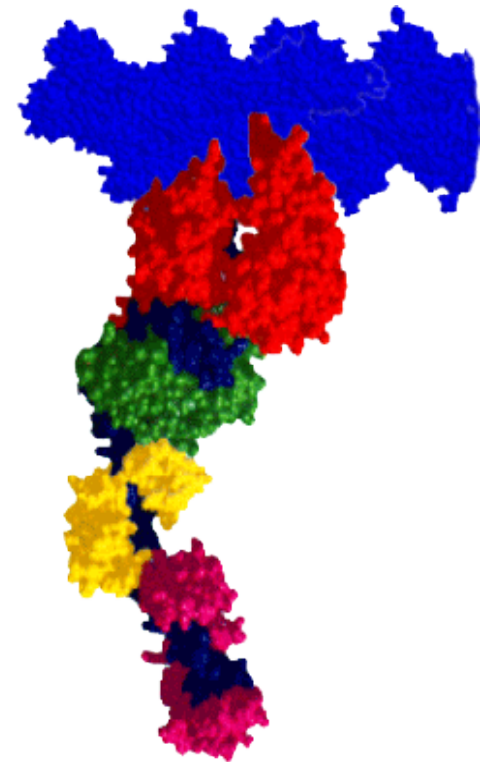
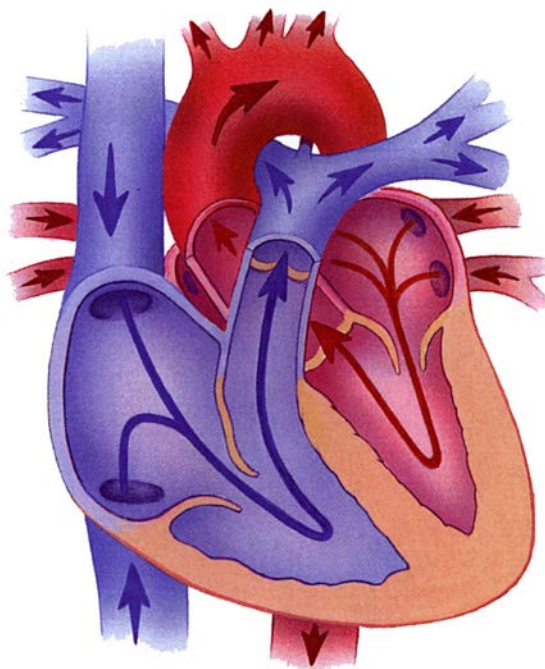


BIGGER ISN'T BETTER: RISKS & REASONS FOR AN ENLARGED HEART

David M. Warshaw, Ph.D.

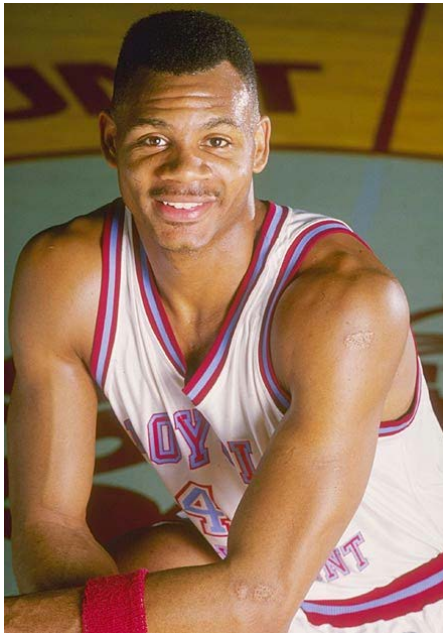
Molecular Physiology & Biophysics

Myosin Molecular Motor



Genetic Defects in Myosin Motor

Hank Gathers



Reggie Lewis



Leading cause of sudden death in young adults.

1 in 500 people have genetic defect (1,250 Vermonters)

Hypertrophic Cardiomyopathy (HCM)



Normal



Dilated Cardiomyopathy (DCM)



Myosin Genetic Mutations

R403Q →

S532P →

2000 amino acids

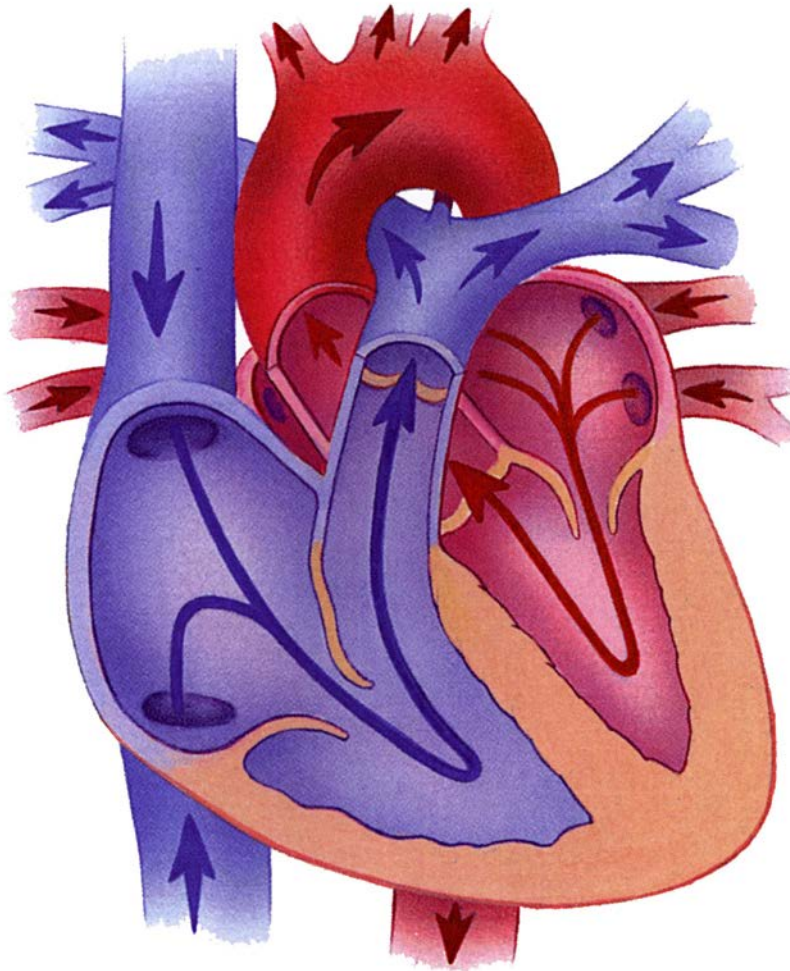
● Hypertrophic



● Dilated



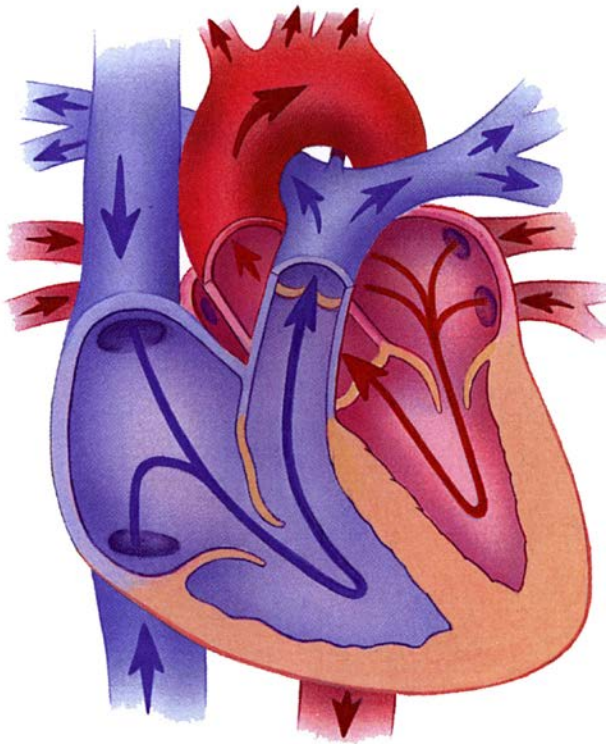
$$\textit{Power} = \textit{Force} \times \textit{Velocity}$$



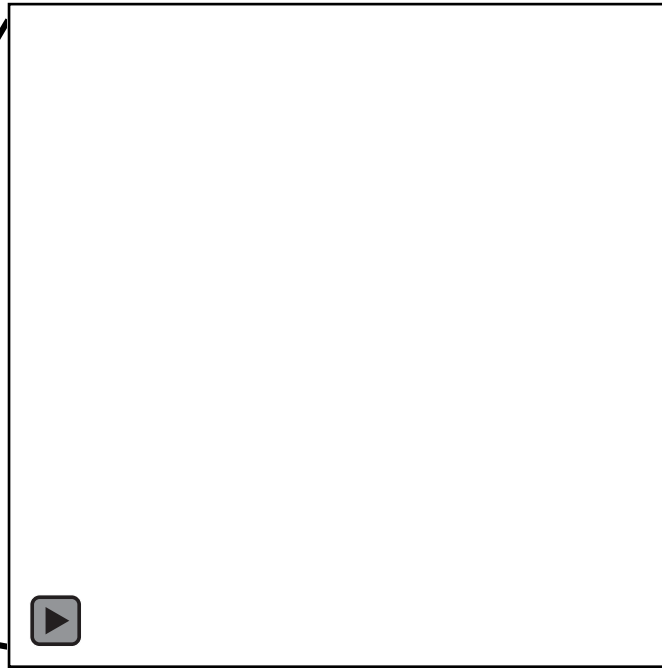
Myosin Molecular Motor



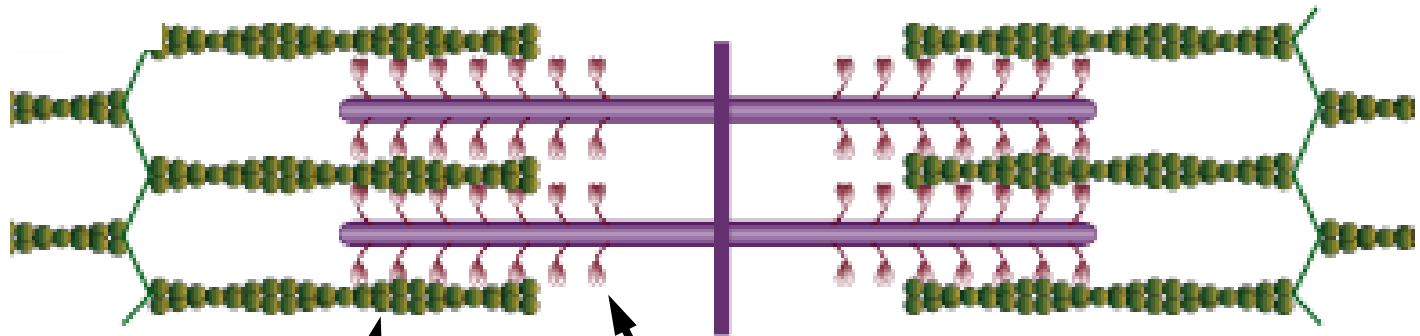
Heart



Cell



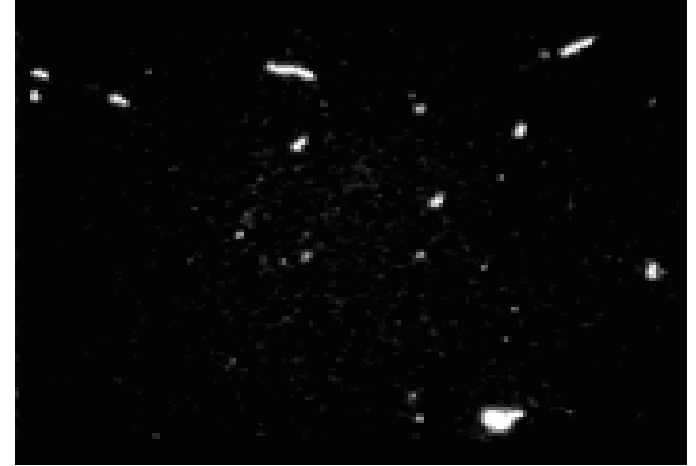
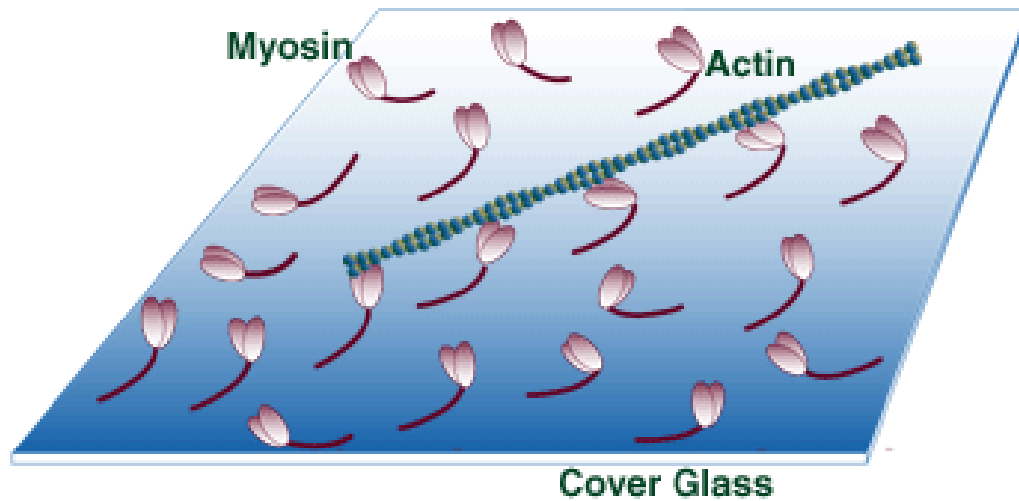
Sarcomere



Actin

Myosin

Motility Assay



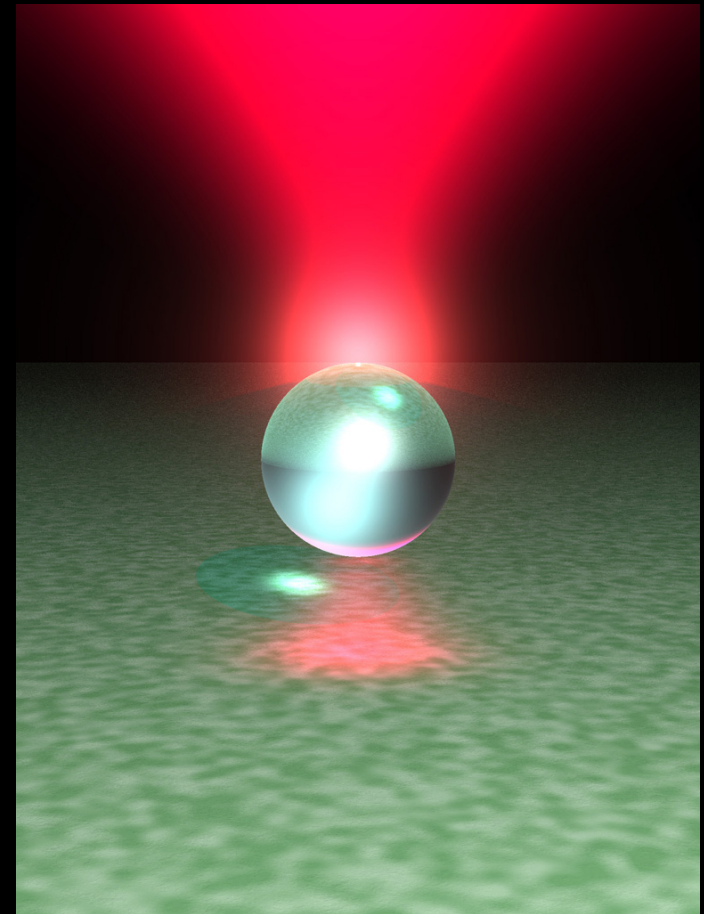
<http://motility.york.ac.uk/>

Actin Filament Velocity ~ Muscle Velocity

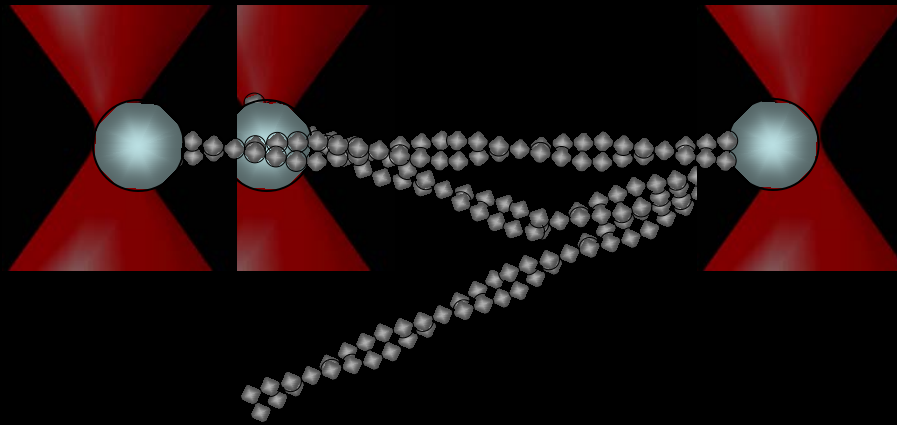
Star Trek Tractor Beam



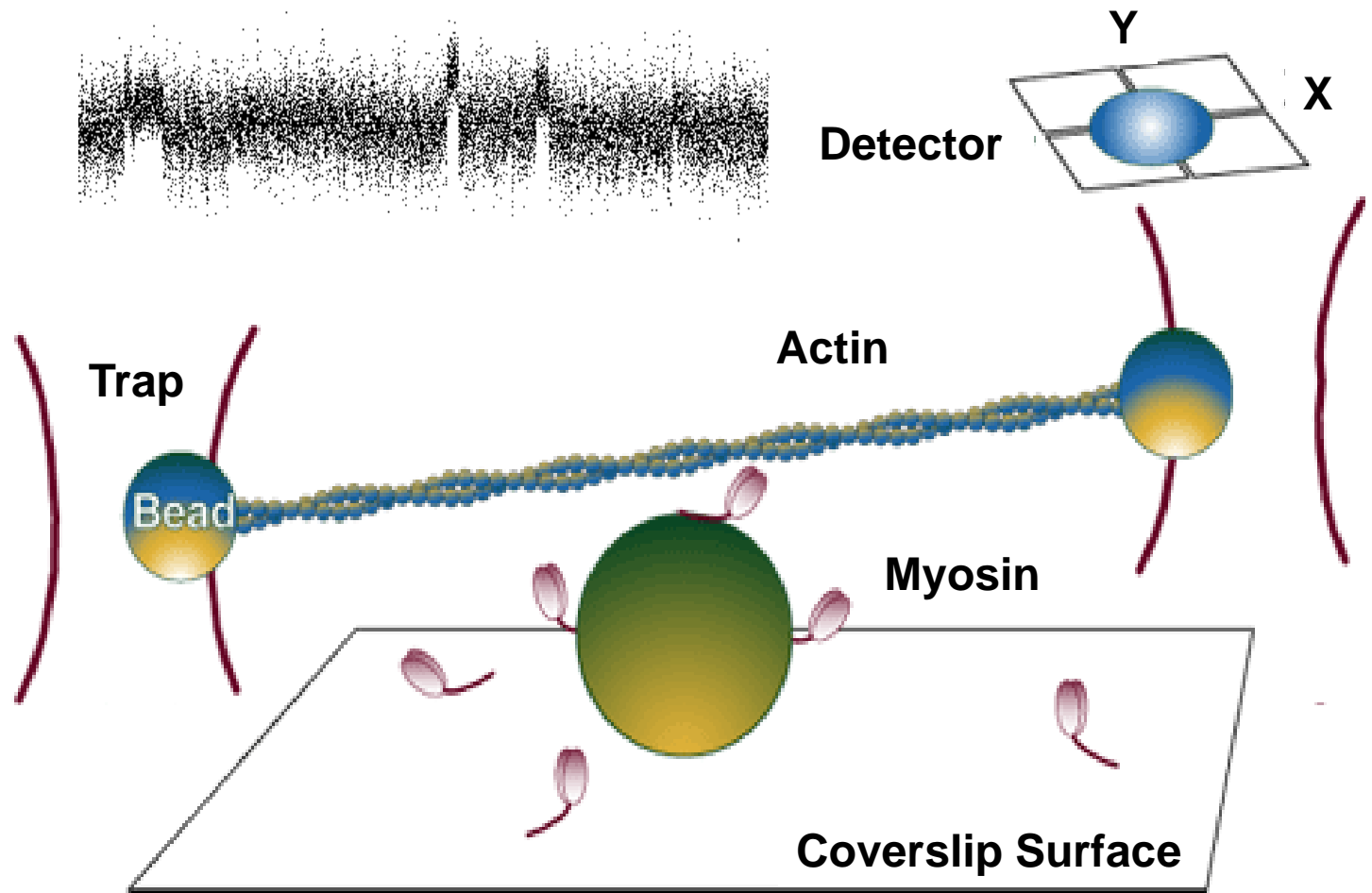
Laser Trap



Single Molecule Laser Trap Assay



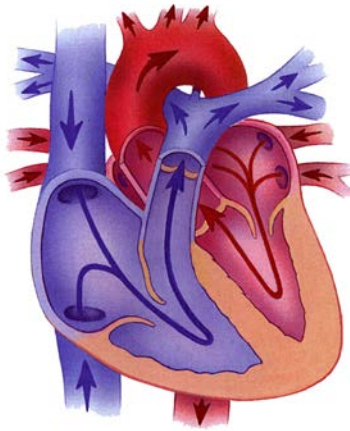
Laser Trap Assay



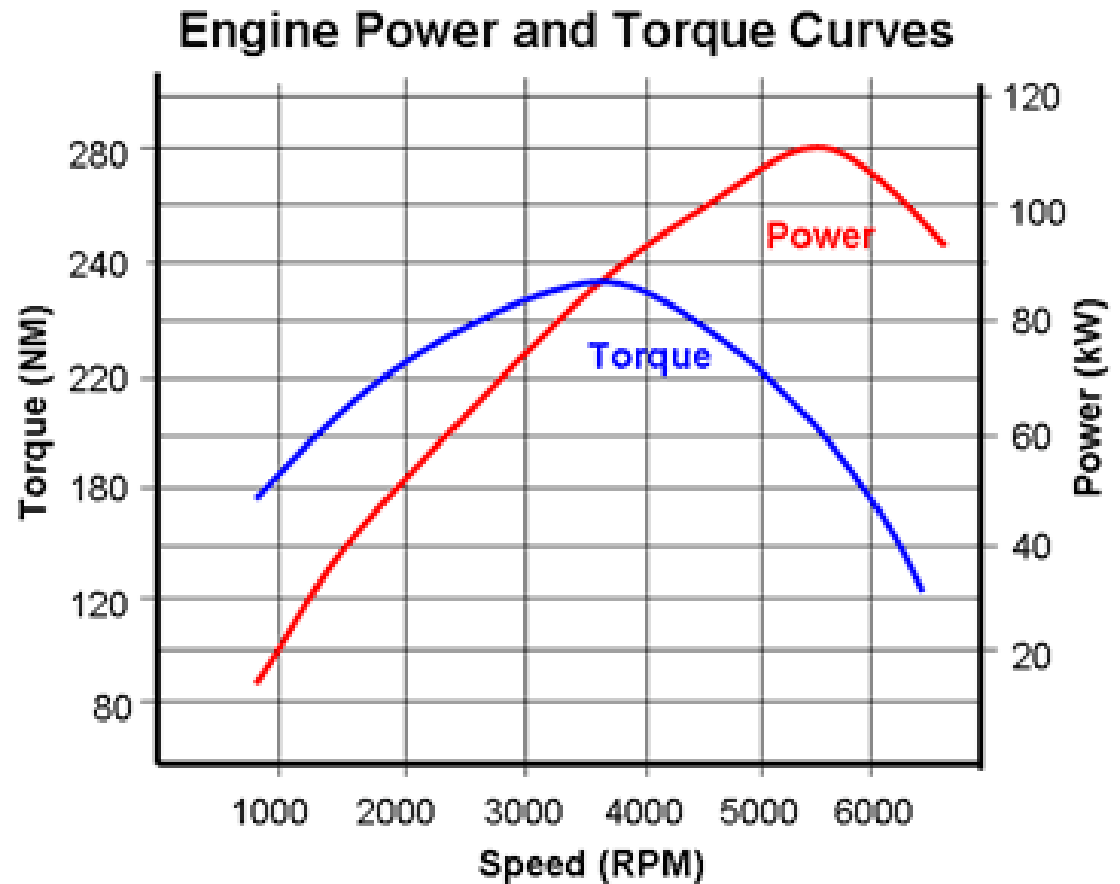
Heart is the Ultimate Power Generator!



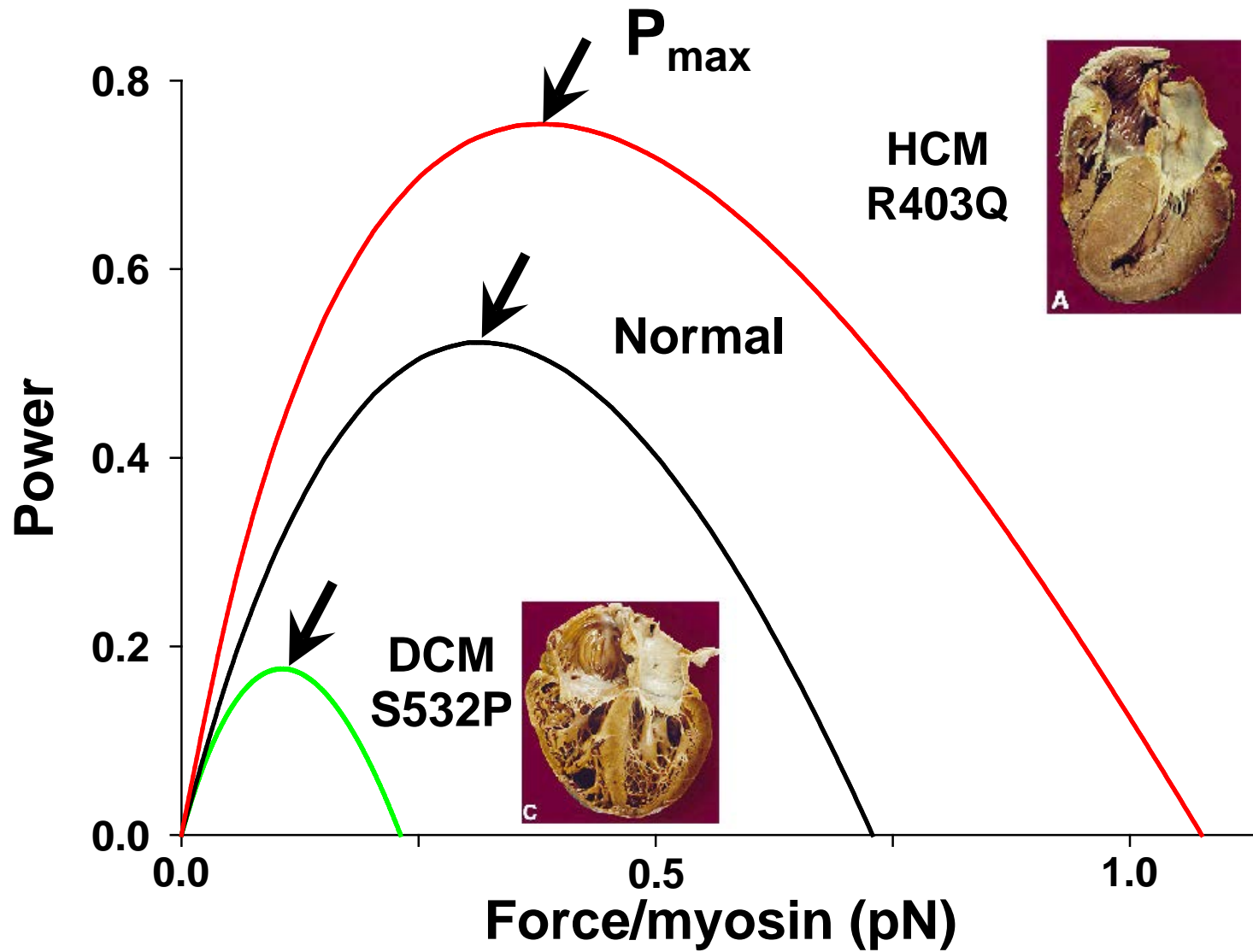
450 Million
Revolutions



3 Billion Beats

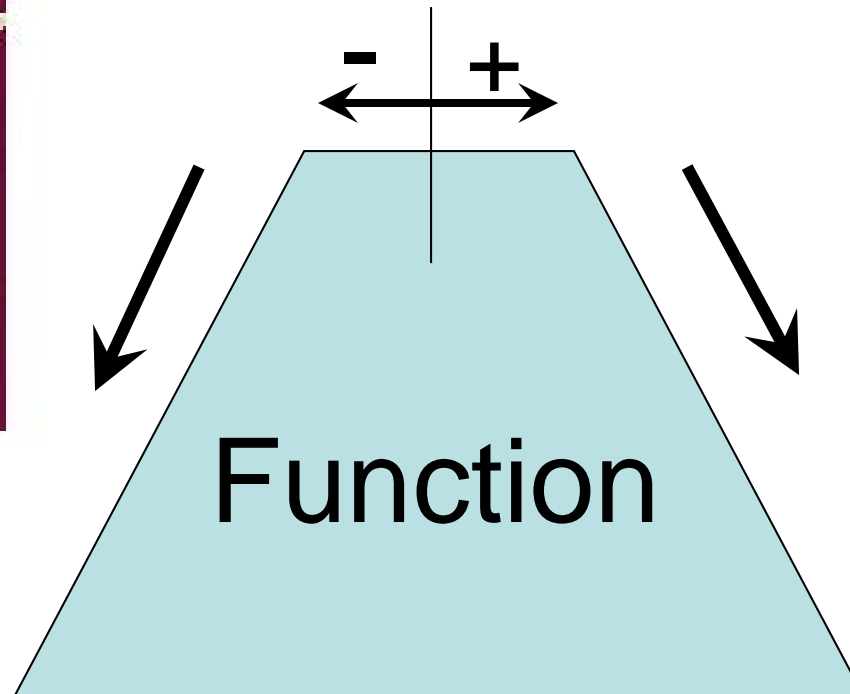
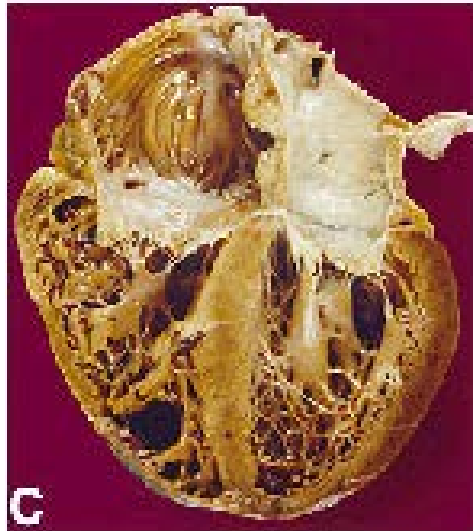


Power vs. Force Relation



Depressed
Motor
Function

Enhanced
Motor
Function



DCM

HCM

CARDIOMYOPATHIES: DEFECTS IN THE MOLECULAR MOTORS THAT POWER THE HEART

Future Perspectives

1. Genetic Testing or Simple EKGs
2. Precision and Individual Therapeutics:

Enhance Myosin Power in Dilated Cardiomyopathy

Reduce Myosin Power in Hypertrophic Cardiomyopathy

SCIENCE

5 FEBRUARY 2016

INSIGHTS | PERSPECTIVES

HEART DISEASE

Throttling back the heart's molecular motor

A small molecule inhibits mutated forms of myosin
that cause cardiac hypertrophy

By **David M. Warshaw**