Self-organization in the slime mold *Dictyostelium discoideum*

CS 790R

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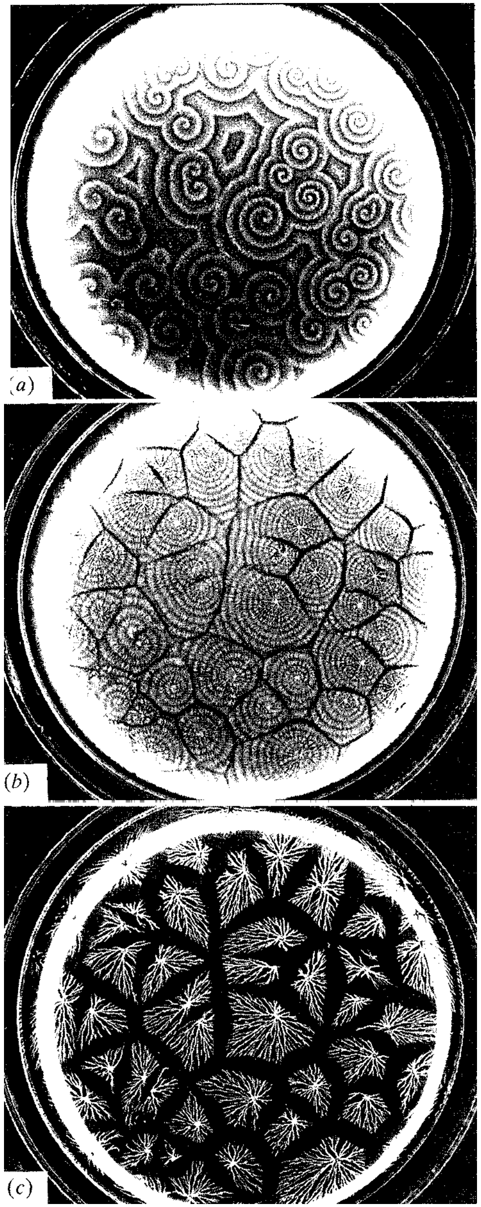
(Hofer et al 1995)

D. Discoideum amoeba starvation response

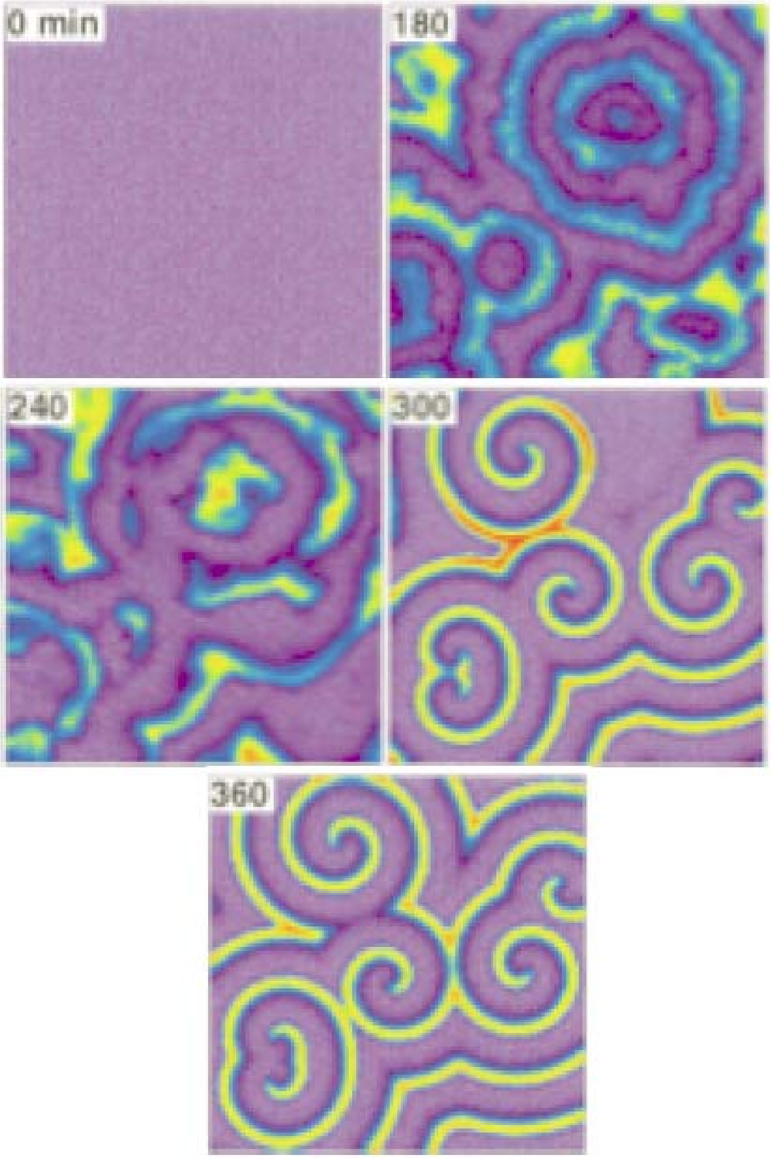


(Hofer et al 1995)

- Upon starvation: unicellular -> multicellular (10^4-10^5 clumps)
- **Excitable**: amoebae readily **relay** cyclic Adenosine Monophosphate (cAMP) signals
  - Extracellular cAMP concentrations trigger the production and release of cAMP as **positive feedback**
  - Wave and spiral patterns of cAMP form
- **Chemotaxis**: amoebae travel up cAMP gradients; (a) spiral pattern emerges (b,c) and amoebae **stream** towards spiral centers
- Eventually form "slug," differentiate (e.g. we notice cell types), produce spores
- But is it self-organization?

The evidence for self-organization

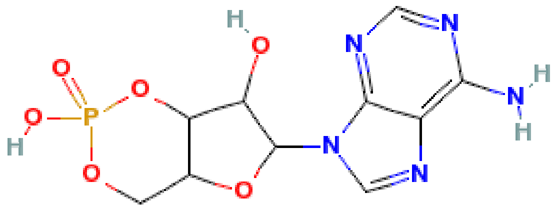
- Each amoeba must be responding to it's **local environment**
- A **global pattern** formed
- Wave "speed & period not generated by a master amoeba," according to experiments
- Could there be *de facto* pacemakers?
  - Those that starve first, by chance



(Lauzeral et al 1997)

cAMP-secretion: Oscillation and Relay

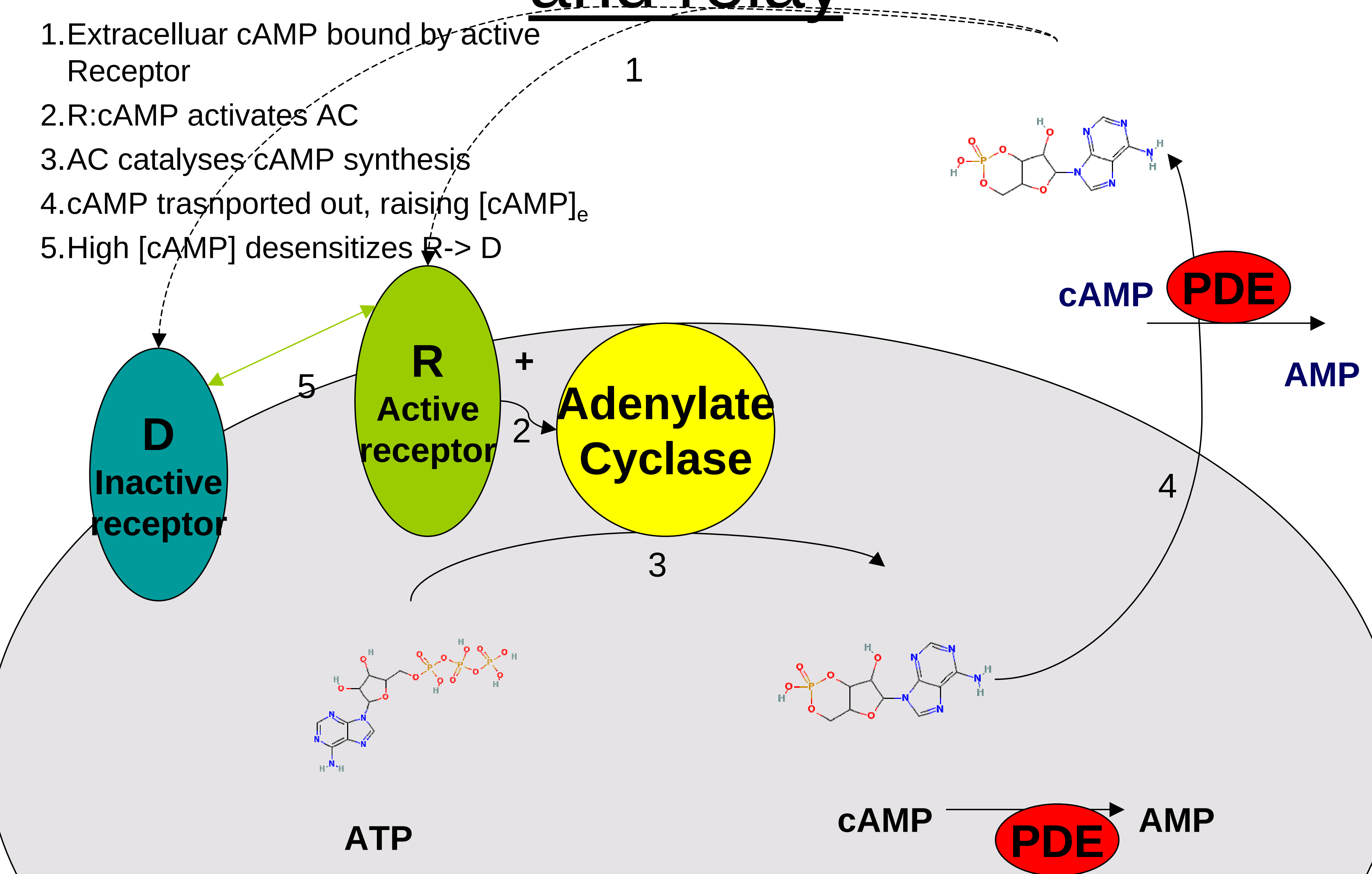
- Oscillatory release
  - Stirred & starved cell suspensions release cAMP in **5-10 minute pulses**
- Relay
  - If a large enough cAMP pulse added to medium…
  - Cells amplify pulse (**positive feedback**)



Cyclic AMP

Basic schematic of cAMP oscillation and relay

1. Extracelluar cAMP bound by active Receptor
2. R:cAMP activates AC
3. AC catalyses cAMP synthesis
4. cAMP trasnported out, raising $[cAMP]_e$
5. High [cAMP] desensitizes R-> D



Modeling cAMP waves

Only three variables needed to model secretion

$$\frac{\partial \gamma}{\partial t} = (k_t \beta / h) - k_e \gamma + D_\gamma \nabla^2 \gamma$$

=rate of change of **extracellular [cAMP]**

Secretion -degradation + diffusion

$$\frac{\partial \beta}{\partial t} = \phi(\rho, \gamma) - k_t \beta - k_i \beta$$

=rate of change of **intracellular [cAMP]**

Synthesis -secretion-degradation

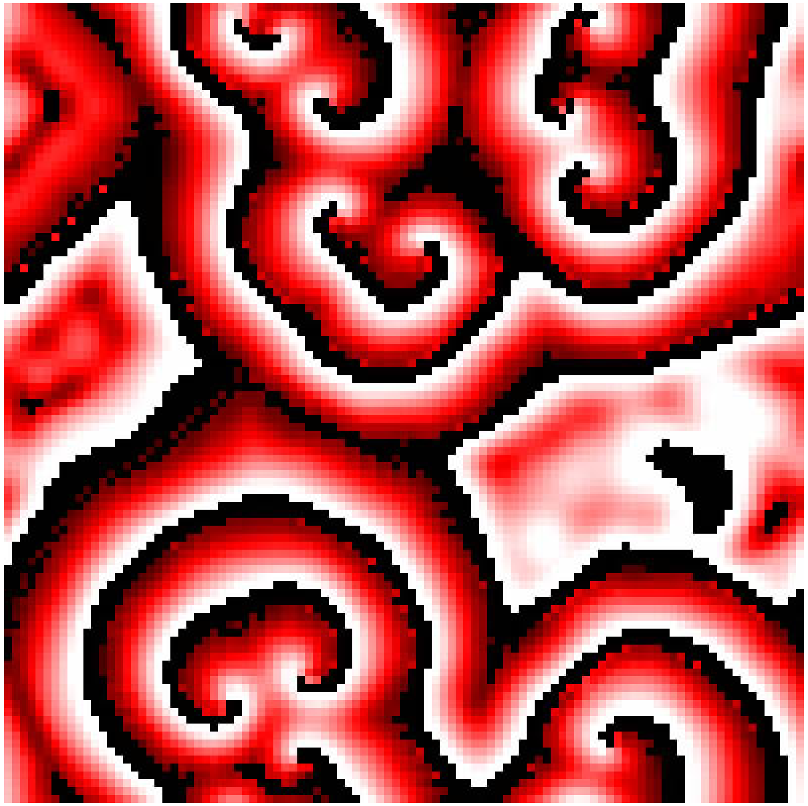
$$\frac{d\rho_T}{dt} = -f_1(\gamma)\rho_T + f_2(\gamma)(1 - \rho_T)$$

=rate of change of **active receptors**

-desensitization + resensitization

NetLogo simulation: BZ

BZ-reactions provide a rough analogy of the cAMP as excitable waves



Modeling cell movement:

- New assumptions
  - Ea. cell detects cAMP gradient & moves up it
  - Prolonged cAMP stimulus desensitizes ability to detect and/or respond to gradients
    - Figure 8.10
    - receptor-mediated desensitizations as before?
    - Polarized motor machinery?
  - Cell-cell adhesions stymie clump dispersal
- $\frac{\partial \gamma}{\partial t}$ is now also a function of local cell density
    - (p.111 if you're interested)

Modeling cell movement: the math

- *Cell diffusion*
  - Variable diffusion coefficient

    $$\mu(n) = \mu_1 + \mu_2 N^4/(N^4 + n^4)$$

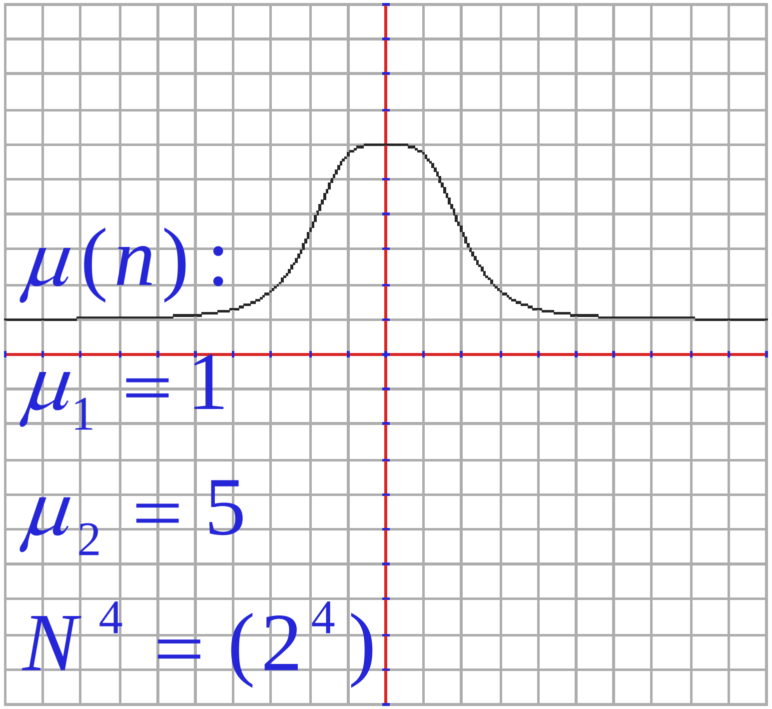
  - Cell density & threshold
- *Chemotaxis*
  - Proportional to [cAMP], density (n), and desensitization (p. 115):

    $$\chi(\rho) = \frac{\chi_0 \rho^m}{A^m + \rho^m}$$

    $\rho =$ active Receptor proportion

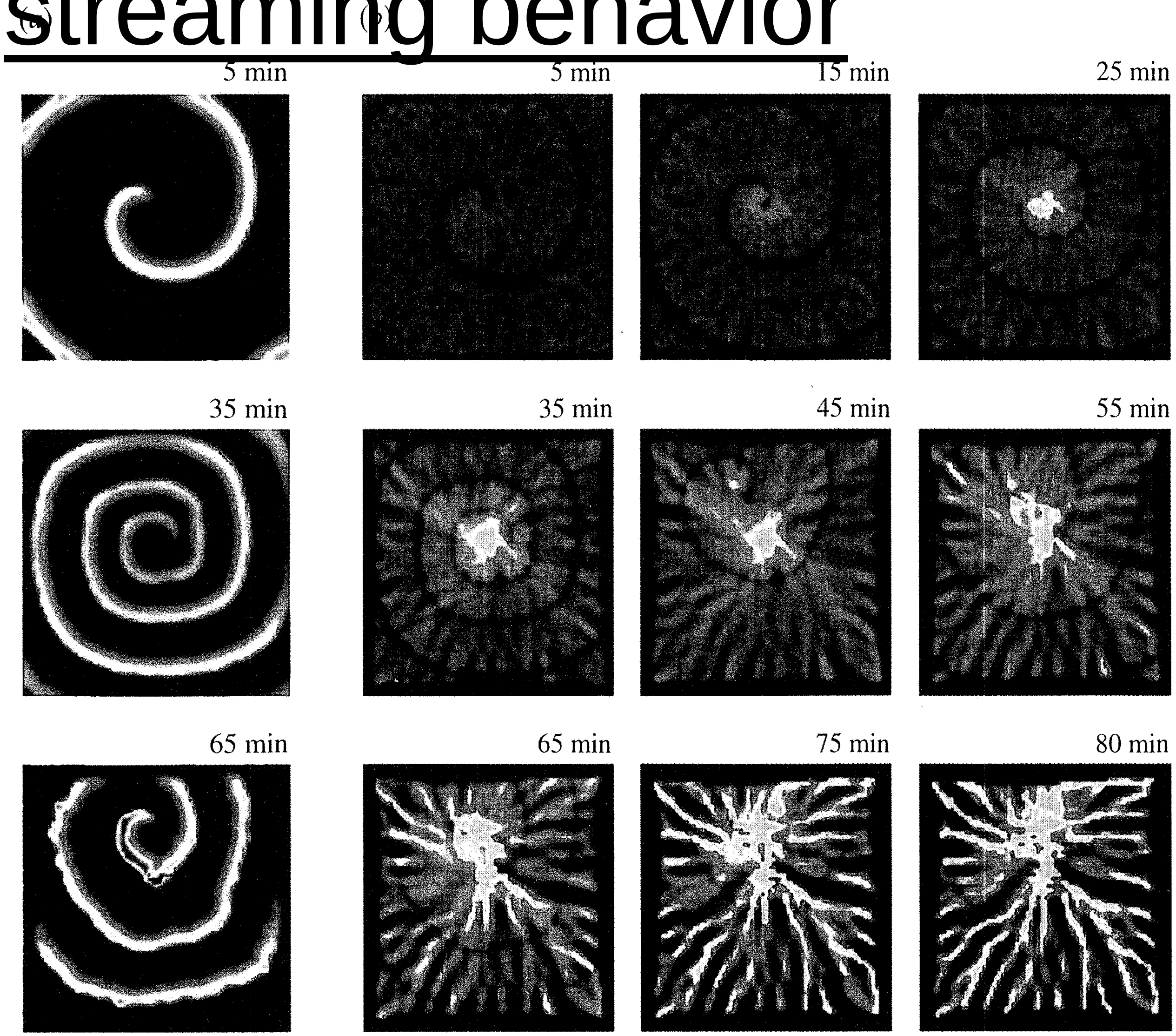
    $A, m =$ constants
- *"They" emphasize shape over specifics here*

$$\frac{\partial n}{\partial t} = \nabla \cdot [\mu(n) \nabla n] - \nabla \cdot [\chi(\rho) n \nabla u]$$



As $n \to N$, $\mu(n)$ falls sharply

Correlating cAMP patterns with streaming behavior



[cAMP] Cell density

Streaming slime “simulation”