

# PSCH 467

## Fundamentals of Neuroscience

### The Goldman Equation for 2 species

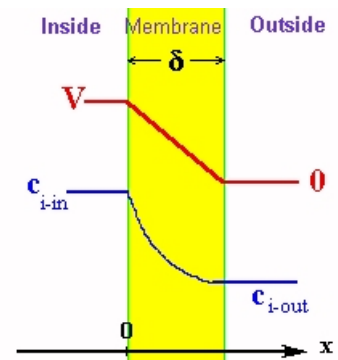
First, consider the current  $I_i$  due to a single species,  $i$  crossing the membrane.

Concentrations of the species on each side of the membrane are given by  $c_{i\text{in}}$  and  $c_{i\text{out}}$  for the two sides of the membrane. Voltage,  $V$ , is measured inside the cell (outside defined as 0) as shown to the right: Membrane thickness is  $\delta$ .

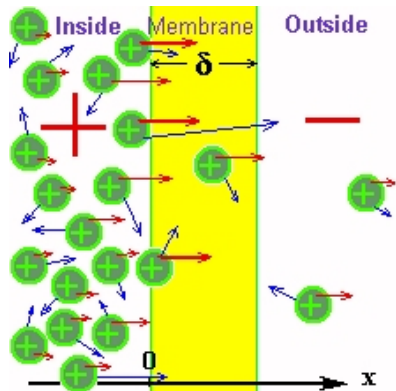
The current is influenced by two forces: **electrical**, and **chemical (diffusion)**. First, consider the *ion flux*, the flow of the ions:

$$\text{Electrical flux: } \Phi_{i,E} = u_i z_i c_i F \frac{dV}{dx}$$

$$\text{Diffusion flux: } \Phi_{i,D} = u_i RT \frac{dc_i}{dx}$$



Where  $F$  is Faraday's constant,  $R$  is Boltzmann's constant,  $T$  is absolute temperature ( $^{\circ}$  Kelvin),  $u_i$  is the mobility of the ion in the membrane, and  $z_i$  is its valence. Note that anything with a subscript ( $i$ ) refers specifically to this species of ion; things without subscripts are “universal” – they apply to all species.



The electrical force is due to the attraction of opposites and repulsion of same charges; the chemical “force” is because the side with more particles has a greater probability of sending one to the other side than the other side has of having particles drift back. This is shown the left. The positively charged particles are all pushed (or pulled) to the right (**red arrows**); they move in random directions (Brownian motion, **blue arrows**), but more end up crossing the membrane from left to right than from right to left. Note that we set this up with a higher concentration on the inside, *and* a positive charge

inside. The negative particles necessary to make both sides electrically neutral and the neutral particles necessary to make the two sides isotonic are not shown.

To convert *ion flux* to electrical current, it must be multiplied by the number of charges on each ion (the valence,  $z_i$ ). The **electrical** flow is due to the attraction (voltage times charge,  $z_i$ , times the available number of particles ( $c_i$ ), times the ability of these ions to travel through the membrane ( $u_i$ , a sort of “conductance”). The **chemical** flow depends on the *difference* in concentration of the species ( $dc_i/dx$ ) times the ability to flow ( $u_i$ ).  $R$  and  $F$  basically adjust units, and  $T$  is needed because warmer substances diffuse more readily than colder. The current due to that ion is therefore the sum of the two currents:

$$I_i = z_i \left( u_i z_i c_i F \frac{dV}{dx} + u_i RT \frac{dc_i}{dx} \right)$$

First, let's get rid of all the stuff that just makes the equations bulky. Collect all the electrical stuff and call it  $E_i$ , where  $E_i = u_i z_i^2 F$ . Collect the diffusion stuff and call it  $D_i$ ,  $D_i = u_i z_i RT$ . So now the current is:

$$I_i = E_i \cdot c_i \frac{dV}{dx} + D_i \frac{dc_i}{dx}$$

Before going on, consider what happens if this is the only ion that can cross the membrane. Then, it must eventually go to equilibrium, which means the current is zero:

$$E_i c_i \frac{dV}{dx} + D_i \frac{dc_i}{dx} = 0$$

Rearranging:

$$\frac{dV}{dx} = -\frac{D_i}{E_i} \frac{dc_i}{c_i}$$

Now integrate both sides with  $x$  going from 0 to  $\delta$ :

$$V \Big|_0^\delta = -\frac{D_i}{E_i} \ln(c_i) \Big|_{c_{i-in}}^{c_{i-out}}$$

where the vertical lines mean "evaluated from (lower) to (upper), and **ln** is the logarithm to the base  $e$  (the "natural logarithm")

$$V_{x=\delta} - V_{x=0} = -\frac{D_i}{E_i} (\ln(c_{out}) - \ln(c_{i-in}))$$

$$0 - V = -\frac{D_i}{E_i} \ln\left(\frac{c_{i-out}}{c_{i-in}}\right)$$

$$V = \frac{D_i}{E_i} \ln\left(\frac{c_{i-out}}{c_{i-in}}\right)$$

Now recall what  $D_i$  and  $E_i$  are, and restore them:

$$V = \frac{u_i z_i RT}{u_i z_i^2 F} \ln\left(\frac{c_{i-out}}{c_{i-in}}\right)$$

Simplify:

$$V = \frac{RT}{z_i F} \ln\left(\frac{c_{i-out}}{c_{i-in}}\right)$$

and lo! The Nernst equation emerges. Note that if  $c_{i-out}$  is larger than  $c_{i-in}$ , the voltage will be positive inside for a cation (negative for an anion). If reversed, the inside will be negative.

Note in general (for the future) that

$$\frac{D_i}{E_i} = \frac{RT}{F z_i}$$

But let's go back to considering that the current might not be zero (because there are other ions crossing the membrane also). Since there are assumed to be no charges inside

the membrane, voltage must change linearly within the membrane (as indicated by the line in the figure). That is

$$dV/dx = \text{constant} = -V/\delta$$

(the slope of the line in the membrane of width  $\delta$ ). The complete current equation for the one species is now:

$$I_i = -\frac{E_i \cdot c_i \cdot V}{\delta} + D_i \frac{dc_i}{dx}$$

which is a first-order linear differential equation in  $c_i$  (as a function of  $x$ , distance through the membrane). The solution of such an equation has the form:

$$c_i = A_i e^{x/\tau_i} + B_i$$

which is an exponential with a “space constant”  $\tau$ . The problem now is to find  $A_i$ ,  $B_i$ , and  $\tau_i$ . Begin by substituting the solution back into the original differential equation (which it must, of course, satisfy to be a solution):

$$I_i = -\frac{E_i \cdot \left( A_i e^{x/\tau_i} + B_i \right) \cdot V}{\delta} + D_i \frac{d\left( A_i e^{x/\tau_i} + B_i \right)}{dx}$$

Taking the derivative in the second term:

$$I_i = -\frac{E_i \cdot \left( A_i e^{x/\tau_i} + B_i \right) \cdot V}{\delta} + D_i \frac{A_i}{\tau_i} e^{x/\tau_i}$$

or

$$I_i = -\left( \frac{E_i A_i e^{x/\tau_i}}{\delta} + \frac{E_i B_i}{\delta} \right) \cdot V + D_i \frac{A_i}{\tau_i} e^{x/\tau_i}$$

Rearranging:

$$I_i = \left( \frac{D_i A_i}{\tau_i} - \frac{E_i A_i V}{\delta} \right) e^{x/\tau_i} - \frac{E_i B_i V}{\delta}$$

First observation: this equation indicates that  $I_i$  is a function of  $x$ , but it cannot be. Kirchoff's current law says the total current passing into and out of any closed volume (an infinitesimal slice of membrane parallel to its faces) must be 0. Current can neither be created nor destroyed. Thus, current must be constant in  $x$ ; so the multiplier on the exponential terms must be zero:

$$\begin{aligned} \left( \frac{D_i A_i}{\tau_i} - \frac{E_i A_i V}{\delta} \right) &= 0 \\ \frac{D_i A_i}{\tau_i} &= \frac{E_i A_i V}{\delta} \\ \frac{D_i A_i \delta}{E_i A_i V} &= \tau_i \\ \tau_i &= \frac{D_i \delta}{E_i V} \end{aligned}$$

Since the first two terms are 0, the equation for  $I_i$  becomes

$$I_i = -\frac{E_i B_i V}{\delta}$$

so

$$B_i = -\frac{I_i \delta}{E_i V}$$

Now, at  $x = 0$  (the inside border of the membrane),  $c_i = c_{i \text{ in}}$ . We also know that the solution at  $x = 0$  is simply  $c_i = A_i + B_i$  (because  $e^0 = 1$ ). Thus

$$c_{i \text{ in}} = A_i + B_i$$

$$c_{i \text{ in}} = A_i - \frac{I_i \delta}{E_i V}$$

so

$$A_i = c_{i \text{ in}} + \frac{I_i \delta}{E_i V}$$

Now, we have  $A_i$ ,  $B_i$ , and  $\delta$ , and can write out the solution for  $c_i$ :

$$c_i = A_i e^{\left(\frac{x}{\tau_i}\right)} + B_i$$

$$c_i = \left( c_{i \text{ in}} + \frac{I_i \delta}{E_i V} \right) e^{\left(\frac{x}{\tau_i}\right)} - \frac{I_i \delta}{E_i V}$$

We still need to get  $x$  out of this. At the outside border of the membrane, where  $x = \delta$ ,  $c_i = c_{i \text{ out}}$  (again, no discontinuity at the membrane). Make use of the solution for  $\tau_i$ :

$$c_{i \text{ out}} = \left( c_{i \text{ in}} + \frac{I_i \delta}{E_i V} \right) e^{\left(\frac{D_i \delta}{E_i V}\right)} - \frac{I_i \delta}{E_i V}$$

Fix the exponential:

$$c_{i \text{ out}} = \left( c_{i \text{ in}} + \frac{I_i \delta}{E_i V} \right) e^{\left(\frac{E_i V}{D_i}\right)} - \frac{I_i \delta}{E_i V}$$

Solve this for  $I_i$ :

$$c_{i \text{ out}} = c_{i \text{ in}} e^{\left(\frac{E_i V}{D_i}\right)} + \frac{I_i \delta}{E_i V} e^{\left(\frac{E_i V}{D_i}\right)} - \frac{I_i \delta}{E_i V}$$

$$c_{i \text{ out}} = c_{i \text{ in}} e^{\left(\frac{E_i V}{D_i}\right)} + \left( \frac{\delta}{E_i V} e^{\left(\frac{E_i V}{D_i}\right)} - \frac{\delta}{E_i V} \right) I_i$$

$$I_i = \frac{c_{i \text{ in}} e^{\left(\frac{E_i V}{D_i}\right)} - c_{i \text{ out}}}{-\left( \frac{\delta}{E_i V} e^{\left(\frac{E_i V}{D_i}\right)} - \frac{\delta}{E_i V} \right)} = \frac{c_{i \text{ in}} e^{\left(\frac{E_i V}{D_i}\right)} - c_{i \text{ out}}}{\frac{\delta}{E_i V} \left( 1 - e^{\left(\frac{E_i V}{D_i}\right)} \right)}$$

$$I_i = \frac{\frac{E_i V}{\delta} \left( c_{i-in} e^{\left(\frac{E_i V}{D_i}\right)} - c_{i-out} \right)}{\left( 1 - e^{\left(\frac{E_i V}{D_i}\right)} \right)}$$

**OK.**

So now we have the current for species  $i$ . Assume there are two species, so there are two currents. One is Na, and one is K. For steady state, the net current through the membrane is 0. That is

$$I_{Na} + I_K = 0$$

$$I_{Na} = -I_K$$

So we can write:

$$\frac{\frac{E_{Na} V}{\delta} \left( c_{Na-in} e^{\left(\frac{E_i V}{D_i}\right)} - c_{Na-out} \right)}{\left( 1 - e^{\left(\frac{E_{Na} V}{D_{Na}}\right)} \right)} = \frac{\frac{E_K V}{\delta} \left( c_{K-in} e^{\left(\frac{E_K V}{D_K}\right)} - c_{K-out} \right)}{\left( 1 - e^{\left(\frac{E_K V}{D_K}\right)} \right)}$$

Now, remember that for both of these species,  $z = 1$ , so for both species

$$\frac{D_i}{E_i} = \frac{RT}{F} \quad \text{so} \quad \frac{E_i}{D_i} = \frac{F}{RT}$$

and

$$\frac{\frac{E_{Na} V}{\delta} \left( c_{Na-in} e^{\left(\frac{F}{RT} V\right)} - c_{Na-out} \right)}{\left( 1 - e^{\left(\frac{F}{RT} V\right)} \right)} = \frac{\frac{E_K V}{\delta} \left( c_{K-in} e^{\left(\frac{F}{RT} V\right)} - c_{K-out} \right)}{\left( 1 - e^{\left(\frac{F}{RT} V\right)} \right)}$$

$$E_{Na} \left( c_{Na-in} e^{\left(\frac{FV}{RT}\right)} - c_{Na-out} \right) = E_K \left( c_{K-in} e^{\left(\frac{FV}{RT}\right)} - c_{K-out} \right)$$

Collect the exponential terms:

$$\begin{aligned} (E_{Na} c_{Na-in} - E_K c_{K-in}) e^{\left(\frac{FV}{RT}\right)} &= (E_{Na} c_{Na-out} - E_K c_{K-out}) \\ e^{\left(\frac{FV}{RT}\right)} &= \frac{(E_{Na} c_{Na-out} - E_K c_{K-out})}{(E_{Na} c_{Na-in} - E_K c_{K-in})} \end{aligned}$$

Taking the natural logarithm ( $\ln$ ) of both sides:

$$\frac{FV}{RT} = \ln \left( \frac{(E_{Na}c_{Na-out} - E_Kc_{K-out})}{(E_{Na}c_{Na-in} - E_Kc_{K-in})} \right)$$

or

$$V = \frac{RT}{F} \ln \left( \frac{(E_{Na}c_{Na-out} - E_Kc_{K-out})}{(E_{Na}c_{Na-in} - E_Kc_{K-in})} \right)$$

Now just substitute for the  $E_i = u_i z_i^2 F$  (and the  $z$  are all +1):

$$V = \frac{RT}{F} \ln \left( \frac{(u_{Na}Fc_{Na-out} - u_KFc_{K-out})}{(u_{Na}Fc_{Na-in} - u_KFc_{K-in})} \right)$$

The F cancels from all terms inside the logarithm, giving:

$$V = \frac{RT}{F} \ln \left( \frac{(u_{Na}c_{Na-out} - u_Kc_{K-out})}{(u_{Na}c_{Na-in} - u_Kc_{K-in})} \right)$$

which is the Goldman Equation.

Define  $b = u_{Na} / u_K$ , the relative mobilities of the two ions. Now

$$V = \frac{RT}{F} \ln \left( \frac{(bc_{Na-out} - c_{K-out})}{(bc_{Na-in} - c_{K-in})} \right)$$

Rule of thumb: use base 10 logs, and  $RT/F$  (at 20°C) is about 58:

$$V = 58 \cdot \log_{10} \left( \frac{(bc_{Na-out} - c_{K-out})}{(bc_{Na-in} - c_{K-in})} \right)$$

Suppose  $b=0$  (that is, Na cannot cross the membrane at all):

$$V = \frac{RT}{F} \ln \left( \frac{(c_{K-out})}{(c_{K-in})} \right) = \frac{RT}{F} \ln \left( \frac{[K^+]_{out}}{[K^+]_{in}} \right)$$

(the negatives cancel in numerator and denominator). This is the Nernst equation for potassium.

If it is potassium that cannot cross ( $u_K \ll u_{Na}$ ),  $b$  approaches infinity, and

$$V = \frac{RT}{F} \ln \left( \frac{(c_{Na-out})}{(c_{Na-in})} \right) = \frac{RT}{F} \ln \left( \frac{[Na^+]_{out}}{[Na^+]_{in}} \right)$$

which is the sodium Nernst equation. For realistic values of  $b$  (about 1/20), notice that the numerator of the full equation is given by both sodium and potassium ( $c_{K-out}$  is small;  $c_{Na-out}$  is large but multiplied by  $b$ ), while the denominator is virtually given by  $c_{K-out}$ .

## Multiple species:

A somewhat more general solution can be found by again saying the sum of all currents is 0:

$$\sum I_i = 0$$

$$0 = \sum \left( \frac{\frac{E_i V}{\delta} \left( c_{i-in} e^{\left( \frac{E_i V}{D_i} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{E_i V}{D_i} \right)}} \right) = \sum \left( \frac{E_i \left( c_{i-in} e^{\left( \frac{E_i V}{D_i} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{E_i V}{D_i} \right)}} \right)$$

### 1. Consider the case in which all species are univalent:

Re-expand the E and D, assuming only univalent ions ( $z=1$  or  $z=-1$ ):

$$0 = \sum \left( \frac{u_i z_i^2 F \left( c_{i-in} e^{\left( \frac{z_i F V}{RT} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{z_i F V}{RT} \right)}} \right) = \sum \left( \frac{u_i F \left( c_{i-in} e^{\left( \frac{z_i F V}{RT} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{z_i F V}{RT} \right)}} \right)$$

The  $z^2$  terms disappeared because  $(-1)^2 = 1$ . Now, if all the species have the same valences all the denominators are the same. If some are positive and some are negative (as long as they are all univalent, that is,  $\pm 1$ ), we invoke the following little trick:

$$(1 - e^{-\alpha}) \cdot (-e^{\alpha}) = -e^{\alpha} + 1 = 1 - e^{\alpha}$$

We can multiply numerator and denominator of the negative  $z$  terms by the negative exponential, and they are gone.

$$0 = \sum_{z=1} \left( \frac{u_i F \left( c_{i-in} e^{\left( \frac{F V}{RT} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{F V}{RT} \right)}} \right) + \sum_{z=-1} \left( \frac{u_i F \left( c_{i-in} e^{\left( \frac{F V}{RT} \right)} - c_{i-out} \right) - e^{\left( \frac{F V}{RT} \right)}}{1 - e^{\left( \frac{F V}{RT} \right)} - e^{\left( \frac{F V}{RT} \right)}} \right)$$

$$0 = \sum_{z=1} \left( \frac{u_i F \left( c_{i-in} e^{\left( \frac{F V}{RT} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{F V}{RT} \right)}} \right) + \sum_{z=-1} \left( \frac{u_i F \left( -c_{i-in} + c_{i-out} e^{\left( \frac{F V}{RT} \right)} \right)}{1 - e^{\left( \frac{F V}{RT} \right)}} \right)$$

$$0 = \sum_{z=1} \left( \frac{u_i F \left( c_{i-in} e^{\left(\frac{FV}{RT}\right)} - c_{i-out} \right)}{1 - e^{\left(\frac{FV}{RT}\right)}} \right) + \sum_{z=-1} \left( \frac{u_i F \left( c_{i-out} e^{\left(\frac{FV}{RT}\right)} - c_{i-in} \right)}{1 - e^{\left(\frac{FV}{RT}\right)}} \right)$$

As with sodium and potassium, the denominators of all terms are the same, so the sum of the numerators must be 0 (and the F can be divided out of each term):

$$0 = \sum_{z=1} u_i \left( c_{i-in} e^{\left(\frac{FV}{RT}\right)} - c_{i-out} \right) + \sum_{z=-1} u_i \left( c_{i-out} e^{\left(\frac{FV}{RT}\right)} - c_{i-in} \right)$$

Collect the terms that have exponentials:

$$0 = \left( \sum_{z=1} u_i c_{i-in} + \sum_{z=-1} u_i c_{i-out} \right) e^{\left(\frac{FV}{RT}\right)} - \left( \sum_{z=1} c_{i-out} + \sum_{z=-1} c_{i-in} \right)$$

$$\left( \sum_{z=1} u_i c_{i-in} + \sum_{z=-1} u_i c_{i-out} \right) e^{\left(\frac{FV}{RT}\right)} = \left( \sum_{z=1} c_{i-out} + \sum_{z=-1} c_{i-in} \right)$$

$$e^{\left(\frac{FV}{RT}\right)} = \frac{\left( \sum_{z=1} c_{i-out} + \sum_{z=-1} c_{i-in} \right)}{\left( \sum_{z=1} u_i c_{i-in} + \sum_{z=-1} u_i c_{i-out} \right)}$$

$$\frac{FV}{RT} = \ln \left( \frac{\left( \sum_{z=1} c_{i-out} + \sum_{z=-1} c_{i-in} \right)}{\left( \sum_{z=1} u_i c_{i-in} + \sum_{z=-1} u_i c_{i-out} \right)} \right)$$

$$V = \frac{RT}{F} \ln \left( \frac{\left( \sum_{z=1} c_{i-out} + \sum_{z=-1} c_{i-in} \right)}{\left( \sum_{z=1} u_i c_{i-in} + \sum_{z=-1} u_i c_{i-out} \right)} \right)$$

as before. Note that *in* and *out* are reversed for the negative ions. If we define  $\mathbf{c} = u_{Cl} / u_K$  for chloride:

$$V = \frac{RT}{F} \ln \left( \frac{c_{K-out} + b \cdot c_{Na-out} + c \cdot c_{Cl-in}}{c_{K-in} + b \cdot c_{Na-in} + c \cdot c_{Cl-out}} \right)$$

Notice that if  $b=0$  and potassium conductance is also 0 (chloride the only thing that crosses the membrane,  $\mathbf{c}$  nearly infinity):

$$V = \frac{RT}{F} \ln \left( \frac{c_{Cl-in}}{c_{Cl-out}} \right)$$

which is the chloride Nernst potential.

We could have written it as

$$V = \frac{RT}{Fz_{Cl}} \ln \left( \frac{c_{Cl-out}}{c_{Cl-in}} \right) = -\frac{RT}{F} \ln \left( \frac{c_{Cl-out}}{c_{Cl-in}} \right) = \frac{RT}{F} \ln \left( \frac{c_{Cl-in}}{c_{Cl-out}} \right)$$

**2. There is a species that is divalent (e.g.: calcium,  $Ca^{+2}$ ), for which  $z_i = 2$ .** Back to the beginning:

$$0 = \sum \left( \frac{u_i z_i^2 F \left( c_{i-in} e^{\left( \frac{z_i FV}{RT} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{z_i FV}{RT} \right)}} \right)$$

Now the  $z$  for  $Ca^{+2}$  are 2, and  $z^2 = 4$ , so that term is:

$$\frac{u_{Ca} 4F \left( c_{Ca-in} e^{\left( \frac{2FV}{RT} \right)} - c_{Ca-out} \right)}{1 - e^{\left( \frac{2FV}{RT} \right)}}$$

and

$$0 = \sum_{z=1} \left( \frac{u_i F \left( c_{i-in} e^{\left( \frac{FV}{RT} \right)} - c_{i-out} \right)}{1 - e^{\left( \frac{FV}{RT} \right)}} \right) + \sum_{z=-1} \left( \frac{u_i F \left( c_{i-out} e^{\left( \frac{FV}{RT} \right)} - c_{i-in} \right)}{1 - e^{\left( \frac{FV}{RT} \right)}} \right) + \frac{u_{Ca} 4F \left( c_{Ca-in} e^{\left( \frac{2FV}{RT} \right)} - c_{Ca-out} \right)}{1 - e^{\left( \frac{2FV}{RT} \right)}}$$

Now note that

$$(1 - e^{2\alpha}) = (1 - e^\alpha) \cdot (1 + e^\alpha)$$

so

$$0 = \sum_{z=1} \frac{u_i F \left( c_{in} e^{\left( \frac{FV}{RT} \right)} - c_o \right) \left( 1 + e^{\left( \frac{FV}{RT} \right)} \right)}{1 - e^{\left( \frac{2FV}{RT} \right)}} + \sum_{z=-1} \frac{u_i F \left( c_o e^{\left( \frac{FV}{RT} \right)} - c_{in} \right) \left( 1 + e^{\left( \frac{FV}{RT} \right)} \right)}{1 - e^{\left( \frac{2FV}{RT} \right)}} + \frac{u_{Ca} 4F \left( c_{in} e^{\left( \frac{2FV}{RT} \right)} - c_o \right)}{1 - e^{\left( \frac{2FV}{RT} \right)}}$$

*(subscripts abbreviated so it fits across...)*

Just consider the positive valences for now (the negatives looks the same but with *in* and *out* reversed). First, all the denominators are the same and can be multiplied out (with F):

$$0 = \sum_{z=1} u_i \left( c_{i-in} e^{\left(\frac{FV}{RT}\right)} - c_{i-out} \right) \left( 1 + e^{\left(\frac{FV}{RT}\right)} \right) + 4u_{Ca} \left( c_{Ca-in} e^{\left(\frac{2FV}{RT}\right)} - c_{Ca-out} \right)$$

$$0 = \sum_{z=1} u_i \left( c_{i-in} e^{\left(\frac{FV}{RT}\right)} - c_{i-out} + c_{i-in} e^{\left(\frac{2FV}{RT}\right)} - c_{i-out} e^{\left(\frac{FV}{RT}\right)} \right) + 4u_{Ca} \left( c_{Ca-in} e^{\left(\frac{2FV}{RT}\right)} - c_{Ca-out} \right)$$

This is a quadratic equation in  $e^{FV/RT}$  -- obviously, the solution is not simple. Therefore, it must be left as an exercise for the student.

Seriously -- let's just find the Nernst equation for the divalent  $c_{Ca}$ . That is, assume nothing else crosses the membrane, so  $I_{Ca} = 0$ :

$$0 = 4u_{Ca} \left( c_{Ca-in} e^{\left(\frac{2FV}{RT}\right)} - c_{Ca-out} \right)$$

$$0 = \left( c_{Ca-in} e^{\left(\frac{2FV}{RT}\right)} - c_{Ca-out} \right)$$

$$c_{Ca-in} e^{\left(\frac{2FV}{RT}\right)} = c_{Ca-out}$$

$$e^{\left(\frac{2FV}{RT}\right)} = \frac{c_{Ca-out}}{c_{Ca-in}}$$

$$2 \frac{FV}{RT} = \ln \left( \frac{c_{Ca-out}}{c_{Ca-in}} \right)$$

$$V = \frac{RT}{2F} \ln \left( \frac{c_{Ca-out}}{c_{Ca-in}} \right)$$

In general, the Nernst equation is (as we saw earlier):

$$V = \frac{RT}{Fz_i} \ln \left( \frac{c_{i-out}}{c_{i-in}} \right)$$

and that works here, as well.