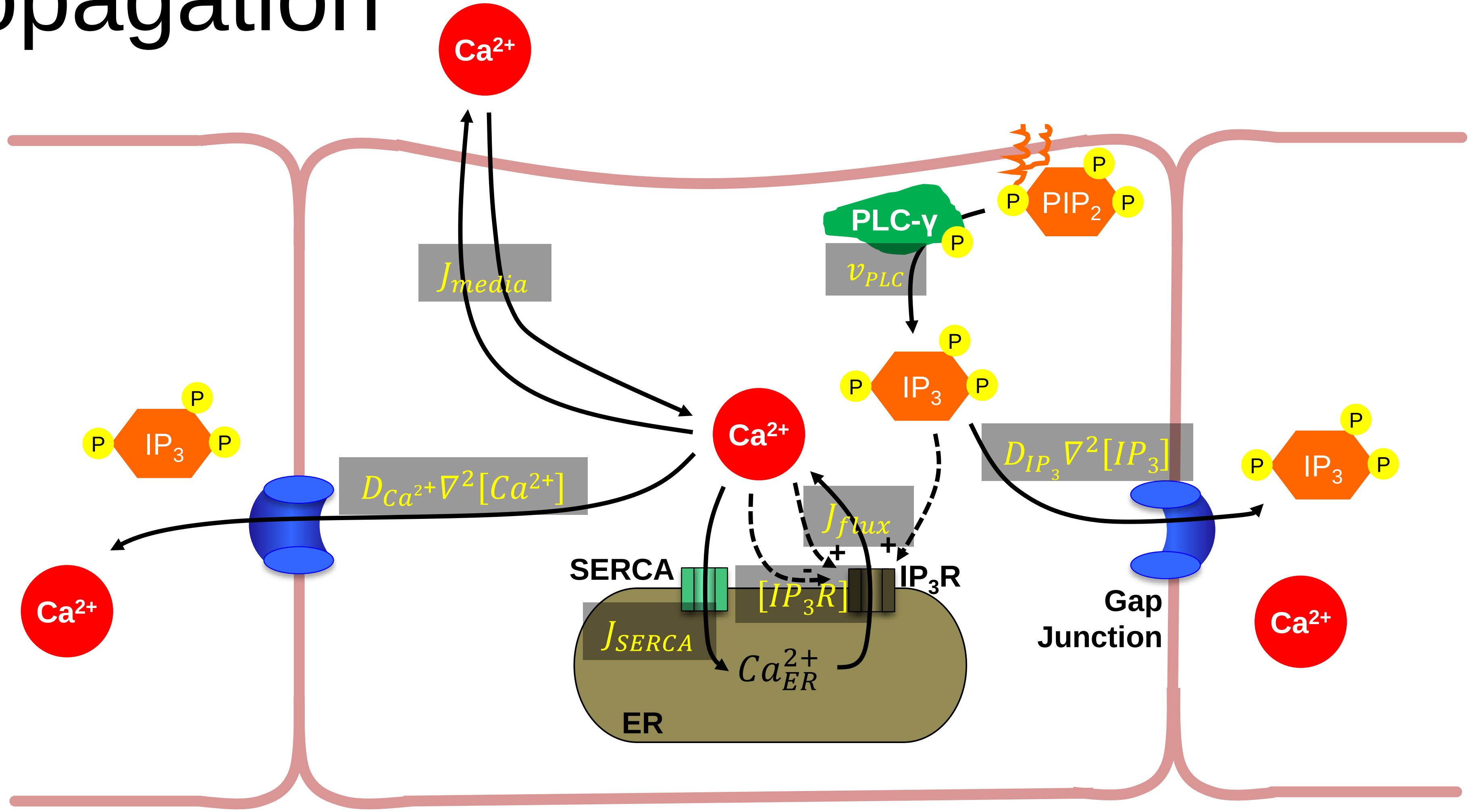
Parameter	Description	Category	When decreased	When increased
k_1	Rate constant of calcium leak from ER[1]	J_{flux}	Frequency↓ Amplitude↓	Waves stop
k_2	Rate constant of calcium release through IP3R[1]		Waves stop	Frequency↑ Speed↑
$K_{Ca^{2+}}$	Half-saturation constant for calcium activation of IP3R[1]		Frequency↑ Amplitude↓	Waves stop
K_{IP_3}	Half-saturation constant for IP3 activation of IP3R[1]		Frequency↑ Amplitude↑	Waves stop
v_{SERCA}	Maximum rate of calcium pumping into the ER[2]	J_{SERCA}	Waves stop	Steady State↓ Amplitude↑
k_{SERCA}	Half-saturation constant for calcium pumping into the ER[2]		Amplitude↑ Steady State↓	Waves stop
v_{leak}	Rate of calcium leak from medium[1]	J_{media}	Frequency↓ Amplitude↑ Speed↓	Waves stop
k_{leak}	Rate constant of calcium flux to the medium[1]		Waves stop	Frequency↑ Amplitude↑ Speed↑
V_{ER}/V	Volumetric fraction of ER[2]	$[Ca_{ER}^{2+}]$	Frequency↓ Amplitude↑ Speed↓ Width↑	Waves stop
k_6	Rate constant of IP3R inactivation[1,2]	$[IP_3R]$	Width↓ Frequency↓ Amplitude↑	No effect
K_i	Half-saturation constant for calcium inhibition of IP3R[1,2]		Waves stop	Frequency↓ Amplitude↑
k_{deg}	Rate constant of IP3 degradation[1]	$[IP_3]$	Speed↑ Amplitude↑ Frequency↑	Waves stop
μ_{PLC}	Mean rate of IP3 generation		Waves stop	Speed↑ Amplitude↑ Frequency↑
D_{IP_3}	Effective diffusivity of IP3[1,2,3]	Diffusion	Random flashes	Speed↑ Amplitude↑
$D_{Ca^{2+}}$	Effective diffusivity of calcium[1,2,3]		Random flashes	No effect

Parameter	Description	Category	Amplitude	Steady state concentration	Frequency	Speed
k_1	Rate constant of calcium leak from ER[1]	J_{flux}	X	X	-	X
k_2	Rate constant of calcium release through IP3R[1]		X	X	-	X
$K_{Ca^{2+}}$	Half-saturation constant for calcium activation of IP3R[1]		X	X	X	-
K_{IP_3}	Half-saturation constant for IP3 activation of IP3R[1]		X	X	X	-
v_{SERCA}	Maximum rate of calcium pumping into the ER[2]	J_{SERCA}	X	X	-	X
k_{SERCA}	Half-saturation constant for calcium pumping into the ER[2]		X	X	-	X
v_{leak}	Rate of calcium leak from medium[1]	J_{media}	X	X	-	X
k_{leak}	Rate constant of calcium flux to the medium[1]		-	-	X	X
V_{ER}/V	Volumetric fraction of ER[2]	$[Ca_{ER}^{2+}]$	-	-	-	-
k_6	Rate constant of IP3R inactivation[1,2]	$[IP_3R]$	-	-	-	-
K_i	Half-saturation constant for calcium inhibition of IP3R[1,2]		X	X	-	-
k_{deg}	Rate constant of IP3 degradation[1]	$[IP_3]$	X	X	X	X
μ_{PLC}	Mean rate of IP3 generation		-	-	-	X
D_{IP_3}	Effective diffusivity of IP3[1,2,3]	Diffusion	-	-	X	X
$D_{Ca^{2+}}$	Effective diffusivity of calcium[1,2,3]		-	-	-	-

1. Höfer, Thomas, Laurent Venance, and Christian Giaume. "Control and plasticity of intercellular calcium waves in astrocytes: a modeling approach." *The Journal of neuroscience* 22.12 (2002): 4850-4859.
2. Sneyd, J. A. M. E. S., et al. "Intercellular calcium waves mediated by diffusion of inositol trisphosphate: a two-dimensional model." *American Journal of Physiology-Cell Physiology* 268.6 (1995): C1537-C1545.
3. Keener, James P., and James Sneyd. *Mathematical physiology*. Vol. 1. New York: Springer, 1998.

Molecular mechanism of calcium propagation



Boundary and initial conditions

No-flux boundary conditions:

$$D_{IP_3}\nabla^2[IP_3] = 0 \; at \; x = \{0, L\}$$

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

Steady-state initial conditions:

$at \; t = 0$:

$$[Ca^{2+}] = 0.05 \; \mu M$$

$$[IP_3] = 0.15 \; \mu M$$

$$[Ca_{ER}^{2+}] = 80 \; \mu M$$

$$[IP_3R] = 1$$

PDE model (Version 1)

$$\frac{\partial[Ca^{2+}]}{\partial t}=\frac{(k_1+k_2[IP_3R][Ca^{2+}]^2[IP_3]^2)([Ca^{2+}_{ER}]-[Ca^{2+}])}{(K^2_{Ca^{2+}}+[Ca^{2+}]^2)(K^2_{IP_3}+[IP_3]^2)}-\frac{v_{SERCA}[Ca^{2+}]^2}{k^2_{SERCA}+[Ca^{2+}]^2}+(v_{leak}-k_{leak}[Ca^{2+}])+D_{Ca^{2+}}\nabla^2[Ca^{2+}]$$

$$\frac{d[Ca^{2+}_{ER}]}{dt}=-\frac{V}{V_{ER}}\left(\frac{(k_1+k_2[IP_3R][Ca^{2+}]^2[IP_3]^2)([Ca^{2+}_{ER}]-[Ca^{2+}])}{(K^2_{Ca^{2+}}+[Ca^{2+}]^2)(K^2_{IP_3}+[IP_3]^2)}-\frac{v_{SERCA}[Ca^{2+}]^2}{k^2_{SERCA}+[Ca^{2+}]^2}\right)$$

$$\frac{\partial[IP_3]}{\partial t}=\Gamma(1,\mu_{PLC})-k_{deg}[IP_3]+D_{IP_3}\nabla^2[IP_3]$$

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

PDE model (Version 2)

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

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

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

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

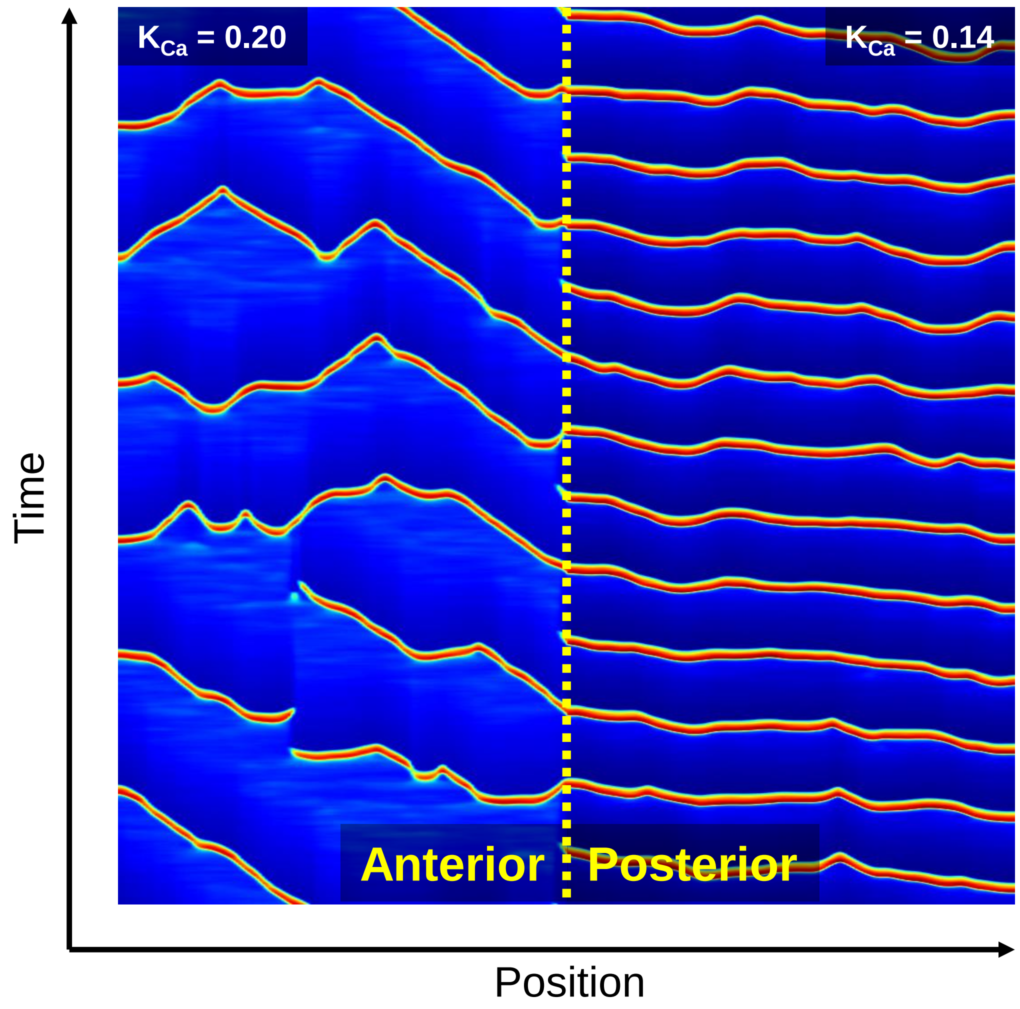
$$J_{flux} = \frac{(k_1 + k_2[IP_3R][Ca^{2+}]^2[IP_3]^2)([Ca_{ER}^{2+}] - [Ca^{2+}])}{(K_{Ca^{2+}}^2 + [Ca^{2+}]^2)(K_{IP_3}^2 + [IP_3]^2)}$$

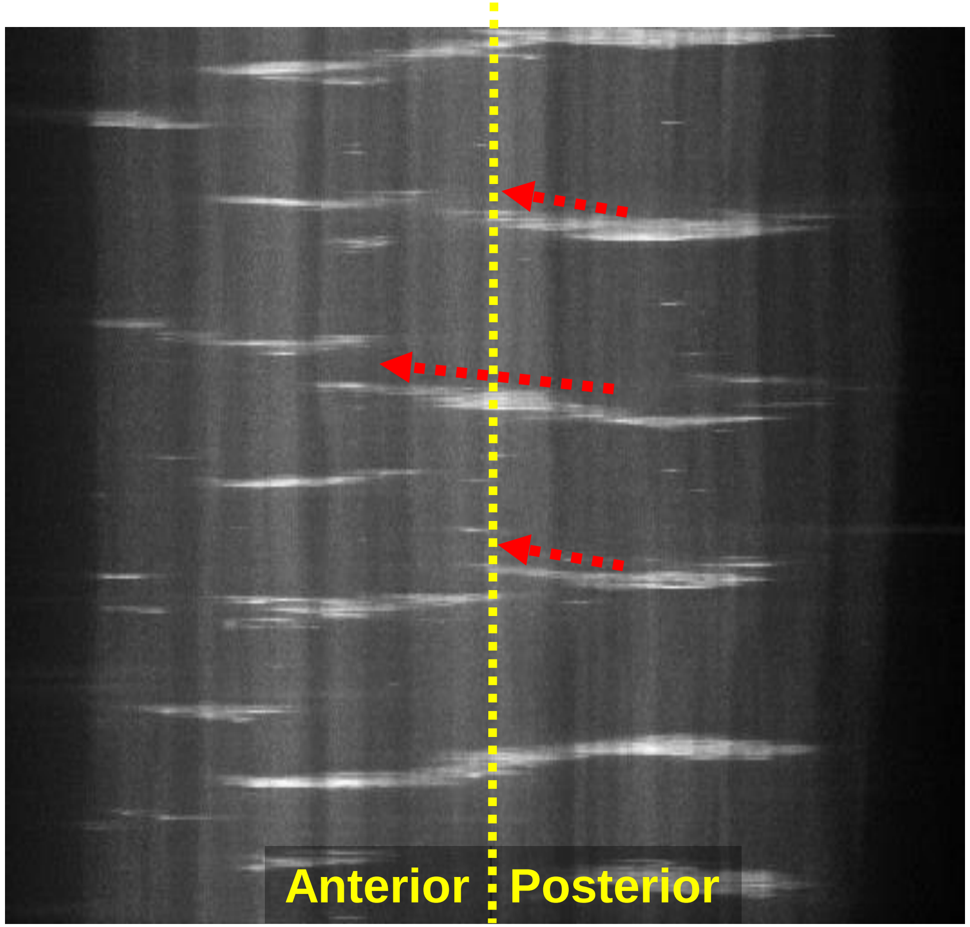
$$J_{SERCA} = \frac{v_{SERCA}[Ca^{2+}]^2}{k_{SERCA}^2 + [Ca^{2+}]^2}$$

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

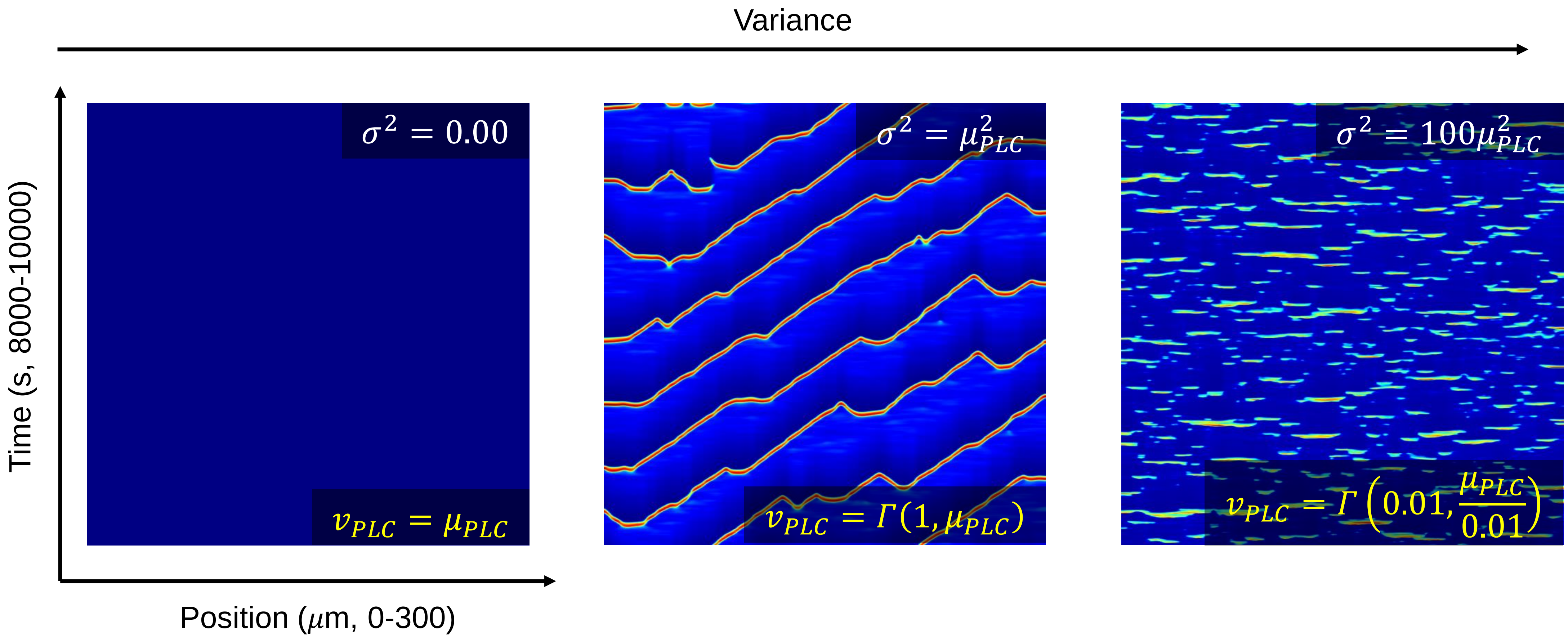
$$v_{PLC} = \Gamma(1, \mu_{PLC})$$

Boundary penetrance may be explained by differential cell properties in compartments





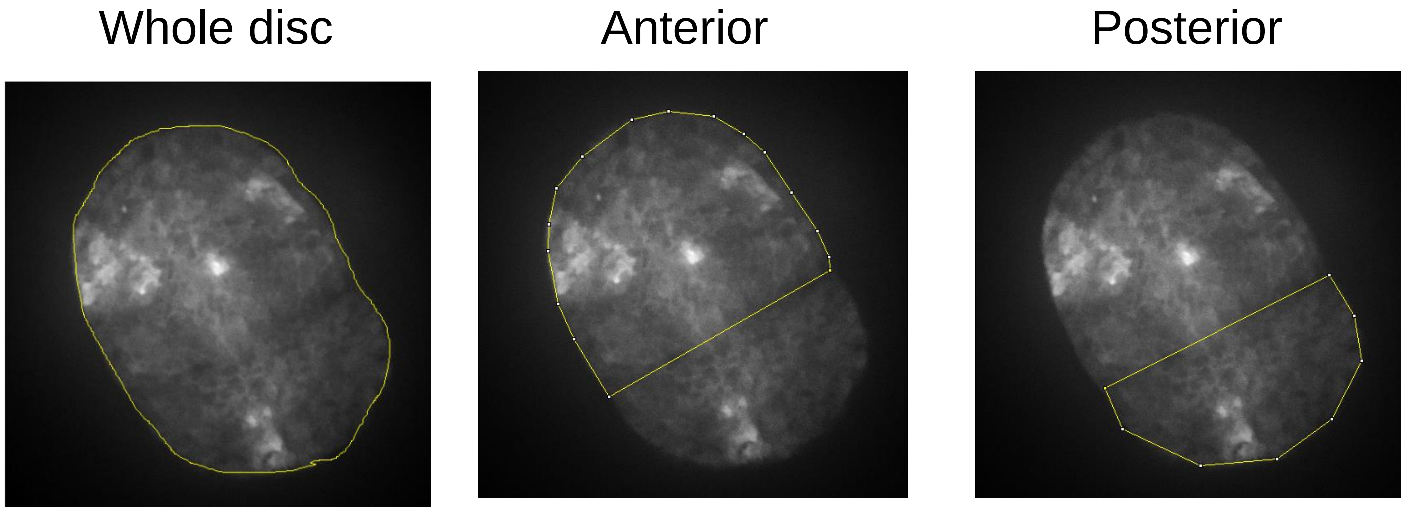
Signal variance may explain pulse to wave transition

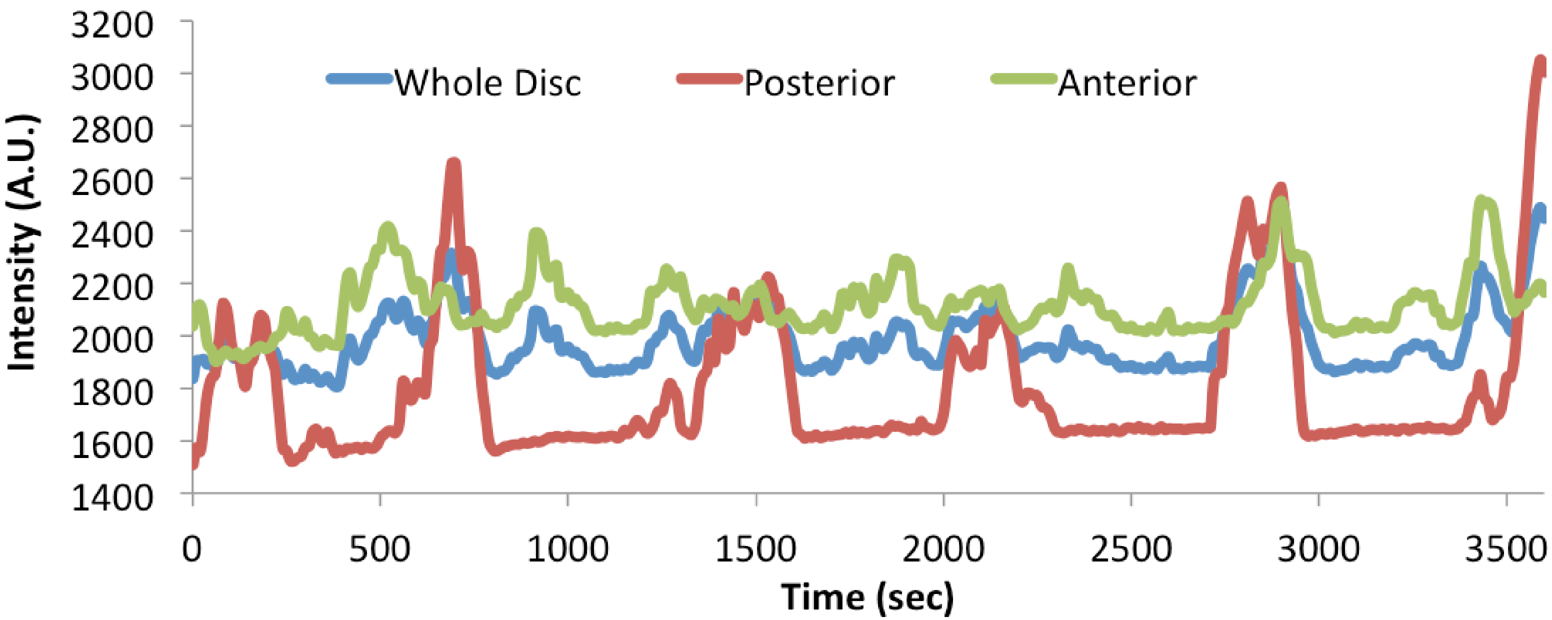


t = 8000s to 10000s

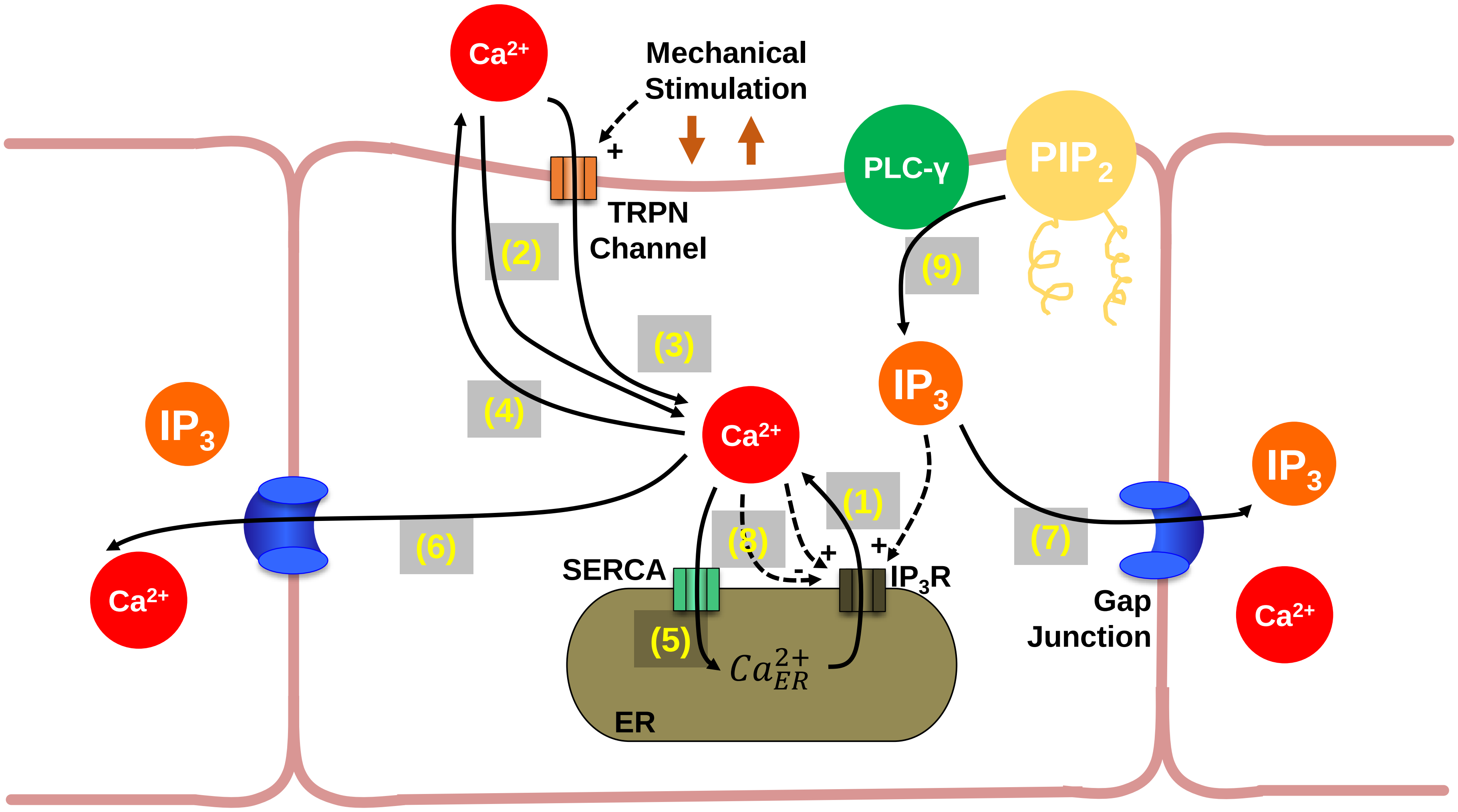
OTHER SLIDES:

Domain specificity of Ca^{2+} transients





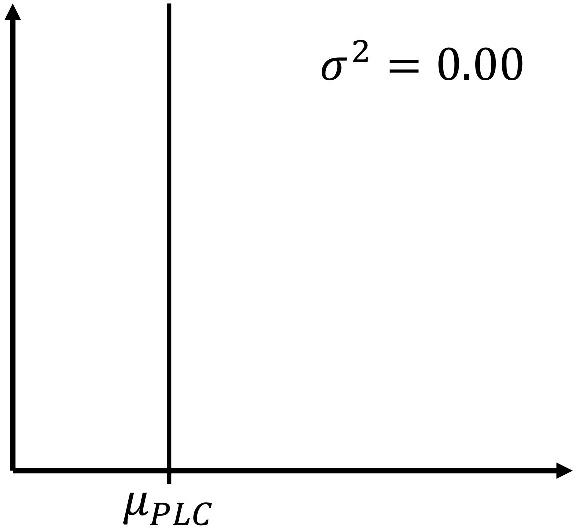
Molecular mechanism of calcium propagation



Probability density functions

$$v_{PLC} = \mu_{PLC}$$

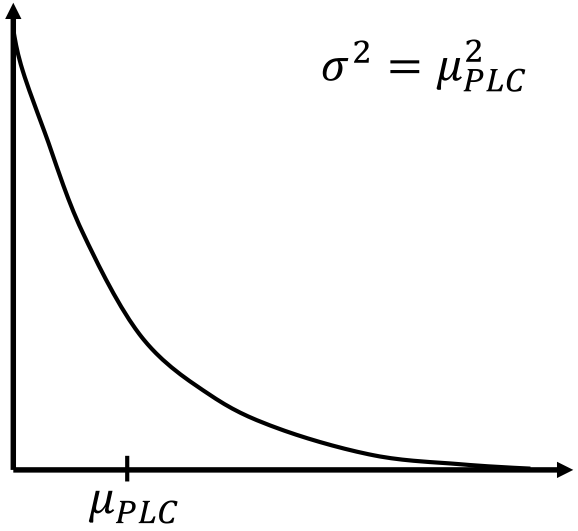
$$\sigma^2 = 0.00$$



Represents an IP_3 generation signal with no noise.

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

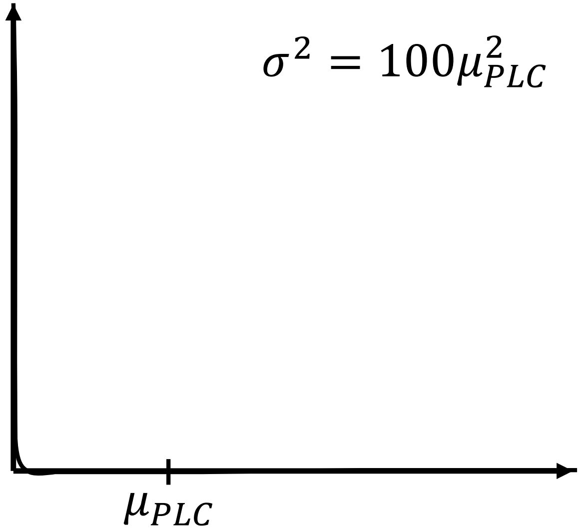
$$\sigma^2 = \mu_{PLC}^2$$



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.

$$v_{PLC} = \Gamma\left(0.01, \frac{\mu_{PLC}}{0.01}\right)$$

$$\sigma^2 = 100\mu_{PLC}^2$$



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.

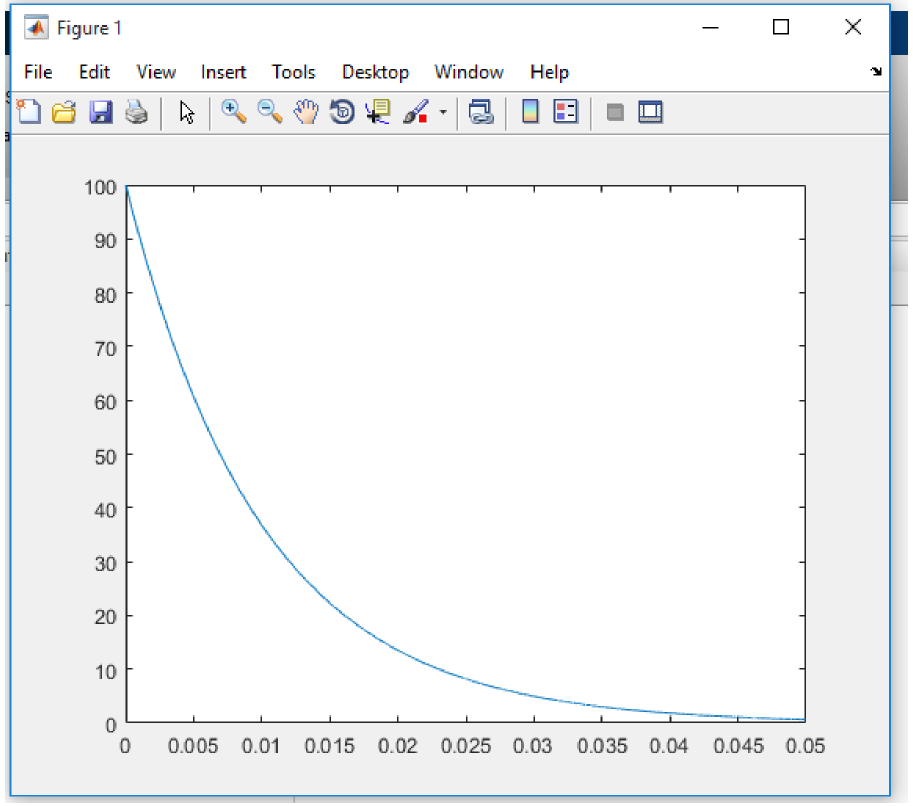


Figure 1
File Edit View Insert Tools Desktop Window Help
100
90
80
70
60
50
40
30
20
10
0
0 0.005 0.01 0.015 0.02 0.025 0.03 0.035 0.04 0.045 0.05

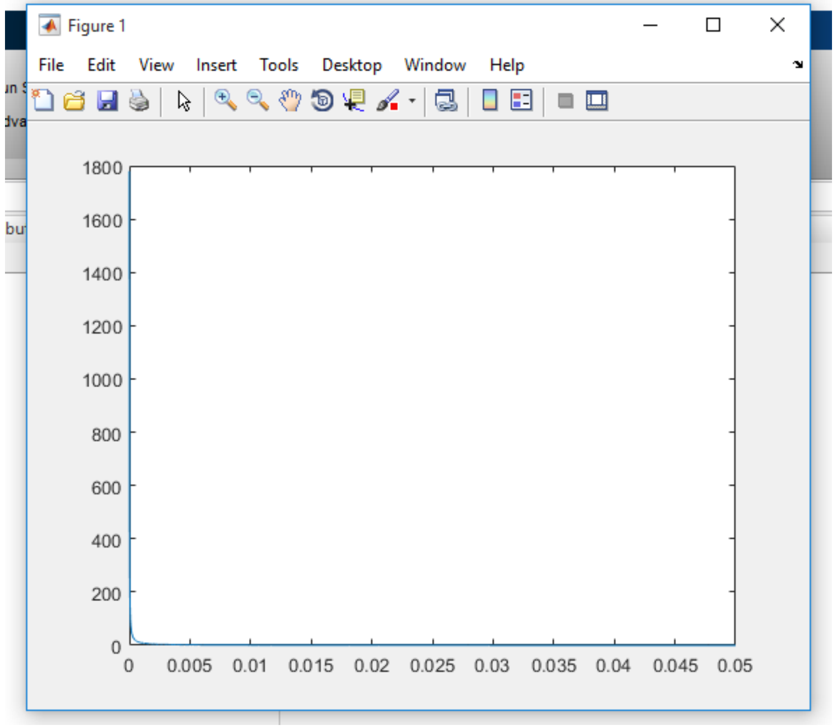


Figure 1
File Edit View Insert Tools Desktop Window Help
1800
1600
1400
1200
1000
800
600
400
200
0
0 0.005 0.01 0.015 0.02 0.025 0.03 0.035 0.04 0.045 0.05