Ion Channels of Excitable Membranes

THIRD EDITION

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```
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<Dimension name="time" t="1"/>
<Dimension name="mass" m="1"/>
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<Dimension name="current" i="1"/>
<Dimension name="charge" i="1" t="1"/>
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<Dimension name="energy_per_kelvin" m="1" l="2" t="-2" k="-1"/>
<Dimension name="energy_per_kelvin_per_mol" m="1" l="2" t="-2" k="-1" n="-1"/>
<Dimension name="charge_per_volt-meter" m="-1" l="-3" i="2" t="4"/>
<Dimension name="energy-time" m="1" l="2" t="-1"/>
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<Dimension name="concentration" n="1" l="-3"/>
<Dimension name="temperature" k="1"/>

<Assertion dimension="resistance" matches="1 / conductance"/>
<Assertion dimension="force" matches="mass * acceleration"/>
<Assertion dimension="energy" matches="force * distance"/>
<Assertion dimension="energy_per_kelvin" matches="energy / kelvin"/>
<Assertion dimension="charge_per_volt-meter" matches="charge / (voltage * distance)"/>
<Assertion dimension="energy-time" matches="energy * time"/>
<Assertion dimension="resistivity" matches="resistance * distance"/>
<Assertion dimension="concentration" matches="mole / volume"/>
<Assertion dimension="conductance" matches="1 / resistance"/>
```

TABLE 1.1 Physical Constants

Avogadro's number	N	$= 6.0221 \times 10^{23}\ \text{mol}^{-1}$
Elementary charge	q_e	$= 1.6022 \times 10^{-19}\ \text{C}$
Faraday's constant	F	$= Nq_e = 9.6485 \times 10^{4}\ \text{C mol}^{-1}$
Absolute temperature	T(K)	$= 273.15 + T$ (°Celsius)
Boltzmann's constant	k_B	$= 1.3807 \times 10^{-23}\ \text{V C K}^{-1}$
		$= 1.3807 \times 10^{-23}\ \text{J K}^{-1}$
Gas constant	R	$= 1.987\ \text{cal mol}^{-1}\ \text{K}^{-1}$
		$= 8.3145\ \text{J mol}^{-1}\ \text{K}^{-1}$
		$= 8.3145\ \text{V C mol}^{-1}\ \text{K}^{-1}$
Polarizability of free space	ε_0	$= 8.8542 \times 10^{-12}\ \text{C V}^{-1}\ \text{m}^{-1}$
Planck's constant	h	$= 6.6261 \times 10^{-34}\ \text{J s}$
One joule	1 J	$= 1\ \text{kg m}^2\ \text{s}^{-2}$
		$= 1\ \text{V C} = 1\ \text{W s}$
		$= 0.2389\ \text{cal}$

```
<Constant name="Avagadro's number" symbol="N" dimension="none" value="6.0221E23"/>

<Constant name="Elementary charge" symbol="q_e" dimension="charge" value="1.6E-19"/>
<Constant name="Boltzmann's constant" symbol="k_B" dimension="energy_per_kelvin" value="1.3807E23"/>
<Constant name="Gas constant" symbol="R" dimension="energy_per_kelvin_per_mol" value="N * k_B"/>
<Constant name="Faraday's constant" symbol="F" dimension="charge_per_mole" value="N * q_e"/>
<Constant name="Polarizability of free space" symbol="epsilon_0" dimension="charge_per_volt-meter"
value="8.8542E-12"/>
<Constant name="Planck's constant" symbol="h" dimension="energy-time" value="6.6261E-34"/>
```

```
 <Unit name="Mole" symbol="mol" dimension="mole"/>
 <Unit name="Per mole" symbol="per_mol" dimension="per_mole"/>
 <Unit symbol="C_per_mol" dimension="charge_per_mole"/>
 <Unit name="Ohm" symbol="ohm" dimension="resistance"/>
 <Unit name="Ohm centimetres" symbol="ohm_cm" dimension="resistivity" power="-2"/>
 <Unit name="farad" symbol="F" dimension="capacitance"/>
 <Unit name="siemens" symbol="S" dimension="conductance"/>
 <Unit name="Molar" symbol="M" dimension="concentration"/>
 <Unit name="milliMolar" symbol="mM" dimension="concentration" power="-3"/>
 <Unit name="microMolar" symbol="uM" dimension="concentration" power="-6"/>
 <Unit name="nanoMolar" symbol="nM" dimension="concentration" power="-9"/>
 <Unit name="milliVolt" symbol="mV" dimension="voltage" power="-3"/>

 <Unit name="Celsius" symbol="C" dimension="temperature" offset="273.5"/>
```

A physicist would begin the problem with the **Boltzmann equation** of statistical mechanics, which gives the relative probabilities at equilibrium of finding a particle in state 1 or in state 2 if the energy difference between these states is $u_2 - u_1$:

$$\frac{p_2}{p_1} = \exp\left(-\frac{u_2 - u_1}{k_B T}\right) \tag{1.7}$$

Here k_B is Boltzmann's constant and T is absolute temperature on the Kelvin scale. This equation conveniently describes the equilibrium distribution of particles in

```
<ComponentType name="ThermalEnvironment">
    <Parameter dimension="kelvin" name="temperature"/>
</ComponentType>

<ComponentType name="BoltzmannState">
    <Parameter name="u" dimension="energy"/>
</ComponentType>

<ComponentType name="BoltzmannSystem">
    <ComponentReference name="env" type="ThermalEnvironment"/>
    <Child name="state1" type="BoltzmannState"/>
    <Child name="state2" type="BoltzmannState"/>
    <Exposure name="p1_over_p2" dimension="none"/>

    <Behavior>
       <DerivedVariable name="u1" dimension="energy" select="state1/u"/>
       <DerivedVariable name="u2" dimension="energy" select="state2/u"/>
       <DerivedVariable name="T" dimension="temperature"
select="env/temperature"/>
       <DerivedVariable exposure="p1_over_p2" dimension="none" value="exp(-
(u2 - u1) / (k_B * T))"/>
     </Behavior>
</ComponentType>
```

Now we have a useful equilibrium relation between concentration ratios and energy differences. In our problem, $U_1 - U_2$ is the molar electrical energy difference of the permeant ion due to a membrane potential difference $E_1 - E_2$. If we consider a mole of an arbitrary ion S with charge z_S, then $U_1 - U_2$ becomes $z_S F(E_1 - E_2)$. Substituting into Equation 1.9 shows that the equilibrium potential E_S is a function of the concentration ratio and the valence:

$$E_S = E_1 - E_2 = \frac{RT}{z_S F} \ln \frac{[S]_2}{[S]_1} \tag{1.10}$$

This well-known relationship is called the **Nernst equation** (Nernst 1888).

```
<ComponentType name="NernstCompartment">
    <Parameter name="concentration" dimension="concentration"/>
</ComponentType>

<ComponentType name="NernstSystem">
    <ComponentReference name="species" type="Species"/>
    <Child name="Inside" type="NernstCompartment"/>
    <Child name="Outside" type="NernstCompartment"/>
    <Exposure name="E_S" dimension="voltage"/>
    <Requirement name="temperature" dimension="temperature"/>

    <Behavior>
        <Build>
            <ChildInstance component="species"/>
        </Build>
        <DerivedVariable name="z_S" select="species/valence" dimension="none"/>
        <DerivedVariable name="T" select="temperature" dimension="temperature"/>
        <DerivedVariable name="Si" select="Inside/concentration"
                         dimension="concentration"/>
         <DerivedVariable name="So" select="Outside/concentration"
                          dimension="concentration"/>
         <DerivedVariable exposure="E_S" value="(R * T) / (z_S * F) * log(So / Si) "/>
    </Behavior>
</ComponentType>
```

TABLE 1.3 Free Ion Concentrations and Equilibrium Potentials for Mammalian Skeletal Muscle

Ion	Extracellular concentration (mM)	Intracellular concentration (mM)	$\frac{[Ion]_o}{[Ion]_i}$	Equilibrium potential[a] (mV)
Na^+	145	12	12	+67
K^+	4	155	0.026	–98
Ca^{2+}	1.5	100 nM	15,000	+129
Cl^-	123	4.2[b]	29[b]	–90[b]

[a] Calculated from Equation 1.11 at 37°C.

[b] Calculated assuming a –90-mV resting potential for the muscle membrane and that Cl^- ions are at equilibrium at rest.

```
<Species id="Sodium" symbol="Na" valence="1"/>
<Species id="Calcium" symbol="Ca" valence="2"/>
<Species id="Potassium" symbol="K" valence="1"/>
<Species id="Chloride" symbol="Cl" valence="-1"/>

 <NernstSystem id="skeletalMuscleChloride" species="Chloride">
         <Inside concentration="4.2 mM"/>
         <Outside concentration="123 mM"/>
 </NernstSystem>

<ComponentType name="EquilibriumCalculation">
     <Parameter name="temperature" dimension="temperature"/>
     <Children name="systems" type="NernstSystem"/>

    <Procedure>
        <Equilibrate/>
            <ForEachComponent select="systems" as="system">
                <Print template="${system/name} \tat ${temperature:C}: \tinside=$
{system/Inside/concentration:mM} \toutside=${system/Outside/concentration:mM} \tpotential=$
{system/E_S:mV}"/>
            </ForEachComponent>
     </Procedure>
</ComponentType>

<EquilibriumCalculation id="potentials" temperature="37 C">
     <Insertion component="skeletalMuscleSodium"/>
     <Insertion component="skeletalMusclePotassium"/>
     <Insertion component="skeletalMuscleCalcium"/>
     <Insertion component="skeletalMuscleChloride"/>
</EquilibriumCalculation>


 <EquilibriumCalculation id="roomTemperaturePotentials" extends="potentials" temperature="21
C"/>

 <EquilibriumCalculation id="freezingPotentials" extends="potentials" temperature="0 C"/>
```

```
NFO - Reading model from /home/rcc/NEUROML-LEMS/eclipse/LEMS/examples/nernst.xml at
org.lemsml.sim.LemsProcess.readModel(LemsProcess.java:103)
INFO - OK:  dimension assertion holds: resistance matches 1 / conductance at org.lemsml.type.Assertion.check(Assertion.java:50)
INFO - OK:  dimension assertion holds: force matches mass * acceleration
INFO - OK:  dimension assertion holds: energy matches force * distance
INFO - OK:  dimension assertion holds: energy_per_kelvin matches energy / kelvin
INFO - OK:  dimension assertion holds: charge_per_volt-meter matches charge / (voltage * distance)
INFO - OK:  dimension assertion holds: energy-time matches energy * time
INFO - OK:  dimension assertion holds: resistivity matches resistance * distance
INFO - OK:  dimension assertion holds: concentration matches mole / volume
INFO - OK:  dimension assertion holds: conductance matches 1 / resistance
INFO - skeletalMuscleSodium   at 37.00 C:       inside=12.00 mM   outside=145.0 mM  potential=66.77 mV at
org.lemsml.run.ExecutablePrint.execute(ExecutablePrint.java:29)
INFO - skeletalMusclePotassium     at 37.00 C:       inside=155.0 mM   outside=4.000 mM  potential=-97.99 mV
INFO - skeletalMuscleCalcium       at 37.00 C:       inside=0.0001mM   outside=1.500 mM  potential=128.8 mV
INFO - skeletalMuscleChloride      at 37.00 C:       inside=4.200 mM   outside=123.0 mM  potential=-90.49 mV
INFO - skeletalMuscleSodium        at 21.00 C:       inside=12.00 mM   outside=145.0 mM  potential=63.33 mV
INFO - skeletalMusclePotassium     at 21.00 C:       inside=155.0 mM   outside=4.000 mM  potential=-92.94 mV
INFO - skeletalMuscleCalcium       at 21.00 C:       inside=0.0001mM   outside=1.500 mM  potential=122.2 mV
INFO - skeletalMuscleChloride      at 21.00 C:       inside=4.200 mM   outside=123.0 mM  potential=-85.82 mV
INFO - skeletalMuscleSodium        at 0.000 C:       inside=12.00 mM   outside=145.0 mM  potential=58.81 mV
INFO - skeletalMusclePotassium     at 0.000 C:       inside=155.0 mM   outside=4.000 mM  potential=-86.31 mV
INFO - skeletalMuscleCalcium       at 0.000 C:       inside=0.0001mM   outside=1.500 mM  potential=113.5 mV
INFO - skeletalMuscleChloride      at 0.000 C:       inside=4.200 mM   outside=123.0 mM  potential=-79.70 mV
```