(ii) chemotaxis

↳ movement in response to chemical signal

model organism: Dictyostelium discoideum (slime mold)

Single-cellular amoeba, eats bacteria

low food → produce cAMP → aggregate

goal: model the process of secreting cAMP & aggregating in response to cAMP gradients

[again, could use cell-level agent-based model, likely to be v. complicated]

how many variables?

two densities { $u(x,t)$ amoebae concentration; $c(x,t)$ concentration of cAMP

PDE model

note: run & tumble behavior

amoebae: diffusion + advection by external field

$v = \nabla c$ = gradient of cAMP

(why not birth & death? always consider relevant timescales)

cAMP: diffusion + creation + degradation

$$\begin{cases} u_t = D_u \Delta u - \chi \nabla \cdot (u \nabla c) \\ c_t = D_c \Delta c + \alpha u - \beta c \end{cases}$$

$\chi \nabla \cdot (u \nabla c)$: advection according to cAMP gradient; χ: strength of response to gradient

αu: prod. by amoebae; βc: degradation

Note: family of spatially homogeneous constant soln's

say we set ~~$c \equiv c_0 \ \forall x$~~ ~~$c(x) \equiv c_0 \ \forall x$~~

$$u(x,0) = u_0$$
$$c(x,0) = c_0 \quad \forall x$$

then $u_t = D_u \Delta u^{0} - \chi \nabla \cdot (u \nabla c)^{0}$

$$c_t = D_c \Delta c^{0} + \alpha u_0 - \beta c_0$$

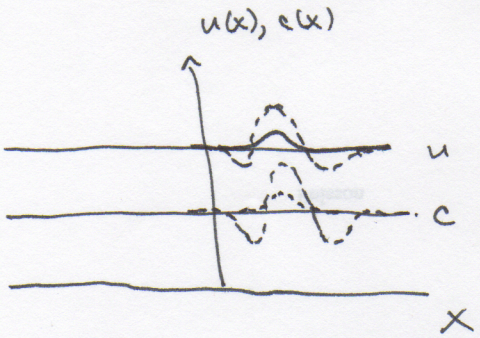
$\Rightarrow$ $u_0 = \frac{\beta c_0}{\alpha}$ is steady soln for any c_0

However, as w/ Turing bifurcation, spatially homogeneous steady state not nec. stable

↳ recall in activator-inhibitor system key was to have inhibitor diffuse much faster than activator to get pattern forming instability

↳ here more complicated, but similar idea, strength (rate of cAMP prod. · rate of response)

roughly speaking want $\alpha \chi$ to dominate βD_u (rate of degradation · diffusion of amoebae)

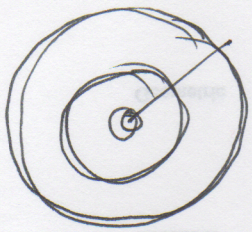


[only do if less than ½ time gone]

(very heuristic, like Bjorn's ex. of Turing)

(If response to cAMP & incr. cAMP prod. dominate diffusion & cAMP degradation can see this kind of pattern forming behavior)

Imagine radial



Spiral Fundamentally 2D - can't look at quite this way

(iii) Calcium waves:

Nature review ~10 yr. ago:

"Almost everything we do is controlled by Ca^{2+} – how we move, how our hearts beat, and how our brains process information and store memories."

→ believe information in signals may have to do w/ wave frequency rather than amplitude

- intracellular oscillations
  - ↳ Xenopus oocytes: spatial waves that propagate through cell
    - full purpose not known, but involved in avoidance of polyspermy (multiple fertilization) & other key developmental processes

like → 1D front

but also see spiral waves 

targets 

- intercellular oscillations
  - ↳ airway epithelial cells: calcium waves generated by mechanical stimuli; purpose likely stimulation of cilia that move mucus: Ca^{2+} waves can coordinate movement of cilia (synchronized beat rhythm)
  - ↳ contraction of heart muscle: [see visualizations on Scholarpedia]

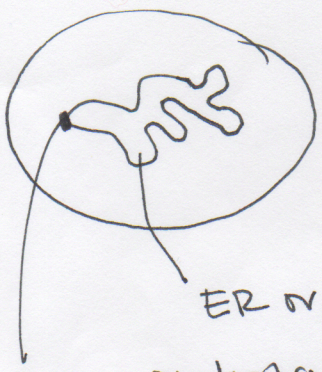
- under normal conditions action potentials propagate along network of Purkinje fibers (Ca^{2+} participates in creation of AP's)

- damaged tissue or changes in cellular structures can lead to abnormally long AP duration & shortened refractory times

↳ can produce spiral waves that lead to tachycardia (heart rates 100-200 bpm)

or ventricular fibrillation (spiral breakup → often fatal)

=



Ca^{2+} concentration in cytosol much lower than surrounding extracellular matrix → actively pumped out (sequested to ER)

* IP_3 → Ca^{2+} released from ER to cytoplasm
* Ca^{2+} exhibits positive feedback on short timescales (incr. activity of IP_3 receptors
* Ca^{2+} exhibits negative feedback on longer timescales

Model for Xenopus oocytes

(can use stochastic Markov-type models for individual receptors — we'll just use density spatio-temporal (PDE) model)

$$P_t = D_p \Delta p - \underbrace{k_p p}_{\text{degradation}}$$

could include production
↳ assume longer timescale/ not relevant here

$$c_t = D_c \Delta c + k_f \underbrace{\left(\mu_0 + \frac{\mu_1 p}{\mu_2 + p}\right)}_{IP_3 \text{ activation}} \underbrace{\left(b + \frac{(1-b)c}{k_1 + c}\right)}_{\text{calcium activation}} h - \underbrace{\frac{\gamma c}{k_\gamma + c}}_{\text{pump out}} + \underbrace{\beta}_{\text{leak}}$$

k_f: rate const. / scaling factor

h: calcium inactivation

[note what happens when $p \to 0, \infty$; $c \to 0, \infty$]

$$\tau h_t = \frac{k_2}{k_2 + c} - h$$

~~say h starts at some const., $c = 0$ what happens~~

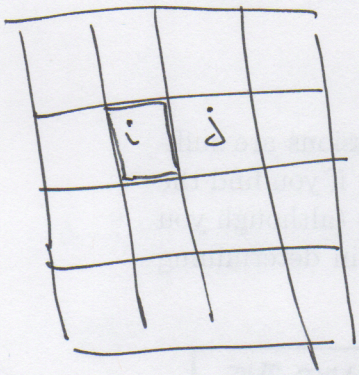
as $c \nearrow$, $\frac{k_2}{k_2 + c} \searrow$ so ~ exponential decay

as h gets small, ($\searrow 0$) influx in c also gets small ($\searrow 0$)

but note time scales not same

↳ this is how we capture initial pos. feedback followed by later neg. feedback

To model intercellular waves, one approach is to use square lattice of cells w same internal dynamics as above, w Ca^{2+} across cells but IP_3 flux via gap junctions.

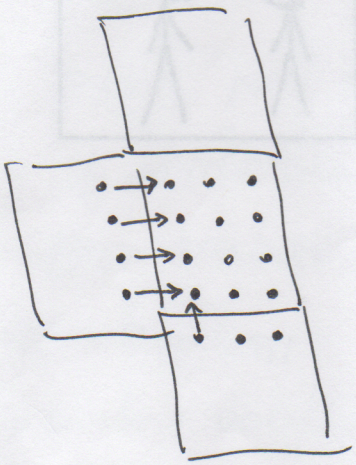


In particular use flux

$k(p_i - p_j)$

to couple cells

Solve numerically using some # of grid points inside cell and some # cells



Just scratching the surface - lots more in papers posted on Canvas if interested

also Sneyd & Keener Math. Physiol.