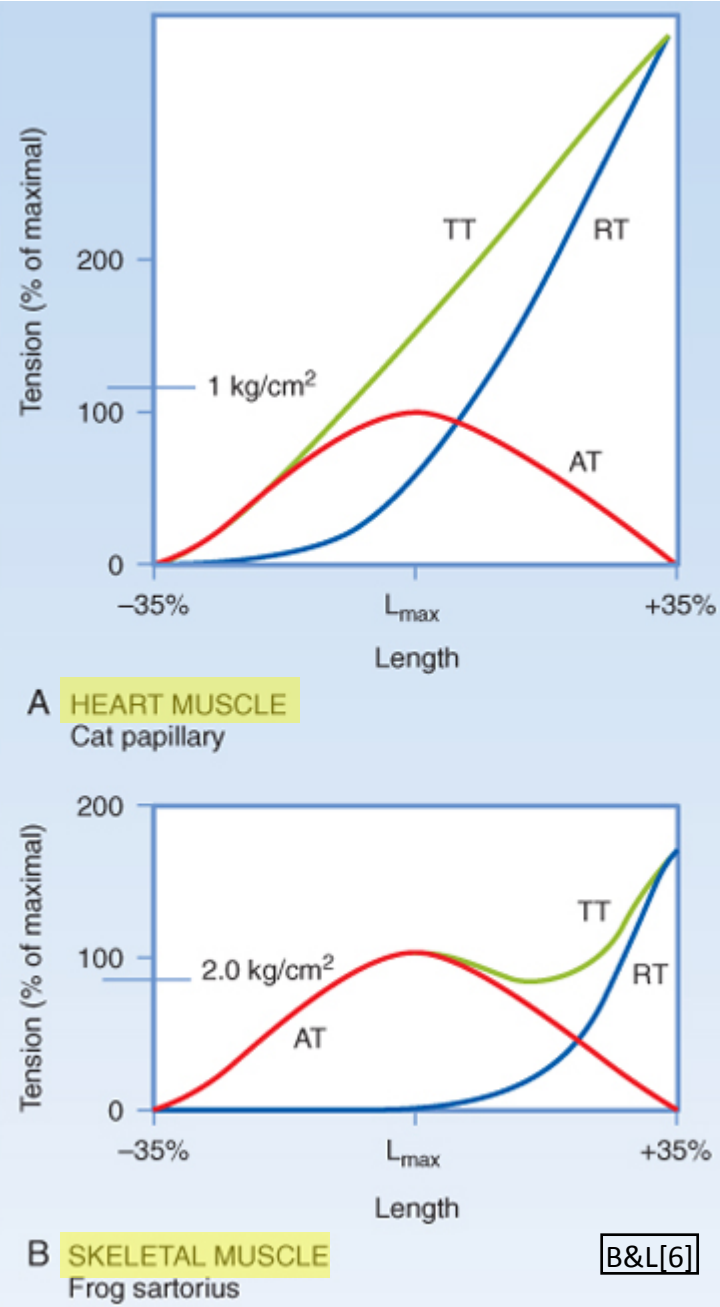


Figure 13-2 Cardiac muscle (panel A) has high resistance to stretch when compared with skeletal muscle (panel B). When either cardiac or skeletal muscle is stretched, there is an increase in resting tension (RT). If the muscle is then stimulated to contract maximally, it generates more tension (termed total tension-TT). The difference between total tension and resting tension at any given length is the force produced by contraction (e.g., active tension-AT). The bell-shaped dependence of active tension on muscle length is consistent with the sliding filament theory of cardiac and skeletal muscle. It is, however, difficult to stretch cardiac muscle beyond its optimal sarcomere length, as evidenced by the rapid rise in resting tension in the middle of the bell-shaped AT curve.

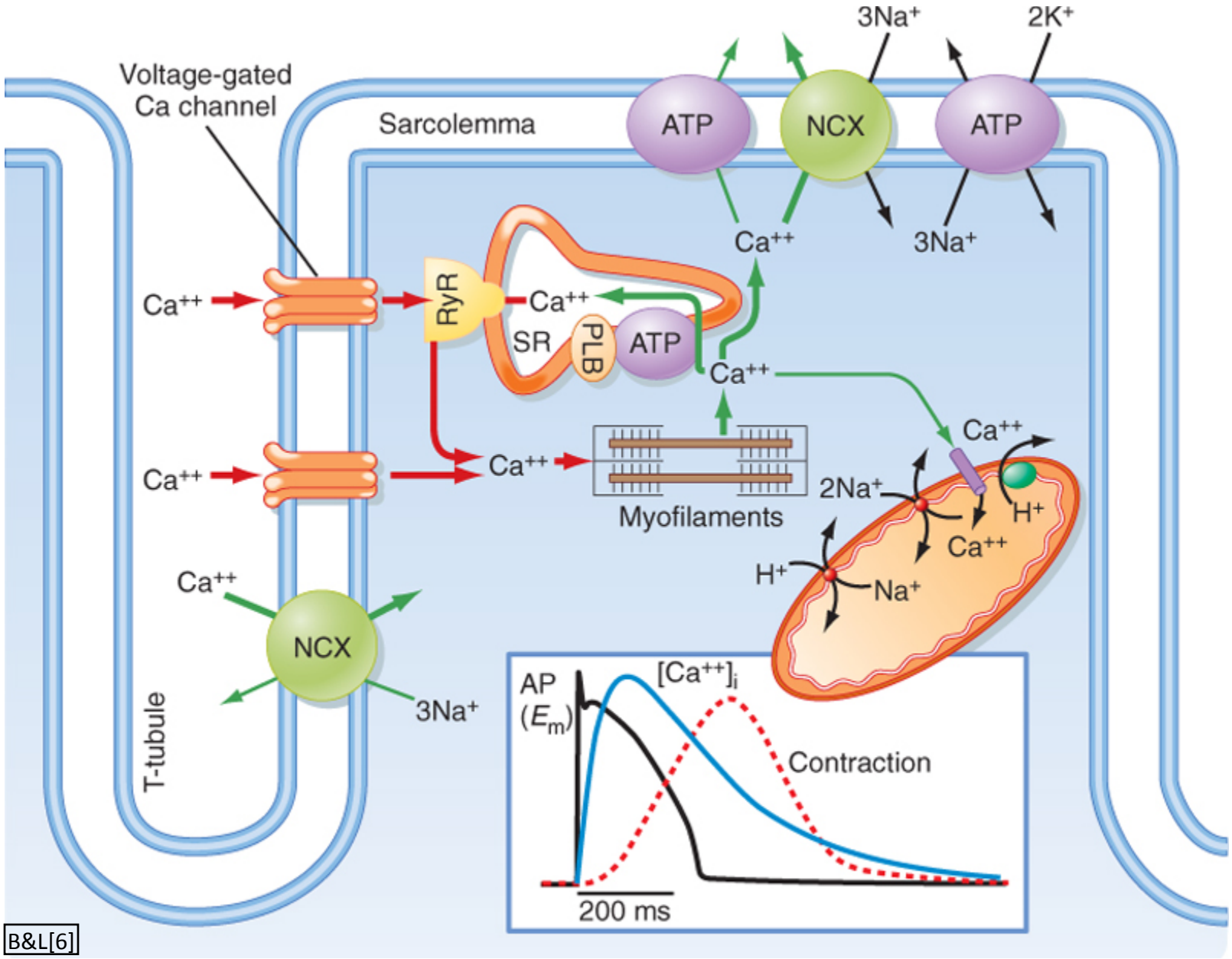


Figure 13-3 Excitation-contraction coupling in the heart requires Ca^{++} influx through L-type Ca^{++} channels in the sarcolemma and T tubules. See text for details. (Redrawn from Bers DM: Nature 415:198-205, 2002.)

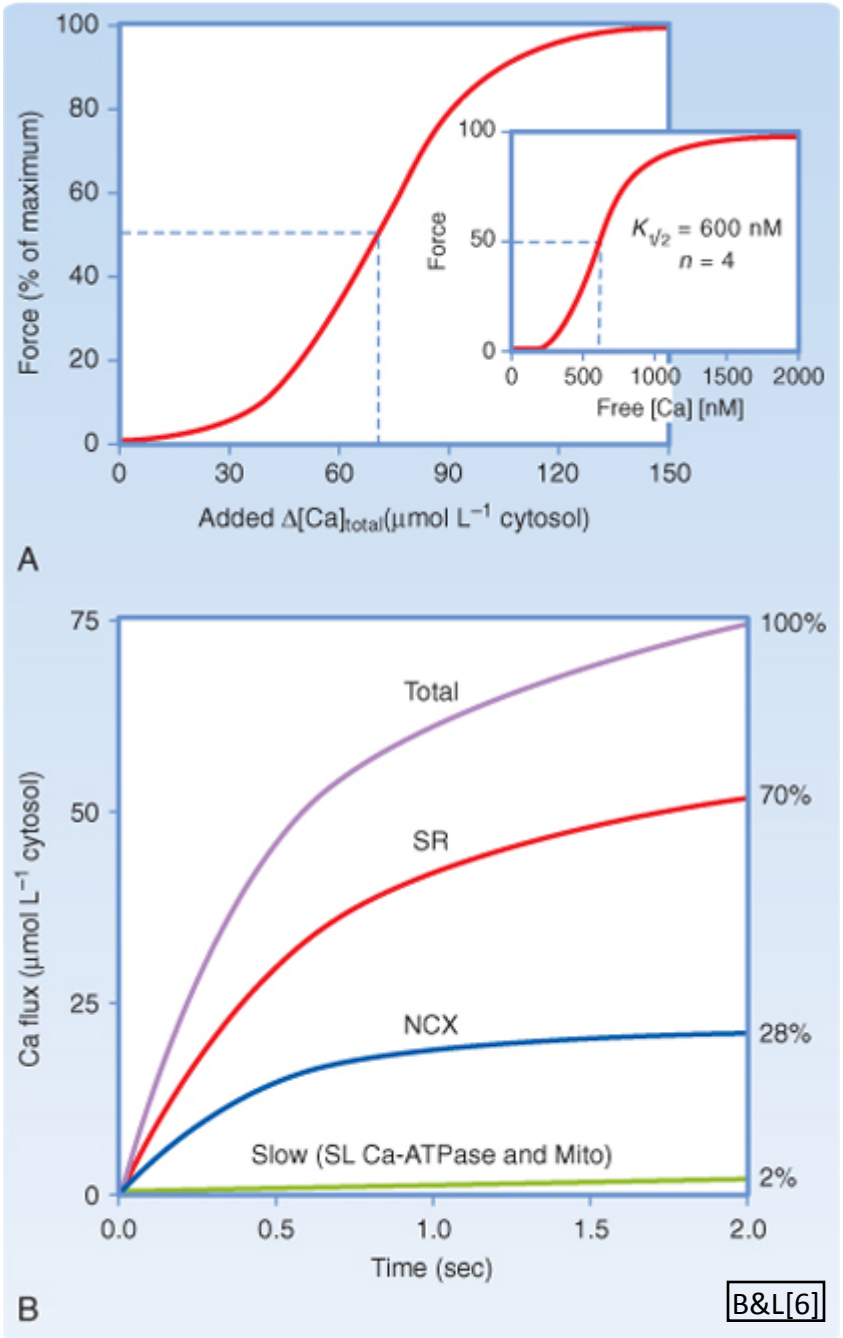
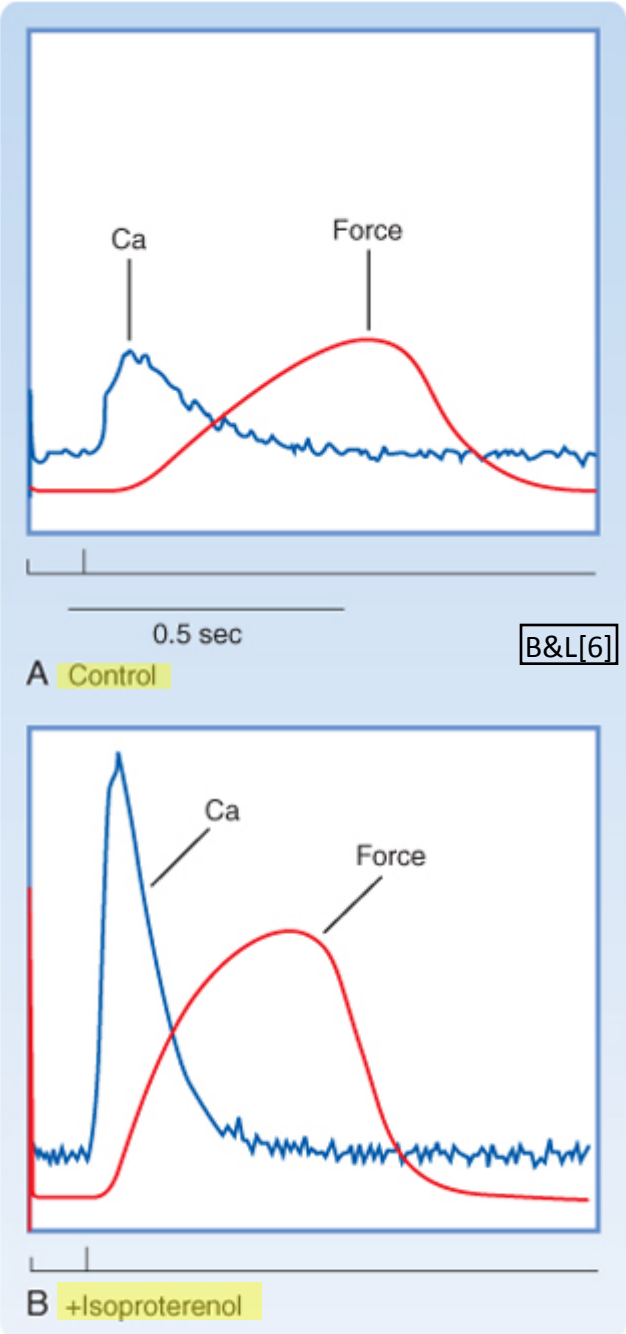


Figure 13-4 Half-maximal force of contraction of cardiac muscles requires a rise in cytosolic free [Ca^{++}] to approximately 600 nM (inset to panel A). Because of the high Ca^{++} buffering capacity of cytosolic proteins (such as parvalbumin and troponin C), this rise in free Ca^{++} requires an increase in total cytosolic [Ca^{++}] of about 70 µM (panel A). Relaxation of the heart occurs by reducing cytosolic free [Ca^{++}], with Ca^{++} sequestration by the SR accounting for the majority of the decrease in cytosolic [Ca^{++}] (≈70%; panel B). Some Ca^{++} extrusion occurs through the $3Na^{+}$-$1Ca^{++}$ antiporter (≈28%), with very little Ca^{++} extrusion by the sarcolemmal Ca^{++} pump (< 2%). NCX, sodium-calcium exchanger. (Redrawn from Bers DM: Nature 415:198-205, 2002.)



B&L[6]

Figure 13-5 Stimulation of β-adrenergic receptors in the heart increases the force of contraction. Electrical stimulation of myocardium results in a transient rise in intracellular [Ca^{++}] and production of force (A). Isoproterenol (a β-adrenergic receptor agonist) increases the amplitude of the intracellular Ca^{++} transient and hence the amount of force generated (B).

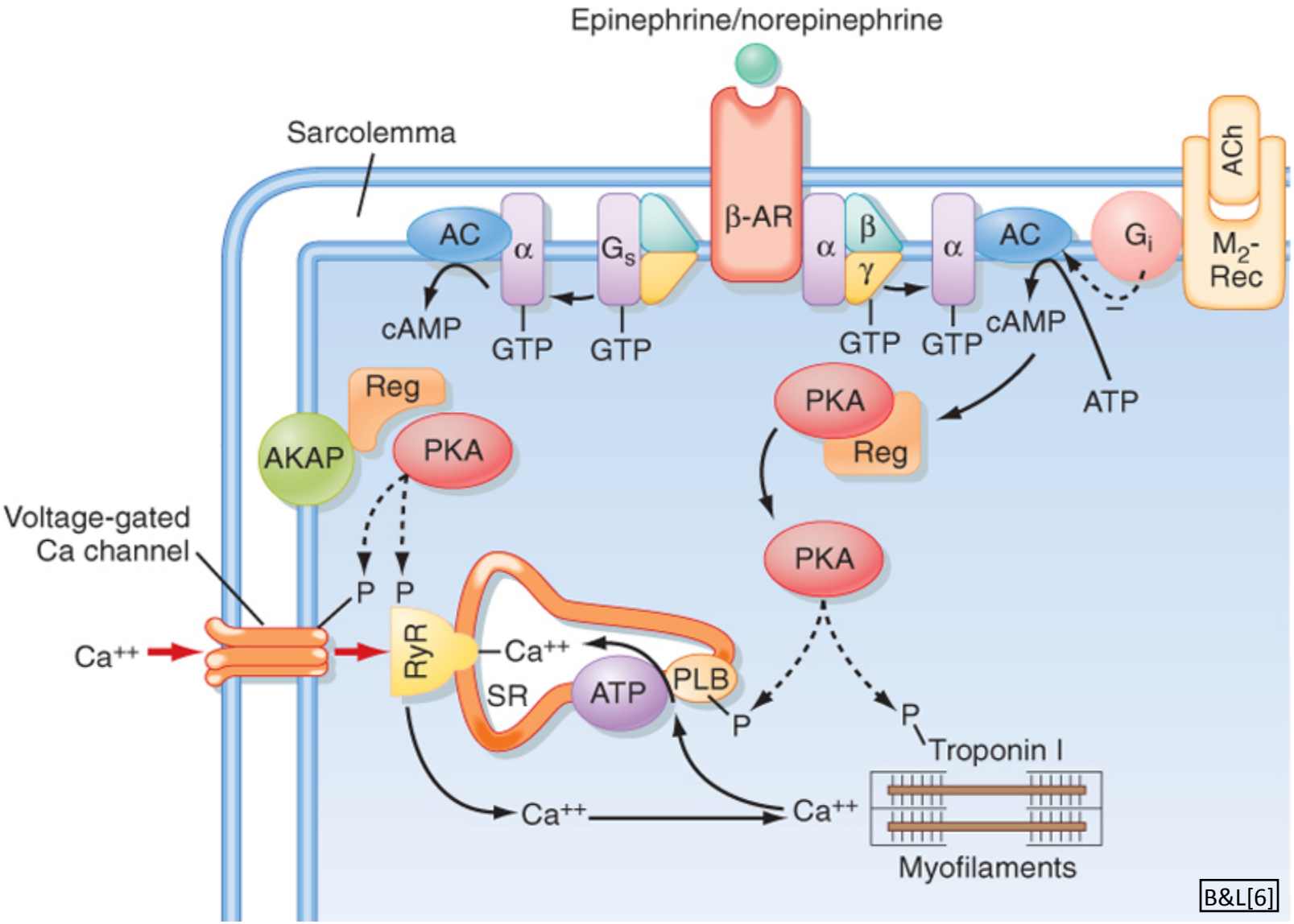


Figure 13-6 Sympathetic stimulation of the heart results in an increase in cytosolic cAMP and hence phosphorylation of several proteins by protein kinase A (PKA). An A kinase adapter protein (AKAP) adjacent to the L-type Ca^{++} channel facilitates phosphorylation of this channel and possibly nearby SR Ca^{++} channels (RyR). Other proteins phosphorylated by PKA include phospholamban (PLB) and troponin I. Muscarinic agonists (e.g., acetylcholine [ACh]), on the other hand, inhibit this sympathetic cascade by inhibiting the production of cAMP by adenylate cyclase (AC). β-AR, β-adrenergic receptor. (Redrawn from Bers DM: Nature 415:198, 2002.)

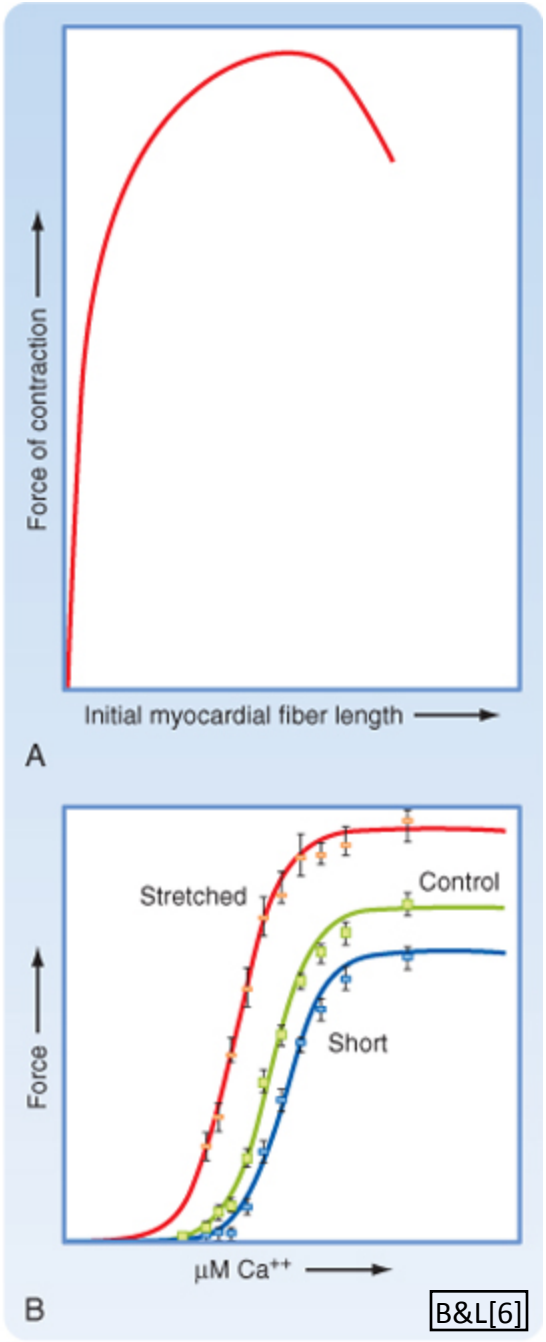


Figure 13-7 Stretching the heart increases the force of contraction (A). This is attributable to both an increase in the maximal force of contraction and an increase in the sensitivity of contraction to Ca^{++} (B) and reflects an intrinsic regulatory process referred to as the Frank-Starling law of the heart.

B&L[6]

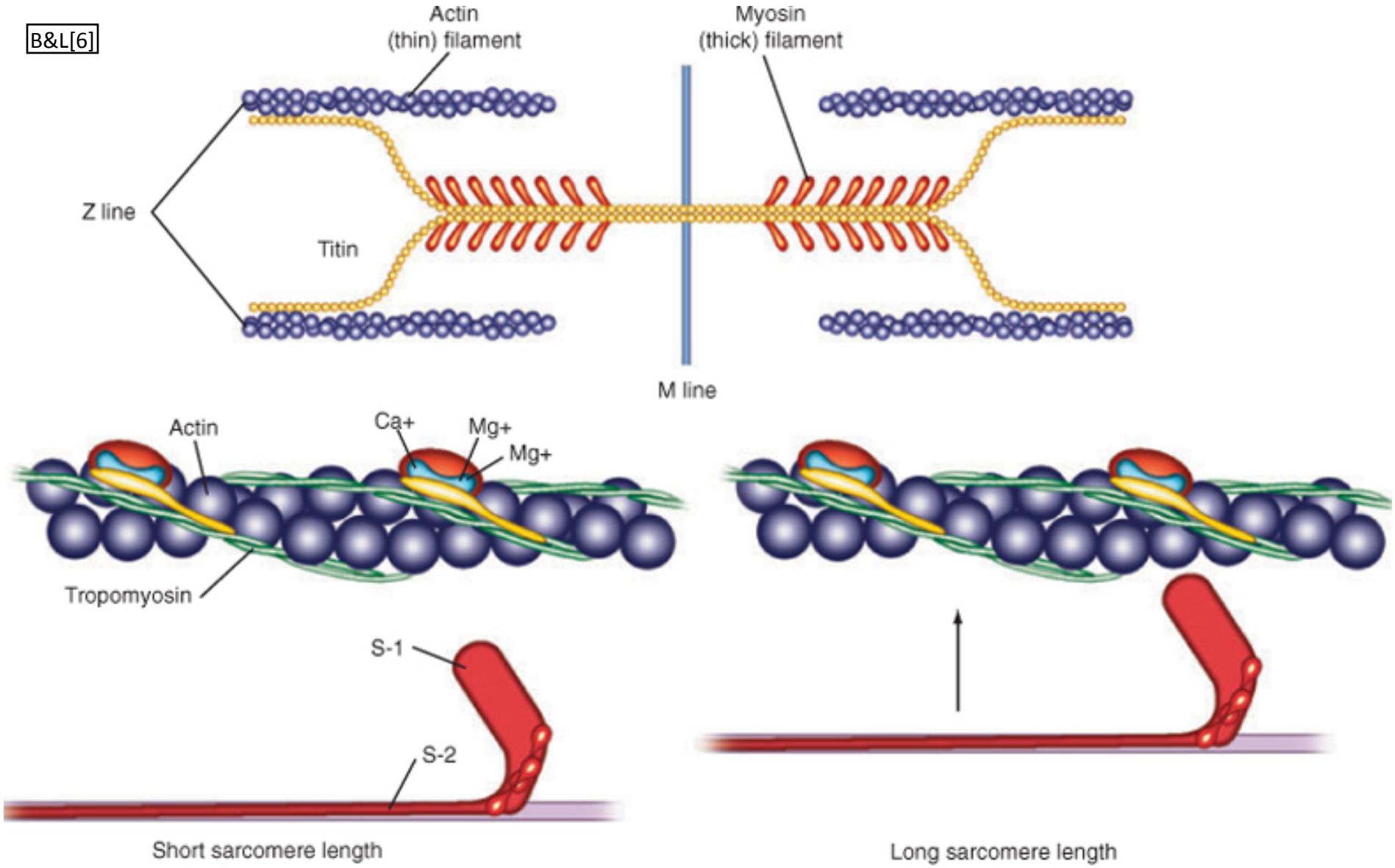


Figure 13-8 Titin may contribute to the ability of stretch to increase the force of contraction of the heart. Titin binds to both myosin and actin such that stretch of the cardiac muscle may bring the actin filament closer to the myosin head and thus increase the number of myosin heads that interact with actin at a given intracellular [Ca^{++}]. (Redrawn from Moss RL, Fitzsimons DP: Circ Res 90:11-13, 2002.)

END

Video 2, Module 5