NCS Cell Equations

The NeoCortical Simulator (NCS) was developed at The University of Nevada, Reno by the Brain Computation Lab under the direction of Dr. Phillip Goodman.
At the single cell level NCS solves a limited and slightly reordered form of the Hodgkin-Huxley Model that is similar to Equation (1). However, during the numerical integration a constant membrane leak is added. This is explained further below.

$$C_N \frac{dV}{dt} - I_M - I_A - I_{AHP} - I_{input} - I_{syn} + I_{leak} = 0 \tag{1}$$

The currents expressed in this equation fall into several different categories that are only briefly explained here. To begin, both I_M and I_{AHP} contribute to the membrane voltage by controlling spike-frequency adaptation. These are small ionic currents that have a long period of activity when the membrane voltage is between rest and threshold.
I_M is the Noninactivating Muscarinic Potassium Current and is defined by

$$I_M = \bar{g}_M S m^P (E_k - V) \tag{2}$$

Where S is a non-dimensional Strength variable added to NCS and P is the power that the activation variable m is raised to. This is essentially decreasing the slope of the activation variable as explained in Section 2.6. The change of that activation variable is defined as

$$\frac{dm}{dt} = \frac{m_\infty - m}{\tau_m} \tag{3}$$

Where

$$\tau_m = \frac{\epsilon}{e^{\left(\frac{V - V_{1/2}}{\omega}\right)} + e^{-\left(\frac{V - V_{1/2}}{\eta}\right)}}$$

$$m_\infty = \frac{1}{1 + e^{-\left(\frac{V - V_{1/2}}{\xi}\right)}}$$

ϵ is the scale factor.
$V_{1/2}$ satisfies the equation $m_\infty(V_{1/2}) = 0.5$.
ω, η and ξ are slope factors affecting the rate of change of the activation variable m.
This channel is defined in NCS through the input file format as:

```
CHANNEL Km
     TYPE                      m
     M_INITIAL                 0.0       0.0
     REVERSAL_POTENTIAL      -80         0
     M_POWER                   1
     E_HALF_MIN_M            -44
     SLOPE_FACTOR_M           40        20        8.8
     TAU_SCALE_FACTOR_M        0.303
     UNITARY_G                 5
     STRENGTH                  0.00015
END_CHANNEL
```

Notice that (2) is different from the traditional equation shown below in Equation (4). This reverse of the driving force explains the sign changes in Equation (1).

$$I_M = \bar{g}_M m_m (V - E_K) \tag{4}$$

I_{AHP} is the current provided by the other small spike-adaptation contributing channel. These are voltage independent potassium channels that are regulated by internal calcium.

$$I_{AHP} = \bar{g}_{AHP} S m^P (E_k - V) \tag{5}$$

Where S is a non-dimensional Strength variable added to NCS and P is the power that the activation variable m is raised to. The change of that activation variable is defined as

$$\frac{dm}{dt} = \frac{m_\infty - m}{\tau_m} \tag{6}$$

$$\tau_m = \frac{\epsilon}{f(Ca) + b}$$

$$m_\infty = \frac{f(Ca)}{f(Ca) + b}$$

Where

ϵ is the scale factor.

b is the backwards rate constant, defined as CA_Half_Min in the NCS documentation.

$f(Ca)$ is the forward rate constant defined by (7).

$$f(Ca) = \kappa [Ca]_i{}^\alpha \tag{7}$$

Internal calcium concentrations are calculated at the compartment level in NCS. Physiologically the calcium concentration of a cell increases when an action potential fires. After the action potential has ended the internal concentration of calcium will diffuse throughout the cell where it is taken up by numerous physiological buffers. In NCS this diffusion/buffering phenomena is modeled by a simple decay equation defined by Equation (8).

$$[Ca]_i(t+1) = [Ca]_i(t) \left(1 - \frac{dt}{\tau_{Ca}}\right) \tag{8}$$

Where

dt is the simulation time step.

τ_{Ca} is the defined time constant for the Ca decay.

When an action potential fires in NCS the internal calcium concentration is increased by a static value specified in the input file.

This channel is defined in the NCS input file format as:

```
CHANNEL Kahp
     TYPE                          ahp1
     SEED                        999999
     M_INITIAL                        0.0          0.0
     REVERSAL_POTENTIAL            -80             0
     M_POWER                          2
     UNITARY_G                        6
     STRENGTH                         0.00015
     CA_SCALE_FACTOR                  0.000125
     CA_EXP_FACTOR                    2
     CA_HALF_MIN                      2.5
     CA_TAU_SCALE_FACTOR              0.01
END_CHANNEL
```

The third and final channel type modeled in NCS is the transient outward potassium current or K_a. This channel requires hyperpolarization for its activation; meaning that the channel will open during inhibitory synaptic input. This is defined by (9).

$$I_K = \bar{g}_M S m^P h^C \left(E_k - V\right) \tag{9}$$

Where as before S is a non-dimensional Strength variable added to NCS, P is the power that the activation variable m is raised to and C is the power that the inactivation variable h is raised to. The change of activation and inactivation variables is defined by (10) and (11).

$$\frac{dm}{dt} = \frac{m_\infty - m}{\tau_m} \tag{10}$$

$$\frac{dh}{dt} = \frac{h_\infty - m}{\tau_h} \tag{11}$$

Where

$$m_\infty = \frac{1}{1 + e^{-\left(\frac{V - V_{1/2m}}{\xi}\right)}}$$

$V_{1/2m}$ satisfies the equation $m_\infty(V_{1/2m}) = 0.5$.

ξ is slope factor affecting the rate of change of the activation variable m.

$$h_\infty = \frac{1}{1 + e^{-\left(\frac{V - V_{1/2h}}{\eta}\right)}}$$

$V_{1/2h}$ satisfies the equation $h_\infty(V_{1/2h}) = 0.5$.

η is slope factor affecting the rate of change of the inactivation variable h.

τ_m and τ_h are voltage dependent. NCS allows this dependence to be defined using an array of values for both the voltages and time constants. This is defined by (12).

$$\tau(V) = \begin{cases} \tau(1) & \text{if } V < V(1), \\ \tau(2) & \text{if } V < V(2), \\ \vdots \\ \tau(n) & \text{if } V < V(n) \\ \tau(n+1) & \text{else} \end{cases} \tag{12}$$

This channel is defined in NCS through the input file format as:

```
CHANNEL Ka
     TYPE                    a
     M_INITIAL               0.0         0.0
     H_INITIAL               1.0         0.0
     REVERSAL_POTENTIAL    -80           0
     M_POWER                 1
     H_POWER                 1
     E_HALF_MIN_M           11
     E_HALF_MIN_H          -56
     SLOPE_FACTOR_M         18
     SLOPE_FACTOR_H         18
     UNITARY_G               0.12
     STRENGTH                2.5
     V_TAU_VALUE_M           0.0002  9999
     V_TAU_VALUE_H           0.03   0.08   0.13   0.18   0.23
     V_TAU_VOLTAGE_M       100
     V_TAU_VOLTAGE_H       -21     -1     10     21
END_CHANNEL
```

The leakage current is voltage-independent and is modeled by (13). Notice that the driving force is expressed using the normal convention. This is the reason the leakage current is subtracted in the membrane voltage equation rather than added, as seen in the traditional membrane voltage equations.

$$I_{leak} = g_{leak}\,(V - E_{leak}) \tag{13}$$

The synaptic currents are calculated by

$$I_{syn} = \bar{g}_{syn} PSG(t)\,(E_{syn} - V) \tag{14}$$

The numerical integration scheme employed by NCS is similar to an Eulerian method however, as mentioned above a constant leak term is added to the discretized form of (1). To begin the current values defined above are summed

$$I_{Total} = I_M + I_A + I_{AHP} + I_{input} + I_{syn} - I_{leak} \tag{15}$$

The new voltage is then calculated as a combination of the defined membrane resting potential, the previously calculated membrane potential, the membrane resistance, capacitive time constant and the total currents.

$$V(t+1) = V_{rest} + (V(t) - V_{rest})\left(1 - \frac{\Delta}{\tau_{mem}}\right) + \Delta\frac{I_{Total}}{C_n} \tag{16}$$

Rearranging for clarity

$$V(t+1) = V(t) + (V_{rest} - V(t))\frac{\Delta}{\tau_{mem}} + \Delta\frac{I_{Total}}{C_n} \tag{17}$$

Where

$C_n = \frac{\tau_{mem}}{R_{mem}}$

R_{mem} is the defined resistance of the membrane.

τ_{mem} is the defined capacitive time constant of the membrane.

Notice the form of (1) in a simple Eulerian integration scheme would be

$$V(t+1) = V(t) + \Delta\frac{I_{Total}}{C_n} \tag{18}$$

The addition of the middle term in Equation (17) numerically drives the membrane voltage of the cell back to a predefined resting potential.