# A basic model of calcium homeostasis in non-excitable cells


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## Supporting Information S5 Program

### Rate equations, parameters, initial concentrations, and calculations for Fig 8B

Calculations in Fig 8B are based on the same model as in Fig 7, where both PMCA and NCX are included. (Fig S1).

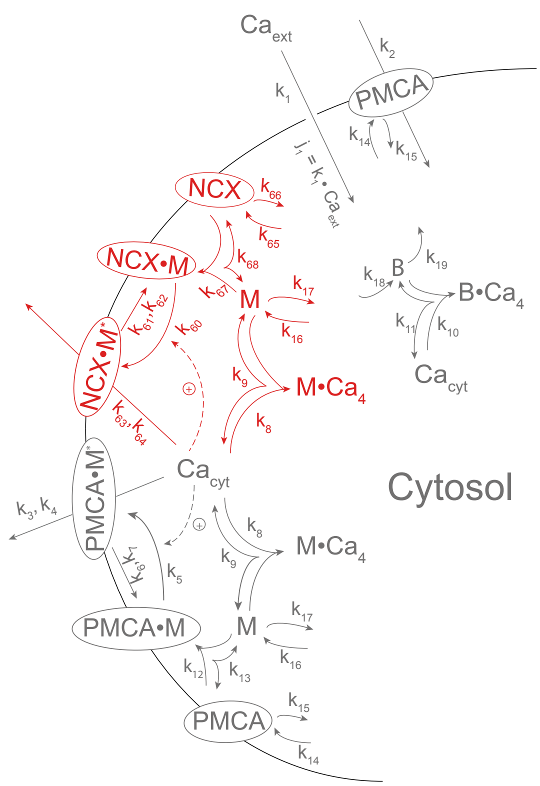


**Figure S1. Model including both PMCA and NCX for cytosolic $Ca^{2+}$ extrusion.** The added NCX part is outlined in red.

The model in Fig 8B is described by the following rate equations:

$$
\begin{aligned}
\frac{dCa^{2+}_{ext}}{dt} &= k_1 \times Ca^{2+}_{ext} - k_2 \times Ca^{2+}_{cyt} \times PMCA - k_3 \times \frac{(PMCA{\bullet}M^*) \times Ca^{2+}_{cyt}}{k_4 + Ca^{2+}_{cyt}} \\
&- 4 \times k_8 \times M \times Ca^{2+}_{cyt} + 4 \times k_9 \times (M{\bullet}Ca_4) - 4 \times k_{10} \times B \times Ca^{2+}_{cyt} \\
&+ 4 \times k_{11} \times (B{\bullet}Ca_4) - \frac{k_{63} \times Ca^{2+}_{cyt} \times (NCX{\bullet}M^*)}{k_{64} + Ca^{2+}_{cyt}}
\end{aligned} \tag{S1}
$$

$$
\frac{d(PMCA{\bullet}M^*)_{ext}}{dt} = k_5 \times Ca^{2+}_{cyt} \times (PMCA{\bullet}M) - \frac{k_6 \times (PMCA{\bullet}M^*)}{k_7 + (PMCA{\bullet}M^*)} \tag{S2}
$$

$$
\frac{dM}{dt} = k_{16} - k_{17} \times M - k_{12} \times M \times PMCA + k_{13} \times (PMCA{\bullet}M) \tag{S3}
$$

$$
+ k_9 \times (M{\bullet}Ca_4) - k_8 \times Ca^{2+}_{cyt} \times M + k_{68} \times (NCX{\bullet}M) \tag{S4}
$$

$$
- k_{67} \times M \times NCX \tag{S5}
$$

$$
\frac{d(M{\bullet}Ca_4)}{dt} = k_8 \times Ca^{2+}_{cyt} \times M - k_9 \times (M{\bullet}Ca_4) \tag{S6}
$$

$$
\frac{dB}{dt} = k_{18} - k_{19} \times B - k_{10} \times B \times Ca^{2+}_{cyt} + k_{11} \times (B{\bullet}Ca_4) \tag{S7}
$$

$$
\frac{d(B{\bullet}Ca_4)}{dt} = k_{10} \times B \times Ca^{2+}_{cyt} - k_{11} \times (B{\bullet}Ca_4) \tag{S8}
$$

$$
\begin{aligned}
\frac{d(PMCA{\bullet}M)}{dt} &= k_{12} \times PMCA \times M - k_{13} \times (PMCA{\bullet}M) \\
&+ \frac{k_6 \times (PMCA{\bullet}M^*)}{k_7 + (PMCA{\bullet}M^*)} - k_5 \times Ca^{2+}_{cyt} \times (PMCA{\bullet}M)
\end{aligned}
$$

$$\frac{dPMCA}{dt} = k_{14} - k_{15}{\times}PMCA - k_{12}{\times}PMCA{\times}M + k_{13}{\times}(PMCA{\bullet}M)$$

$$\frac{d(NCX{\bullet}M^*)}{dt} = k_{60}{\times}(NCX{\bullet}M){\times}Ca^{2+}_{cyt} - \frac{k_{61}{\times}(NCX{\bullet}M^*)}{k_{62} + (NCX{\bullet}M^*)}$$

$$\frac{d(NCX{\bullet}M)}{dt} = k_{67}{\times}M{\times}NCX - k_{68}{\times}(NCX{\bullet}M) - k_{60}{\times}NCX{\bullet}M{\times}Ca^{2+}_{cyt} + \frac{k_{61}{\times}(NCX{\bullet}M^*)}{k_{62} + (NCX{\bullet}M^*)}$$

$$\frac{dNCX}{dt} = k_{65} - k_{66}{\times}NCX - k_{67}{\times}M{\times}NCX + k_{68}{\times}(NCX{\bullet}M)$$

The time steps during LSODE integration is $1.0{\times}10^{-2}$s, with 4 phases having intervals of 20s, 150s, 180s, and 225s.

The rate constants in phase 1 are given as: $k_1 = 0.0s^{-1}$, $k_2 = 0.0s^{-1}$, $k_3 = 5.0{\times}10^3 s^{-1}$, $k_4 = 1.2\mu M$, $k_5 = 16.0\mu M^{-1}s^{-1}$, $k_6 = 8.0{\times}10^{-3}\mu M/s$, $k_7 = 1.0{\times}10^{-6}\mu M$, $k_8 = 2.5s^{-1}$, $k_9 = 5.0s^{-1}$, $k_{10} = 1.0{\times}10^2\mu M^{-1}s^{-1}$, $k_{11} = 80.0s^{-1}$, $k_{12} = 1.0{*}10^{-2}\mu M^{-1}s^{-1}$, $k_{13} = 1.0{\times}10^{-1}\mu M^{-1}s^{-1}$, $k_{14} = 0.0\mu M/s$, $k_{15} = 0.0s^{-1}$, $k_{16} = 0.0\mu M/s$, $k_{17} = 0.0s^{-1}$, $k_{18} = 0.0\mu M/s$, $k_{19} = 0.0s^{-1}$, $k_{60} = 16.0\mu M^{-1}s^{-1}$, $k_{61} = 8.0{\times}10^{-3}\mu M/s$, $k_{62} = 1.0{\times}10^{-6}\mu M$, $k_{63} = 0.0s^{-1}$, $k_{64} = 1.0{\times}10^2\mu M$, $k_{65} = 0.0\mu M/s$, $k_{66} = 0.0s^{-1}$, $k_{67} = 1.0{\times}10^{-2}\mu M^{-1}s^{-1}$, $k_{68} = 1.0{\times}10^{-1}s^{-1}$.

Changed rate constants in phases 2-4:

$k^{max}_{1,ph2}$ (phase 2, Eq 10) = $2.0{\times}10^{-2}s^{-1}$, $\alpha$ (phase 2, Eq 10) = $1.3{\times}10^{-2}s^{-1}$; $\beta$ (phase 2, Eq 12) = $1.2{\times}10^2 s^{-2}$; $k_1$, phases 3-4 = $0.0s^{-1}$; $k_3$, phases 3-4 = $0.0s^{-1}$; $k_{63}$, phases 2-3 =$0.0s^{-1}$; $k_{63}$, phase 4 = $1.0{\times}10^5 s^{-1}$. Other rate constants as described for phase 1 above.

Initial concentrations (all in $\mu$M): $Ca^{2+}{}_{cyt} = 1.0247{\times}10^{-1}$, PMCA•M* = $1.0973{\times}10^{-4}$, $Ca^{2+}{}_{ext} = 2{\times}10^3$, M = 9.5161, M•Ca4 = $4.8886{\times}10^{-1}$, B = $1.7859{\times}10^2$, B•Ca4 = 22.936, PMCA•M = $4.8225{\times}10^{-3}$, PMCA = $5.0677{\times}10^{-3}$, NCX•M* = $1.0973{\times}10^{-4}$, NCX•M = $4.8225{\times}10^{-3}$, NCX = $5.0677{\times}10^{-3}$.

The executables `careg64v5` (Mac OSX) and `careg64v5.exe` (Windows) are found in the `fortran` subdirectory. Rate parameters together with the initial concentrations are read from the input file `CAREG64v5.INP`.

### Compiling `CAREG64v5.f`

We have compiled `CAREG64v5.f` with 64 bits encoding using the Mac Terminal and Windows Cmd prompt together with Absoft's ProFortran compilers for Mac OSX and Windows:

Mac OSX: `f77 -o careg64v5 -m64 -O2 CAREG64v5.f libV77.a`
Windows: `f77 -o careg64v5.exe -m64 -O2 CAREG64v5.f vms.lib`
with the (enclosed) 64 bits libraries `libV77.a` and `vms.lib`.

### Running the model

If gnuplot and Perl are installed, on Mac OSX one runs the script file `careg64v5.sh` by using the terminal command `./careg64v6.sh`. On Windows computers you use the Cmd prompt and type `careg64v5.cmd`. The numerical output will be created, i.e. concentrations in file `CAREG64v6-07.txt` and fluxes in file `CAREG64v5-65_fluxes.txt`. `CAREG64v5-65` is our run identifier (which can be changed in the input file `CAREG64v5.INP`).

The following four graphs (Fig S2) (in pdf format) will be generated and should be opened automatically by the default pdf viewer.

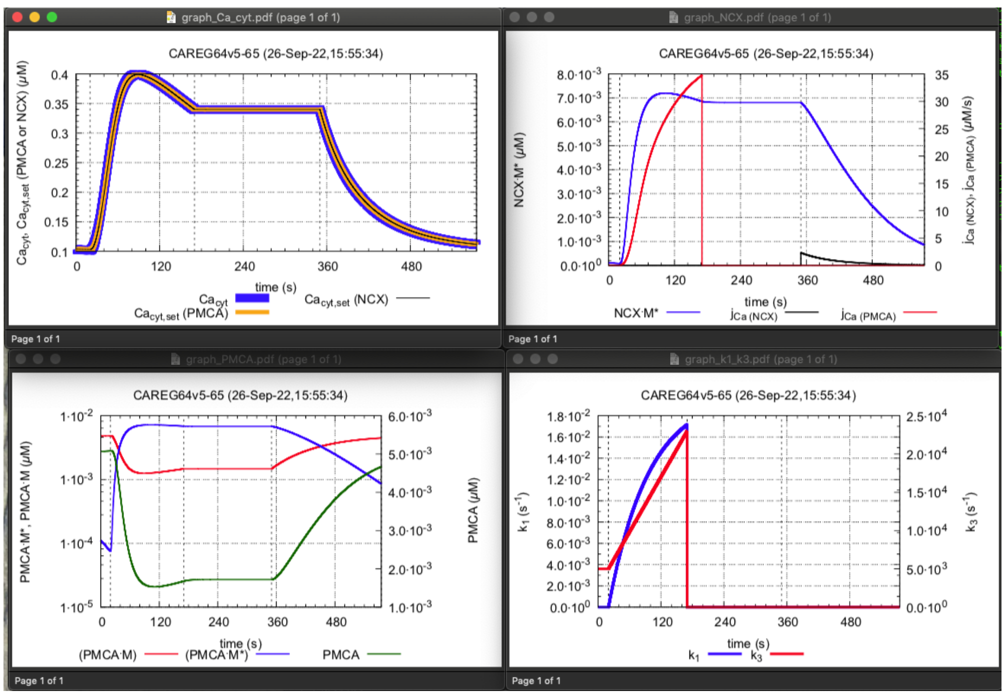


**Figure S2. Graphs created when running `careg64v5.sh` or `careg64v5.exe` with Perl and gnuplot installed.** $j_{\mathrm{Ca\ (PMCA)}}$ and $j_{\mathrm{Ca\ (NCX)}}$ are the velocities by which PMCA and NCX pump calcium out of the cell.

If Perl or gnuplot are not installed you execute the provided binary files `CAREG64v5` (Mac) or `CAREG64v5-65.exe`, which will generate the concentration and flux data files `CAREG64v5-65.txt` and `CAREG64v5-65_fluxes.txt`. Graphs can then be created by a custom graphing program if it allows to plot numerical column data. The graphs in Fig S2 involve the following comma-delimited columns:

File `CAREG64v5-65.txt`:

column 1: time (s)
column 2: $\mathrm{Ca_{cyt}}$ ($\mu$M)
column 3: (PMCA•M$^*$) ($\mu$M)
column 10: $\mathrm{Ca_{cyt,\ set}}$ (PMCA) ($\mu$M)
column 11: $\mathrm{Ca_{cyt,\ set}}$ (NCX) ($\mu$M)
column 27: PMCA•M ($\mu$M)
column 29: PMCA ($\mu$M)
column 30: $k_3$ (1/s)
column 31: $k_1$ (1/s)
column 32: $(NCX{\bullet}M^*)$ ($\mu$M)

File `CAREG64v5-65_fluxes.txt`:
column 1: time (s)
column 4: $\mathrm{j_{Ca\ (PMCA)}}$ ($\mu$M/s)
column 14: $\mathrm{j_{Ca\ (NCX)}}$ ($\mu$M/s)