Transporters

J. Abramson, I. Smirnova, et al. (2003) Structure and mechanism of the lactose permease of *Escherichia coli.* *Science* 301:610-615.

J.D. Horisberger (2004) Recent insights into the structure and mechanism of the sodium pump. *Physiology* 19:377-387

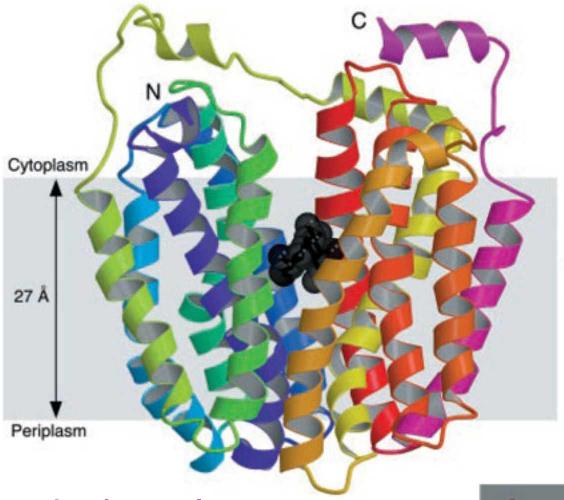
P. Läuger (1987) Voltage dependence of sodium-calcium exchange: Predictions from kinetic models. *J. Membrane Biol.* 99:1-11.

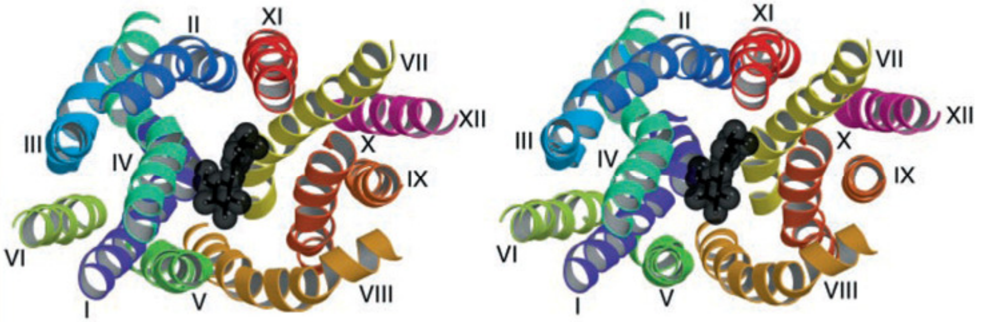
N. Reyes and D.C. Gadsby (2006) Ion permeation through the Na^+, K^+ - ATPase. *Nature* 443:470-474.

T. Shinoda, H. Ogawa, et al. (2009) Crystal structure of the sodium-potassium pump at 2.4 Å resolution. *Nature* 459:446-450.

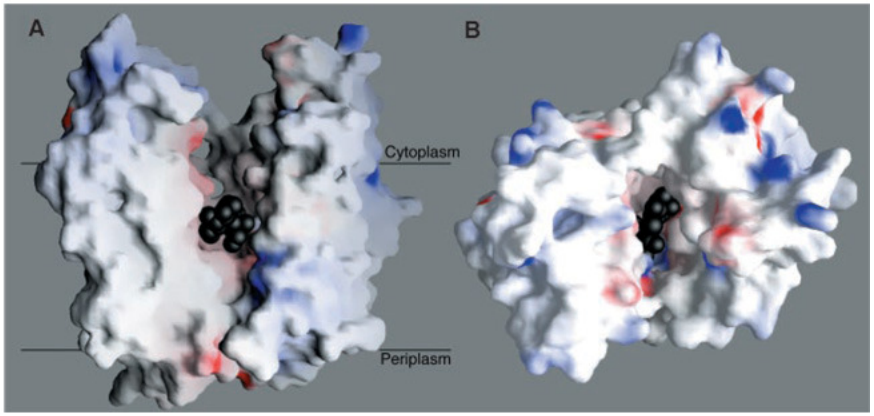
Structure of a bacterial transporter, LacY, which transports lactose into the cell using energy stored in the gradient of H^+ ions.

The molecule has 12 transmembrane α helices forming a cavity. The solved version was a mutated form of the molecule that is thought to be trapped in the structure with the cavity open to the cytoplasm. It is shown with a high-affinity substrate in the transport cavity.



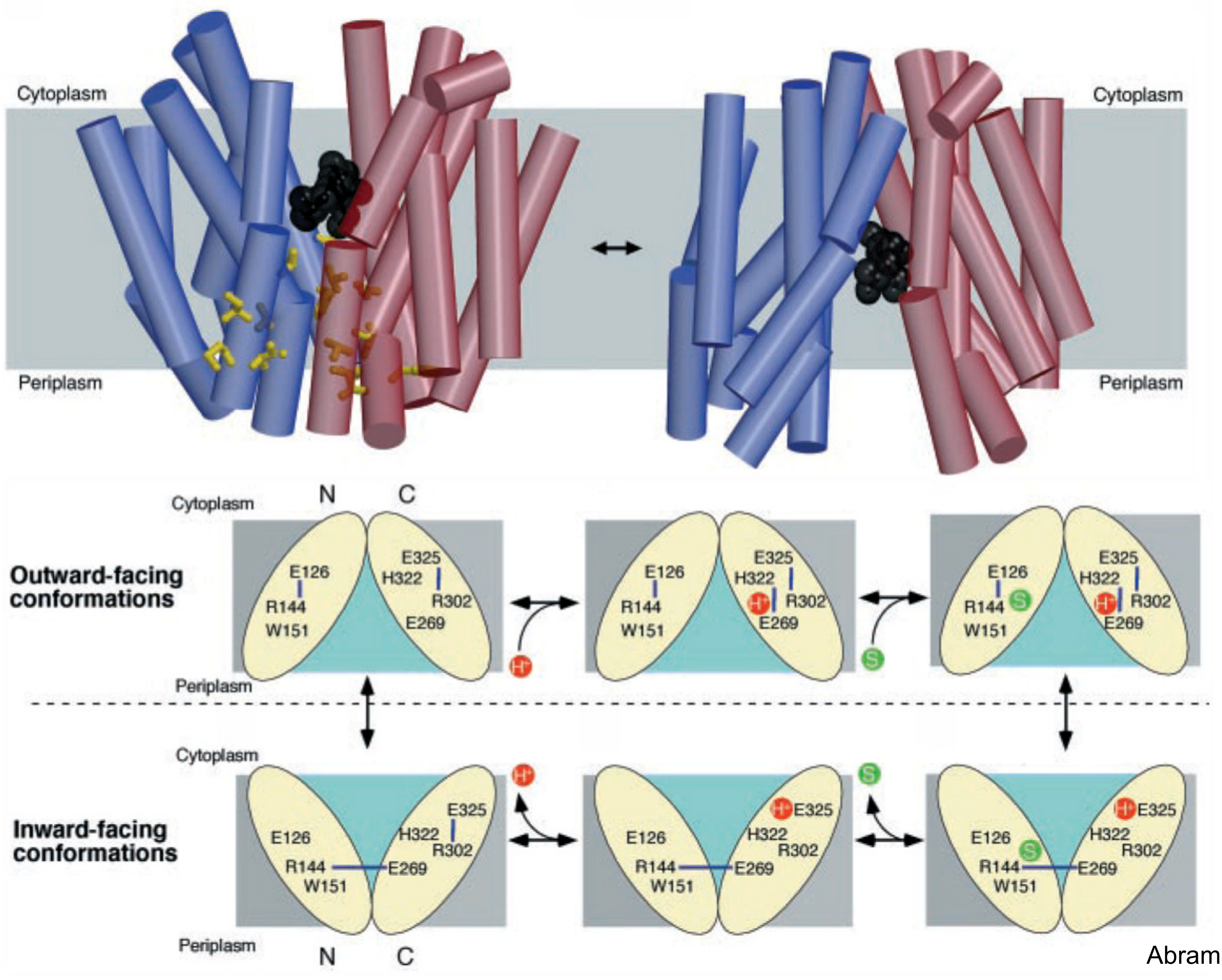


N-terminal purple
C-terminal pink



Abramson et al. 2003

Presumed transport mechanism. A cycle involving H^+ binding, lactose binding, translocation, unbinding, and reverse-translocation.



The blue lines are H bonds.

Abramson et al. 2003

Na-K ATPase is a member of a gene family containing various cation transporters (including SERCA pumps in heart cells), Ca ATPase (PMCA), and others.

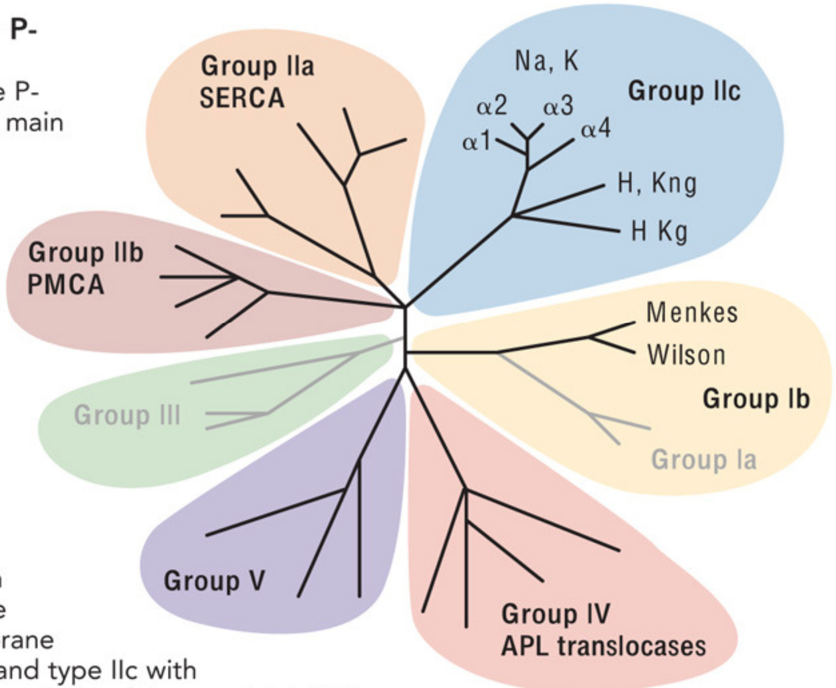
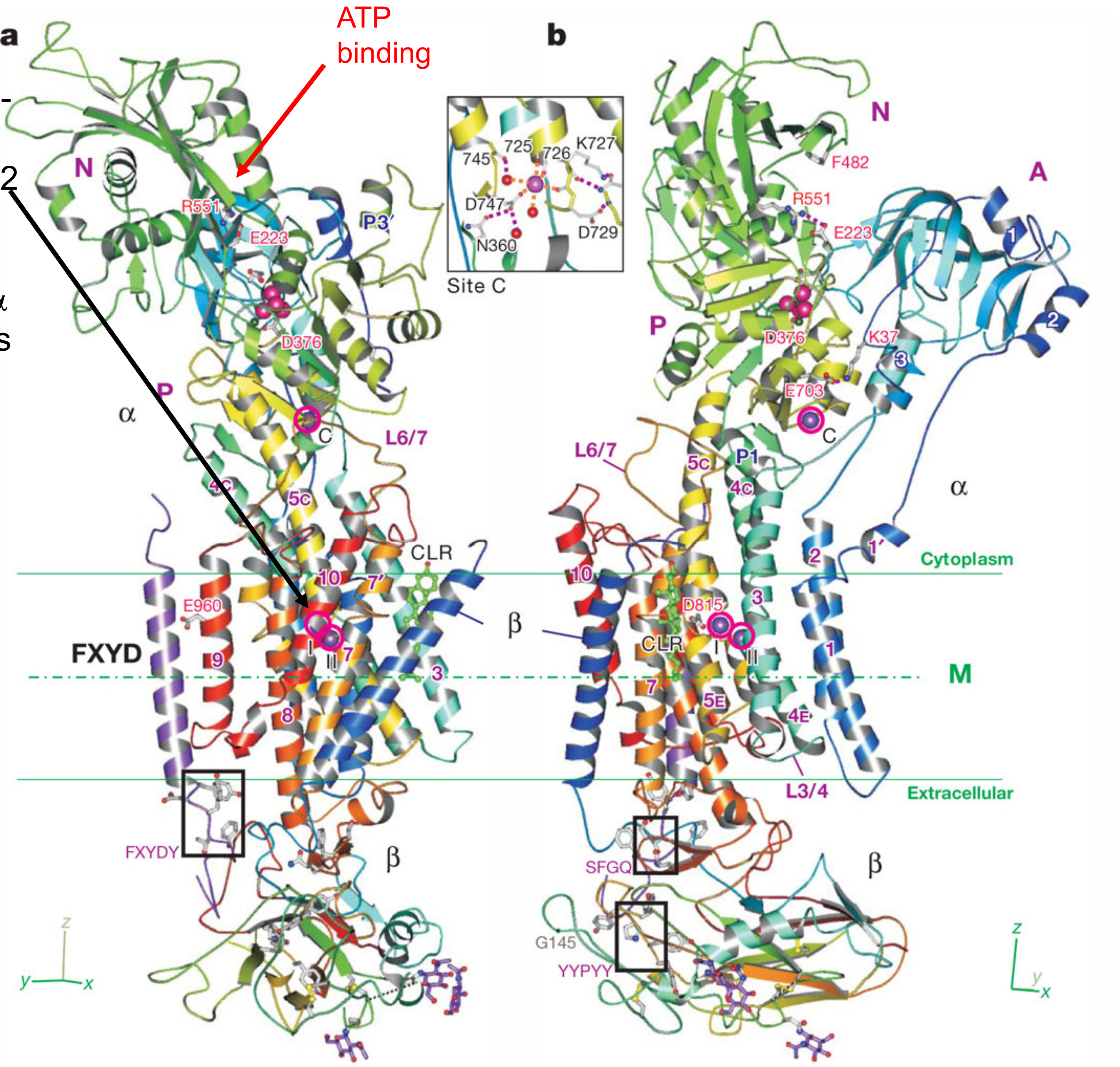


FIGURE 1. **Schematic phylogenetic tree of the P-ATPase family**
This simplified and schematic phylogenetic tree of the P-ATPase family illustrates the relationship between the main branches of this family. A more complete version of this tree can be found in the P-type ATPase Database internet site (http://biobase.dk/~axe/Patbase.html) maintained by K. B. Axelsen. The branches represent the genes present in the human genome (black lines) and, in addition, groups Ib and III (gray lines), which are not found in animal cells. Group I includes the B subunit of the bacterial KDP system (Ia) and a very large family (Ib) of cation pumps able to transport various metal ions (Cu^{2+}, Ag^{+}, Cd^{2+}, etc.). The human genome contains 2 group Ib ATPases that are both known to transport copper (the Menkes and Wilson proteins). Group II includes the sarcoplasmic-endoplasmic reticulum calcium pumps (SERCA; group IIa; in human 3 SERCA genes + 2 other genes corresponding to the secretory pathway calcium pumps), the plasma membrane calcium pump (PMCA; group IIb, 4 genes in human), and type IIc with the 4 isoforms of the Na-K-ATPase α-subunit and the gastric and "nongastric" H-K-ATPase α-subunits. Type III P-ATPases are proton ATPases (or Mg-ATPases) found in yeast, plant, and protozoa but not in multicellular animals. Up to 14 group IV genes have been found in the human genome (although some of them might be pseudogenes), and one of these genes has been characterized as an aminophospholipid (APL) transporter or "flippase" in protozoa and mammals, but very little is known about their function. No functional data are available concerning the group V P-ATPases.

Horisberger, 2004

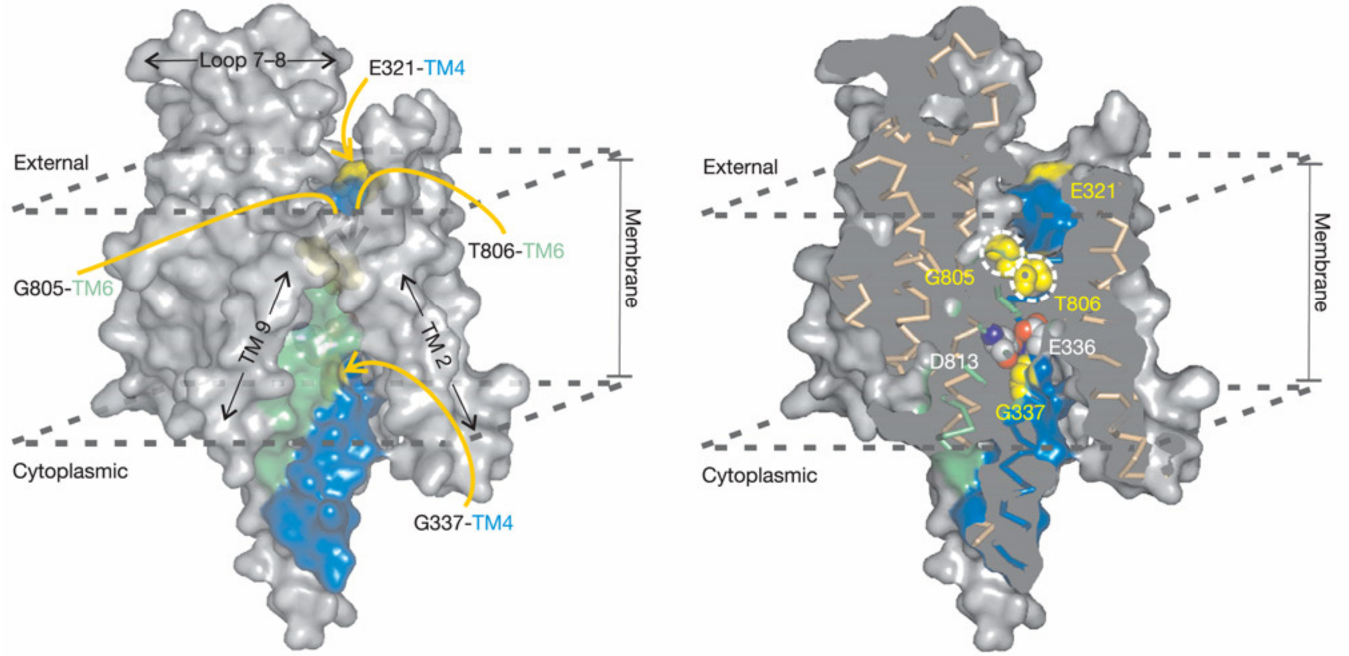
The structure of a Na-K ATPase with the molecule frozen with 2 K$^+$ ions bound. Two subunits of the enzyme are shown (α and β) from two views about 90° apart.



N-terminal blue
C-terminal red

Shinoda et al. 2009

The structure contains an internal-facing and external-facing vestibule. Presumably, these are the binding sites for Na and K, but the nature of occlusion is not clear.

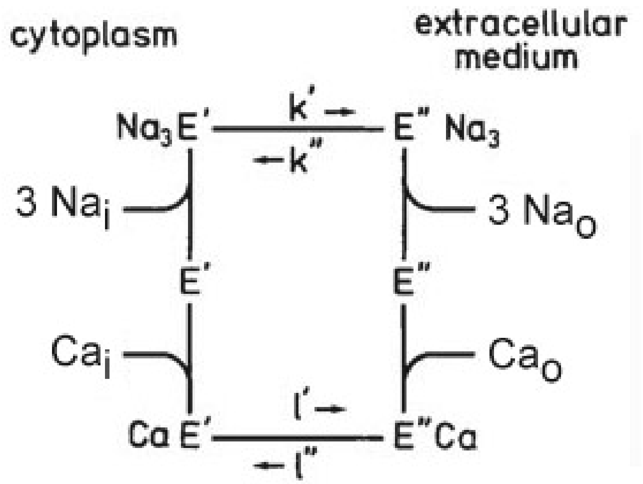


Reyes and Gadsby 2006

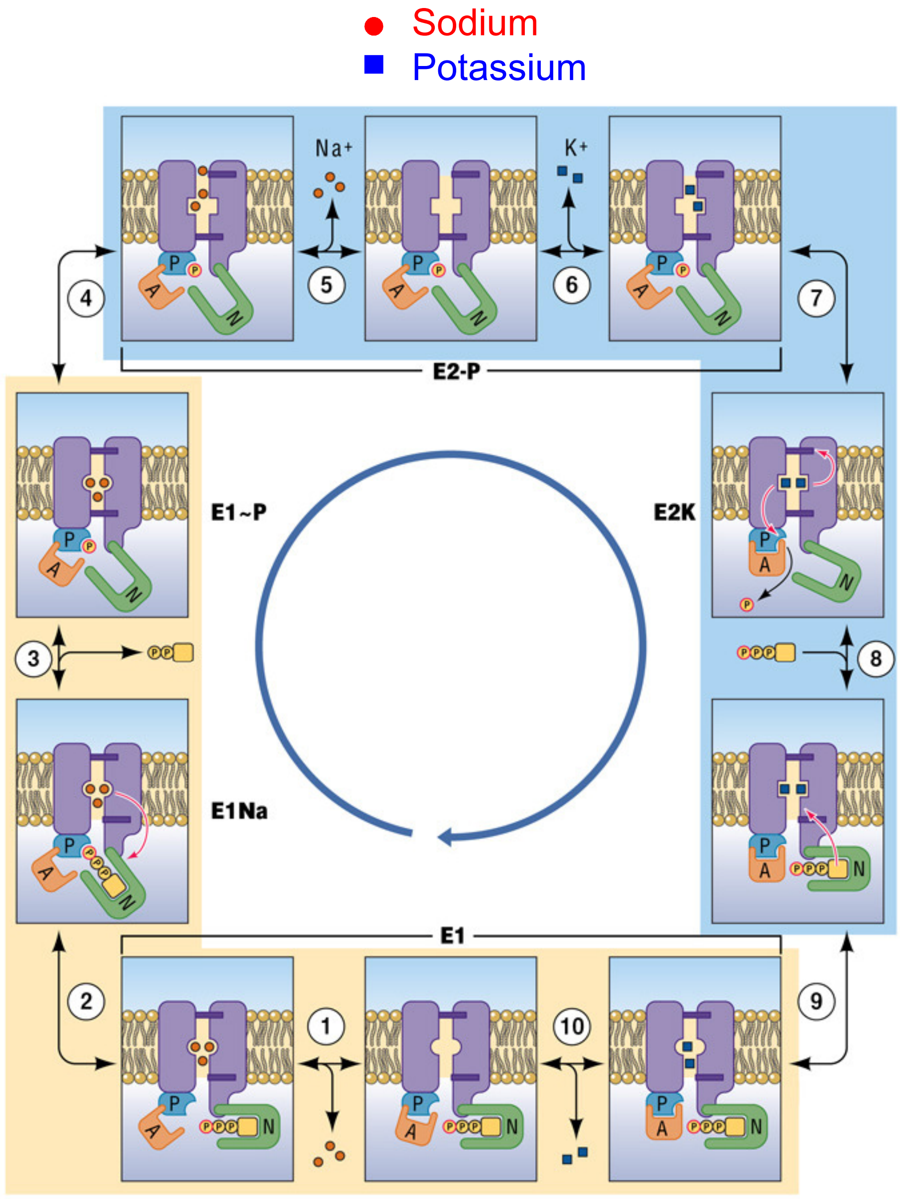
The sequence of steps in the Na-K ATPase is complex, involving separate transport of Na out, K in, and ATP cleavage.

Note the gates (black) that occlude the Na and K during the transport step.

Motivated by this model Läuger and others have analyzed a slightly simpler transporter, the Na-Ca cotransporter with a similar scheme.



P. Läuger 1987



Horisberger, 2004