

Homogenized model

$$\frac{\partial [Ca^{2+}]}{\partial t} = J_{flux} - J_{SERCA} + J_{media} + D_{Ca^{2+}} \nabla^2 [Ca^{2+}]$$

$$\frac{d[IP_3R]}{dt} = k_6 \left(\frac{K_i^2}{K_i^2 + [Ca^{2+}]^2} - [IP_3R] \right)$$

$$\frac{d[Ca_{ER}^{2+}]}{dt} = -\frac{V}{V_{ER}} (J_{flux} - J_{SERCA})$$

$$\frac{\partial [IP_3]}{\partial t} = v_{PLC} - k_{deg}[IP_3] + D_{IP_3} \nabla^2 [IP_3]$$

$$J_{flux} = \frac{(k_1 + k_2[IP_3R][Ca^{2+}]^2[IP_3]^2)([Ca_{ER}^{2+}] - [Ca^{2+}])}{(K_{Ca^{2+}}^2 + [Ca^{2+}]^2)(K_{IP_3}^2 + [IP_3]^2)}$$

$$J_{SERCA} = \frac{v_{SERCA}[Ca^{2+}]^2}{k_{SERCA}^2 + [Ca^{2+}]^2}$$

$$J_{media} = v_{leak} - k_{leak}[Ca^{2+}]$$

$$v_{PLC} = \Gamma(1, \mu_{PLC})$$

Boundary and initial conditions

No-flux boundary conditions:

$$\nabla[IP_3] = 0 \text{ at } x = \{0, L\}$$
$$\nabla[Ca^{2+}] = 0 \text{ at } x = \{0, L\}$$

Spatial domain is 0 to L

Steady-state initial conditions:

$$\begin{aligned} \text{at } t = 0: \quad & [Ca^{2+}] = 0.05 \mu M \\ & [IP_3] = 0.15 \mu M \\ & [Ca_{ER}^{2+}] = 80 \mu M \\ & [IP_3R] = 1 \end{aligned}$$

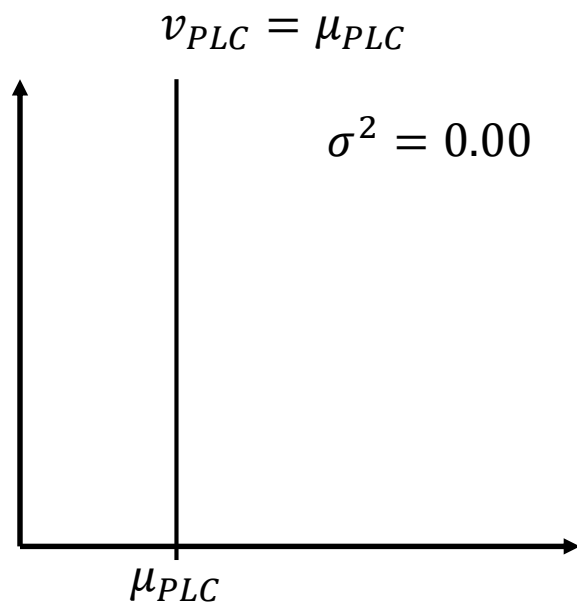
Parameter	Description	Value
k_1	Rate constant of calcium leak from ER ¹	4e-4 [1/s]
k_2	Rate constant of calcium release through IP3R ¹	0.08 [1/s]
$K_{Ca^{2+}}$	Half-saturation constant for calcium activation of IP3R ¹	0.2 [uM]
K_{IP_3}	Half-saturation constant for IP3 activation of IP3R ¹	0.3 [uM]
v_{SERCA}	Maximum rate of calcium pumping into the ER ²	0.08 [uM/s]
k_{SERCA}	Half-saturation constant for calcium pumping into the ER ²	0.02 [uM]
v_{leak}	Rate of calcium leak from medium ¹	0.51 [1/s]
k_{leak}	Rate constant of calcium flux to the medium ¹	0.035 [uM]
V_{ER}/V	Volumetric fraction of ER ²	20
k_6	Rate constant of IP3R inactivation ^{1,2}	11.3 [1/s]
K_i	Half-saturation constant for calcium inhibition of IP3R ^{1,2}	0.09 [uM]
k_{deg}	Rate constant of IP3 degradation ¹	0.08 [1/s]
μ_{PLC}	Mean rate of IP3 generation	1e-2 [uM/s]
D_{IP_3}	Diffusivity of IP3 ^{1,2,3}	280 [uM/s^2]
$D_{Ca^{2+}}$	Diffusivity of calcium ^{1,2,3}	20 [uM/s^2]
D_{IP_3}	Permeability of IP3 ^{1,2,3}	1 [uM/s]
$D_{Ca^{2+}}$	Permeability of calcium ^{1,2,3}	0.01 [uM/s]

Homogenization

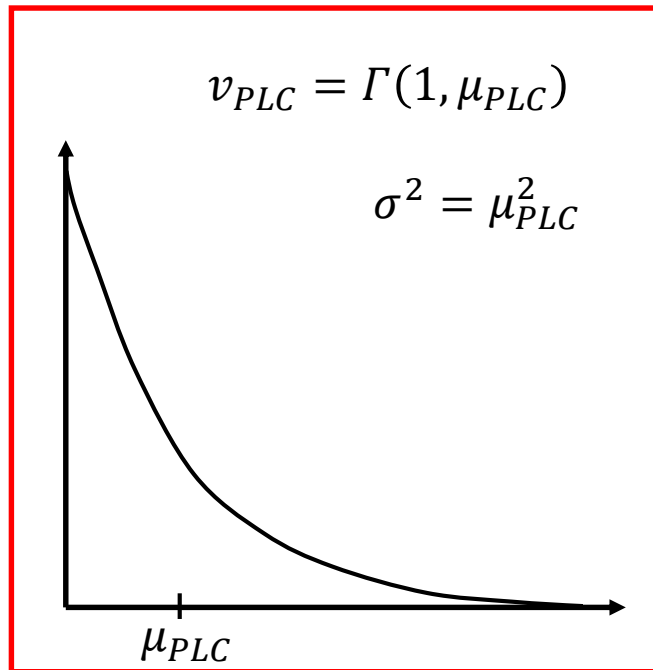
- Cell topology was ignored through homogenization as described in¹
- Permeability and Diffusivity terms were combined to obtain effective diffusivity for calcium and IP3
- Effective diffusivities (after accounting for cell boundaries) are:
 - IP3: $9.66 \text{ } \mu\text{M/s}^2$
 - Calcium: $0.10 \text{ } \mu\text{M/s}^2$

1. Keener, James P., and James Sneyd. *Mathematical physiology*. Vol. 1. New York: Springer, 1998.

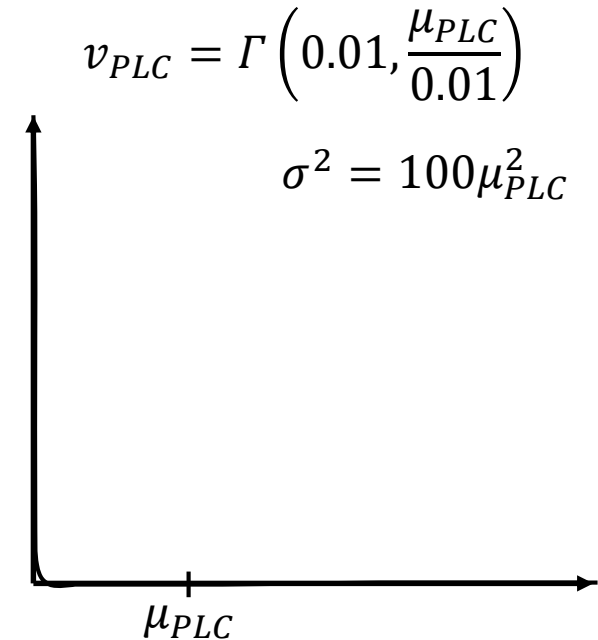
v_{PLC} Probability density function



Represents an IP_3 generation signal with no noise.



Represents variable IP_3 generation signal where very high production rates can rarely occur, but production on average is the same as in pdf 1.



IP_3 signal with even higher variance than pdf 2. Here production rates will generally be very low but a greater frequency of high-rate events results in an average generation equal to pdf 1 and 2.

I called [gamrnd](#) in MATLAB to generate random numbers on this distribution

Stochastic term

- I used multiple pdf's including Gaussian for the stochastic term and always saw a transition as the variance increased with constant mean. I went with Gamma for this exploratory analysis because it most resembled the distribution of stimulus in discs in absence of serum

- The following is the term used for the AlChE model:

$$v_{PLC} = \Gamma(1, \mu_{PLC}) = \text{Gamma}(1, \mu_{PLC})$$

- The formal pdf for this term is:

$$P\left(x, k, \frac{\mu_{PLC}}{k}\right) = \frac{x^{k-1} e^{-\frac{xk}{\mu_{PLC}}}}{\frac{\mu_{PLC}^k}{k} \int_0^\infty x^{k-1} e^{-x} dx}$$

$$P(x, 1, \mu_{PLC}) = \frac{e^{-\frac{x}{\mu_{PLC}}}}{\mu_{PLC} \int_0^\infty e^{-x} dx}$$

- I called [gamrnd](#) in MATLAB to generate random numbers on this distribution