A Systems Approach to Biology

MCB 195

Lecture 4
Tuesday, 15 Feb 2005

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LINEAR SYSTEMS

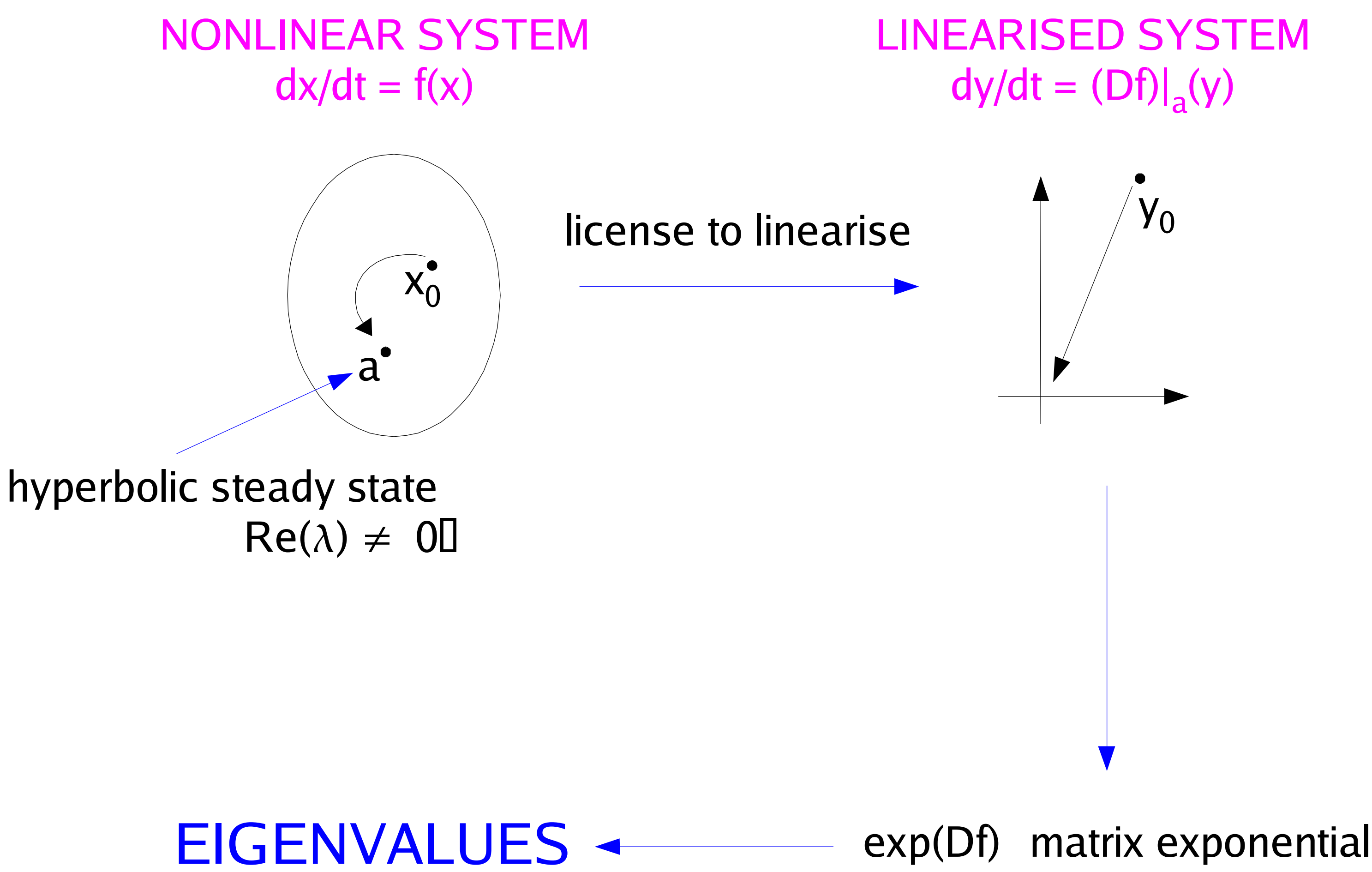
more about those dreaded
eigenvalues

and then

BISTABILITY

Why do we need to know about eigenvalues?

Because they tell us what trajectories look like near a steady state


NONLINEAR SYSTEM
$dx/dt = f(x)$
LINEARISED SYSTEM
$dy/dt = (Df)|_a(y)$
license to linearise
x_0
a
y_0
hyperbolic steady state
$Re(\lambda) \neq 0$
EIGENVALUES
exp(Df) matrix exponential

$$Au = \lambda u \quad u \neq 0$$

characteristic equation $\quad \det(A - \lambda I) = 0$

$$\begin{pmatrix} a & b \\ c & d \end{pmatrix}$$

$$\lambda^2 - (a + d)\lambda + (ad - bc) = 0$$

2 distinct real roots	2 equal real roots	2 complex conjugate roots
$(\lambda - 1)(\lambda - 2) = 0$	$(\lambda - 1)^2 = 0$	$\lambda^2 + 1 = 0$

$$\frac{dx}{dt} = Ax$$

if A has a real eigenvalue λ with eigenvector u

$$Au = \lambda u$$

exp(At) has eigenvalue exp(λt) for the same eigenvector

if the linear system is started anywhere along the line defined by u, it remains on that line and moves exponentially at rate λ

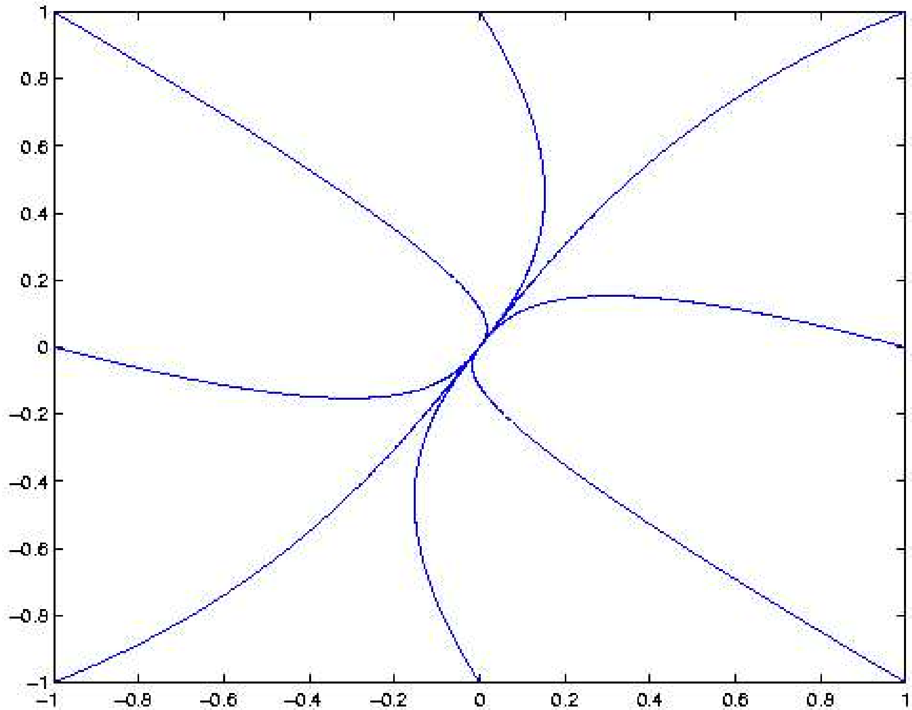
THE SIMPLE CASE

distinct real eigenvalues

$$\frac{dx}{dt} = Ax \qquad A = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$$

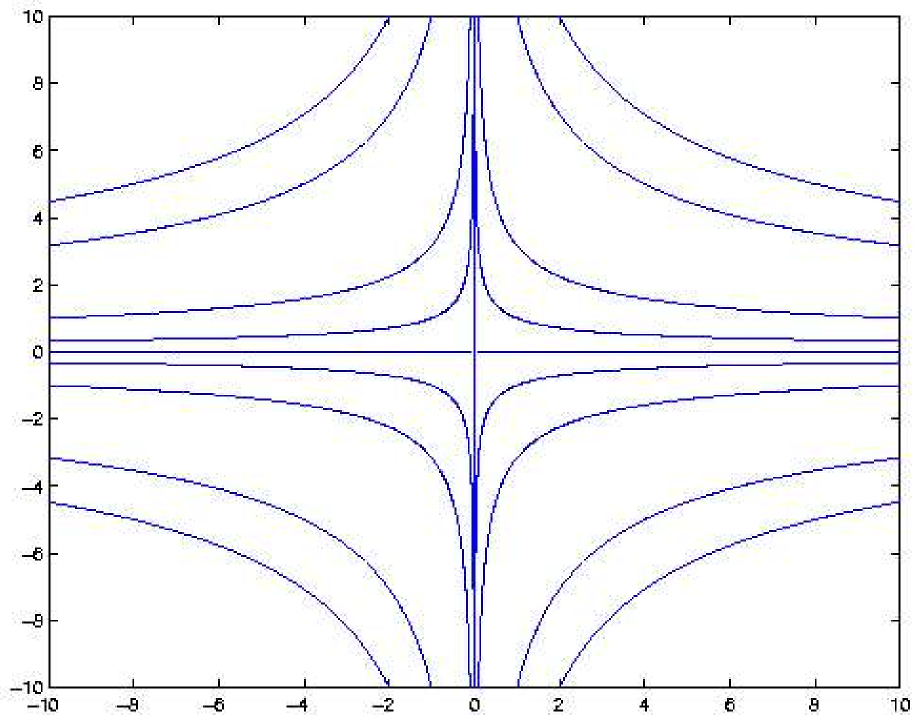
$$Au = \lambda u \qquad Av = \mu v$$

unstable node	saddle	stable node
$\lambda, \ \mu > 0$	$\lambda > 0, \ \mu < 0$	$\lambda, \ \mu < 0$



$$\begin{pmatrix} -3 & 1 \\ 1 & -2 \end{pmatrix}$$

stable node



$$\begin{pmatrix} 2 & 0 \\ 0 & -1 \end{pmatrix}$$

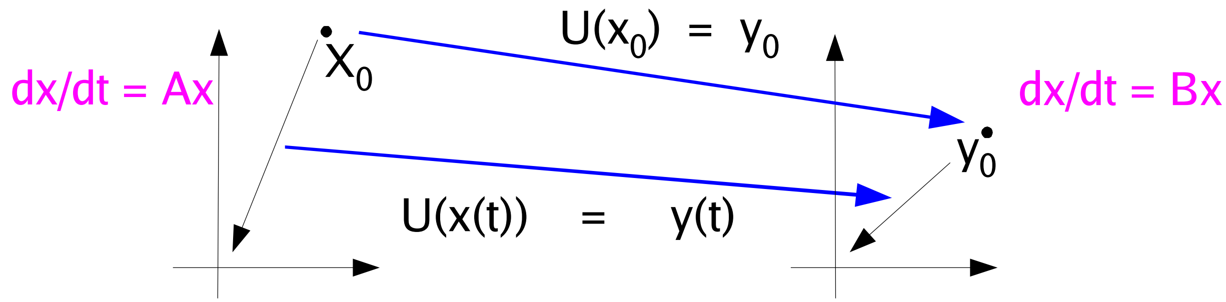
saddle

A and B are conjugate if there is an invertible matrix U such that

$$B = UAU^{-1}$$

conjugate matrices have identical eigenvalues

conjugate matrices have identical dynamics



THE INTERESTING CASE

complex eigenvalues

$$A = \begin{pmatrix} a & -b \\ b & a \end{pmatrix}$$

can always find a conjugate matrix of this form

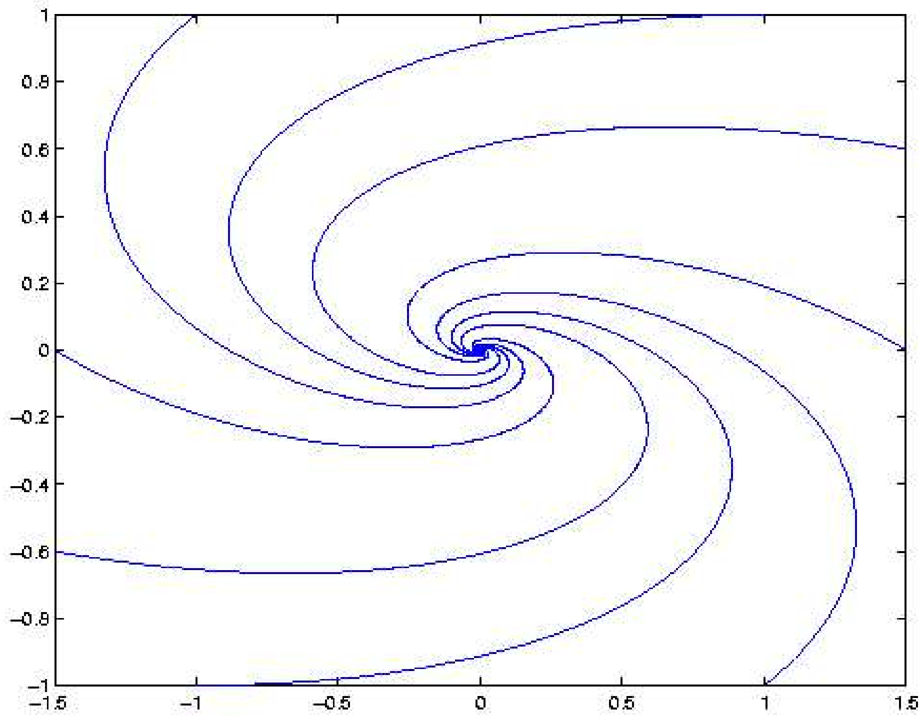
$$\begin{pmatrix} a & -b \\ b & a \end{pmatrix} \longleftrightarrow a + ib$$

sums and products of matrices ⟷ sums and products of complex numbers

exp(A) ⟷ exp(a+ib) = exp(a) exp(ib)

$$\exp(a)\begin{pmatrix} \cos(b) & -\sin(b) \\ \sin(b) & \cos(b) \end{pmatrix} \longleftrightarrow \exp(a)\,(\cos(b) + i\sin(b))$$

complex eigenvalues imply SPIRALS
or damped oscillations

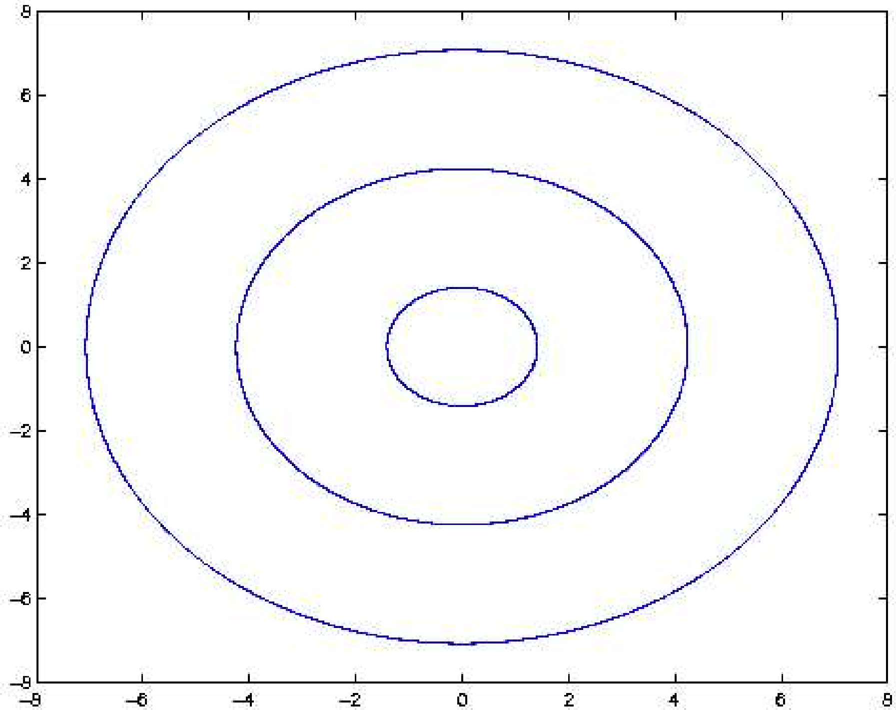


$$\begin{pmatrix} -2 & -5 \\ 1 & -1 \end{pmatrix}$$

stable spiral

x(t) = exp(at)cos(bt)x(0) - exp(at)sin(bt)y(0)
y(t) = exp(at)sin(bt)x(0) + exp(at)cos(bt)y(0)

except when a = 0
we get a CENTER



THIS IS NON-HYPERBOLIC !!

THE AWKWARD CASE

equal real eigenvalues

$$A = \begin{pmatrix} a & b \\ 0 & a \end{pmatrix}$$

can always find a conjugate matrix of this form

$$\exp(A) = \exp(a) \begin{pmatrix} 1 & b \\ 0 & 1 \end{pmatrix}$$

degenerate case which cant make up its mind whether to be a node or a spiral

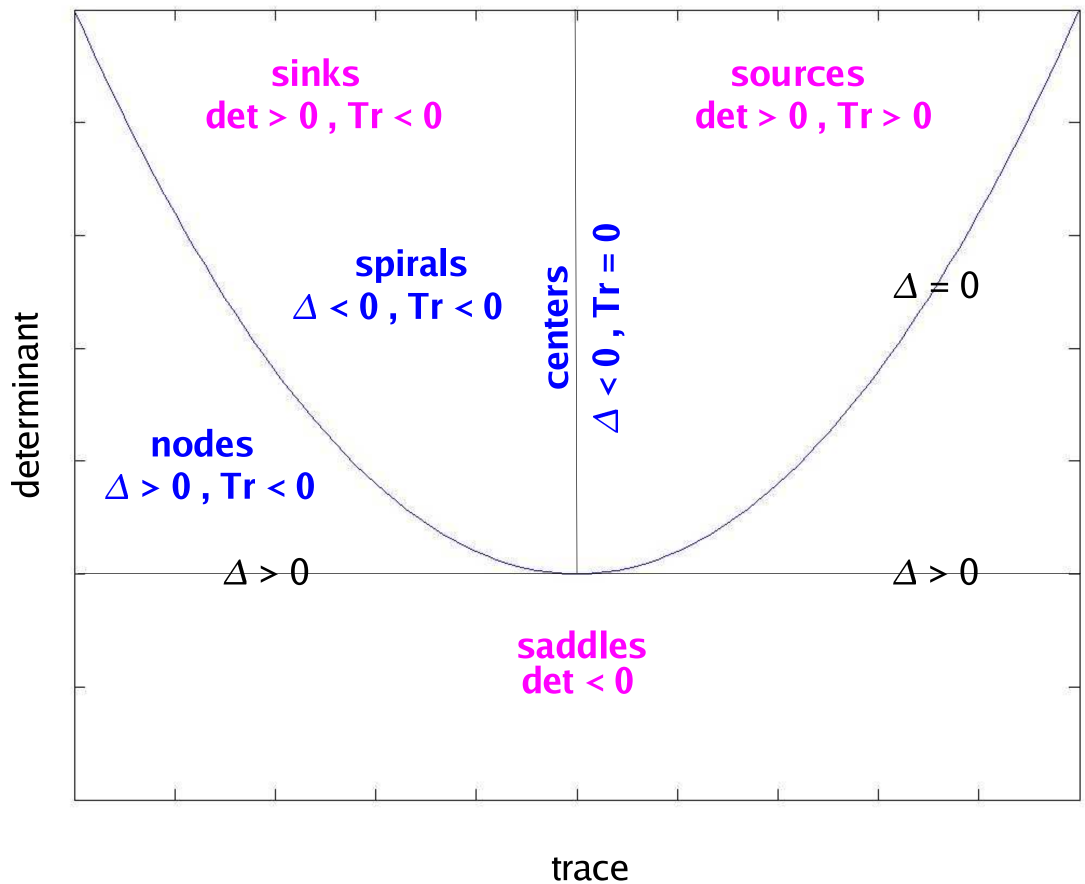
$$A = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$$

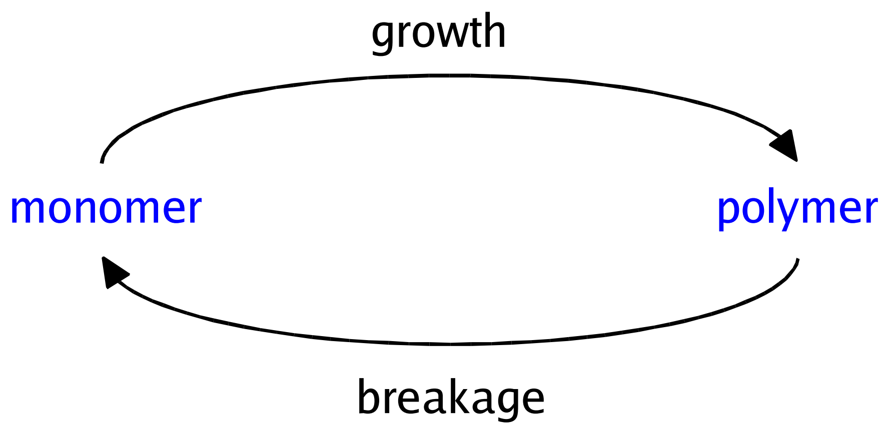
$$\lambda^2 - (a + d)\lambda + (ad - bc) = 0 \qquad \lambda^2 - Tr(A)\lambda + det(A) = 0$$

eigenvalues are $$\lambda = \frac{Tr(A) \pm \{ (Tr(A)^2 - 4\, det(A) \}^{1/2}}{2}$$

$$\Delta = Tr(A)^2 - 4det(A)$$ DISCRIMINANT

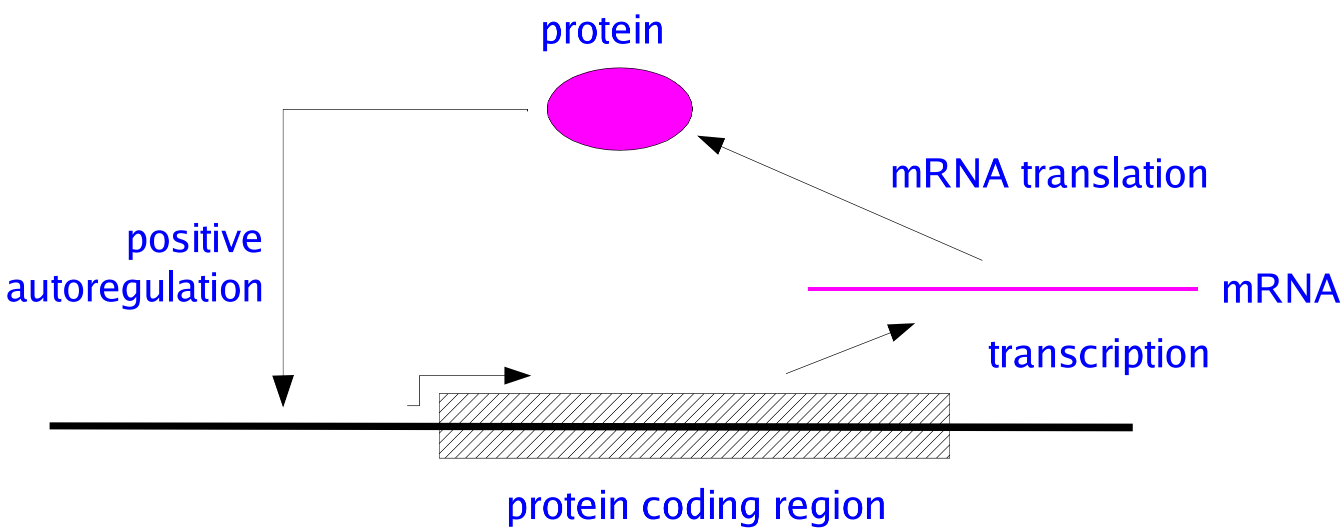
$\Delta > 0$	$\Delta = 0$	$\Delta < 0$
distinct real roots	equal real roots	complex roots


sinks
det > 0 , Tr < 0
sources
det > 0 , Tr > 0
spirals
Δ < 0 , Tr < 0
centers
Δ < 0 , Tr = 0
Δ = 0
nodes
Δ > 0 , Tr < 0
Δ > 0
Δ > 0
saddles
det < 0
determinant
trace



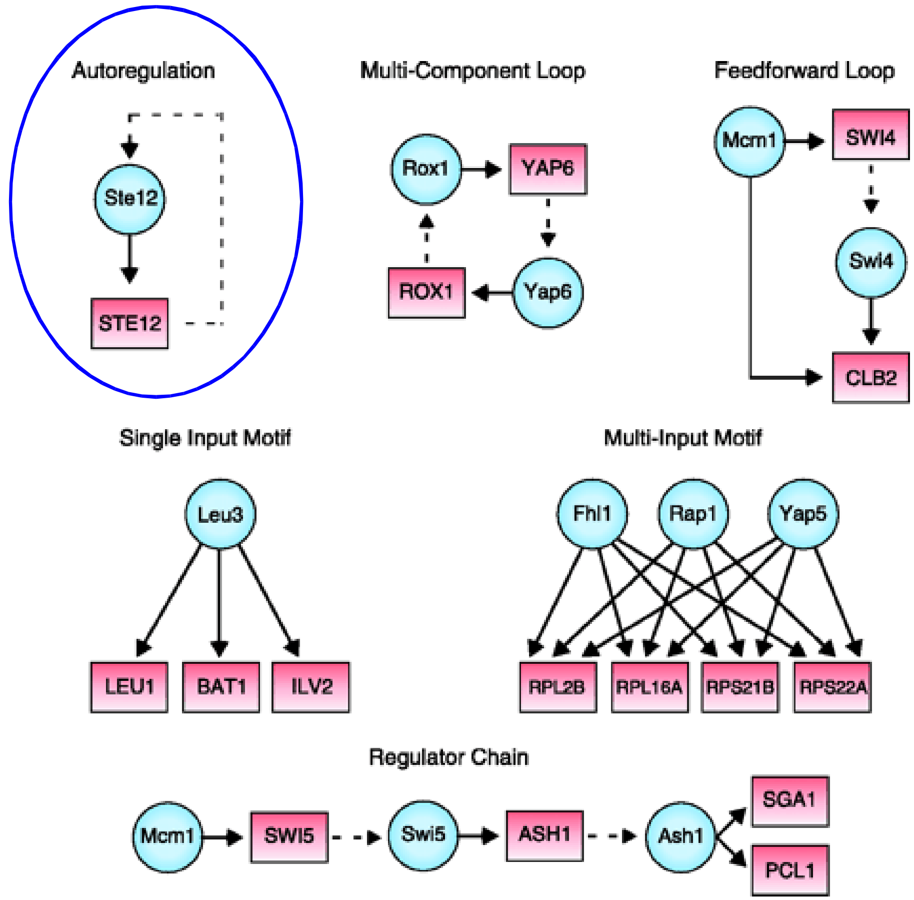
POSITIVE FEEDBACK

GENETIC AUTOREGULATORY LOOP



POSITIVE FEEDBACK

SIGNIFICANT REGULATORY MOTIF IN YEAST



Lee et al, *"Transcriptional regulatory networks in Saccharomyces cerevisiae"* Science **298**:799-804 2002

AND MORE COMPLEX ORGANISMS ...

Helms et al, *"Autoregulation and multiple enhancers control Math1 expression in the developing nervous system"*, Development **127**:1185-96 2000

x	=	protein concentration
y	=	mRNA concentration

$$\frac{dx}{dt} = \lambda y - ax$$

$$\frac{dy}{dt} = \frac{\alpha x^c}{k + x^c} - by$$

λ	translation rate	$(\text{time})^{-1}$
a	protein degradation rate	$(\text{time})^{-1}$
α	maximum gene expression rate	$(\text{mols})(\text{time})^{-1}$
k	“Michaelis-Menten” constant	(mols)
b	mRNA dedgradation rate	$(\text{time})^{-1}$
c	cooperativity	