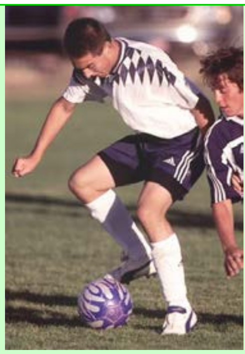
Creatine Kinase Reaction

You have heard or read about creatine supplementation, or the role of creatine phosphate in intense or powerful muscle contractions. However, you may have never studied the substrates and products of this reaction from a chemical structure perspective. You may also never have understood the purpose of this reaction to the bigger picture of cellular energy transfer. I hope this Topic "opens your eyes" to the bigger picture of the role of this reaction to skeletal muscle function during a variety of exercise conditions, including the recovery from prior exercise and the capacity to perform intense intermittent exercise.



The **creatine kinase** reaction (Equation 1 and Figure 1) is an **equilibrium reaction** *in vivo* within skeletal muscle. As such, the reaction is very sensitive to changing substrate and product concentrations.

As previously explained, the capacity of this reaction during sustained intense exercise is determined by the concentration of **creatine phosphate (CrP)**. For sustained intense exercise, the muscle concentration of CrP at approximately 30 mmol/kg wet wt may last < 10 s. The less intense the exercise, the longer the time for CrP to decrease to low values. Only during very intense exercise will CrP concentrations fall close to zero.

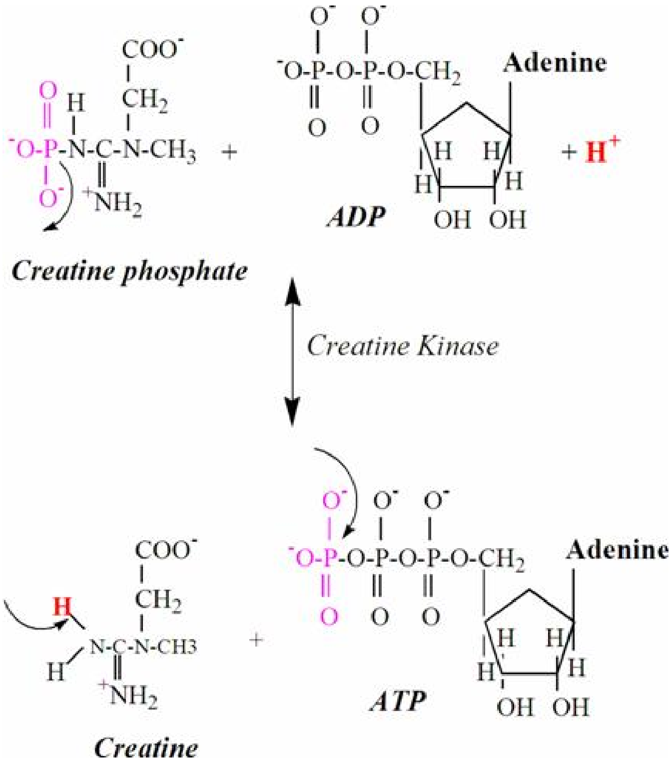


Figure 1. The chemical structures of the substrates and products of the creatine kinase reaction.

$$CrP + ADP + H^{+} \overset{\text{creatine kinase}}{\leftrightarrow} Cr + ATP \qquad \text{Equation 1}$$

It is important to know that the creatine kinase enzyme is located in solution throughout the cytosol, as well as bound to the outer mitochondrial membrane. This latter location has relevance to the role of CrP in the transfer of phosphate from the mitochondria to the cytosol, which will be discussed in subsequent sections.

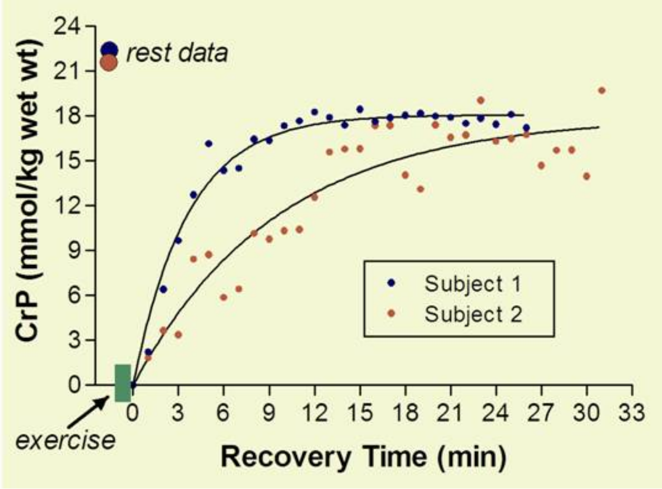


Figure 2. The change in creatine phosphate during intense exercise of the gastrocnemius muscle and the subsequent passive recovery period for two subjects.

During intermittent intense exercise, the capacity of this reaction during the entire intermittent exercise period is dependent on both the CrP concentration, and the rate or recovery of CrP during the rest interval. This fact is important for sports performance, where short bursts of exercise are separated by periods of both active and passive recovery. Figure 2 shows some data for CrP changes during intense exercise and recovery intervals for two subjects in one of our recent studies of muscle phosphate energy metabolism. Notice the near complete degradation of CrP during the exercise period. During the recovery interval, there is a rapid rate of CrP regeneration. The kinetics of this CrP recovery is very individualistic, and is known to be largely determined by the muscle mitochondrial density and oxygen availability. When concerned with muscle mitochondria, this would mean that the endurance training status of the contracting skeletal muscles and their genetically expressed fiber type (motor unit) proportions will dictate the kinetics of CrP recovery.

As you know, the creatine kinase reaction is an equilibrium reaction. This means that the ratio of products to substrates in resting muscle in vivo, the mass action ratio (L), reflects the proportionality of products to substrates at equilibrium. This is referred to as the **creatine kinase equilibrium constant**, and is calculated in Equation 2.

$$For\ the\ following\ conditions: [CrP] = 42\ mmol/L; [Cr] = 5\ mmol/L;\ ATP = 10.5\ mmol/L;$$
$$[ADP] = 0.001\ mmol/L;\ pH = 7.0 = 0.0001\ mmol/L$$
$$L = \frac{10.5 \times 5}{42 \times 0.0001 \times 0.001} = \frac{52.5}{0.0000042} = 12.5 \times 10^6$$

Equation 2

I wanted to show you this to avoid the temptation you might have by assuming that at equilibrium, product and substrate concentrations must be equal. This is not true. To ascertain why, go back to the sections on bioenergetics, and in particular the section on quantifying Gibbs' free energy to re-learn or better still, understand, the equation for calculating the absolute delta G (ΔG). Remember that to calculate the ΔG, the mass action ratio is altered by the absolute temperature, the molar gas constant, and the standard delta G (ΔGº').

Glossary Words

creatine kinase is the enzyme that catalyzes the conversion of creatine phosphate and ADP and a H+ to ATP and creatine, in this direction during muscle contraction. The reaction is reversed during exercise recovery.

equilibrium reaction has a $\Delta G=0$ Kcals/mol during rest, or low energy demand conditions. Directionality is governed by changes in substrate and/or product concentrations.

creatine phosphate (CrP) is one of the substrates of the creatine kinase reaction in the direction of ATP regeneration. It has a concentration in non-exercised muscle approximating 30 mmol/kg wet wt.