<u>What is this?</u>

The **Em Calculator** is designed to compute *membrane potential* (Em, other common names are *resting potential*, *or zero-current potential*), depending on extra- and intracellular concentrations of two cations (Na$^+$ and K$^+$) and one anion (Cl$^-$) and their relative permeabilities/conductances. Two different equations (that give two different results!) are used for this, and the main purpose of this calculator is to compare the results produced by these two equations. One is the Goldman-Hodgkin-Katz equation (also known as the GHK equation or Goldman equation), which is by far the most popular way to determine Em.

GHK equation:

$$Em = \frac{RT}{F} \ln \frac{P_{Na}[Na^+]_o + P_K[K^+]_o + P_{Cl}[Cl^-]_i}{P_{Na}[Na^+]_i + P_K[K^+]_i + P_{Cl}[Cl^-]_o}$$

where R is the universal gas constant, T is absolute temperature, F is the Faraday constant, $[K^+]_o$, $[Na^+]_o$, and $[Cl^-]_o$ are extracellular concentrations of K$^+$, Na$^+$, and Cl$^-$, respectively; $[K^+]_i$, $[Na^+]_i$, and $[Cl^-]_i$ are their intracellular concentrations; P$_K$, P$_{Na}$, and P$_{Cl}$ are their permeabilities. In the calculator we use *relative permeabilities*; for this both numerator and denominator in the expression under the logarithm was divided by P$_{Na}$:

$$Em = \frac{RT}{F} \ln \frac{[Na^+]_o + p_K[K^+]_o + p_{Cl}[Cl^-]_i}{[Na^+]_i + p_K[K^+]_i + p_{Cl}[Cl^-]_o}$$

where p$_K$ = P$_K$/P$_{Na}$ and p$_{Cl}$ = P$_{Cl}$/P$_{Na}$. P$_{Na}$ was chosen because it is usually the smallest of the three permeabilities under consideration.

The other equation is based on Kirchhoff's Law, used less often, and usually called the Chord conductance equation (abbreviated here as the CC equation). The CC equation can be derived from an electrical equivalent circuit that consists of resistances and batteries for Na$^+$, K$^+$, and Cl$^-$. To learn more about the CC equation, read an article by Ernst Niebur (2008,

Electrical Properties of Cell Membranes, Scholarpedia, 3(6):7166.
doi:10.4249/scholarpedia.7166).

CC equation:

$$Em = (\frac{RT}{F}\ln\frac{[Na^+]_o}{[Na^+]_i}g_{Na} + \frac{RT}{F}\ln\frac{[K^+]_o}{[K^+]_i}g_K - \frac{RT}{F}\ln\frac{[Cl^-]_0}{[Cl^-]_i}g_{Cl}) / (g_{Na} + g_K + g_{Cl})$$

where g_{Na}, g_K, and g_{Cl} are conductances of Na^+, K^+, and Cl^-. Cl^- caries a negative charge, so the expression for Cl^- is subtracted.

What are the inputs in the calculator?

The windows for input data (active) and results (inactive) for each ion are grouped in three rows marked "Na+", "K+", and "Cl-". Three columns of active windows can be used to enter data. These columns from left to right are: extracellular concentrations of ions ("Out", in mM), intracellular concentrations of ions ("In", in mM), and dimensionless "Relative permeability/conductance". The latter column is used for both the relative permeability (for GHK) and the relative conductance (for CC). Both permeability and conductance reflect the ease with which the ions cross the membrane, and for both the GHK and CC equations the ratio of this ease for different ions is important, not their absolute values. Conductance is directly related to permeability (Kuffler, Nicholls, Martin. From Neuron to Brain, 2nd Edition, 1984); accordingly, if P_K/P_{Na} = 5, then g_K/g_{Na} = 5, and both relative permeability and relative conductances would be 5 for K^+ and 1 for Na^+. The relative permeability/conductance of Na^+ was selected as a reference point, and the corresponding field in the calculator interface is always 1.

Two additional active windows in the lower left corner are for temperature (in $^{\circ}$C) and for a coefficient consisting of the fundamental constants (RT/F) adjusted for decimal logarithm, that is, the value in the window is 2.3026*RT/F. These windows are reciprocally connected and a direct input in one of them will result in an appropriate change in the other.

Note: Please remember that this is a simple calculator, and it has no protection from an erroneous input (for instance, 0 for any concentration or a negative value of a relative permeability/conductance).

What does the calculator compute?

Three columns of inactive windows serve to display results of calculations. The column in the middle ("Eeq", in mV) shows the equilibrium (Nernst) potentials for each ion, calculated as followed:

$$E_{Na} = \frac{RT}{F} \ln \frac{[Na^+]_o}{[Na^+]_i}$$

$$E_K = \frac{RT}{F} \ln \frac{[K^+]_o}{[K^+]_i}$$

$$E_{Cl} = -\frac{RT}{F} \ln \frac{[Cl^-]_o}{[Cl^-]_i}$$

where E_{Na}, E_K and E_{Cl} are equilibrium potentials for Na^+, K^+, and Cl^-, respectively. Thus, the CC equation can be expressed in simpler form in terms of equilibrium potentials:

$Em = (E_{Na} g_{Na} + E_K g_K + E_{Cl} g_{Cl}) / (g_{Na} + g_K + g_{Cl})$

The two columns on the right marked "GHK" and "CC" depend on the equations that are used for calculation of (from top to bottom) individual

ionic currents for Na$^+$, K$^+$, and Cl$^-$, total currents ("Total") and the resting potential ("Em"). The total current must be 0 to confirm that calculated values of Em are indeed resting, or zero-current, potential from the point of view of the theories at the base of the GHK and CC equations. Accordingly, the individual currents are calculated differently in models associated with GHK and CC. In CC they are determined by Ohm's law:

$$I_{Na} = (E_{Na} - Em)$$

$$I_K = (E_K - Em)\ g_K/g_{Na}$$

$$I_{Cl} = (E_{Cl} - Em)\ g_{Cl}/g_{Na}$$

$$I_{tot} = I_{Na} + I_K + I_{Cl}$$

where I_{Na}, I_K, and I_{Cl} are relative currents for Na$^+$, K$^+$, and Cl$^-$, respectively, and I_{tot} is the total transmembrane current. For the cations the positive current is codirected with influx of the ion, and for Cl$^-$ the positive current means efflux.

The GHK equation is based on electro-diffusion theory (see Kuffler, Nicholls, Martin. From Neuron to Brain, 2nd Edition, 1984) and the ionic currents are:

$$I_{Na} = P_{Na}\ F\ V'\ ([Na^+]_o - [Na^+]_i\ e^{V'})/(e^{V'} - 1)$$

$$I_K = P_K\ F\ V'\ ([K^+]_o - [K^+]_i\ e^{V'})/(e^{V'} - 1)$$

$$I_{Cl} = P_{Cl}\ F\ V'\ ([Cl^-]_i - [Cl^-]_o\ e^{V'})/(e^{V'} - 1)$$

where V' = Em F/RT. After taking out the factor $FV'/(e^{V'}-1)$ and converting to relative permeability, the relative currents can be presented in a shorter form:

$$I_{Na} = [Na^+]_o - [Na^+]_i \, e^{V'}$$

$$I_K = p_K \, ([K^+]_o - [K^+]_i \, e^{V'})$$

$$I_{Cl} = p_{Cl} \, ([Cl^-]_i - [Cl^-]_o \, e^{V'})$$

The shorter form permits Em = 0; in this case $e^{V'}$ = 1 and the currents are simply proportional to the difference in outer and inner concentrations. Again, the positive current is influx for cations and efflux for Cl⁻.

Values of constants used in calculations:

R = 8.314 joules/(°K*Mol)

T = 273.15 + temperature in °C

F = 96485 (coulomb/Mol)

ln(10) = log(10) * 2.302585093