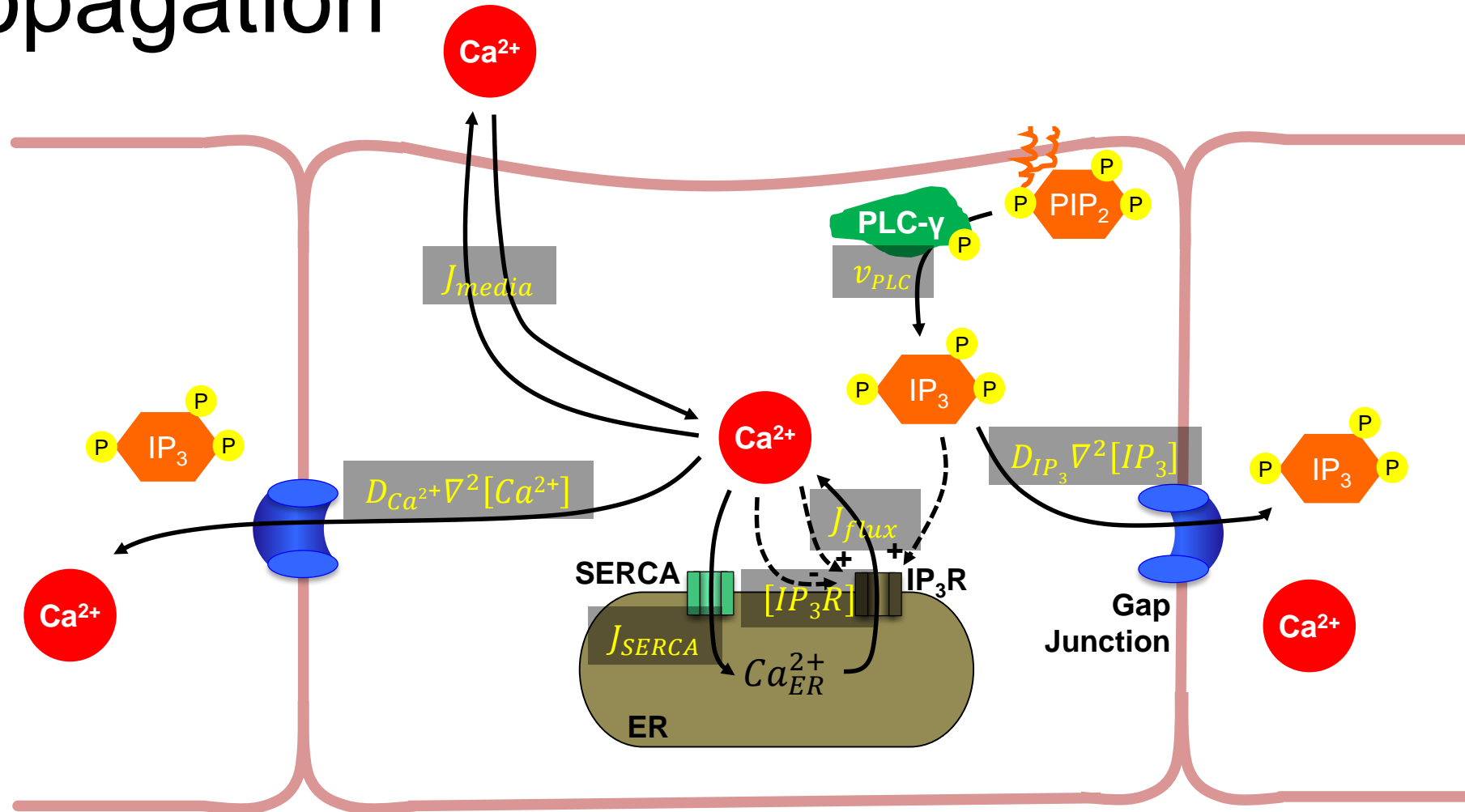


Molecular mechanism of calcium propagation



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.

Boundary and initial conditions

No-flux boundary conditions:

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

Steady-state initial conditions:

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

PDE model (Version 1)

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

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

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

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

PDE model (Version 2)

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

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

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

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

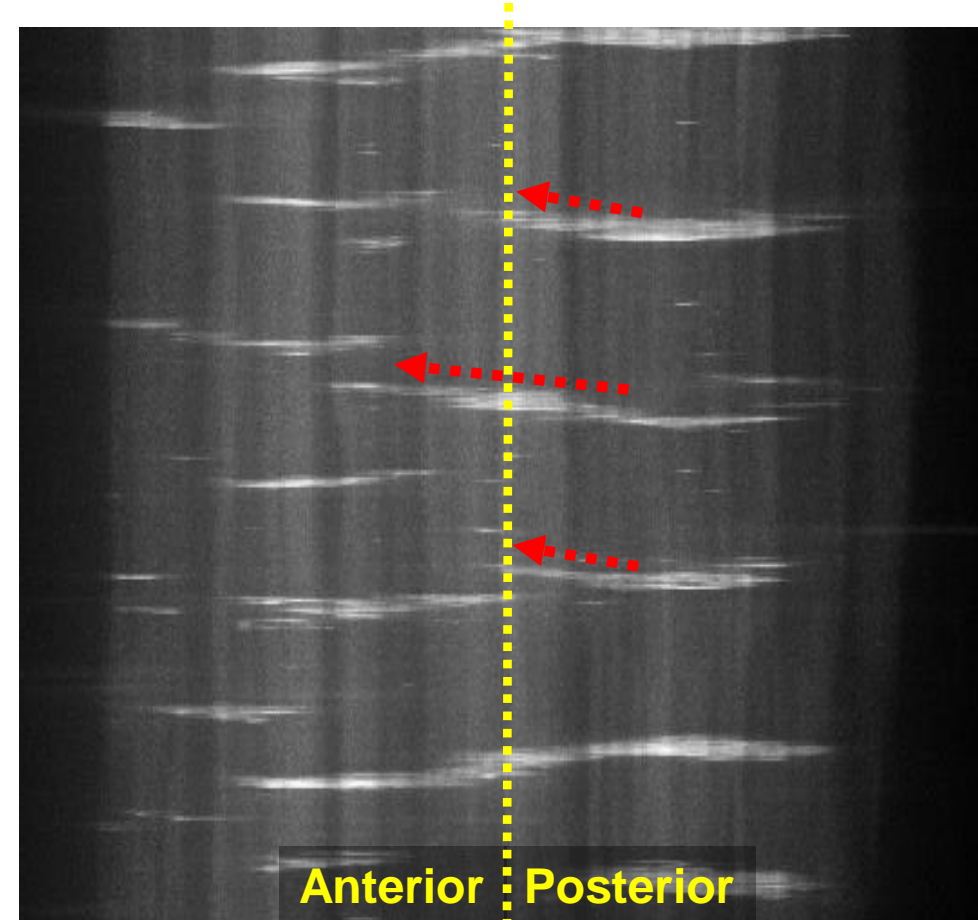
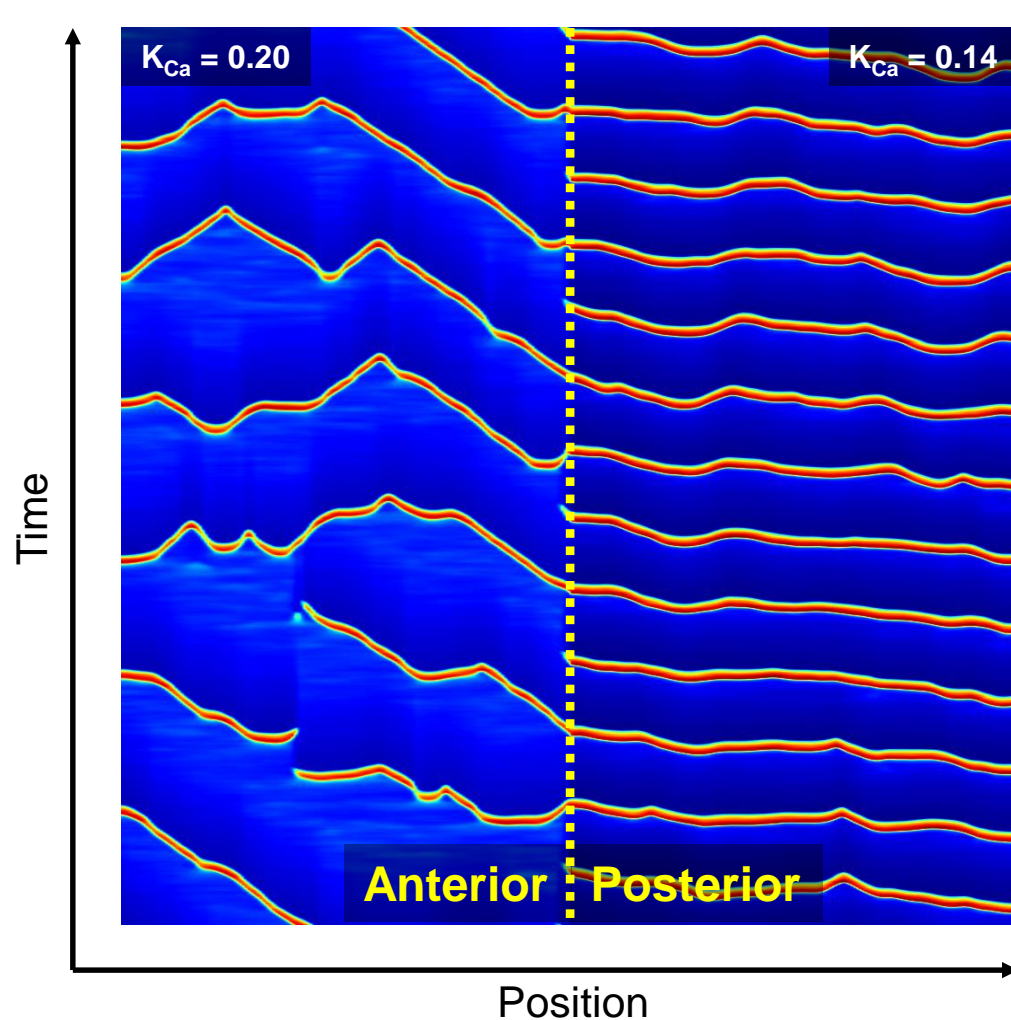
$$J_{flux} = \frac{(k_1 + k_2[IP_3R][Ca^{2+}]^2[IP_3]^2)([Ca_{ER}^{2+}] - [Ca^{2+}])}{(K_{Ca^{2+}}^2 + [Ca^{2+}]^2)(K_{IP_3}^2 + [IP_3]^2)}$$

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

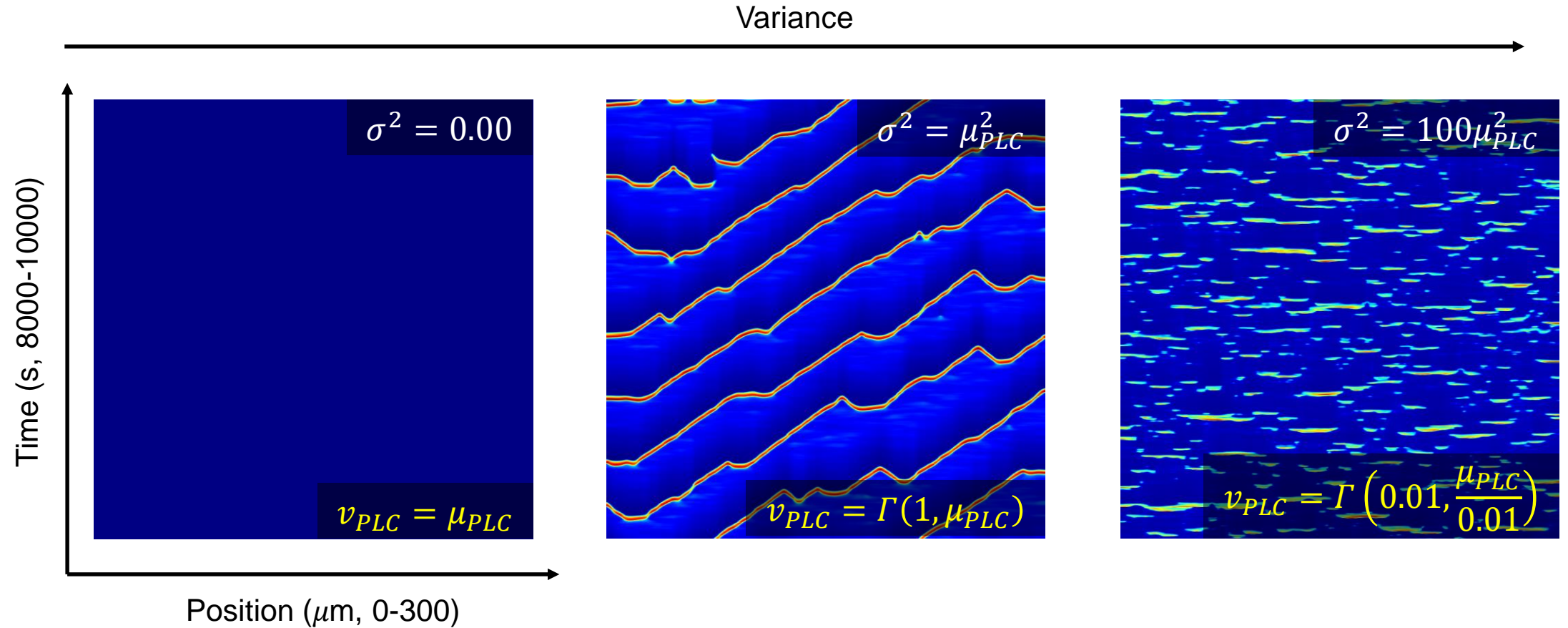
$$J_{media} = v_{leak} - k_{leak}[Ca^{2+}]$$

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

Boundary penetrance may be explained by differential cell properties in compartments



Signal variance may explain pulse to wave transition

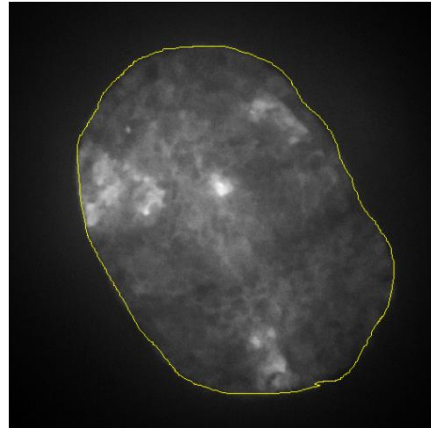


t = 8000s to 10000s

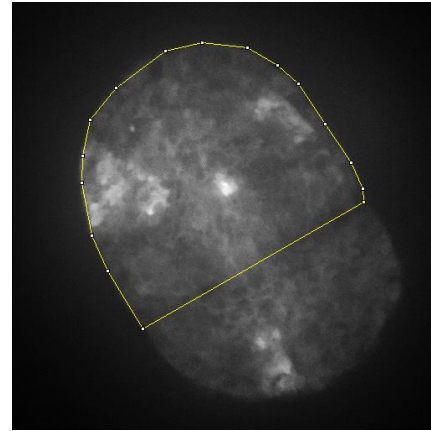
OTHER SLIDES:

Domain specificity of Ca^{2+} transients

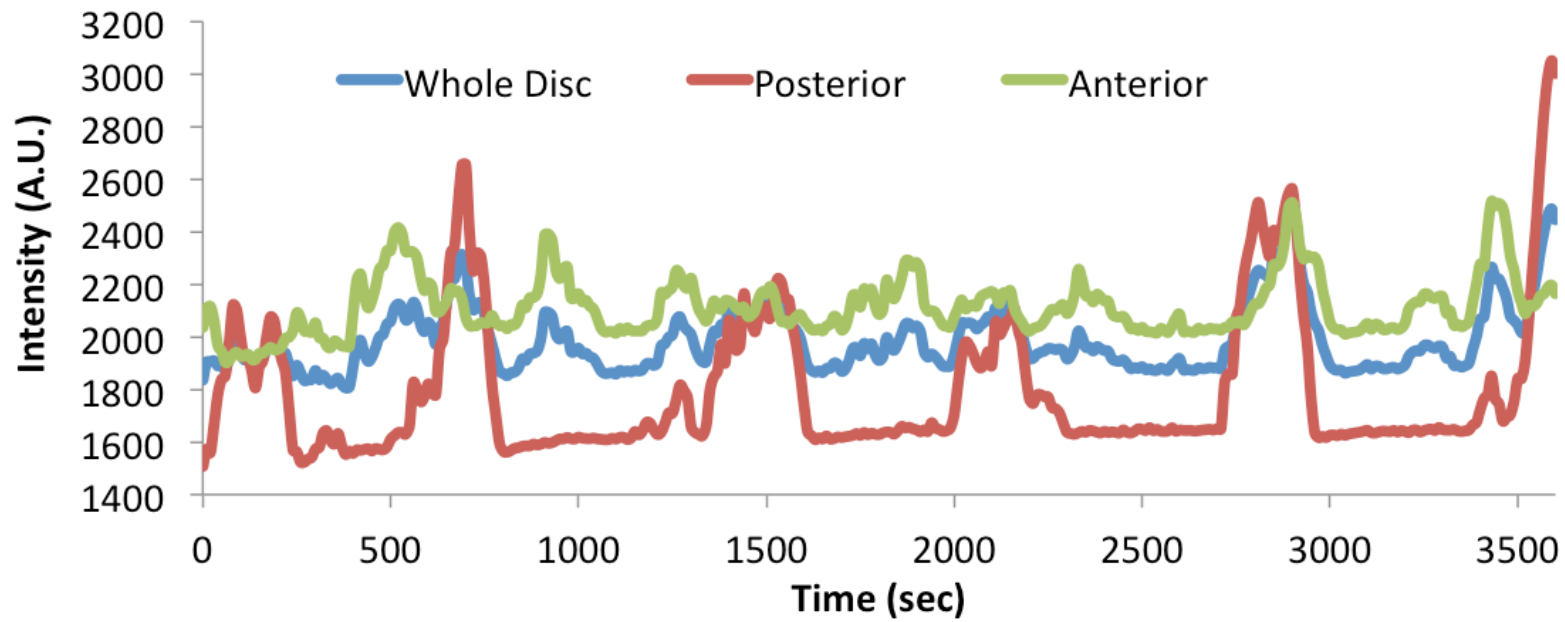
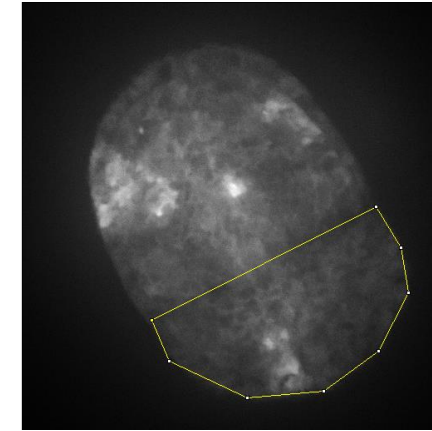
Whole disc

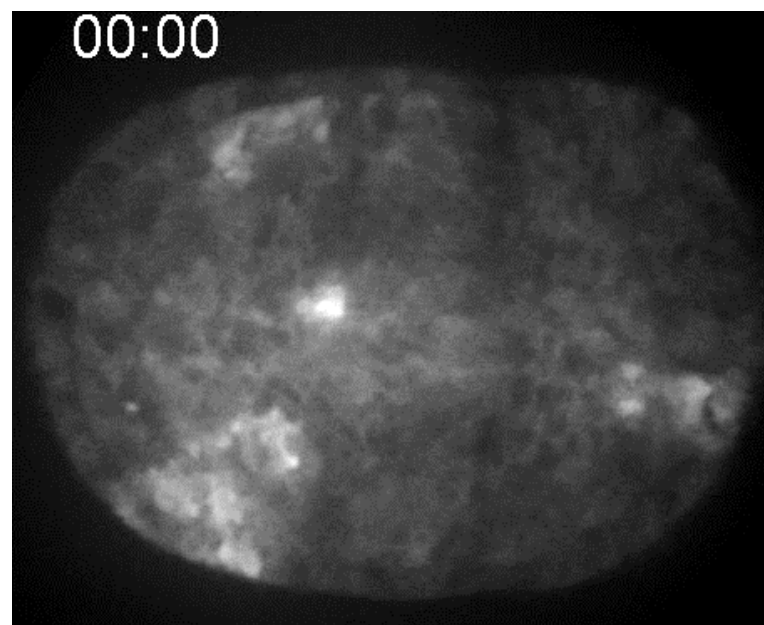


Anterior



Posterior





Molecular mechanism of calcium propagation

