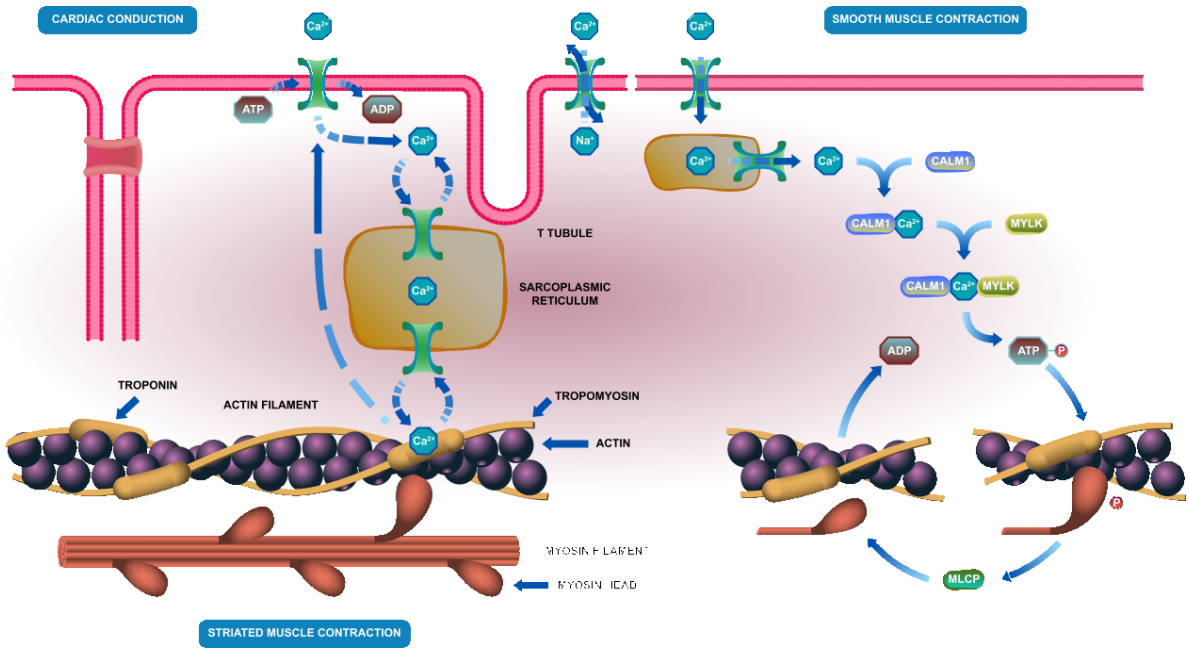
# Muscle contraction

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# Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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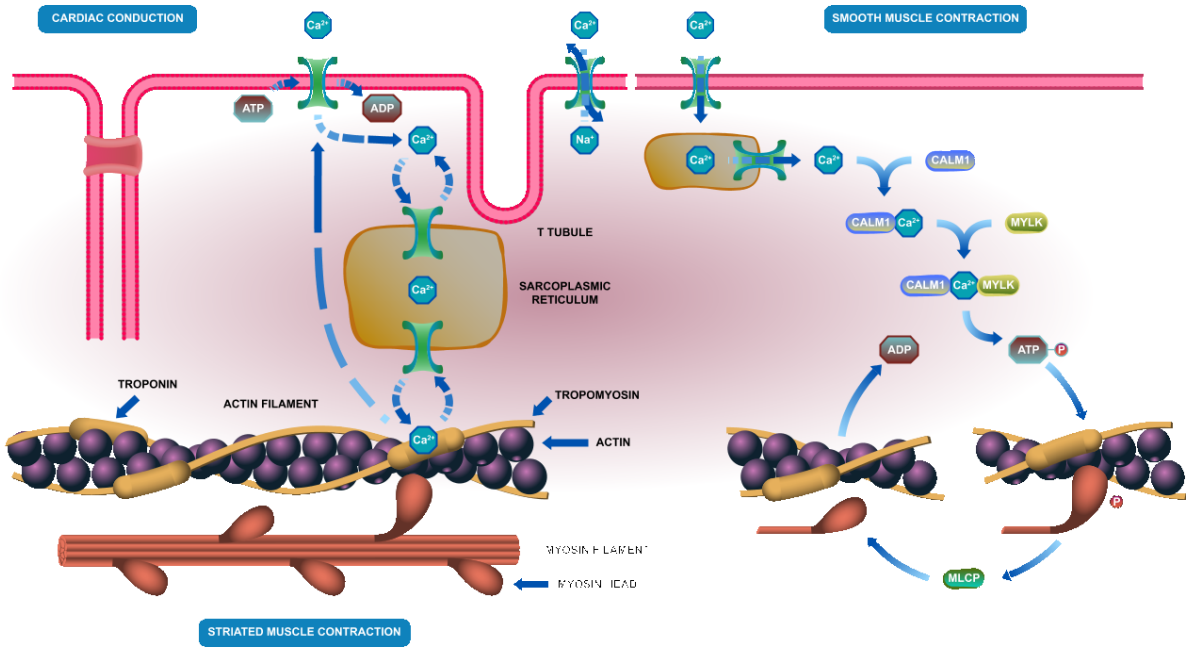
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

## Muscle contraction ↗

**Stable identifier:** R-HSA-397014

**Compartments:** cytosol, plasma membrane




In this module, the processes by which calcium binding triggers actin - myosin interactions and force generation in smooth and striated muscle tissues are annotated.

## Editions

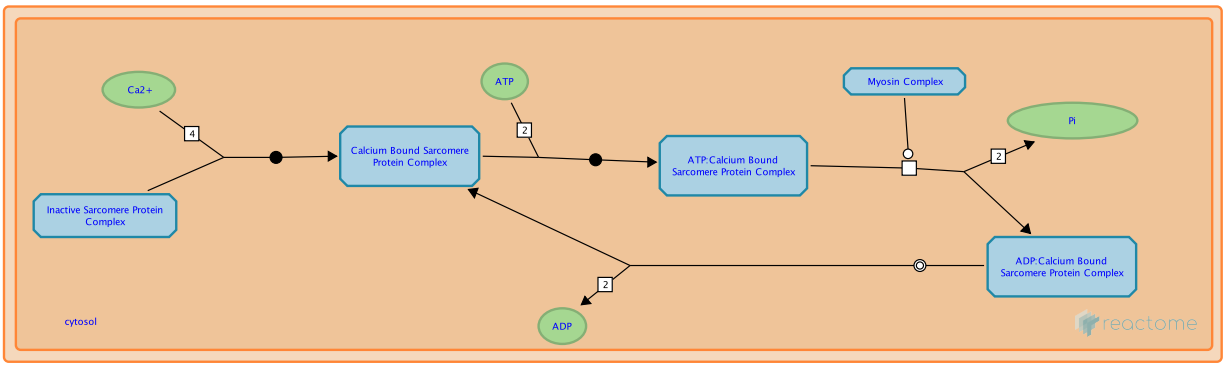
| | | |
|---|---|---|
| 2009-02-10 | Authored | Gillespie, ME. |
| 2009-03-11 | Edited | Gillespie, ME. |

## Striated Muscle Contraction ↗

**Location:** Muscle contraction

**Stable identifier:** R-HSA-390522

**Compartments:** cytosol




Striated muscle contraction is a process whereby force is generated within striated muscle tissue, resulting in a change in muscle geometry, or in short, increased force being exerted on the tendons. Force generation involves a chemo-mechanical energy conversion step that is carried out by the actin/myosin complex activity, which generates force through ATP hydrolysis. Striated muscle is a type of muscle composed of myofibrils, containing repeating units called sarcomeres, in which the contractile myofibrils are arranged in parallel to the axis of the cell, resulting in transverse or oblique striations observable at the level of the light microscope.

Here striated muscle contraction is represented on the basis of calcium binding to the troponin complex, which exposes the active sites of actin. Once the active sites of actin are exposed, the myosin complex bound to ADP can bind actin and the myosin head can pivot, pulling the thin actin and thick myosin filaments past one another. Once the myosin head pivots, ADP is ejected, a fresh ATP can be bound and the energy from the hydrolysis of ATP to ADP is channeled into kinetic energy by resetting the myosin head. With repeated rounds of this cycle the sarcomere containing the thin and thick filaments effectively shortens, forming the basis of muscle contraction.

## Literature references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## Editions

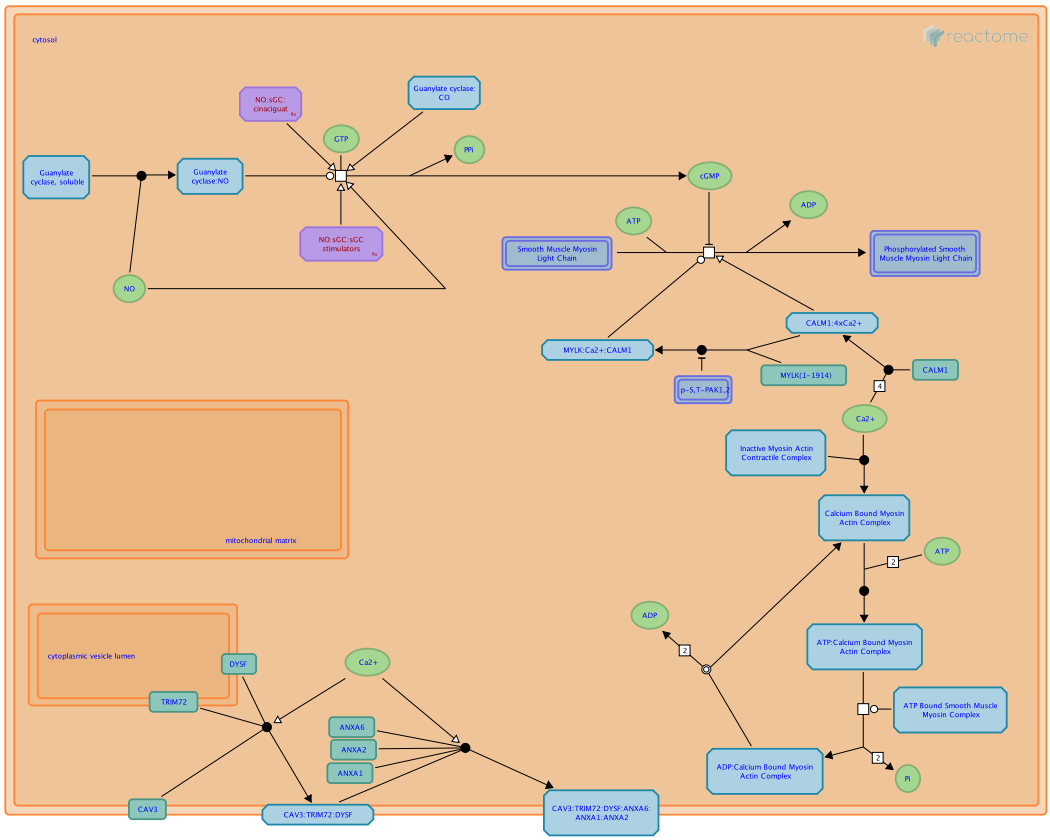
| | | |
|---|---|---|
| 2008-01-11 | Reviewed | Rush, MG. |
| 2009-02-10 | Authored | Gillespie, ME. |
| 2009-03-11 | Edited | Gillespie, ME. |

## Smooth Muscle Contraction ↗

**Location:** Muscle contraction

**Stable identifier:** R-HSA-445355

**Compartments:** cytosol, plasma membrane




Layers of smooth muscle cells can be found in the walls of numerous organs and tissues within the body. Smooth muscle tissue lacks the striated banding pattern characteristic of skeletal and cardiac muscle. Smooth muscle is triggered to contract by the autonomic nervous system, hormones, autocrine/paracrine agents, local chemical signals, and changes in load or length.

Actin:myosin cross bridging is used to develop force with the influx of calcium ions (Ca2+) initiating contraction. Two separate protein pathways, both triggered by calcium influx contribute to contraction, a calmodulin driven kinase pathway, and a caldesmon driven pathway.

Recent evidence suggests that actin, myosin, and intermediate filaments may be far more volatile then previously suspected, and that changes in these cytoskeletal elements along with alterations of the focal adhesions that anchor these proteins may contribute to the contractile cycle.

Contraction in smooth muscle generally uses a variant of the same sliding filament model found in striated muscle, except in smooth muscle the actin and myosin filaments are anchored to focal adhesions, and dense bodies, spread over the surface of the smooth muscle cell. When actin and myosin move across one another focal adhesions are drawn towards dense bodies, effectively squeezing the cell into a smaller conformation. The sliding is triggered by calcium:caldesmon binding, caldesmon acting in an analogous fashion to troponin in striated muscle. Phosphorylation of myosin light chains also is involved in the initiation of an effective contraction.

## Literature references

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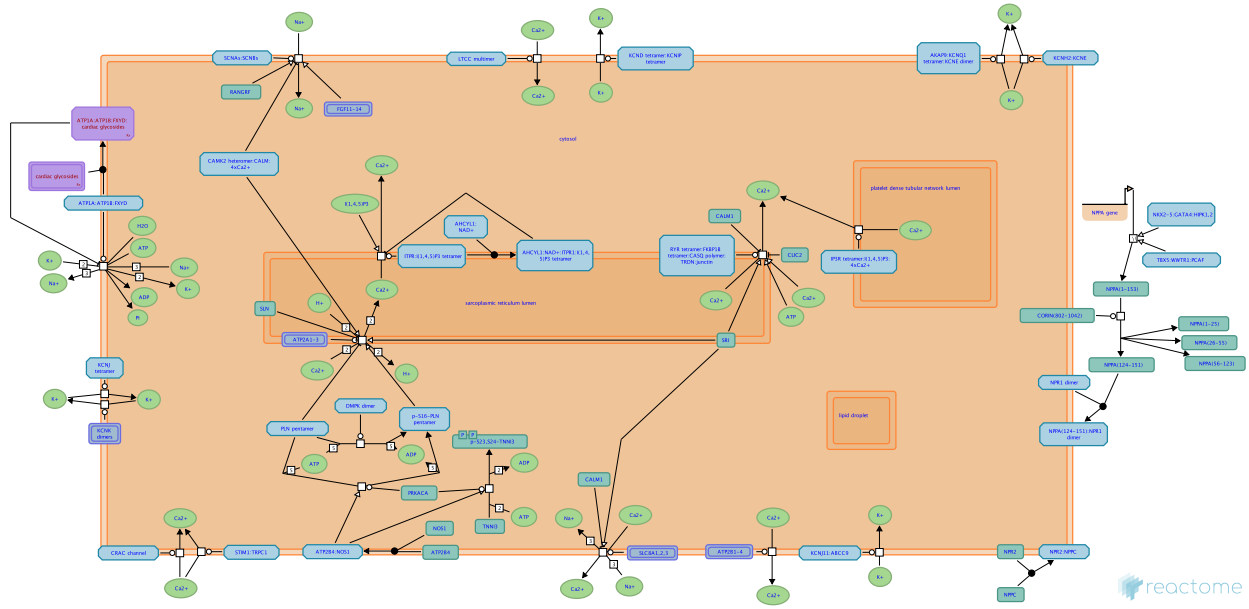
## Editions

| | | |
|---|---|---|
| 2008-01-11 | Reviewed | Rush, MG. |
| 2009-03-09 | Authored | Gillespie, ME. |
| 2009-11-18 | Edited | Gillespie, ME. |

## Cardiac conduction ↗

**Location:** Muscle contraction

**Stable identifier:** R-HSA-5576891




The normal sequence of contraction of atria and ventricles of the heart require activation of groups of cardiac cells. The mechanism must elicit rapid changes in heart rate and respond to changes in autonomic tone. The cardiac action potential controls these functions. Action potentials are generated by the movement of ions through transmembrane ion channels in cardiac cells. Like skeletal myocytes (and axons), in the resting state, a given cardiac myocyte has a negative membrane potential. In both muscle types, after a delay (the absolute refractory period), K+ channels reopen and the resulting flow of K+ out of the cell causes repolarisation. The voltage-gated Ca2+ channels on the cardiac sarcolemma membrane are generally triggered by an influx of Na+ during phase 0 of the action potential. Cardiac muscle cells are so tightly bound that when one of these cells is excited the action potential spreads to all of them. The standard model used to understand the cardiac action potential is the action potential of the ventricular myocyte (Park & Fishman 2011, Grant 2009).

The action potential has 5 phases (numbered 0-4). Phase 4 describes the membrane potential when a cell is not being stimulated. The normal resting potential in the ventricular myocardium is between -85 to -95 mV. The K+ gradient across the cell membrane is the key determinant in the normal resting potential. Phase 0 is the rapid depolarisation phase in which electrical stimulation of a cell opens the closed, fast Na+ channels, causing a large influx of Na+ creating a Na+ current ($I_{Na+}$). This causes depolarisation of the cell. The slope of phase 0 represents the maximum rate of potential change and differs in contractile and pacemaker cells. Phase 1 is the inactivation of the fast Na+ channels. The transient net outward current causing the small downward deflection (the "notch" of the action potetial) is due to the movement of K+ and Cl- ions. In pacemaker cells, this phase is due to rapid K+ efflux and closure of L-type Ca2+ channels. Phase 2 is the plateau phase which is sustained by a balance of Ca2+ influx and K+ efflux. This phase sustains muscle contraction. Phase 3 of the action potential is where a concerted action of two outward delayed currents brings about repolarisation back down to the resting potential (Bartos et al. 2015).

## Literature references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| 2014-05-27 | Authored, Edited | Jassal, B. |
| 2015-11-09 | Reviewed | Colotti, G. |

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