Mathematical Cell Biology Graduate Summer Course

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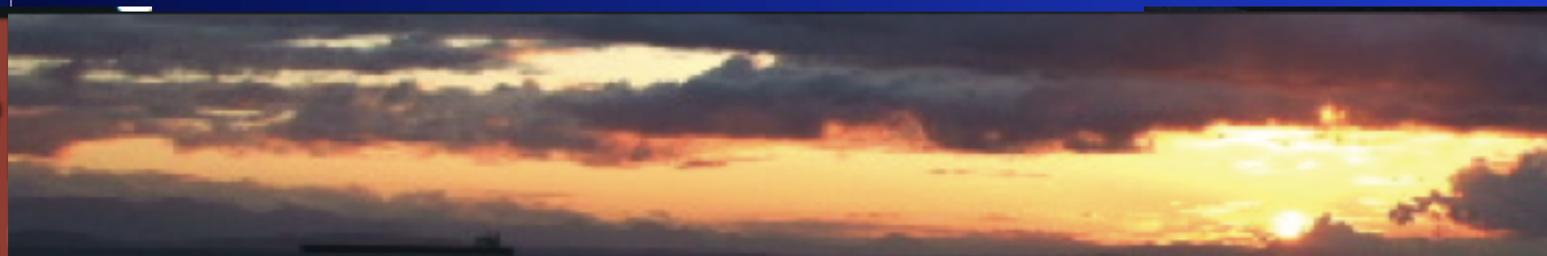
Diffusion, Reaction, and Biological pattern formation, cont'd



mprime

PIMS

www.math.ubc.ca/~keshet/MCB2012/

Reaction diffusion systems and Patterns

Example: (Schnakenberg)

$$\frac{\partial A}{\partial t} = f(A,B) + D_A \frac{\partial^2 A}{\partial x^2}$$

$$\frac{\partial B}{\partial t} = g(A,B) + D_B \frac{\partial^2 B}{\partial x^2}$$

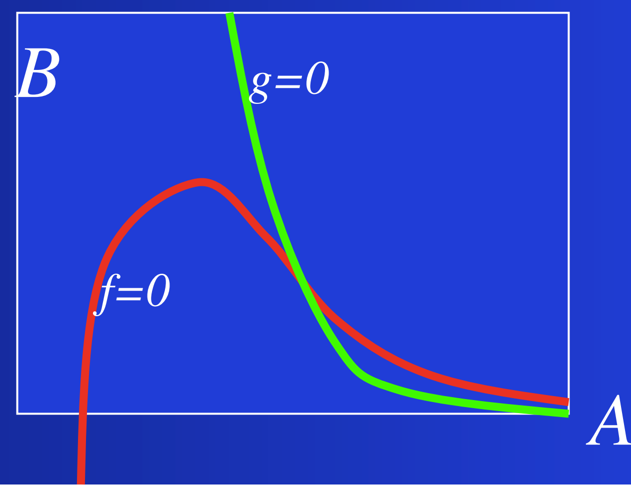
$$S_1 \Leftrightarrow A$$

$$S_2 \xrightarrow{k4} B$$

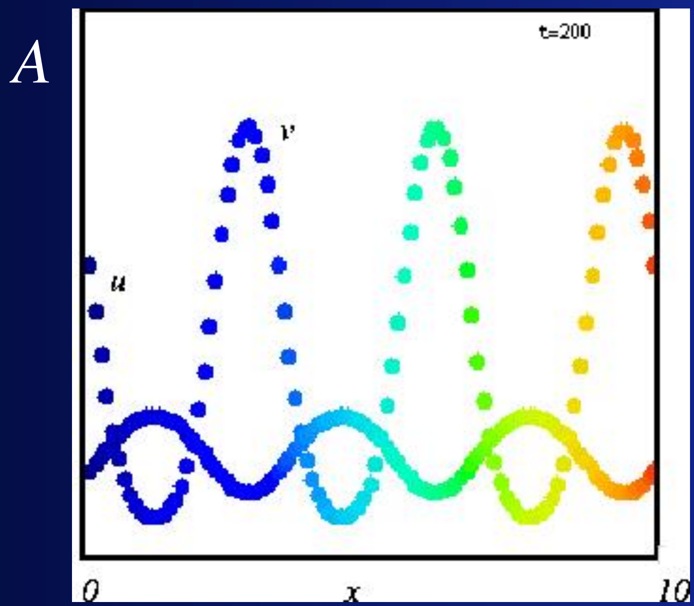
$$B + 2A \xrightarrow{k3} 3A$$

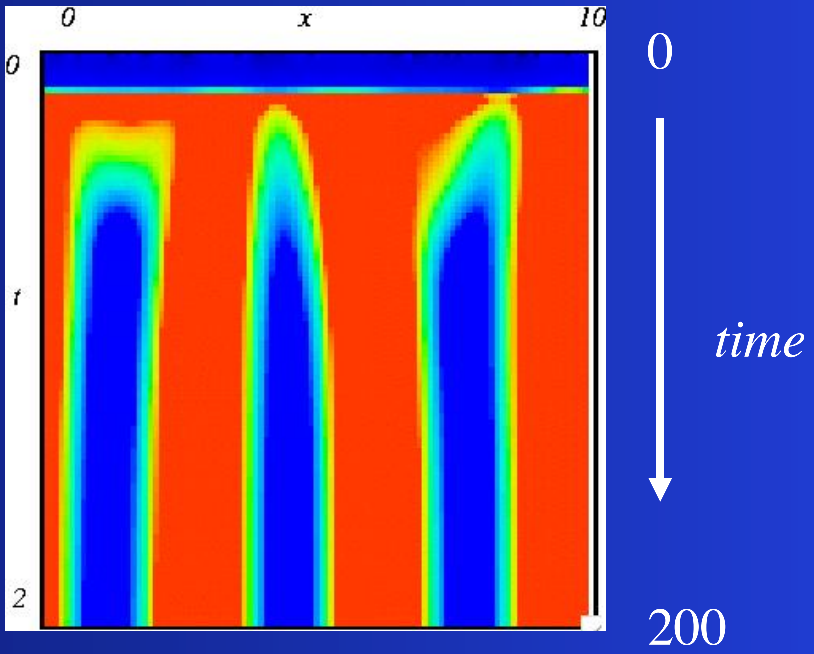
$$f(A,B) = k_1 - k_2 A + k_3 A^2 B$$

$$g(A,B) = k_4 - k_3 A^2 B$$



Example: Shnakenberg RD system





Starting close to the HSS, the system evolves a spatial pattern that persists with time.

How do we find the right parameter regime?

- Equations:

$$\frac{\partial C_1}{\partial t} = R_1(C_1, C_2) + D_1 \frac{\partial^2 C_1}{\partial x_2},$$

$$\frac{\partial C_2}{\partial t} = R_2(C_1, C_2) + D_2 \frac{\partial^2 C_2}{\partial x^2}.$$

- BC's: sealed domain (no flux, i.e. Neumann)

Find the homogeneous steady state

- $(\overline{C}_1, \overline{C}_2)$ such that

$$R_1(\overline{C}_1, \overline{C}_2) = 0,$$
$$R_2(\overline{C}_1, \overline{C}_2) = 0.$$

Compute the Jacobian Matrix

$$a_{11} = \left.\frac{\partial R_1}{\partial C_1}\right|_{\bar{c}_1, \bar{c}_2}, \qquad a_{12} = \left.\frac{\partial R_1}{\partial C_2}\right|_{\bar{c}_1, \bar{c}_2},$$

$$a_{21} = \left.\frac{\partial R_2}{\partial C_1}\right|_{\bar{c}_1, \bar{c}_2}, \qquad a_{22} = \left.\frac{\partial R_2}{\partial C_2}\right|_{\bar{c}_1, \bar{c}_2},$$

Evaluate at the HSS

Stability of the homogeneous steady state (HSS)

$$(\overline{C}_1, \overline{C}_2)$$

- Stability of reaction system on its own (with no diffusion. Requires:

$$a_{11} + a_{22} < 0,$$
$$a_{11}a_{22} - a_{12}a_{21} > 0,$$

Consider small perturbations

$$\begin{pmatrix} C_1' \\ C_2' \end{pmatrix} = \begin{pmatrix} \alpha_1 \\ \alpha_2 \end{pmatrix} \cos qx \, e^{\sigma t}.$$

Ask whether positive values of sigma can exist (implies growth of pattern)

Conditions for instability (pattern formation):

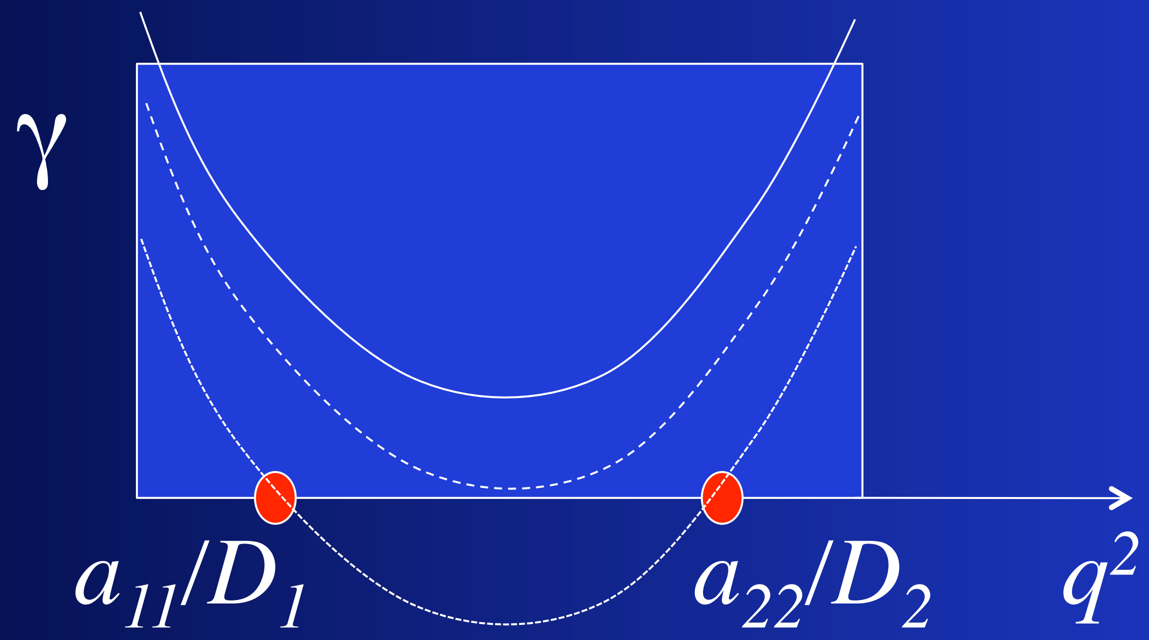
$$
\begin{aligned}
a_{11} + a_{22} &< 0, \\
a_{11}a_{22} - a_{12}a_{21} &> 0, \\
a_{11}D_2 + a_{22}D_1 &> 2\sqrt{D_1 D_2}(a_{11}a_{22} - a_{12}a_{21})^{1/2} > 0.
\end{aligned}
$$

Characteristic equation for σ:

- Eqn $\sigma^2 - \beta\sigma + \gamma = 0$
- β is always negative if SS is stable
- $\gamma = (a_{11} - D_1 q^2)(a_{22} - D_2 q^2) - a_{12}a_{21}$
- Negative γ will ensure that the growth σ is positive.

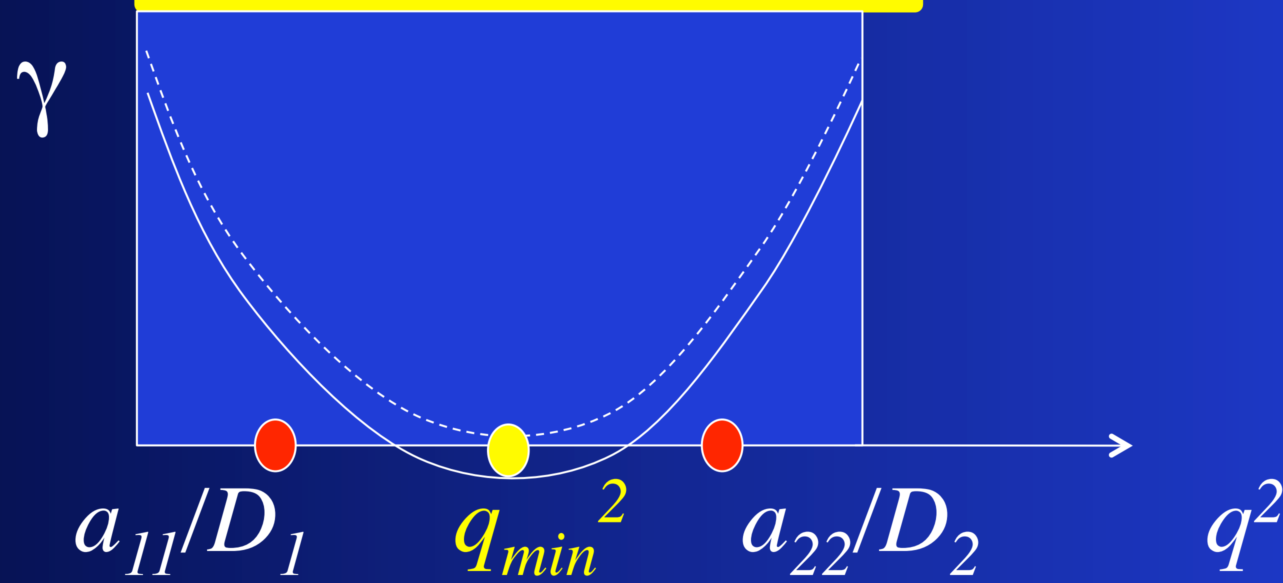
Ask: when is γ negative?

- γ = $(a_{11} - D_1 q^2)(a_{22} - D_2 q^2) - a_{12}a_{21}$



Local minimum for γ at the wavenumber

$$q_{\min}^2 = \frac{1}{2}\left(\frac{a_{22}}{D_2} + \frac{a_{11}}{D_1}\right)$$



Existence of such minimum

$$q_{\min}^2 = \frac{1}{2}\left(\frac{a_{22}}{D_2} + \frac{a_{11}}{D_1}\right)$$

- For q_{min} to exist, need
- $$\frac{a_{22}}{D_2} + \frac{a_{11}}{D_1} > 0$$

Combining results

$$a_{11} + a_{22} < 0,$$ (stability of HSS)

$$\frac{a_{22}}{D_2} + \frac{a_{11}}{D_1} > 0$$

At least one, but not both a_{11} a_{22} negative

D_1 and D_2 cannot be equal (otherwise contradiction)

Sign pattern

At least one, but not both a_{11} a_{22} negative

Suppose $a_{11} > 0$ then $a_{22} < 0$

But, stability of HSS implies

$$a_{11}a_{22} - a_{12}a_{21} > 0,$$

(negative) $- a_{12}\ a_{21} > 0$

Conclude a_{12} a_{21} have opposite signs.

Interpretation

- Case 1: $a_{12} < 0, \qquad a_{21} > 0$
- Case 2: $a_{12} > 0, \qquad a_{21} < 0$
- In either case, need $D_1 < D_2$

Possible interactions

- Case 1:

$$\mathbf{M} = \begin{pmatrix} + & - \\ + & - \end{pmatrix}$$

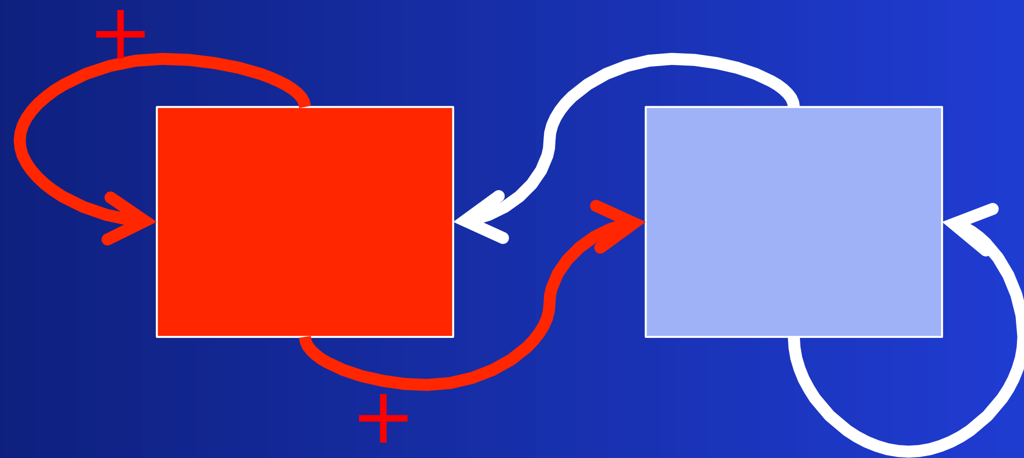
- Case 2:

$$\mathbf{M} = \begin{pmatrix} + & + \\ - & - \end{pmatrix}.$$

Possible interactions

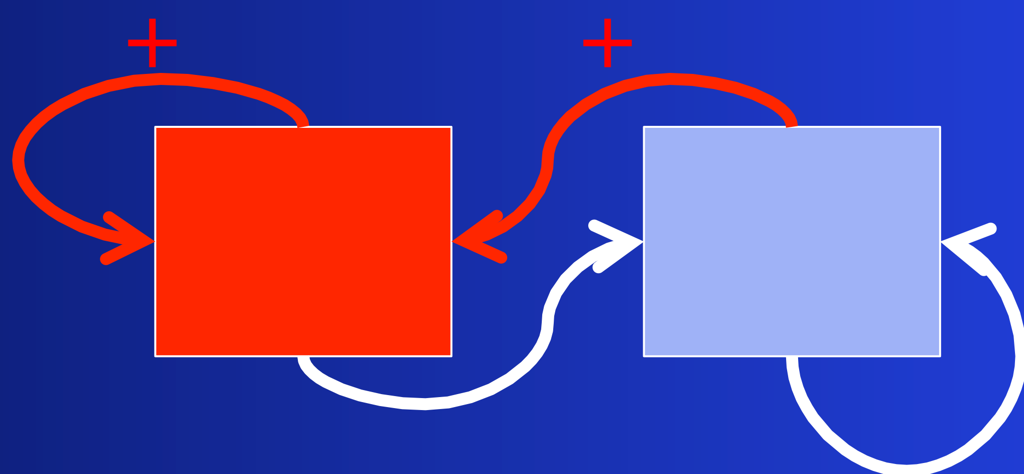
Activator-inhibitor

$$\mathbf{M} = \begin{pmatrix} + & - \\ + & - \end{pmatrix}$$



Substrate-depletion

$$\mathbf{M} = \begin{pmatrix} + & + \\ - & - \end{pmatrix}.$$



RD Simulations

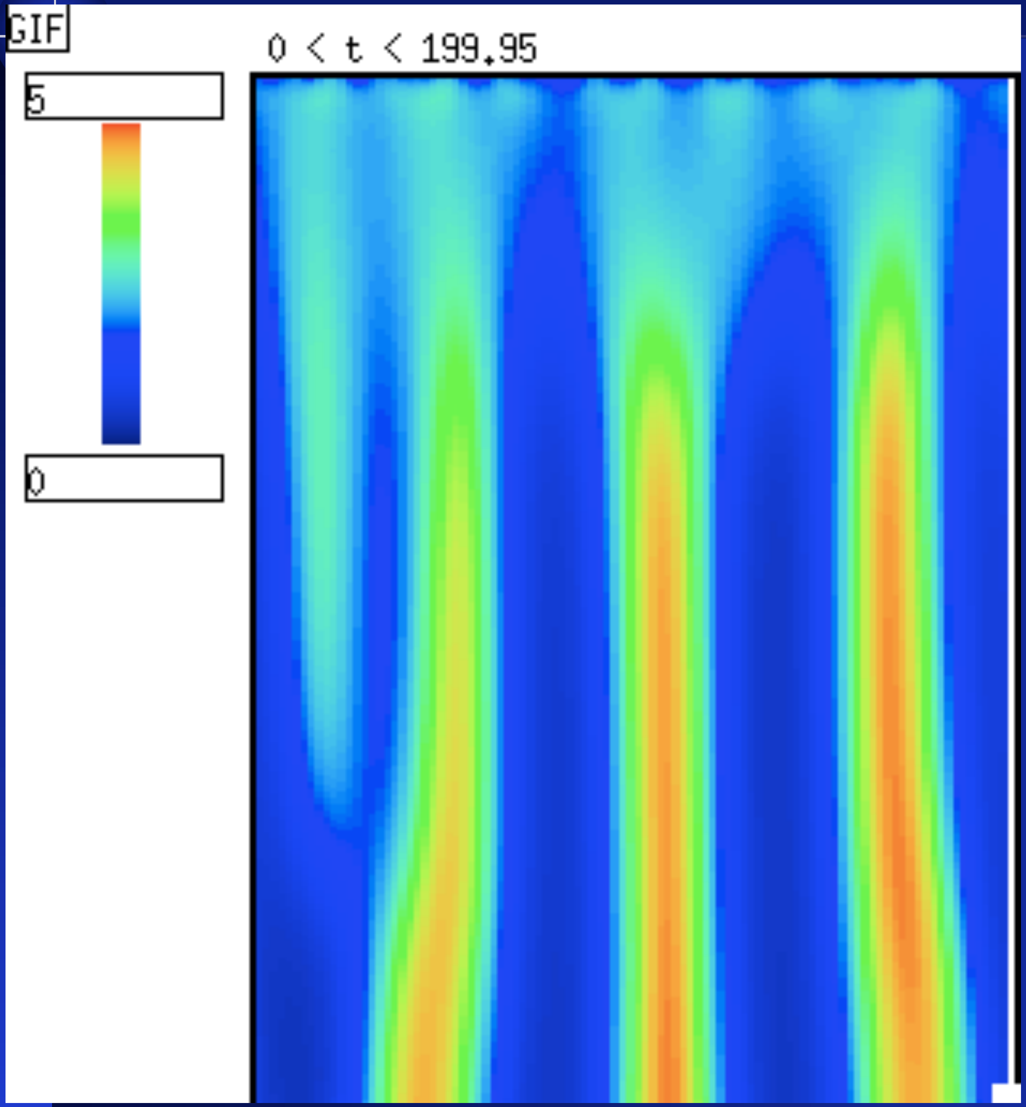
```
# SchnakenRD.ode
# Reaction diffusion system

f(u,v)=gamma*(a-u+u^2*v)
g(u,v)=gamma*(b-u^2*v)
```

Schnakenberg Reaction kinetics

```
%[2..99]
u[j]'=f(u[j],v[j])+du*(u[j+1]+u[j-1]-2*u[j])/h^2
v[j]'=g(u[j],v[j])+dv*(v[j+1]+v[j-1]-2*v[j])/h^2
%
```

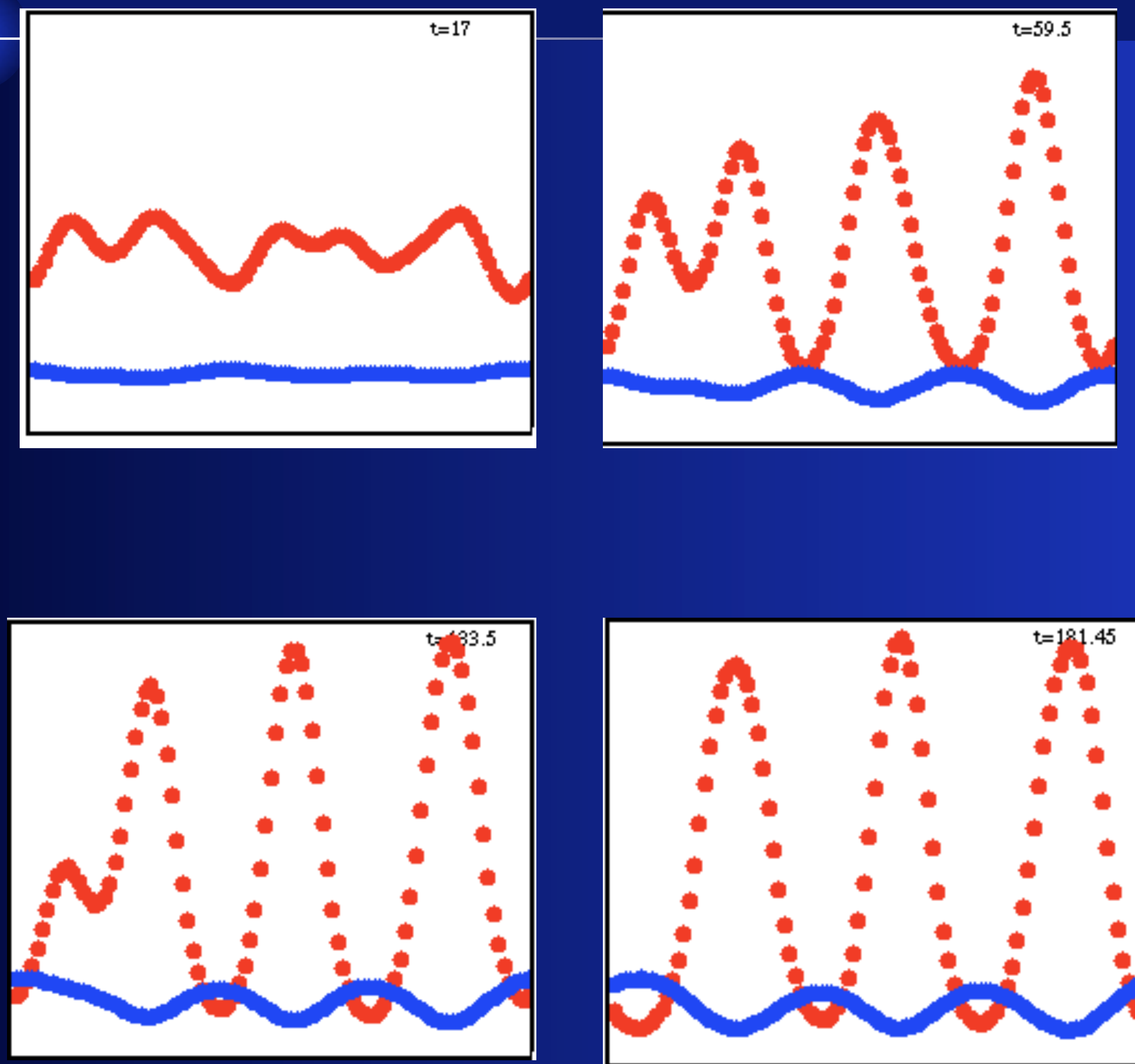
Array plot



XPP Animation file

```
# animation for the array
# cable100a.ani
vtext .8;.95;t=;t
fcircle [1..100]/100;(u[j])/5;.02;$RED
fcircle [1..100]/100;(v[j])/3;.02;$BLUE
end
```

Schnakenberg simulations



Recap

- System of 2 RD equations (2 chemicals) : finding param regime for patterns entails satisfying several inequalities (obtained from quadratic char eqn for the eigenvalues).
- For system of N chemicals (N RD eqs), char eqn is N'th order polynomial.. Much much harder to find the conditions.

Recap

- Turing analysis: only describe patterns that arise from tiny noise.. Not other kinds of pattern formation.
- Once pattern starts to grow, analysis no longer predictive .. Need simulations.
- Other methods of parameter identification useful (esp for larger systems) ← provides motivation for talks by Bill Holmes