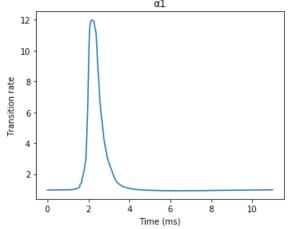
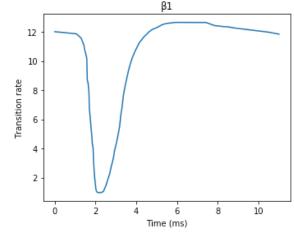
Paper Figures

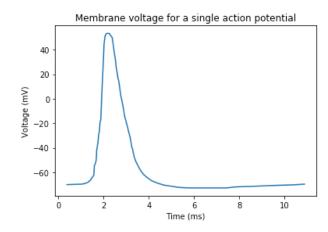
1. Multinomial Markov

Voltage-Gated Calcium Channel

$$C0\frac{\alpha_{\scriptscriptstyle I}(V)}{\overline{\beta_{\scriptscriptstyle I}(V)}}C1\frac{\alpha_{\scriptscriptstyle 2}(V)}{\overline{\beta_{\scriptscriptstyle 2}(V)}}C2\frac{\alpha_{\scriptscriptstyle 3}(V)}{\overline{\beta_{\scriptscriptstyle 3}(V)}}C3\frac{\alpha_{\scriptscriptstyle 4}(V)}{\overline{\beta_{\scriptscriptstyle 4}(V)}}O$$







$$\alpha_i(V) = \alpha_{io} \exp(V/V_i)$$

$$\beta_i(V) = \beta_{io} \exp(V/V_i)$$

$$\alpha_i \Delta t$$

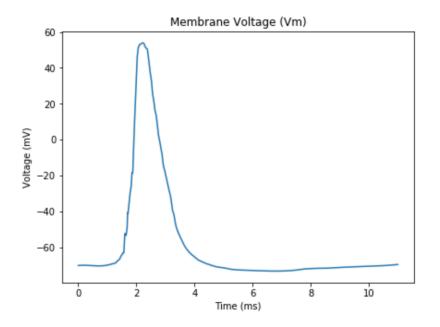
$$\beta_i \Delta t$$

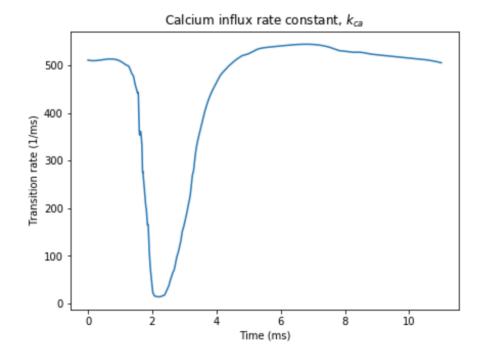
Membrane Voltage (Vm) **Action Potential and State Transitions** -20 VDCC transition, α_3 VDCC transition, α_1 VDCC transition, α_2 VDCC transition, α_4 25 12 120 10 20 100 Transition rate Transition rate Transition rate 8 80 60 40 20 10 10 10 Time (ms) Time (ms) Time (ms) Time (ms) VDCC transition, β_1 VDCC transition, β3 VDCC transition, β_2 VDCC transition, β_4 30 35 30 25 30 25 Transition rate ate 20 ate 25 Transition rate 20 **Fransition** 15 15 10 10 10 10 10 Time (ms) Time (ms) Time (ms) Time (ms)

Calcium Influx

$$C0 \xrightarrow{\alpha_1(V)} C1 \xrightarrow{\alpha_2(V)} C2 \xrightarrow{\alpha_3(V)} C3 \xrightarrow{\alpha_4(V)} C3 \xrightarrow{\beta_4(V)} C3 \xrightarrow{\beta_4(V)} C3 \xrightarrow{\alpha_4(V)} C3$$

$$k_{Ca}(V_m) = \frac{\gamma V_m N_A \left(0.393 - e^{\frac{-V_m}{80.36}}\right)}{2F\left(1 - e^{\frac{V_m}{80.36}}\right)}$$





VDCC Solutions - MCell

VDCC Solutions - ODE

$$C0 \frac{\alpha_{\scriptscriptstyle 1}(V)}{\overline{\beta_{\scriptscriptstyle 1}(V)}} C1 \frac{\alpha_{\scriptscriptstyle 2}(V)}{\overline{\beta_{\scriptscriptstyle 2}(V)}} C2 \frac{\alpha_{\scriptscriptstyle 3}(V)}{\overline{\beta_{\scriptscriptstyle 3}(V)}} C3 \frac{\alpha_{\scriptscriptstyle 4}(V)}{\overline{\beta_{\scriptscriptstyle 4}(V)}} C3 \frac{ca^{2+}}{\overline{\beta_{\scriptscriptstyle 4}(V)}}$$

$$\frac{dC0}{dt} = \beta_1(V)C1 - \alpha_1(V)C0$$

$$\frac{dC1}{dt} = \alpha_1(V)C0 + \beta_2(V)C2 - (\beta_1(V) + \alpha_2(V))C1$$

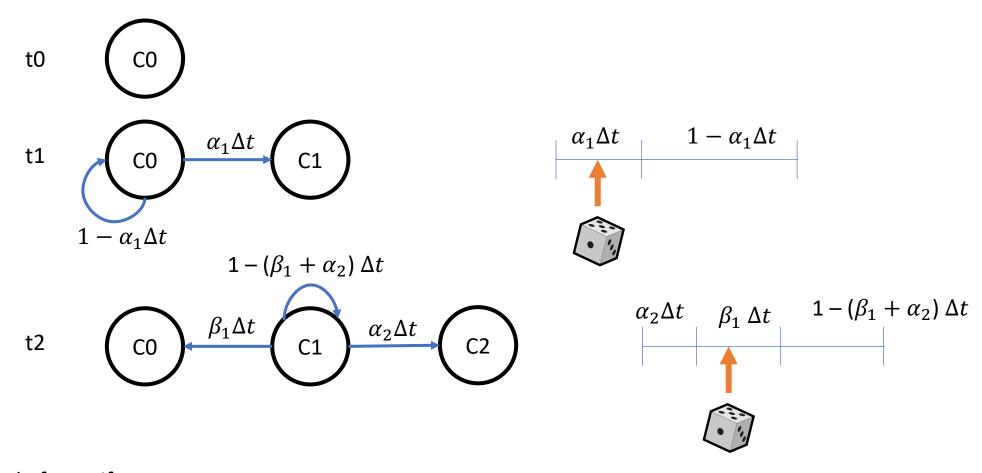
$$\frac{dC2}{dt} = \alpha_2(V)C1 + \beta_3(V)C3 - (\beta_2(V) + \alpha_3(V))C2$$

$$\frac{dC3}{dt} = \alpha_3(V)C2 + \beta_4(V)O - (\beta_3(V) + \alpha_4(V))C3$$

$$\frac{dO}{dt} = \alpha_4(V)C3 - \beta_4(V)O$$

$$\frac{dCa}{dt} = k_{Ca}(V)O$$

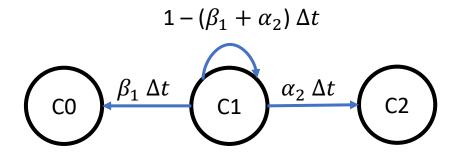
VDCC Solutions - Markov



- 1. Sample for Unif
- Compare to probabilities to find out

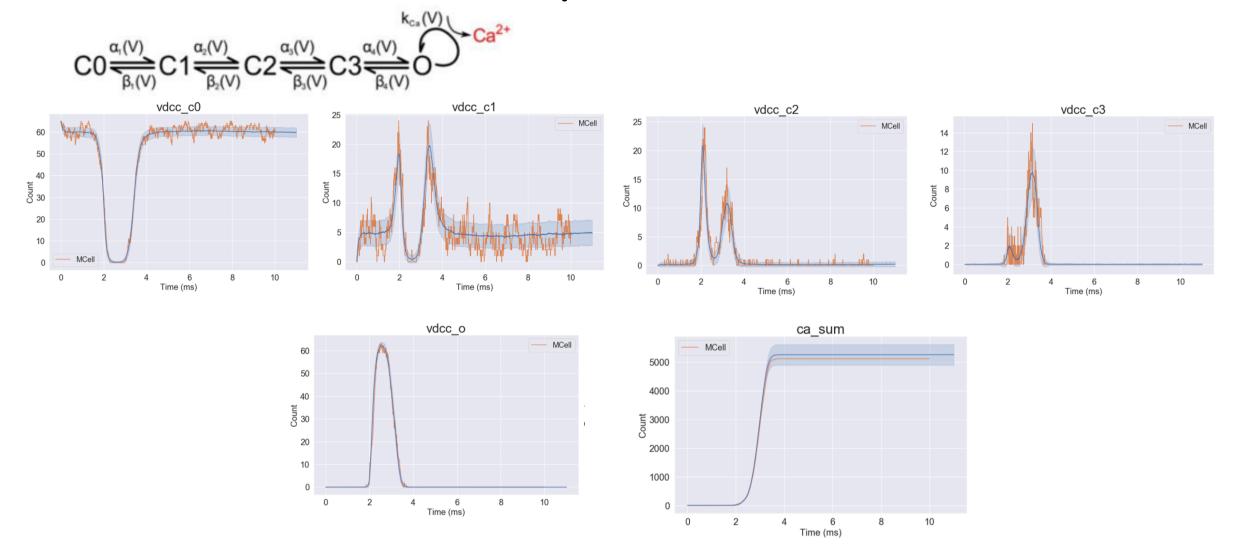
VDCC Solutions – Multinomial Markov

$$\begin{aligned} P_{C1 \to C2} &= \alpha_2 \, \Delta t \\ P_{C1 \to C0} &= \beta_1 \, \Delta t \\ P_{C0 \to C0} &= \beta_1 \, 1 - (\beta_1 + \alpha_2) \, \Delta t \end{aligned}$$

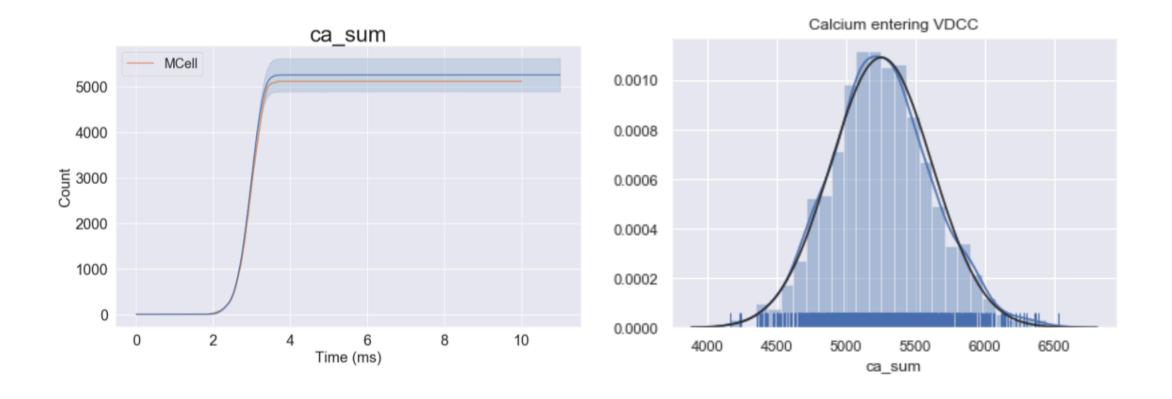


	$P_{C1 \rightarrow C2}$	$P_{C1 \rightarrow C0}$	$P_{C0 \rightarrow C0}$	
n = 1 channel	0	1	0	$\sum = 1$
n = 20 channels	4	9	7	$\sum = 20$

VDCC Solutions Comparison



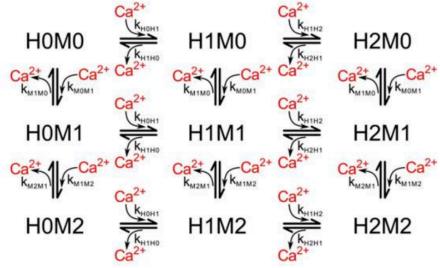
Calcium Influx



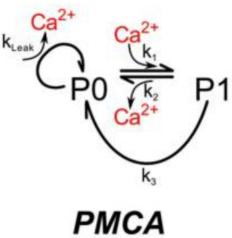
2. Operator Splitting

Calcium binding and diffusion upon influx into axon.

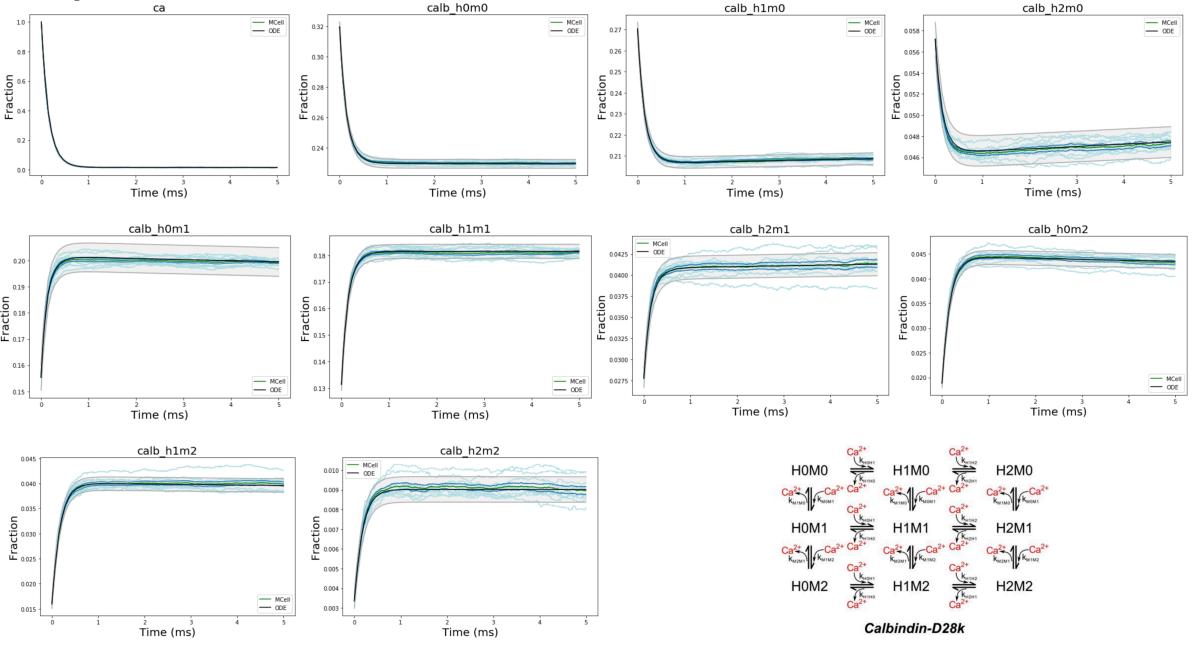
Calcium Binding



Calbindin-D28k



Impact of Calbindin



Impact of PMCA