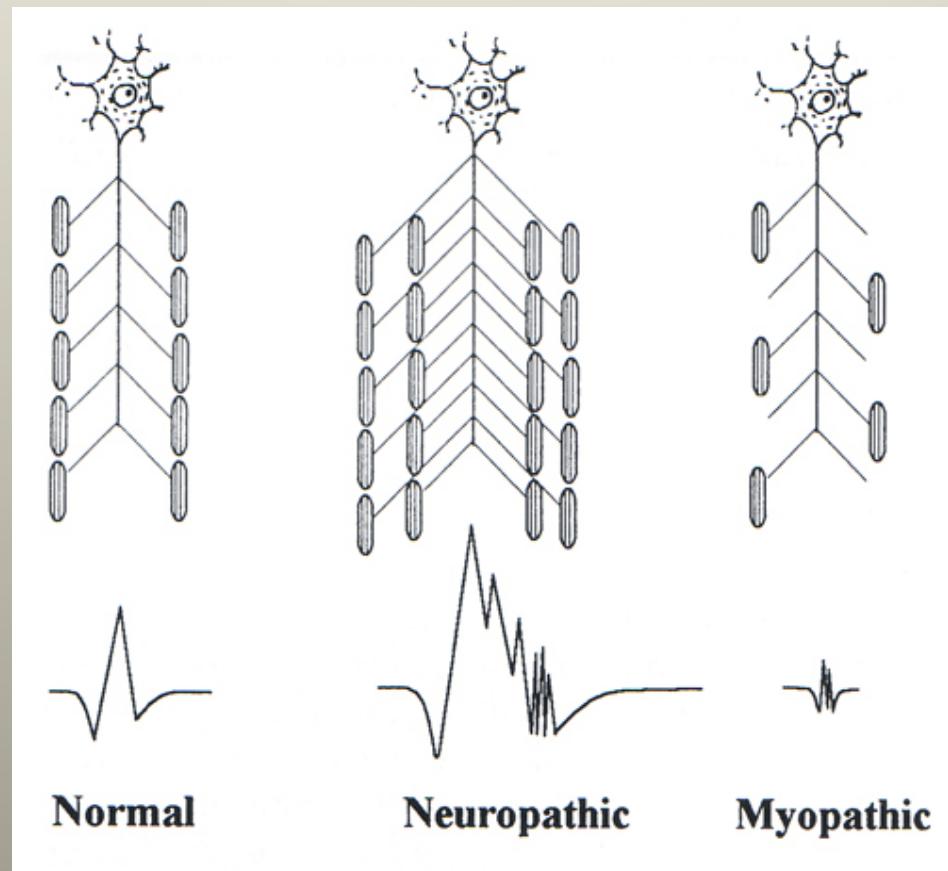


Dr. W. David Arnold, OSU

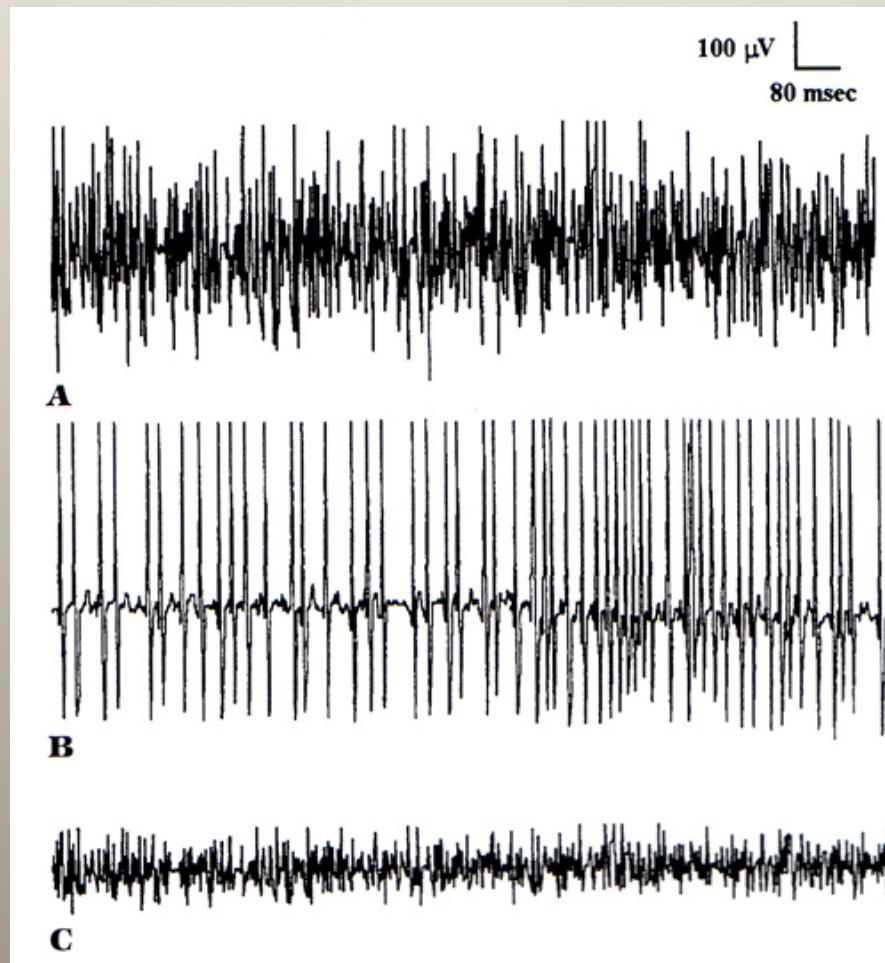
Compound Muscle Action Potential



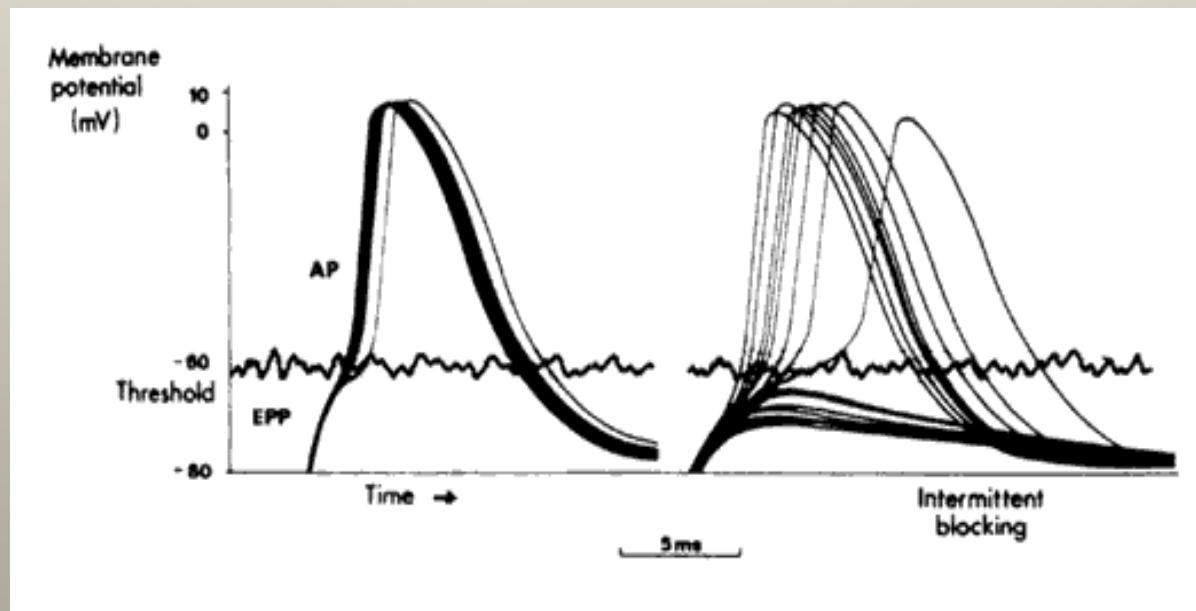
Patterns of motor unit electrical signals In nerve and muscle diseases



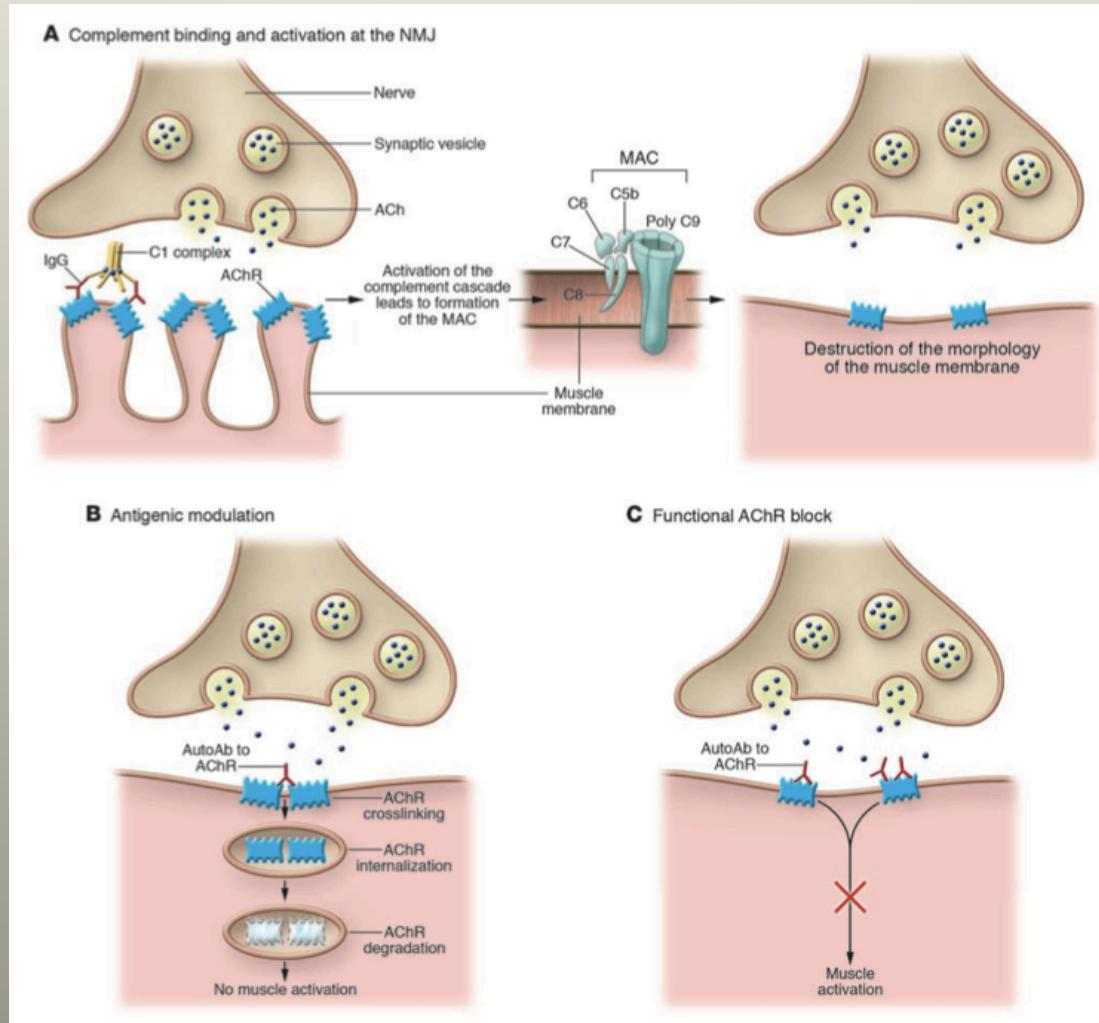
Recruitment of motor units



Problem with CMAP

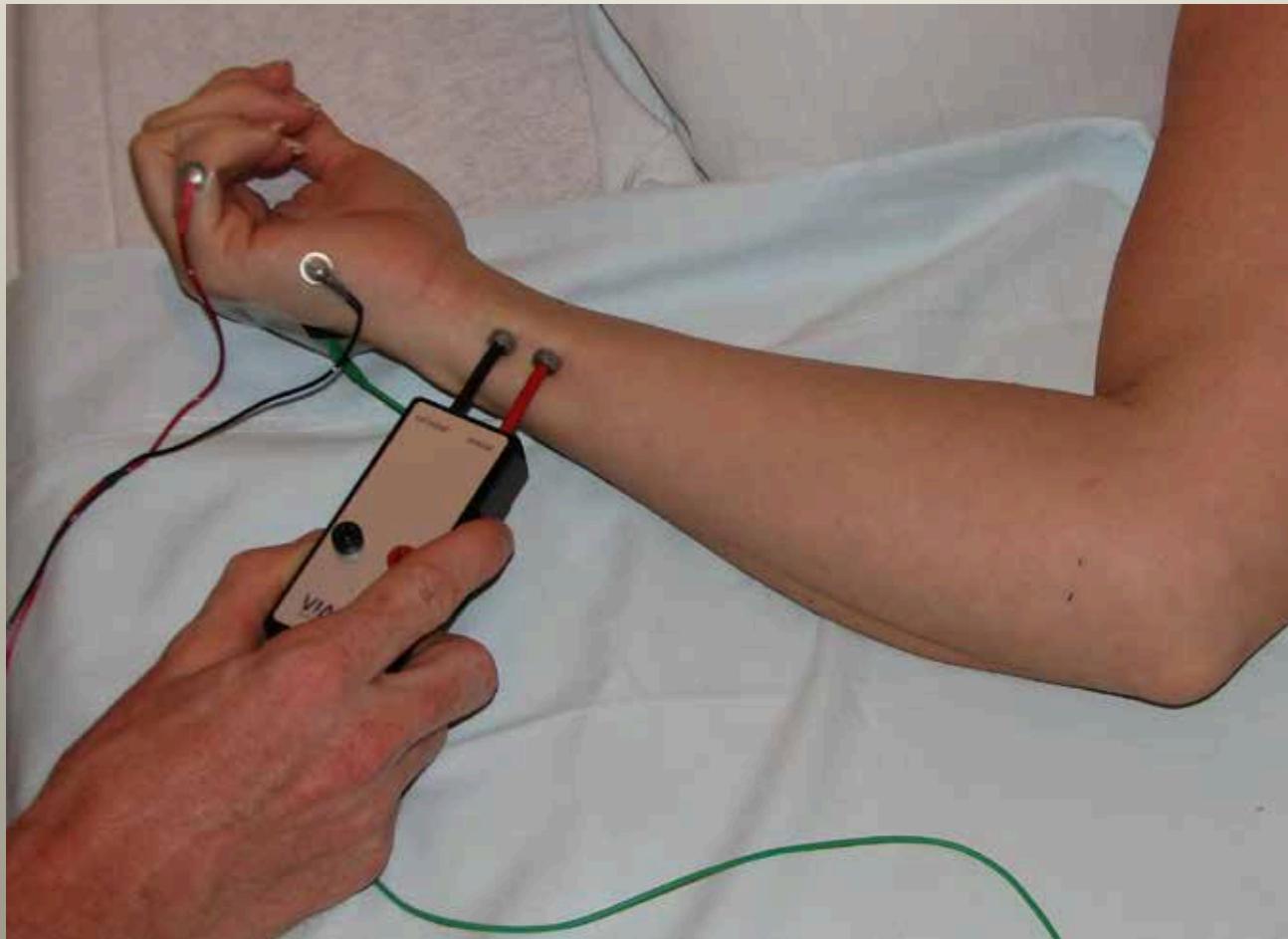


Myasthenia Gravis



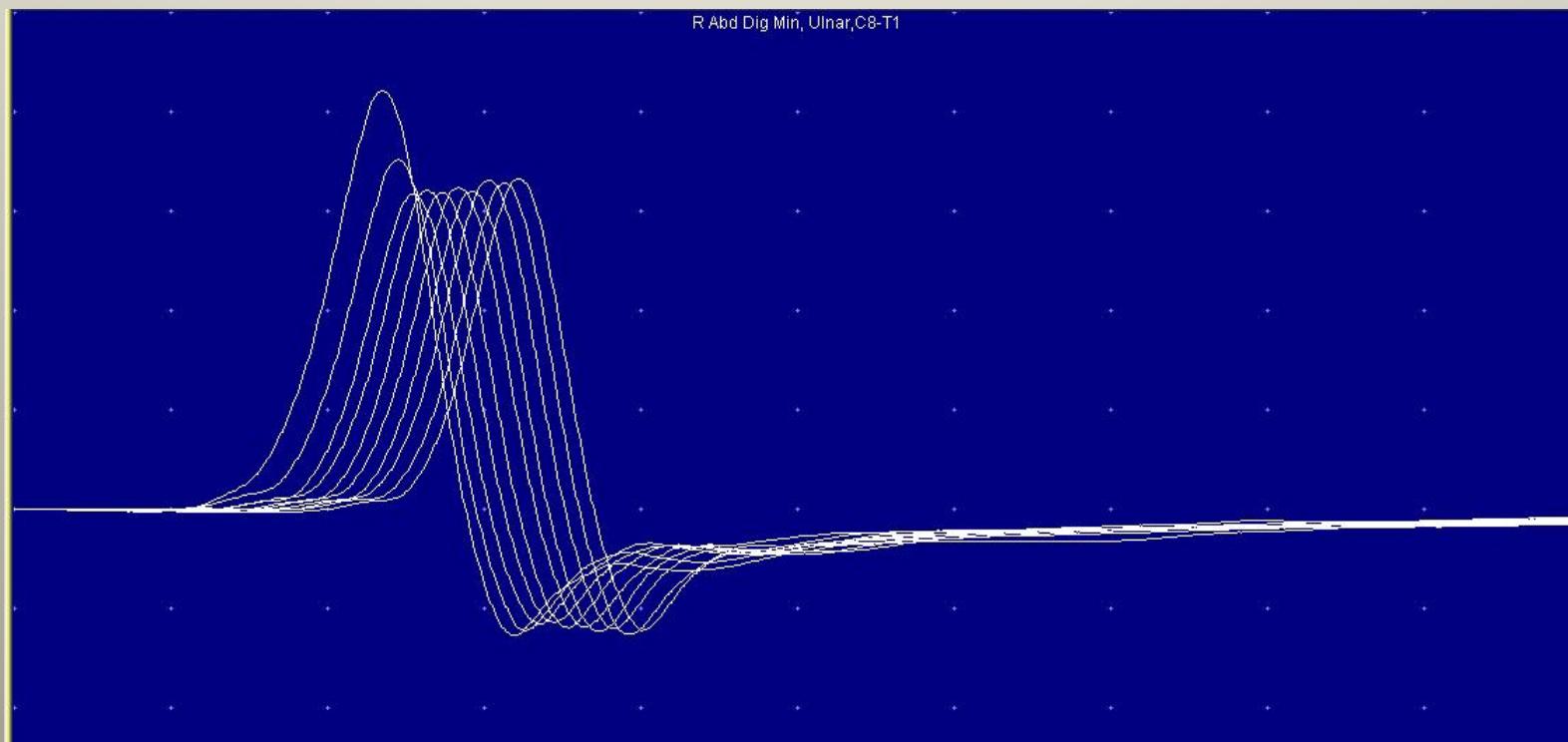
Conte-Fine, et al (2006) J. Clin. Invest.

RNS setup



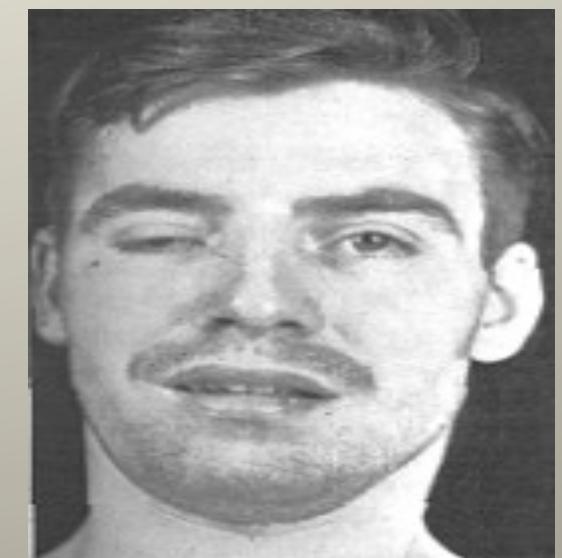
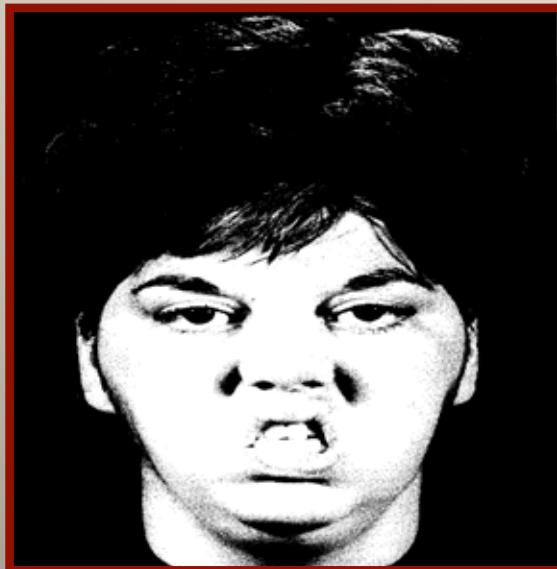
Dr. W. David Arnold, OSU

Myasthenia Gravis



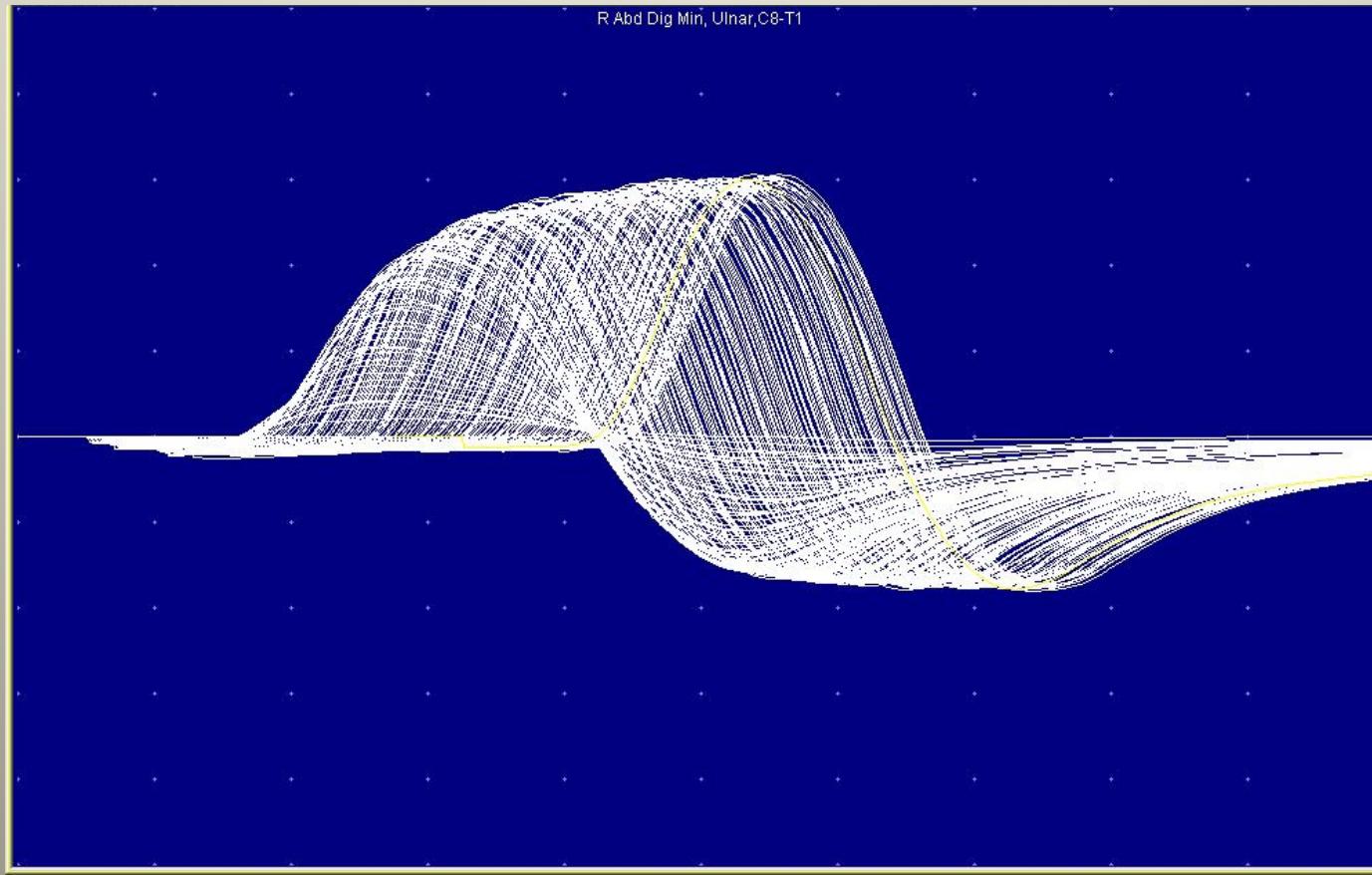
Dr. W. David Arnold, OSU

Myasthenia Gravis



Dr. W. David Arnold, OSU

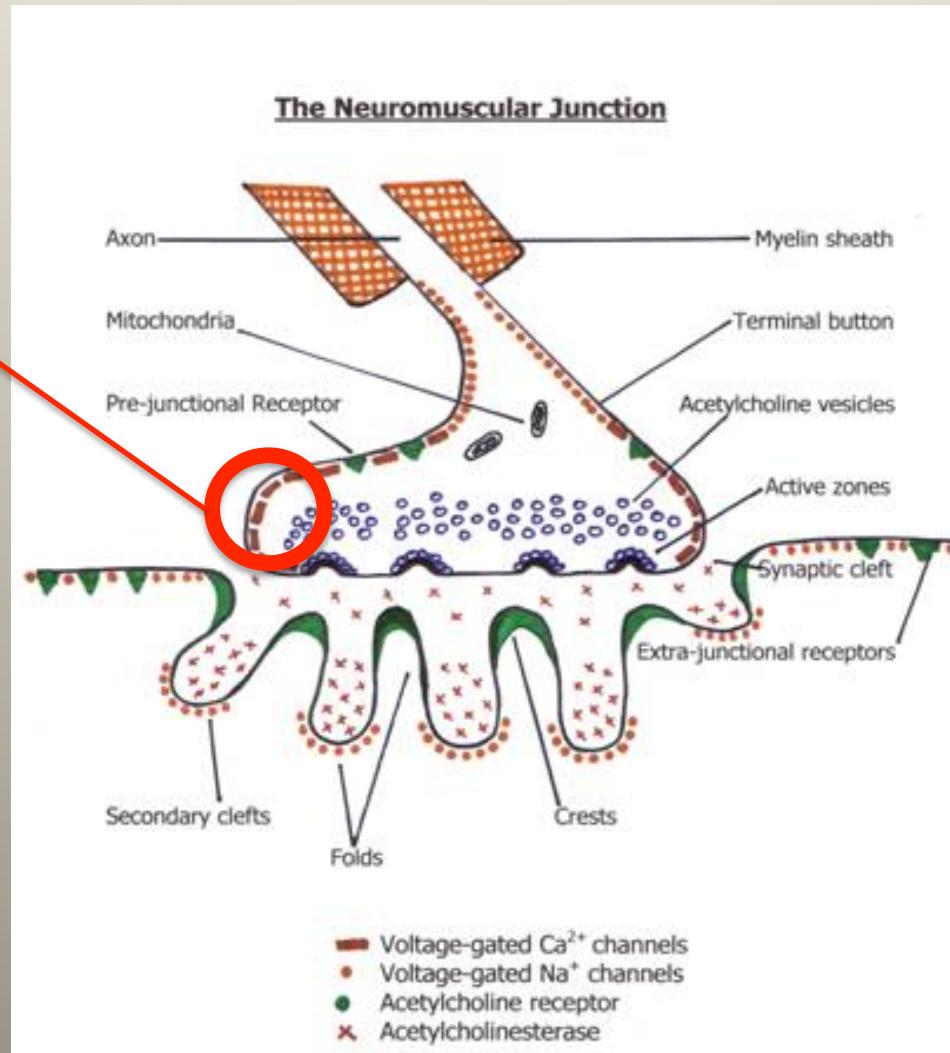
What's going on here?



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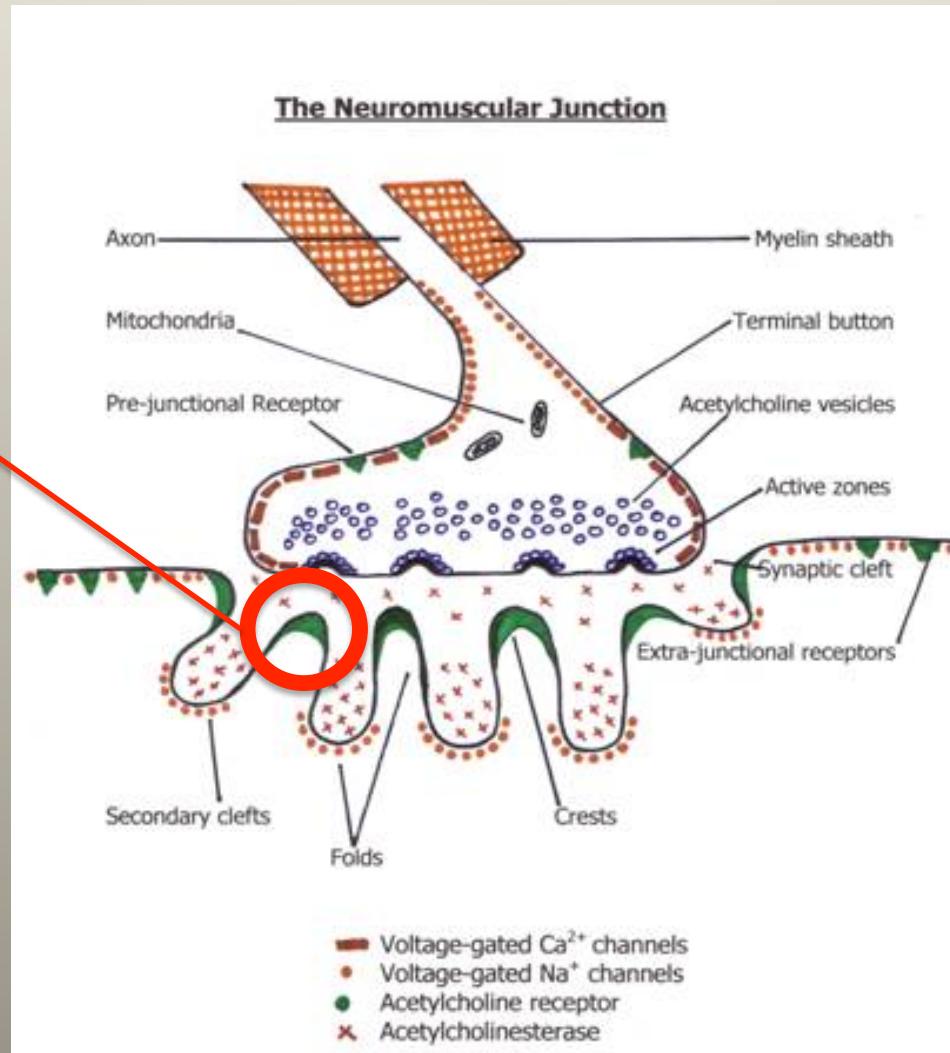
Many Opportunities for Disease

Lambert-Eaton
Syndrome



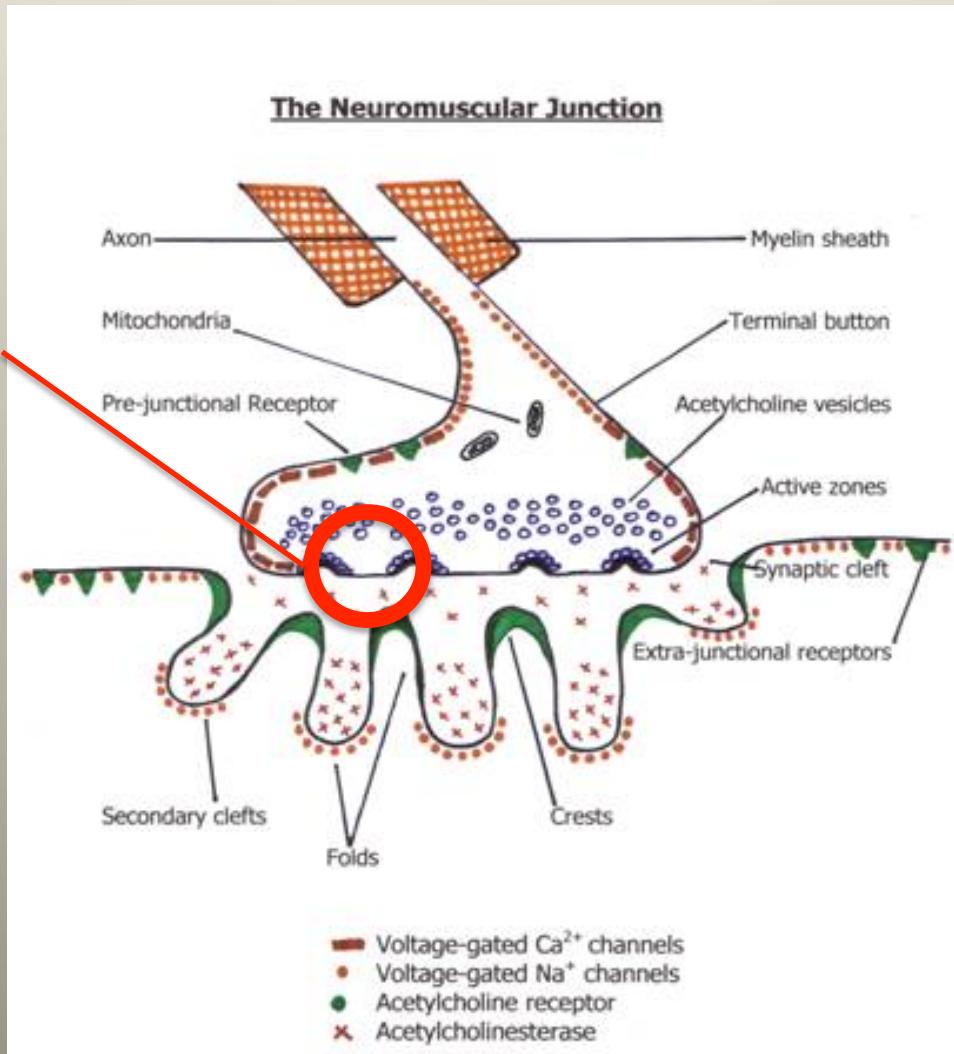
Many opportunities for disease

Myasthenia
Gravis

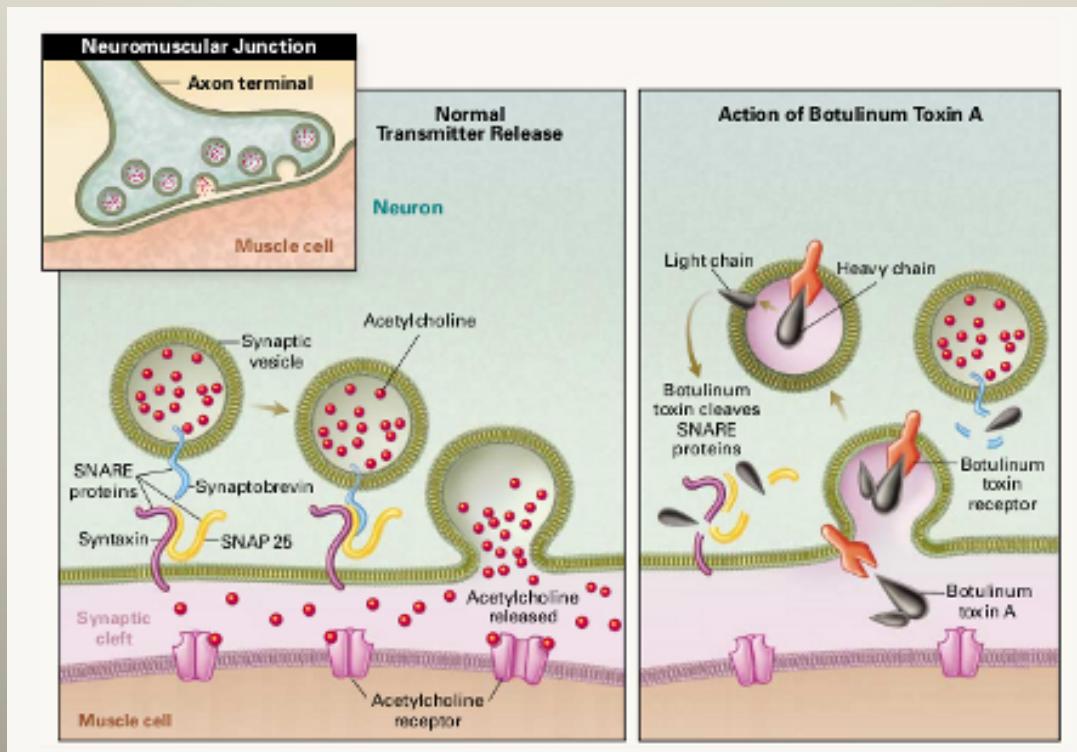


Many Opportunities for Disease

Botulism Toxin



Botulism Toxin Prevents Vesicle Docking



Rowland (2002) N. Engl. J. Med.

Botulism Toxin Prevents Vesicle Docking



Kornberg (2001) JAMA

Summary of NMJ Disorders

Pre-synaptic: Nerve

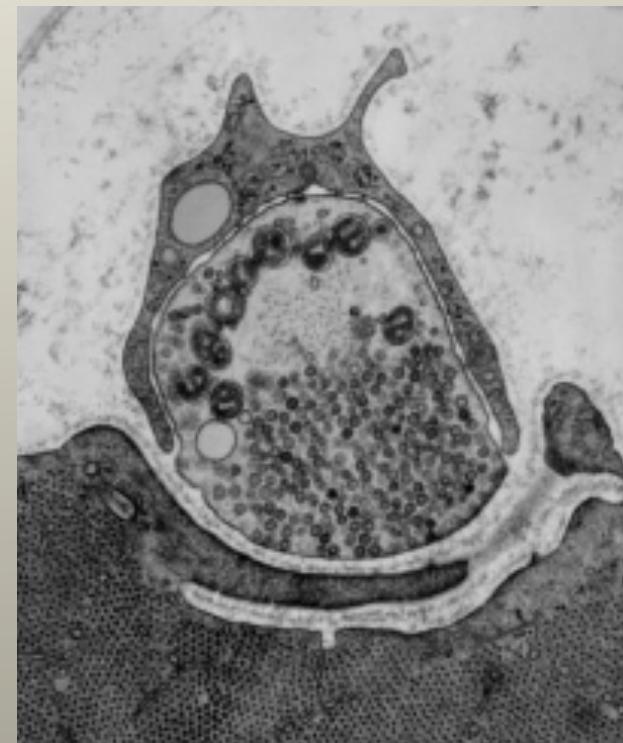
- Lambert Eaton
- Botulism
- Congenital MG

Synaptic

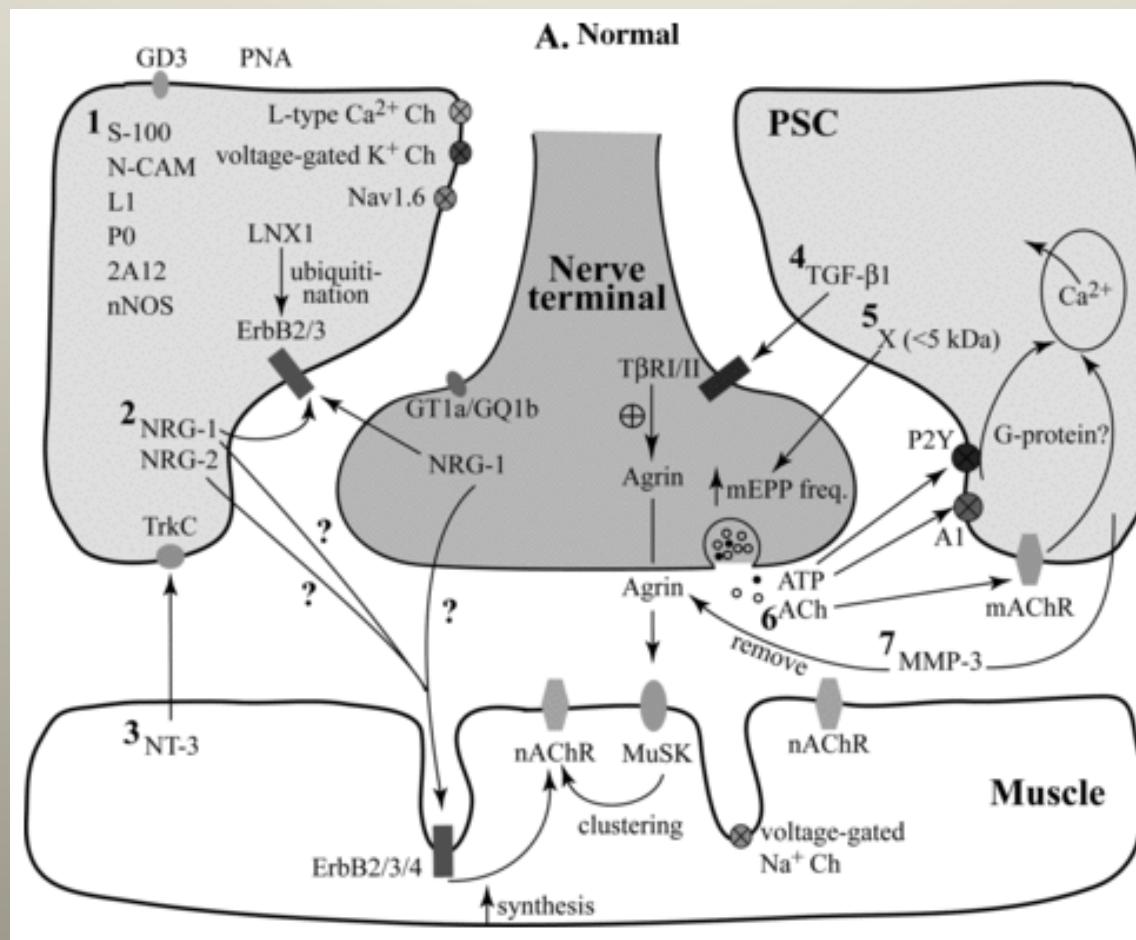
- Congenital MG
(Endplate acetylcholinesterase deficiency)
- Excess anti-acetylcholinesterase medications

Post-synaptic: Muscle

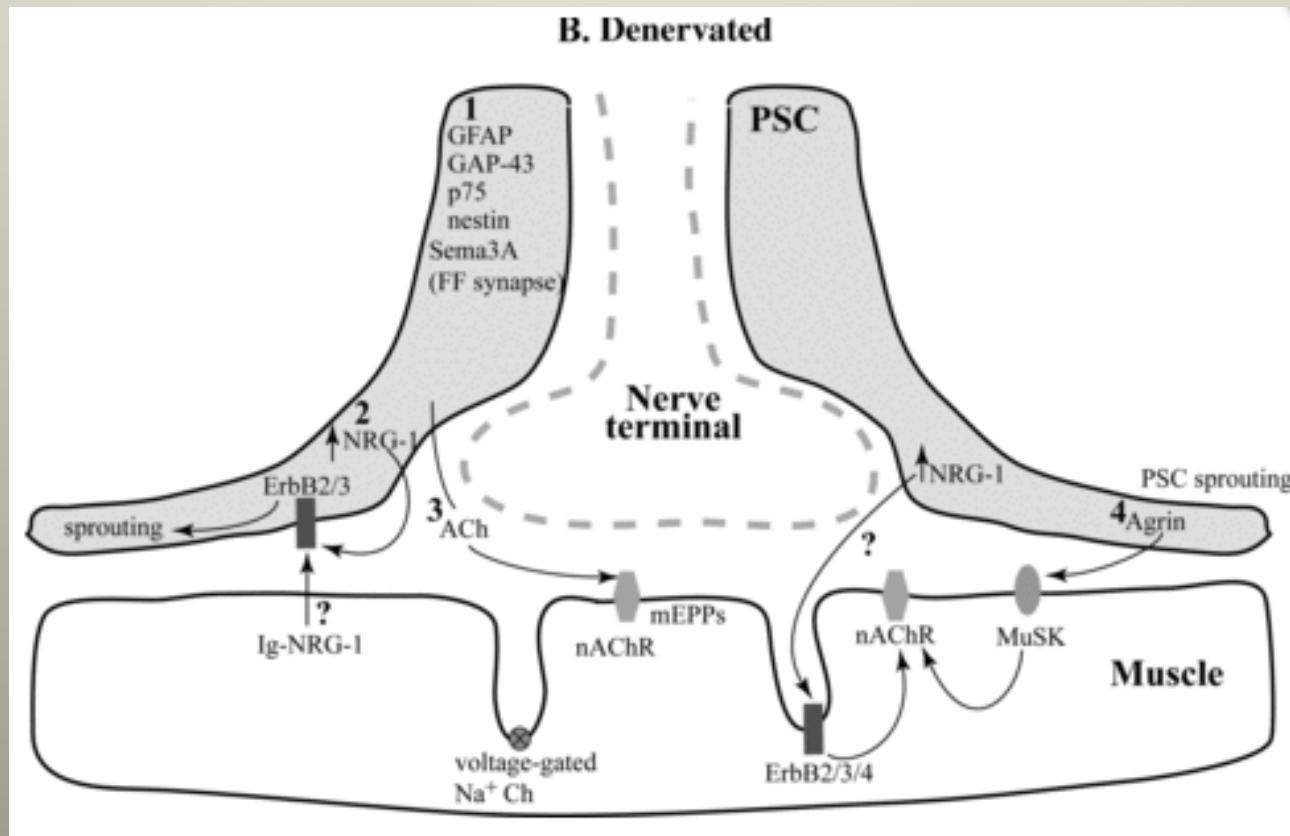
- Myasthenia gravis
- Congenital MG



Presynaptic Schwann Cell Interactions



Presynaptic Schwann Cell Interactions





Dr. Thomas Caceci, Virginia Tech

Structure of the Neuromuscular Junction

Introduction to physiology

April 19th, 2012

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Department of Neurology

Department of Molecular & Cellular Biochemistry

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Wexner
Medical
Center