Chapter 6 Solutions

1) Multiple answers are possible. Transport phase: tetrahedral Cu(I) bound to cysteinate/sulfide ligands. Release phase: O_2- or some other oxidant-mediated disulfide formation and oxidation to Cu(II). Oxidation of the Cu(I) to Cu(II) will worsen its "fit" in a tetrahedral ligand environment, since Cu(II) prefers to be square-planar. Furthermore, Cu(II) will have less affinity for a sulfur-only ligand environment than Cu(I). Additionally, an oxidizing environment can convert two cysteinates to a cystine, which will have no appreciable metal-binding ability and will expedite metal-release. Uptake phase: glutathione (a tripeptide containing a cysteine residue) reduces Cu(II) to Cu(I) and cystines to cysteines.

2) Simply put, a polynuclear cluster would require more than one copper ion to form. Since detoxification pathways, like any pathways, require energy, an overly sensitive switch will waste energy and a cell's resources. Requiring multiple copper ions, even if they bind cooperatively, will decrease the sensitivity of the switch and decrease the likelihood of a false turn-on. Similarly, if seven copper ions need to bind, even cooperatively, other trace transition metal ions will be far less likely to turn on the detoxification pathway.

3) Co(II) has a very high ligand exchange rate, whereas Co(III) is many times more inert. If a protein were to use Co(II) and the cobalt were to be oxidized, the resultant Co(III) would be extremely difficult to release from the protein. Chromium would have an analogous problem (i.e. Cr(II) is labile, Cr(III) is inert)

4) The Nernst equation is as follows:

$$V = [(R*T)/(Z*F)]*\ln(C_{out}/C_{in})$$

where R is the universal gas constant (8.314 $J*mol^{-1}*K^{-1}$), T is the temperature (310 K), Z is the charge of the ion (+2 for Ca^{2+}), F is Faraday's constant $9.6485*10^4$ $C*mol^{-1}$, C_{in} is the intracellular calcium concentration, and C_{out} is the extracellular concentration of calcium (1000 µM). Note that it takes 1 joule of energy to move 1 coulomb across 1 volt of potential, so R is now equalt to 8.314 $C*V*mol^{-1}*K^{-1}$)

$= [(8.314*310)/(2*9.6485*10^4)]$ volts $* \ln(C_{out}/C_{in})$
$= 13.4$ mV $* \ln(C_{out}/C_{in})$

when $C_{in} = 0.1$ µM
$V = 13.4$ mV $* \ln(1000/0.1) = 123$ mV

when $C_{in} = 10$ µM
$V = 13.4$ mV $* \ln(1000/10) = 61.7$ mV

5) Carbonyl oxygens from the protein backbone bind to the cationic sodium ions in the channel pore. Presumably, the protons on the iminium nitrogens in tetrodotoxin and saxitoxin will interact with the same nucleophilic oxygens in a similar, if not stronger, manner. This

interaction is possible because the iminium functionality is cationic (thermodynamically favorable) and relatively small (kinetically accessible).

6) A triethylalkylammonium ion is relatively big. Even though the positive charge on the nitrogen provides a coulombic driving force for interacting with the carbonyl oxygens in the channel, the triethylammonium group cannot enter the channel when closed. However, depolarizing the membrane opens the channel and allows the triethylammonium group to enter and block the channel.