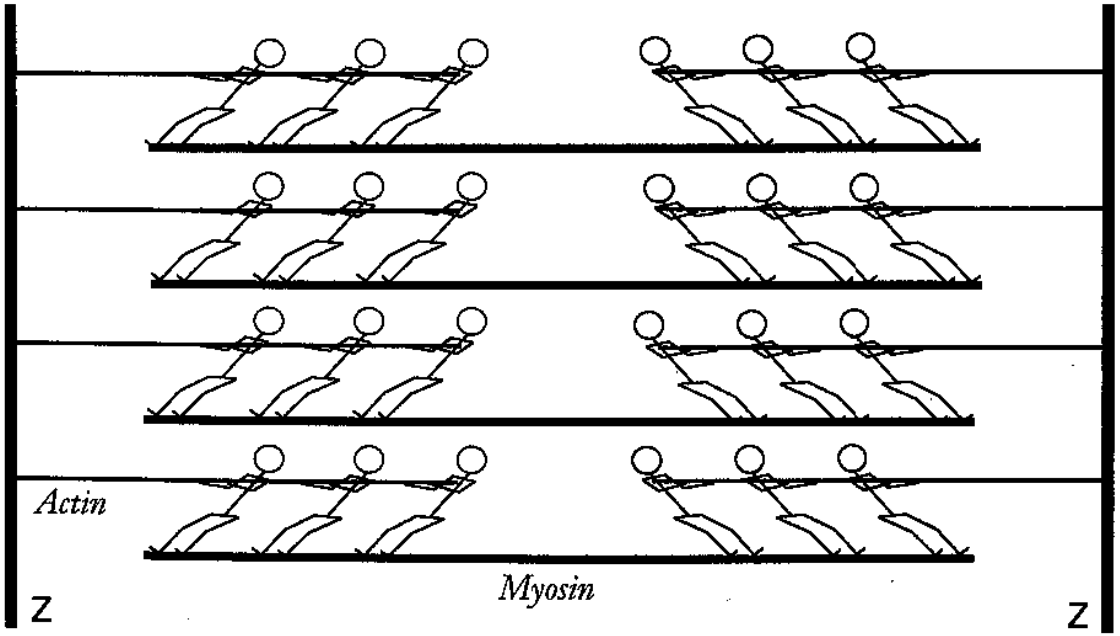
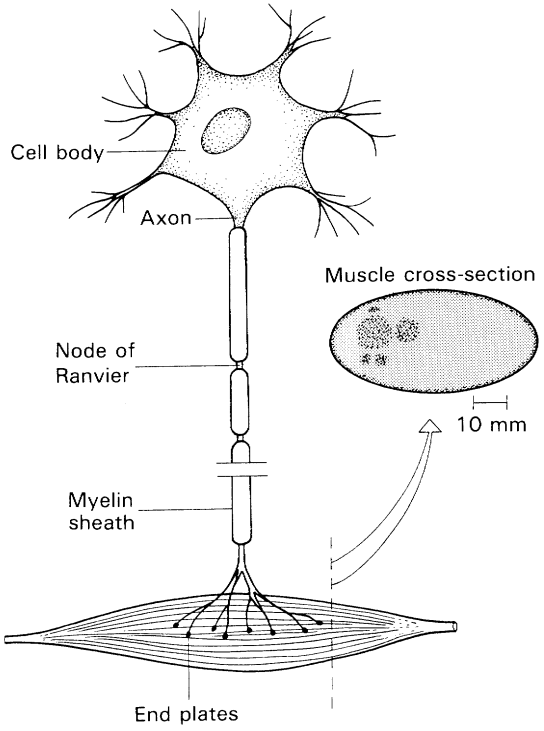
Skeletal muscle physiology



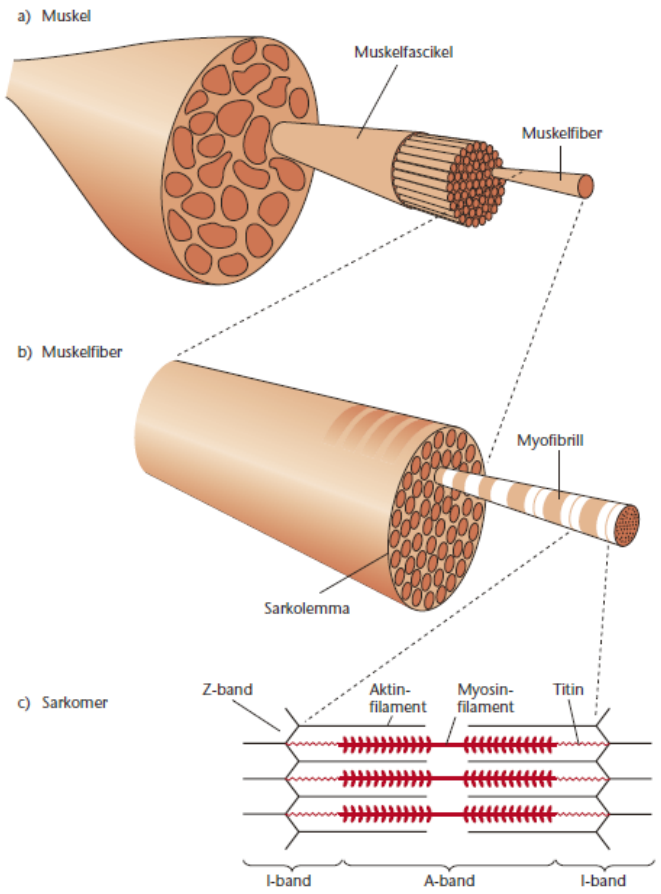
Block 2
Nervcellsfysiologi
Eric Hanse

Motor unit

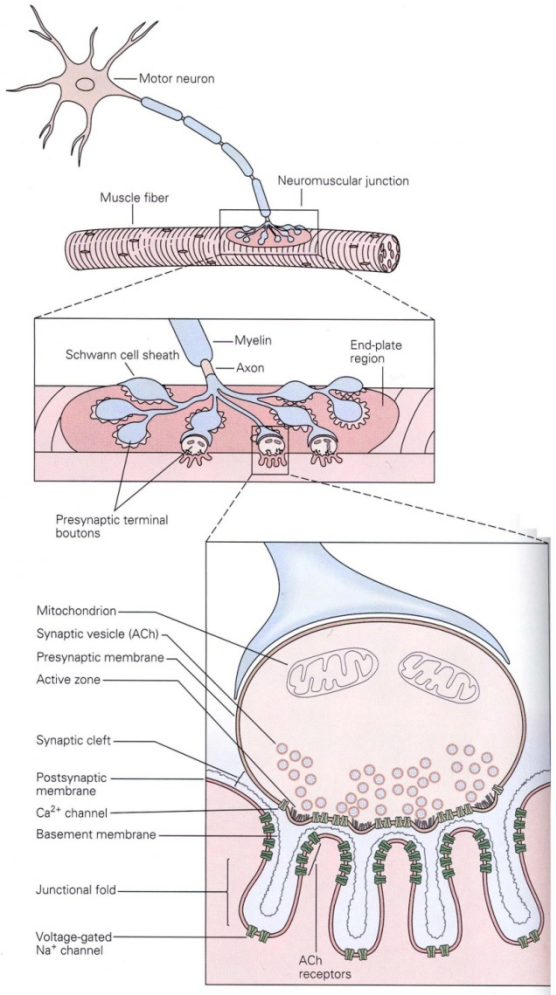
The α-motorneuron and the muscle fibrers innervated by the α-motorneuron



The skeletal muscle consists of sarcomeres in series and in parallel



The neuromuscular junction



A very large synapse consisting of several hundreds of release sites

High ”safety” – produces a suprathreshold postsynaptic potential

AchE hydrolyses most of the Ach within 1 ms

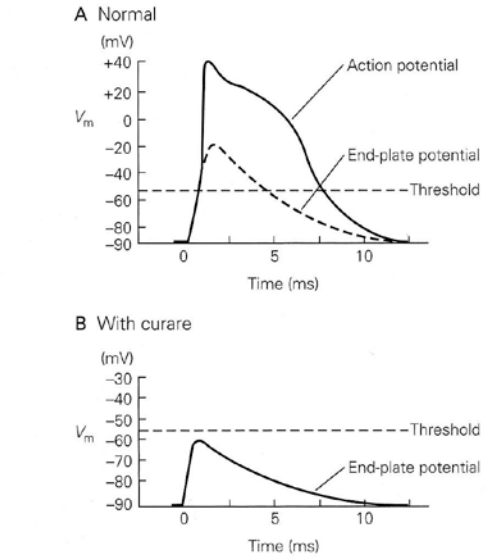


Figure 11-4 The end-plate potential can be isolated pharmacologically for study.

Pharmacological aspects

- **Postsynaptic**

AchR antagonists Curare (Eg. Tubocurarine, pancuronium, vecuronium, atracurium)

Myasthenia Gravis (antibodies against nAChR, α1-subunit)

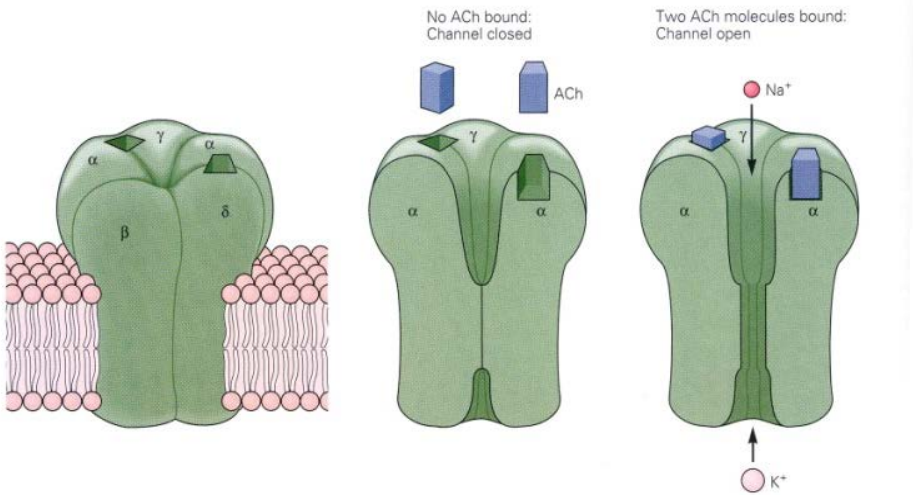
AchR agonists

Desensitisation of AChR (Eg. Suxamethonium)

AchE-inhibitors

Reversible (eg. neostigmine och physostigmine)
- Treatment of av mysthenia gravis

Irreversible –"nerve gases" (eg. sarin, Dyflos, ecothiopate, parathion)



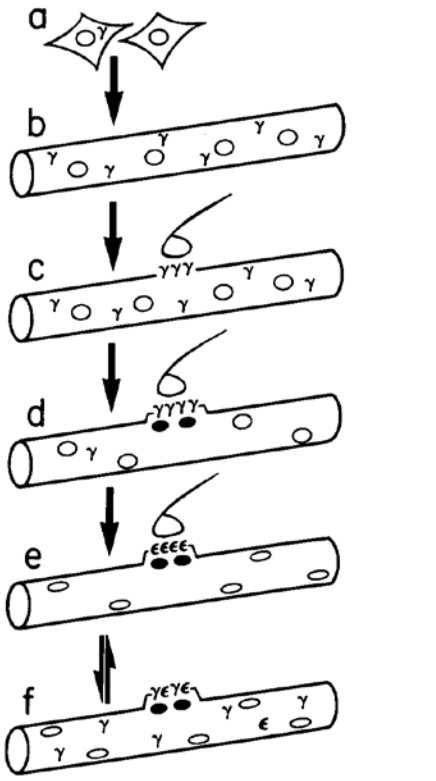
- **Presynaptic**

Inhibition of choline transport (Ex. hemicholinium)

Lambert-Eatons syndrome (antibodies against presynaptic voltage-gated calcium channels)

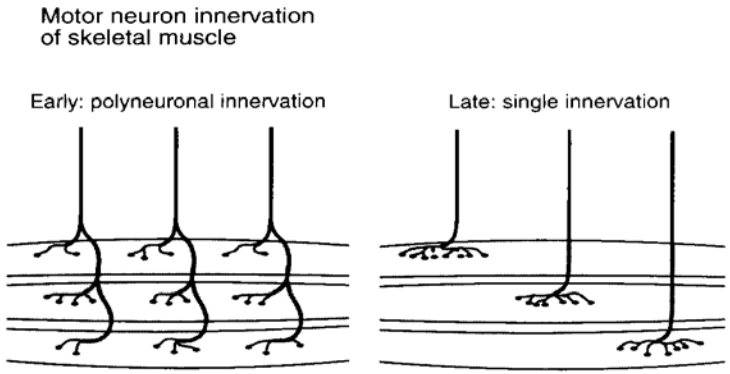
Botulinus toxin – proteolysis of SNARE proteins

Developmental aspects



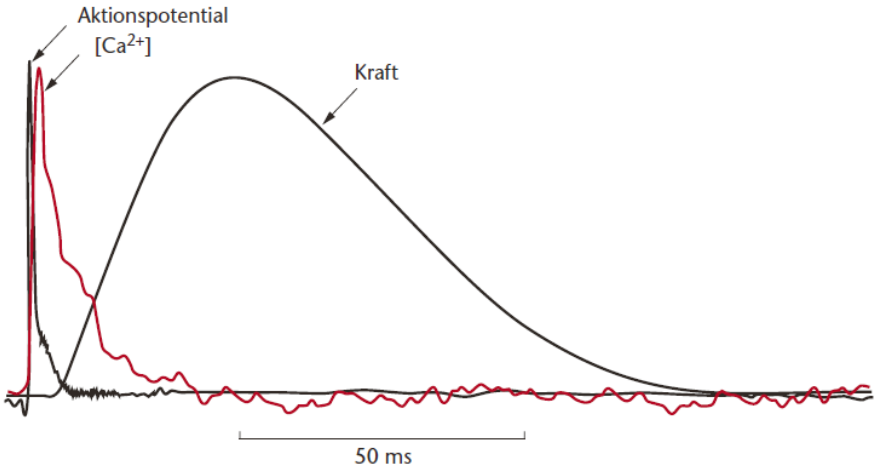
Distribution of AChRs in Developing and Denervated Muscle

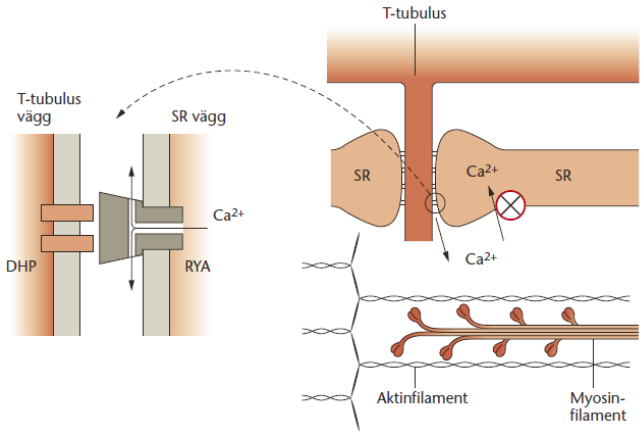
Innervation promotes clustering of AChR and switch of subunits
-reversible upon denervation



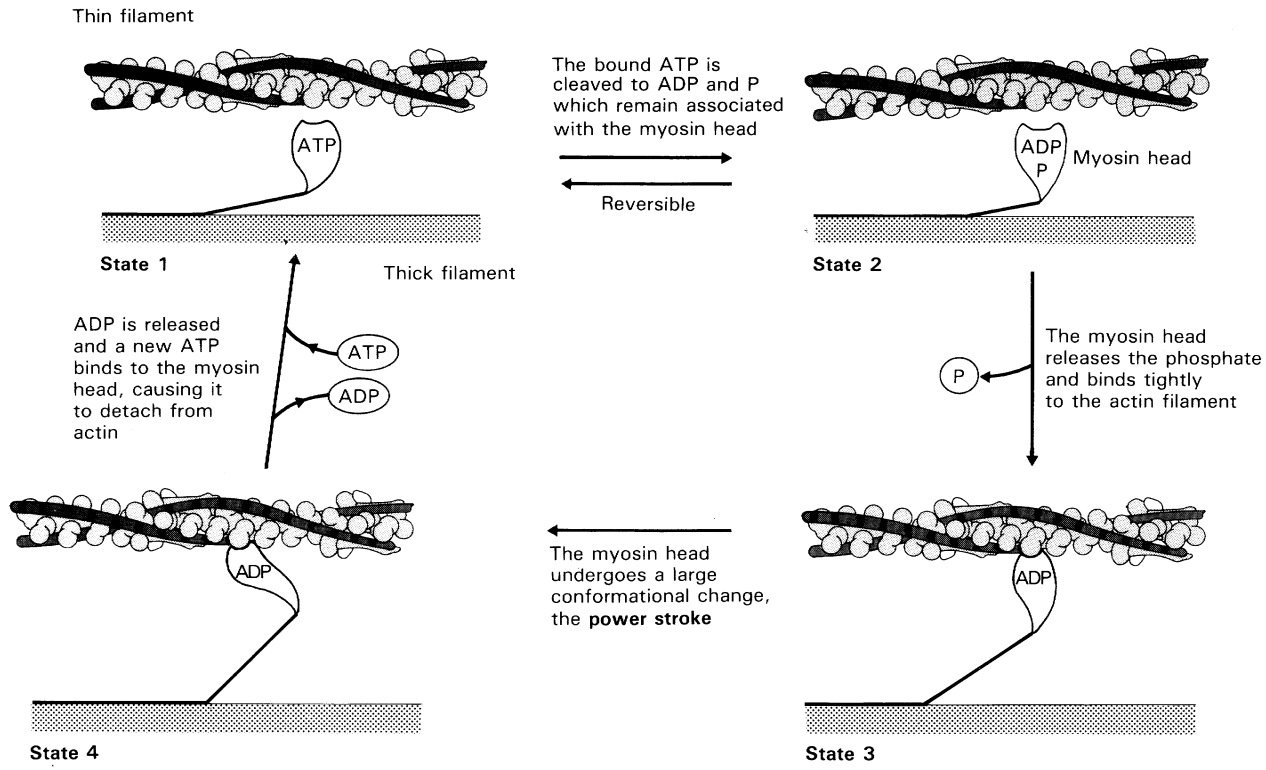
Polyneuronal innervation initially

Calcium, from the sarcoplasmatic reticulum, is necessary for myosin binding to actin



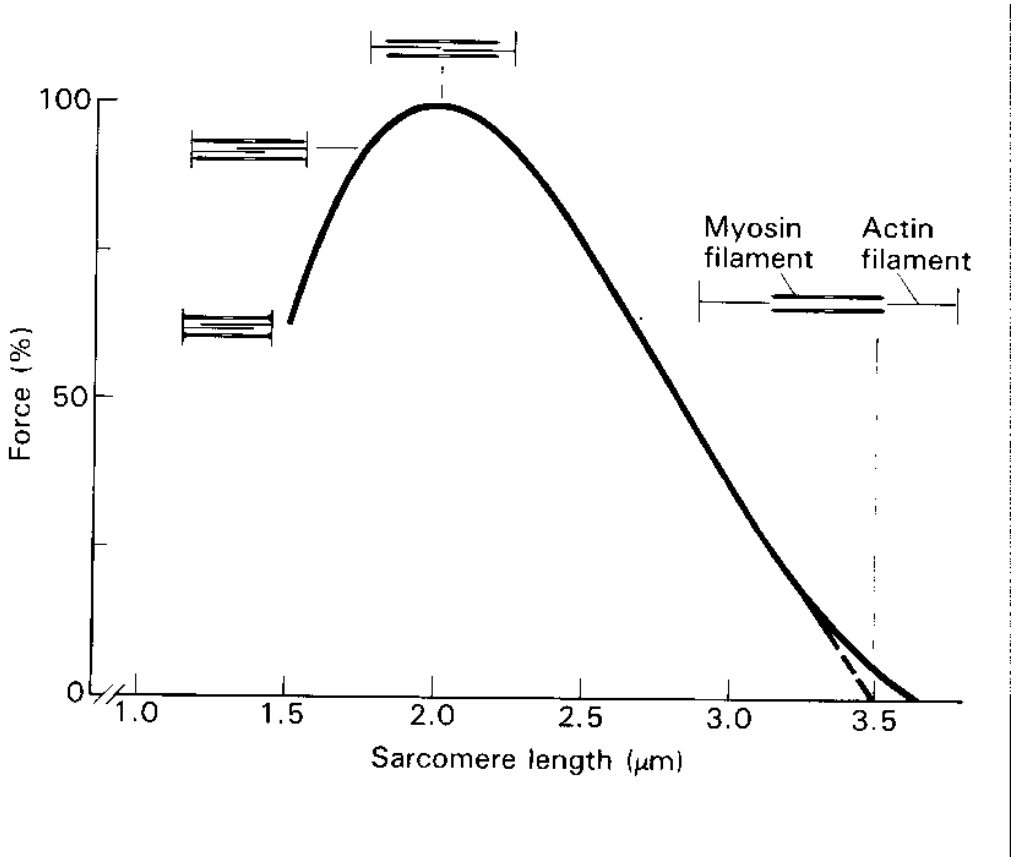


ATP transfer energy to myosin, and decreases the affinity between myosin and actin

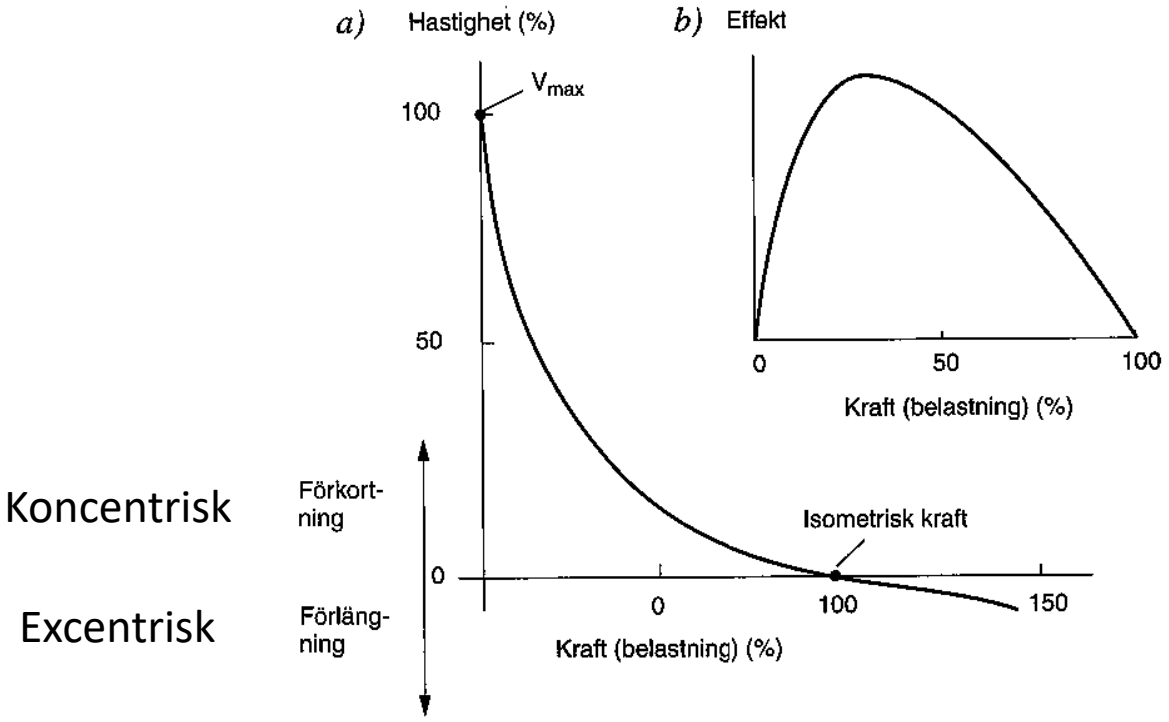


The contraction force is proportionell to the number of parallel actin-myosin bindings at any given moment

The muscle is strongest at an optimal length

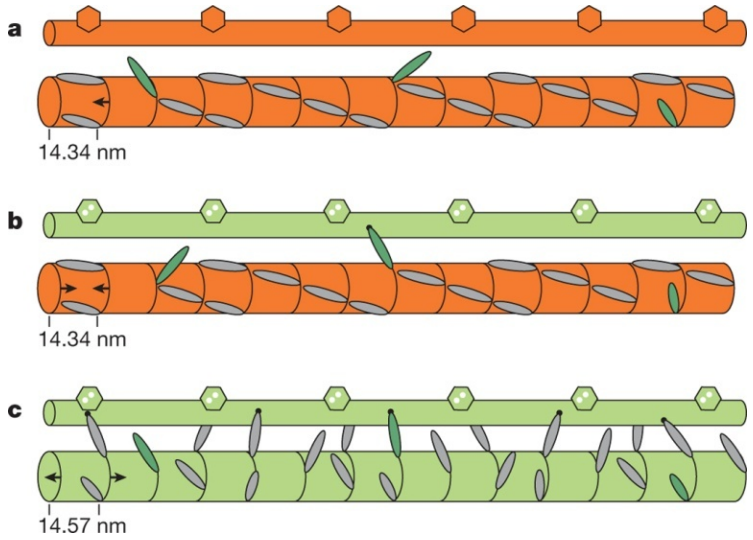


The higher contraction velocity, the lower force



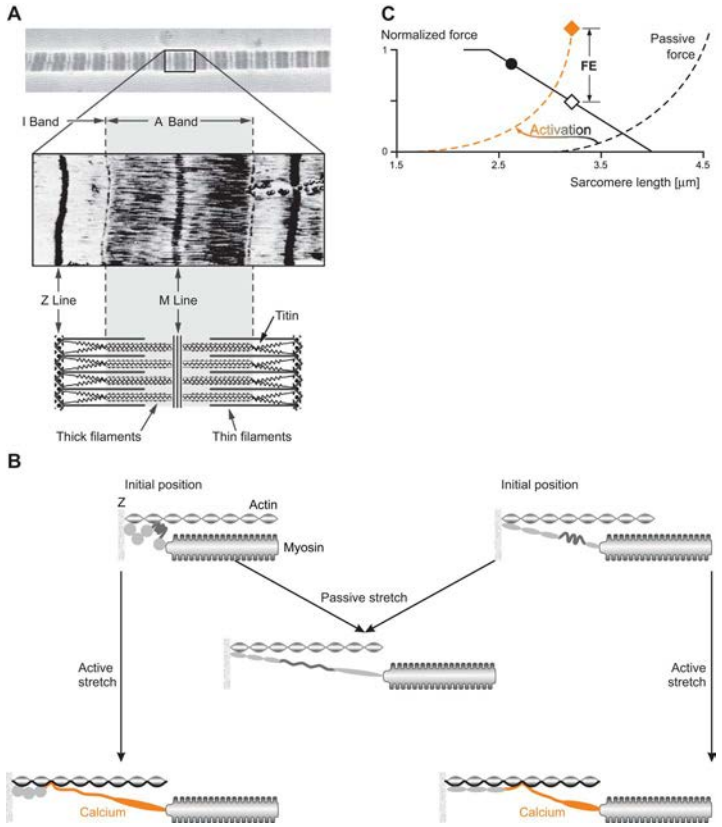
Figur 6.14 a) Förhållandet mellan kraft och hastighet. När hastigheten = 0 råder isometriska förhållanden. Maximal förkortningshastighet (V_{max}) ses när kraften (belastningen) = 0. Störst kraftutveckling ses när muskeln förlängs (excentrisk kontraktion). b) Effektutveckling (kraft × hastighet) hos en muskel är maximal vid 30–40% av den maximala isometriska kraften.

Higher tension recruits more myosin filaments



M Linari *et al. Nature 528:*276 10 DEC 2015

Calcium makes the titin stiffer



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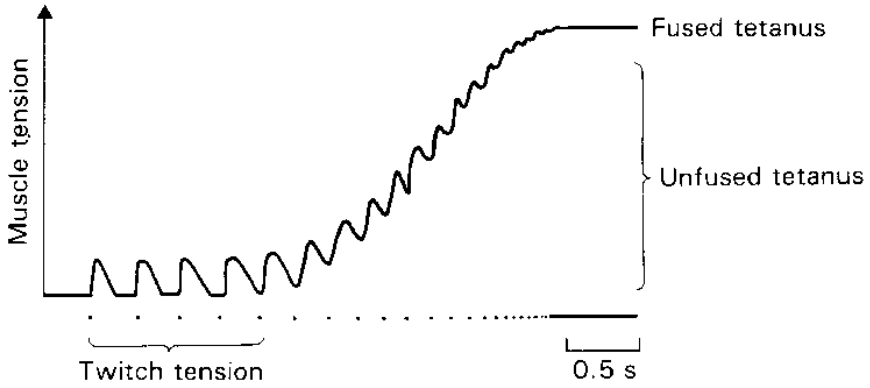
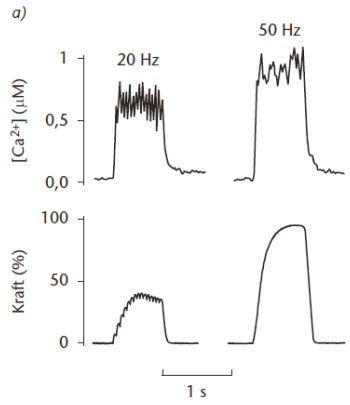
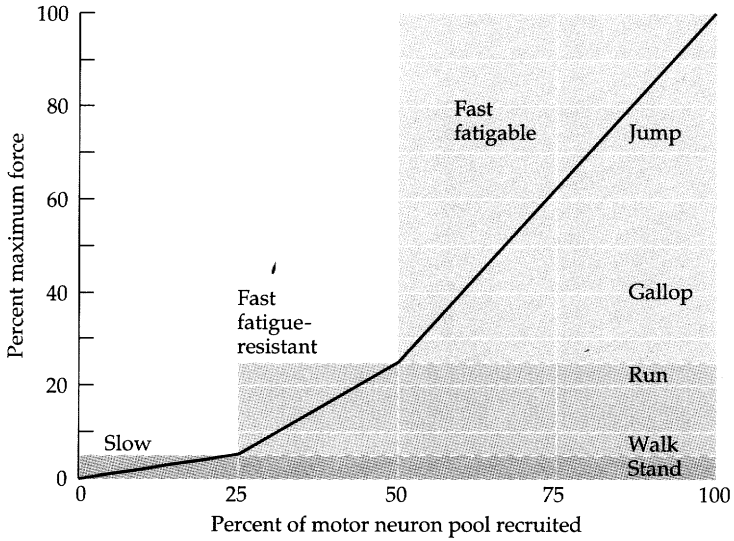
The nervous system regulates contraction force by summation and recruitment





Summation

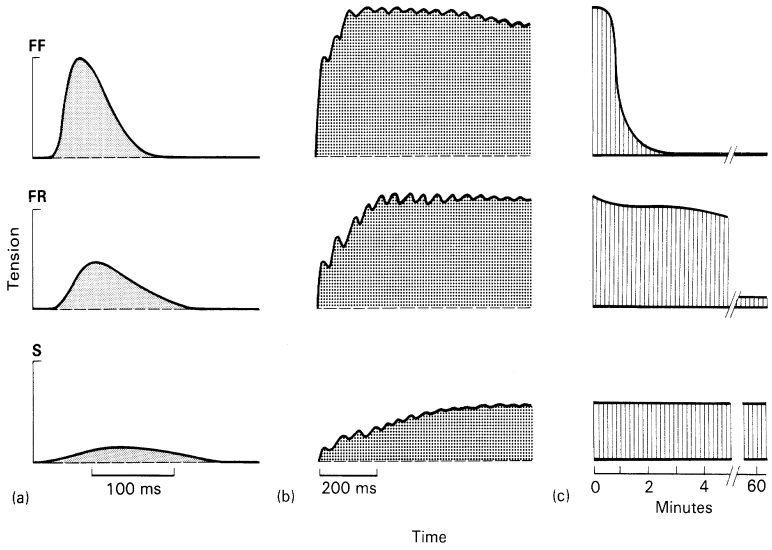
-summates contractions mainly because of higher calcium concentrations in response to higher frequencies of action potentials



Recruitment

of motor units according to a pre-determined order, type I (S) first

Different motor units



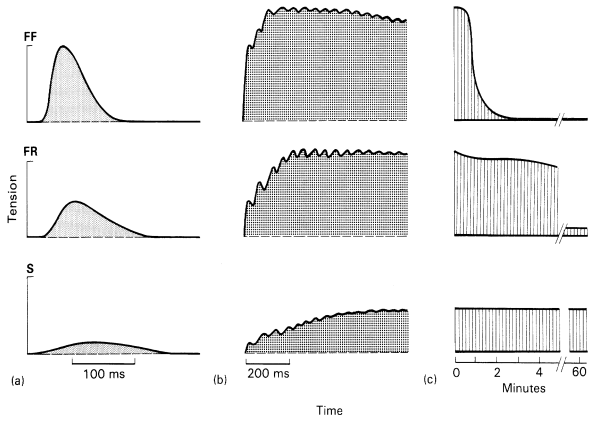
Tabell 6.1

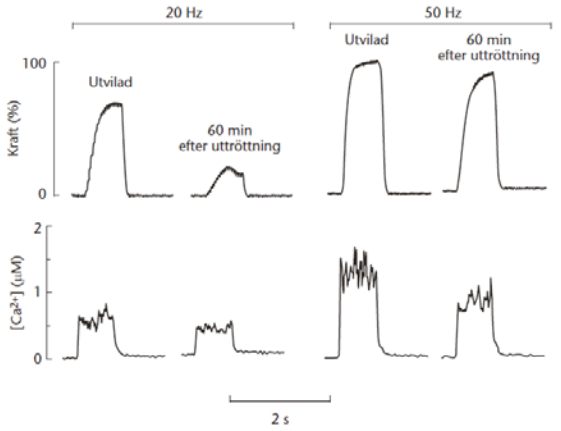
Histokemisk indelning:	IIX/IIB	IIA	I
myofibrillär ATP-nedbrytning	+++	++	+
mitokondriehalt, halt av oxidativa enzymer	+	++	+++
halt av glykolytiska enzymer	+++	+++	+
ungefärlig andel hos människa (totalt sett; varierar något mellan olika muskler)	20%	30%	50%
Motsvarande funktionell indelning	FF (fast fatiguing)	FR (fast, fatigue resistant)	S (slow)
kontraktionstid (twitch)	snabb (20–50 ms)	snabb (20–50 ms)	långsam (100 ms)
tröttas	lätt	relativt uthålliga	mycket uthålliga
α-motorneuron	stora	mindre	minst
aktiveringströskel	hög	lägre	lägst
motoriska enheter	stora	mindre	minst
användning	snabba rörelser, stor kraft	ngt långsammare rörelser, mindre kraft, långvarigt arbete	långsamma rörelser, minst kraft, tonus

Fatigue

Central and peripheral fatigue

Peripheral fatigue
1) Reduced force
2) Slower shortening velocity
3) Slower relaxation





Muscle growth