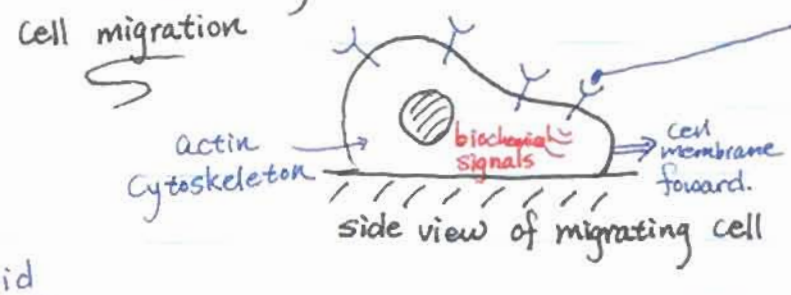
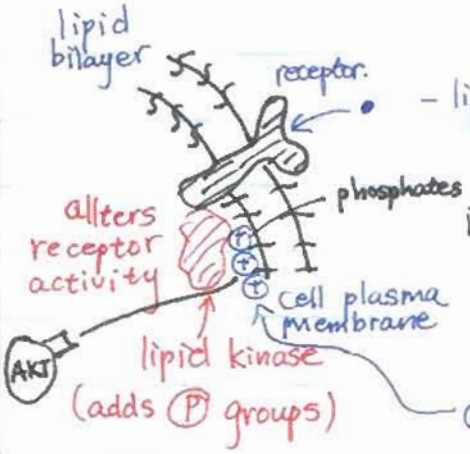
11/3/04

One more chemical subsystem

- diffusion + reaction problem
- processes occuring within / at cell membrane



- chemotactic (influences cell direction
- chemokinetic (influences cell speed)



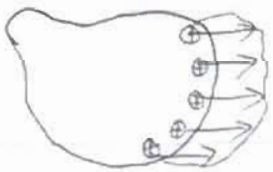
- lipid bilayer is a barrier

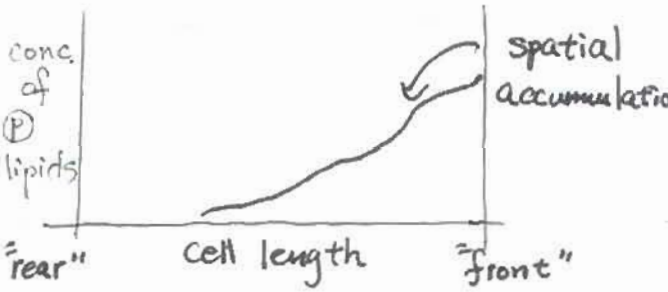
Diffusion + rxn process within / at plasma membrane.

Crucial point

⊗ actin polymerization ∝ to how much the membrane has phosphate groups added on to it.

Top View of all





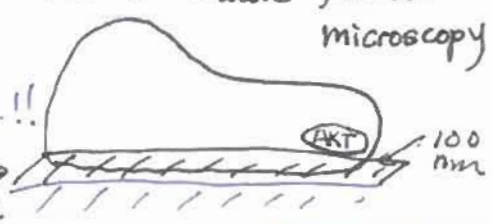
AKT activates the phosphorilayation process by attaching itself on it.

more green, more AKT, more ~~mem~~ Phosphates

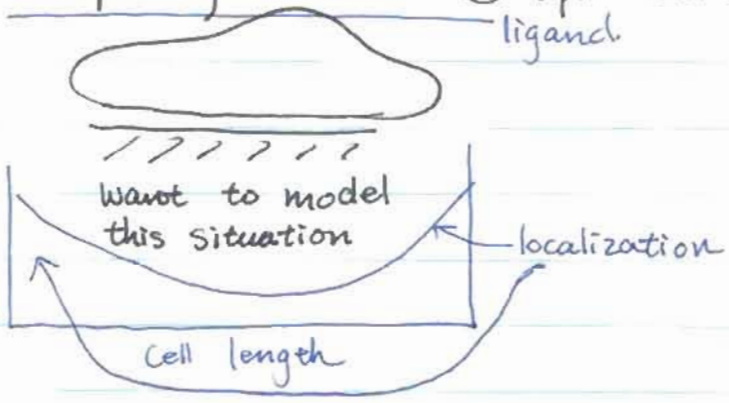
Expt'l measurement:

- express AKt-GFF

Evanescent wave flourescente microscopy



In the absence of any external ligand concentration gradient, cells generate a spatially - localized Ⓟ lipid (Akt-GFP) distribution



Internal symmetry breaking in the direction of the gradient.

Quantity of interest

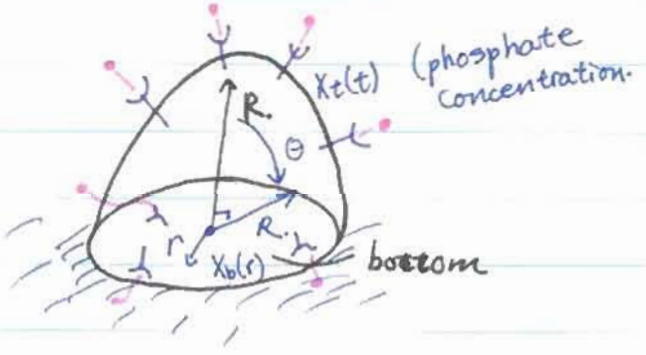
X

molecules

Ⓟ-lipids/μm^2 cell membrane

Geometry of the problem

isotropic medium ⇒ no angular gradients.



Chemical process:

$L + R \rightleftharpoons C$

lipid receptor complex

lipid precision.

V velocity of rxn

Ⓟ-lipid

Akt-GFP

Kc

Consumption

Bottom domain

mass cons. on ⓟ-lipid. (#/area)

$$\frac{\partial X_b}{\partial t} = D \nabla_r^2 X_b - k_c X_b + V_b f(t)$$

(k_c: C-R binding dynamics)

$$\nabla_r^2 = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial}{\partial r}\right) \qquad 0 \le r \le R.$$

I.C. $X_b(r, 0) = X_0$

B.C. $r=0, \quad \nabla_r X_b = 0$

$r=R, \quad D\frac{\partial X_b}{\partial r} = g(t) =$ flux from top domain

Top domain

k_c: L-R binding dynamics

$$\#/\text{area}\ \frac{\partial X_t}{\partial t} = D \nabla_\theta^2 X_t - k_c X_t + V_t f(t)$$

$$\nabla_\theta^2 = \frac{1}{R^2 \sin\theta}\frac{\partial}{\partial \theta}\left(\sin\theta \frac{\partial}{\partial \theta}\right)$$

Transform θ coordinates to η coordinates where $\eta = \cos\theta$

$$\Rightarrow \nabla_\eta^2 = \frac{1}{R^2(1-\eta^2)}\frac{\partial^2}{\partial \eta^2}$$

IC: $X_t(\eta, 0) = X_0$

BC: $\eta = 1, \quad \nabla_\eta X_t = 0$

$\eta = 0, \quad RD\frac{\partial X_t}{\partial \eta} = g(t)$ ← flux to bottom

Is $D_t \approx D_b$?

good for lipids

$V_t \neq V_b$ rxn velocity terms

"integrin adhesion receptors"

- very active on the bottom that's adhesive to the substrate,
- very dynamic

Scale variables

$\rho = \frac{r}{R}$, $\tau = k_c t$, $V_t = \frac{V_t}{k_c}$, $V_b = \frac{b_b}{k_c}$ $\qquad \frac{k_c R^2}{D} \equiv \alpha^2$ Damkohler number.

$$\frac{\partial X_b}{\partial \tau} = \frac{1}{\alpha^2}\nabla^2_\rho X_b - X_b + V_b f(\tau)$$

$$\frac{\partial X_t}{\partial \tau} = \frac{1}{\alpha^2}\nabla^2_\eta X_t - X_t + V_t f(\tau)$$

IC: $X_b(\rho, 0) = X_0$

$X_t(\eta, 0) = X_0$

B.C.: $\frac{\partial X_b}{\partial \rho} = 0, \rho = 0$; $\frac{\partial X_t}{\partial \eta} = 0, \eta = 1$

$\frac{\partial X_b}{\partial \rho} = g(\tau) = \frac{\partial X_t}{\partial \eta}$ $\quad \rho = 1, \eta = 0$

- play w/ different geometries.

You can solve (linear PDEs) by separation of variables or finite fourier transform or Sturville operator theory
- Details are in Haugh supplement on BE.430 website.

Result: $X_b(\rho, \tau \to \infty)$, steady-state solution
(how long does it take to attain?

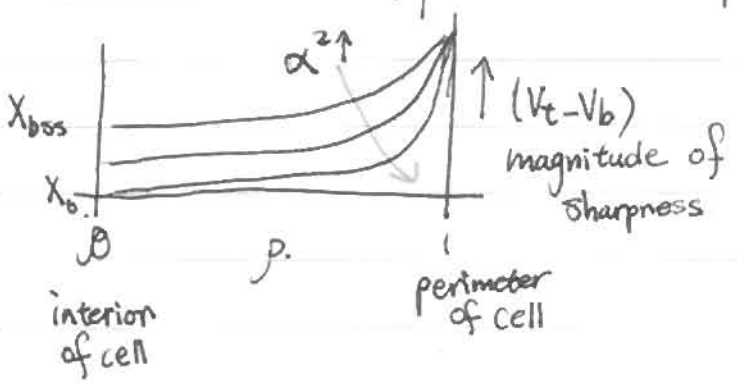
$\tau_{0.5}$, $\tau_{0.95}$?

$$X_{bss}(\rho) = V_b + \frac{(V_t - V_b)\,\alpha\, I_0(\alpha\rho)}{\alpha I_0(\alpha) + \beta(\alpha) I_1(\alpha)}$$

I_0, I Bessel Functions.

$$\beta(\alpha) = \sum_{n=0}^{\infty} \frac{(4n+1) P^2_{2n}(0)}{1 + 2n(2n+1)\alpha^2}$$

Legendre Polynomial



$\alpha^2 = 3$

$D = 0.5\ \mu m^2/s$

$k_c \sim 1\ min^{-1}$ → $\tau_{0.5} \sim 30$ sec.

$R \sim 20\ \mu m$

$V_t - V_b$ = hypothesis, predicted by model
experimental test.