Modeling with partial differential equations

Part 2

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Outline: Part 2

The Reaction-Diffusion equation

Why does it occur so frequently?

Some PDE examples from the literature

Simulations of intracellular calcium

Predicted effect of cell shape on signaling

Predictions and experimental validation of kinase activity

1-D cable equation vs. epithelial reaction-diffusion equation

Cable equation:

diffusion

reaction that increases or decreases voltage

$$C_m \frac{\partial V}{\partial t} = \boxed{\frac{a}{2\rho_i} \frac{\partial^2 V}{\partial x^2}} - \boxed{I_{ion}}$$

Diffusion of [HCO_3] across epithelium:

reaction that consumes [HCO3]

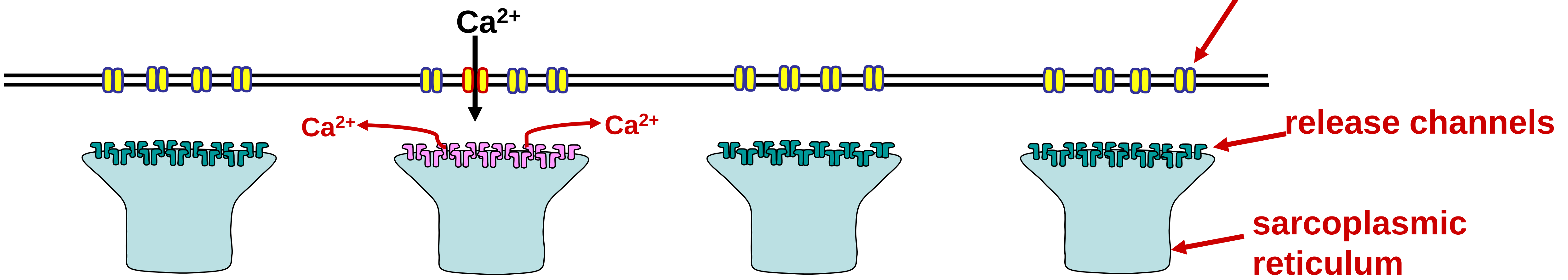
$$\frac{\partial [HCO_3]_i}{\partial t} = \boxed{D_{HCO_3} \frac{\partial^2 [HCO_3]}{\partial x}} - \boxed{k[HCO_3]}$$

diffusion

Other examples of reaction-diffusion equations

Changes in intracellular [Ca^{2+}] during release

Ca^{2+} in heart cells is released from discrete clusters of channels

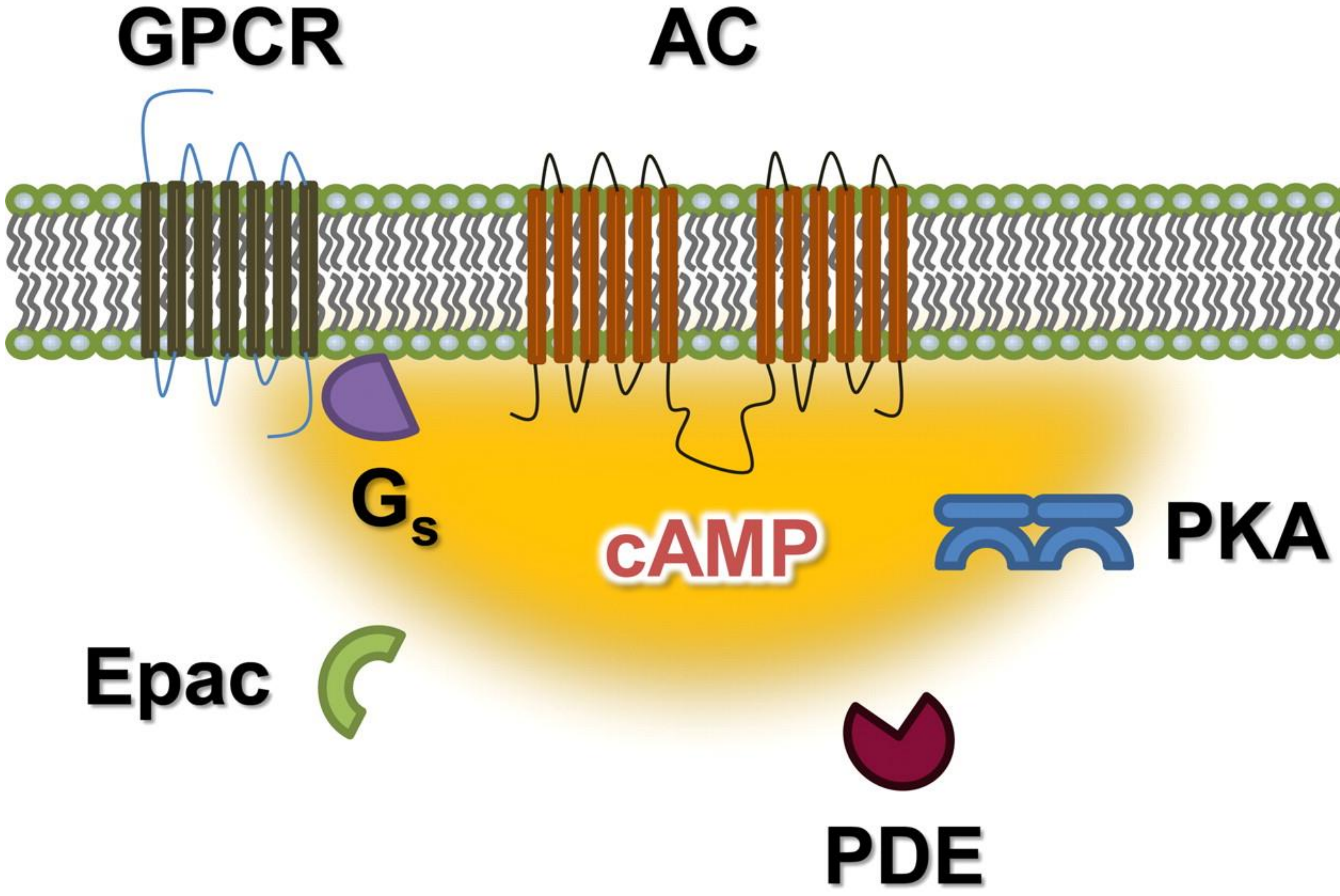


Released Ca^{2+} *diffuses* within cytoplasm

Reaction: **Release of Ca^{2+} and buffering reactions in cytoplasm**

Other examples of reaction-diffusion equations

Other intracellular second messengers, e.g. cAMP

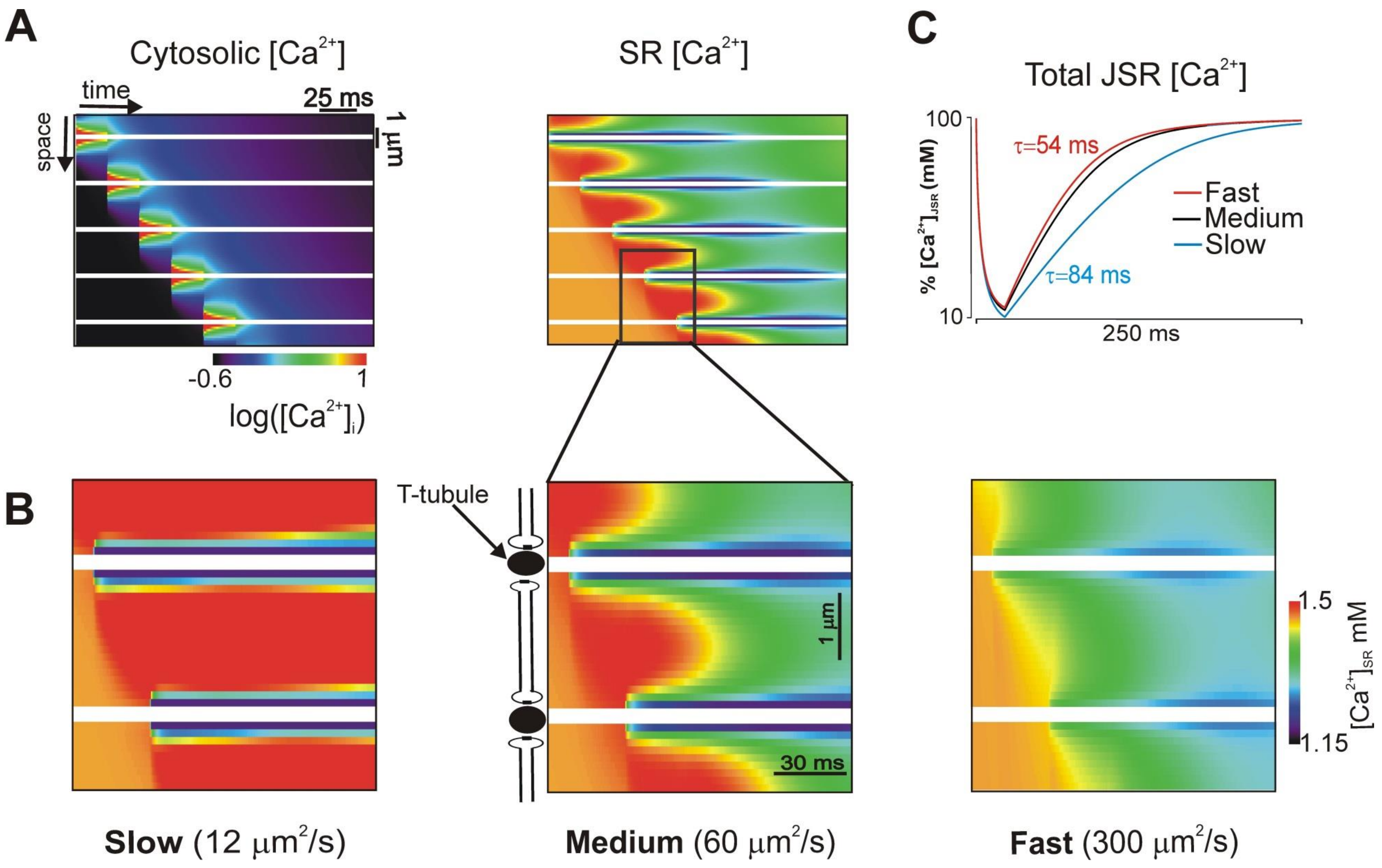


Harvey, (2011) *Am J Physiol* 301:C775-C776.

These processes are common → so are reaction-diffusion equations

PDE-based modeling studies

Example 1: Ca^{2+} in cytosol and sarcoplasmic reticulum (SR) during release

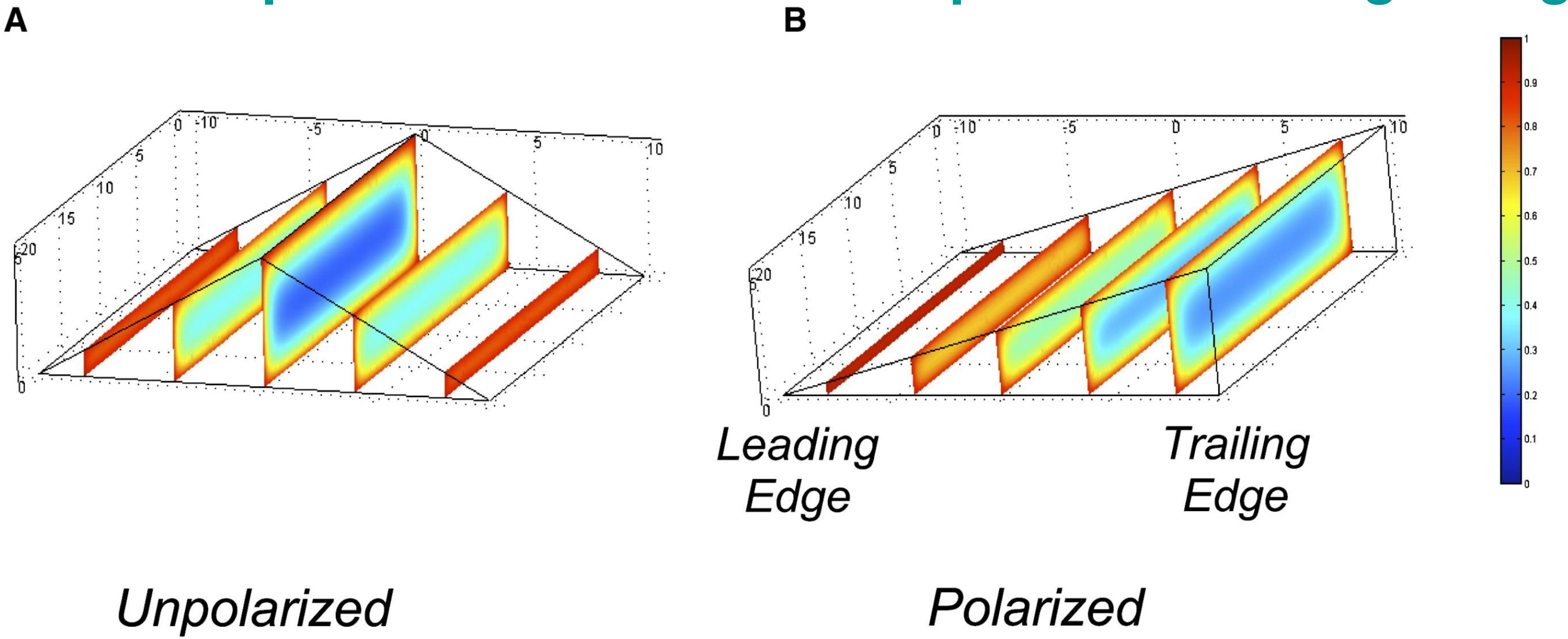


Message: Ca^{2+} diffusion within SR matters as much as diffusion in cytosol

Ramay, Jafri, Lederer, Sobie (2010) *Biophys J* 98:2515-2523.

PDE-based modeling studies

Example 2: How does cell shape influence signaling?

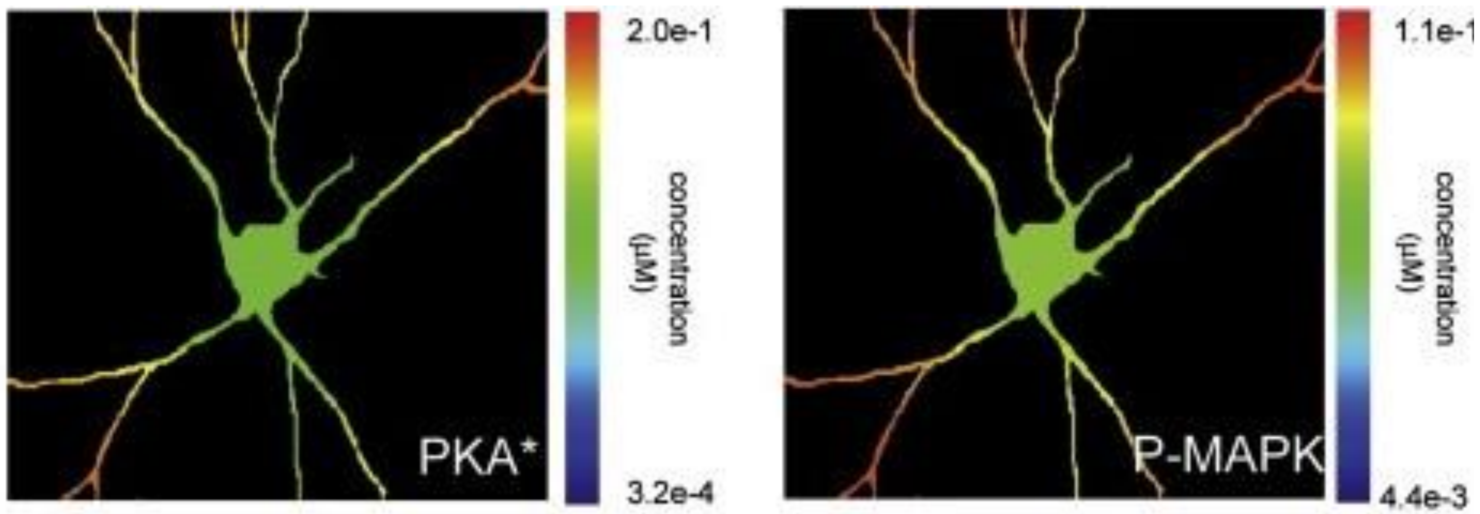


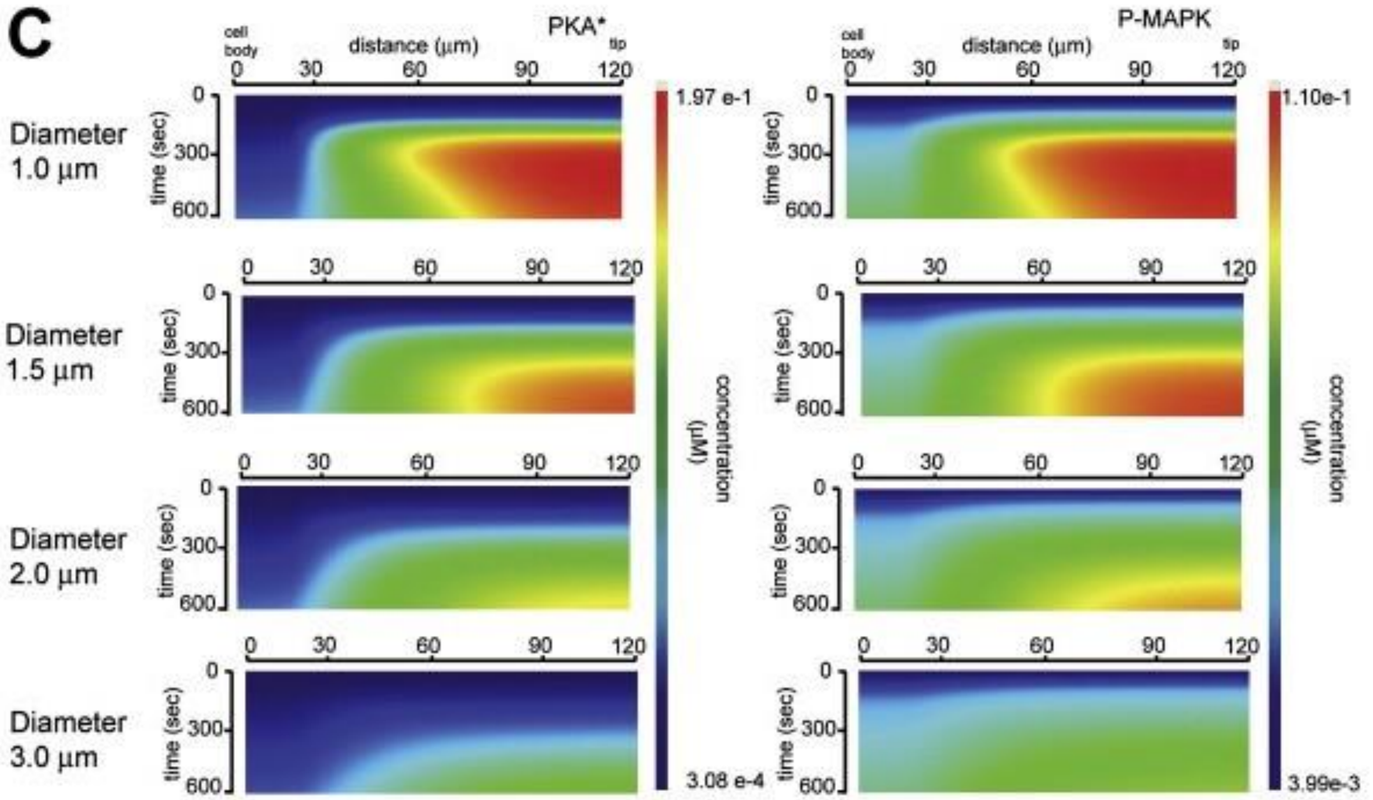
Meyers, Craig, Odde (2006) *Curr Biol* 16:1685-1693.

Message: Geometry matters. The degree of phosphorylation will be different in thin and thick regions of a cell.

PDE-based modeling studies

Example 3: Prediction/measurement of signaling spatial gradients



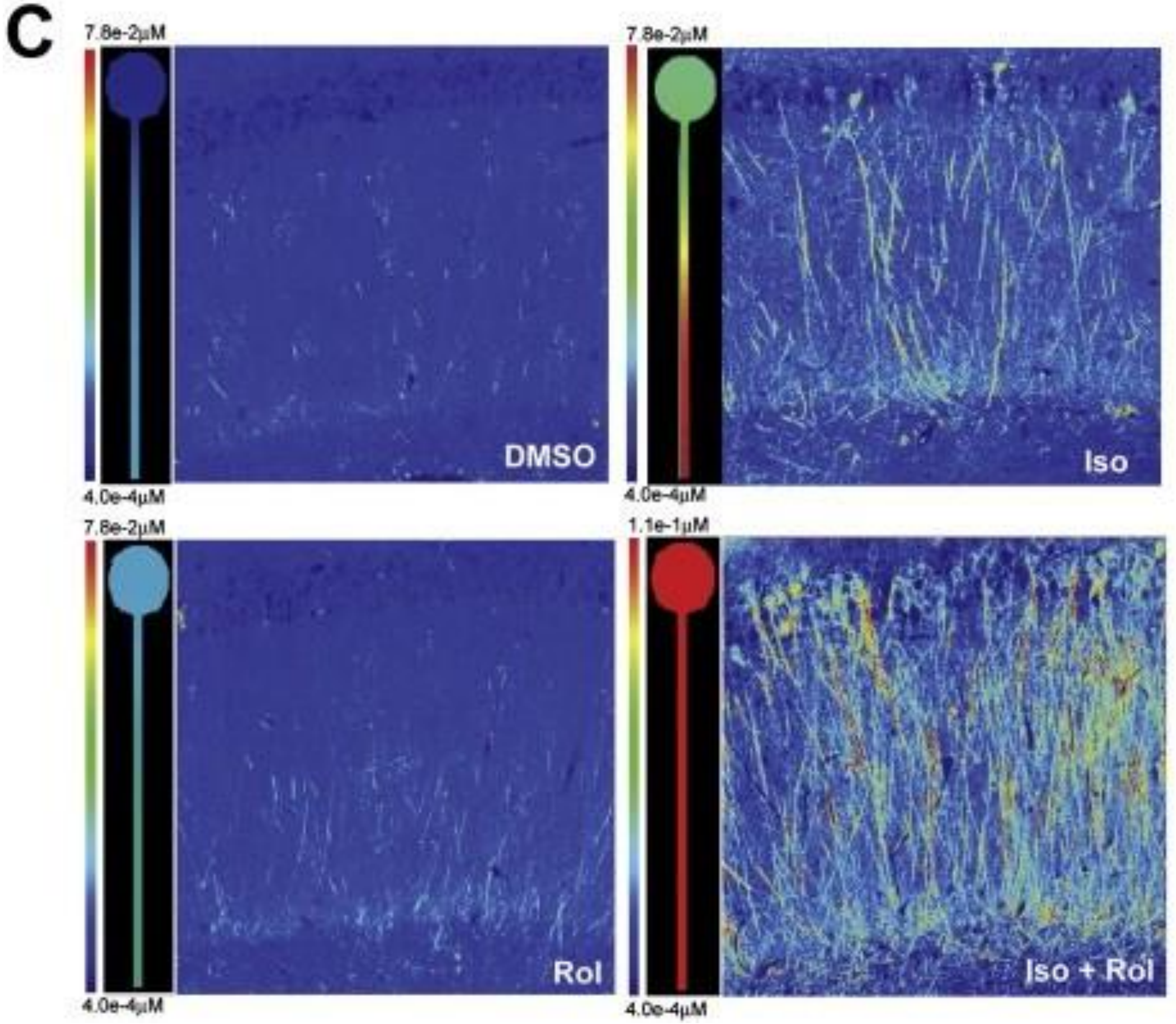


Neves et al. (2008) *Cell* 133:666-680

Message: **Spatial signals depend on geometry, but they depend equally on processes that turn signals off.**

PDE-based modeling studies

Example 3: Prediction/measurement of signaling spatial gradients



Neves et al. (2008) *Cell* 133:666-680

Predictions made in the models were confirmed experimentally

Summary

Reaction-diffusion equations occur repeatedly in biology, whenever the processes producing and degrading a species are spatially separated.

Modeling studies based on PDEs can provide insight into the relative importance of biological versus geometrical factors.