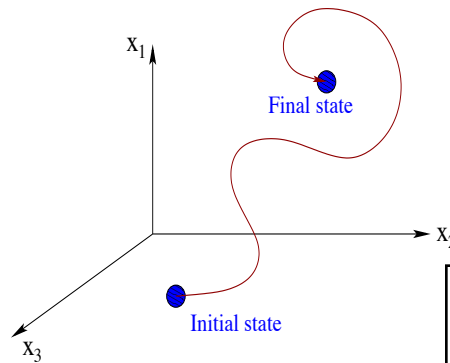
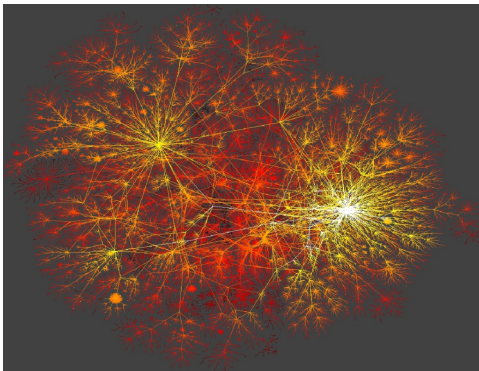


# Linear Network Control



A dynamical system is controllable if it can be driven from **any** initial state to **any** desired final state **in finite time** by suitable choice of input control signals.

General Mathematical framework: **Kalman's Controllability Rank Condition**

Focus of existing works: **minimal number of signals** required to control the network

Structural controllability: Y.-Y. Liu, J.-J. Slotine, and A.-L. Barabasi, "Controllability of complex networks," e.g., *Nature* **473**, 167 (2011)

Exact controllability: Z.-Z. Yuan, C. Zhao, Z.-R. Di, W.-X. Wang, and Y.-C. Lai, "Exact controllability of complex networks," *Nat. Commun.* **4**, 2447 (2013)

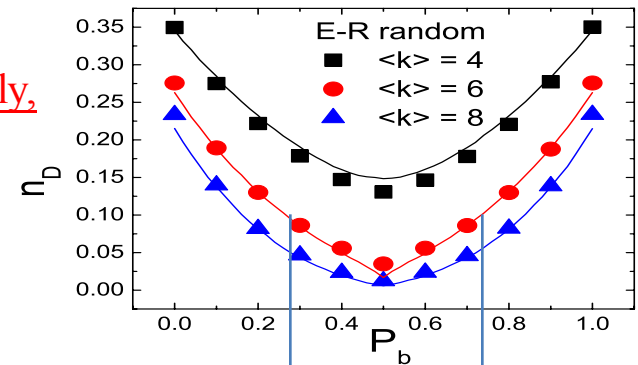
Issue: controllability is mathematically well defined but physically, control may be difficult

In terms of **ENERGY**

Energy bounds: G. Yan, J. Ren, Y.-C. Lai, C. H. Lai, B. Li, "Controlling complex networks: how much energy is needed?" *Phys. Rev. Lett.* **108**, 218703 (2012).

Energy scaling: Y.-Z. Chen, L.-Z. Wang, W.-X. Wang, and Y.-C. Lai, "Energy scaling and reduction in controlling complex networks," *Roy. Soc. Open Sci.* **3**, 160064 (2016).

Physical controllability: L.-Z. Wang, Y.-Z. Chen, W.-X. Wang, and Y.-C. Lai, "Physical controllability of complex networks," *Sci. Rep.* **7**, 40198 (2017).



High probability of energy divergence



# Optimal Control Input and Energy

$$\mathbf{u}_t = \mathbf{B}^T \cdot \exp[\mathbf{A}^T (T_f - t)] \cdot \mathbf{W}_{T_f}^{-1} \cdot \mathbf{v}_{T_f}, \text{ where}$$

$$\mathbf{W}_{T_f} \equiv \int_0^{T_f} \exp(\mathbf{A}t) \cdot \mathbf{B} \cdot \mathbf{B}^T \cdot \exp(\mathbf{A}^T t) dt \quad \text{and}$$

$$\mathbf{v}_{T_f} \equiv \mathbf{x}_{T_f} - \exp(\mathbf{A}T_f) \cdot \mathbf{x}_0$$

$$\text{Energy } \varepsilon(T_f) \equiv \int_0^{T_f} \|\mathbf{u}_t\|^2 dt = \mathbf{v}_{T_f}^T \cdot \mathbf{W}_{T_f}^{-1} \cdot \mathbf{v}_{T_f}$$

W - Symmetric **Gramian matrix** (positive definite if system is controllable)

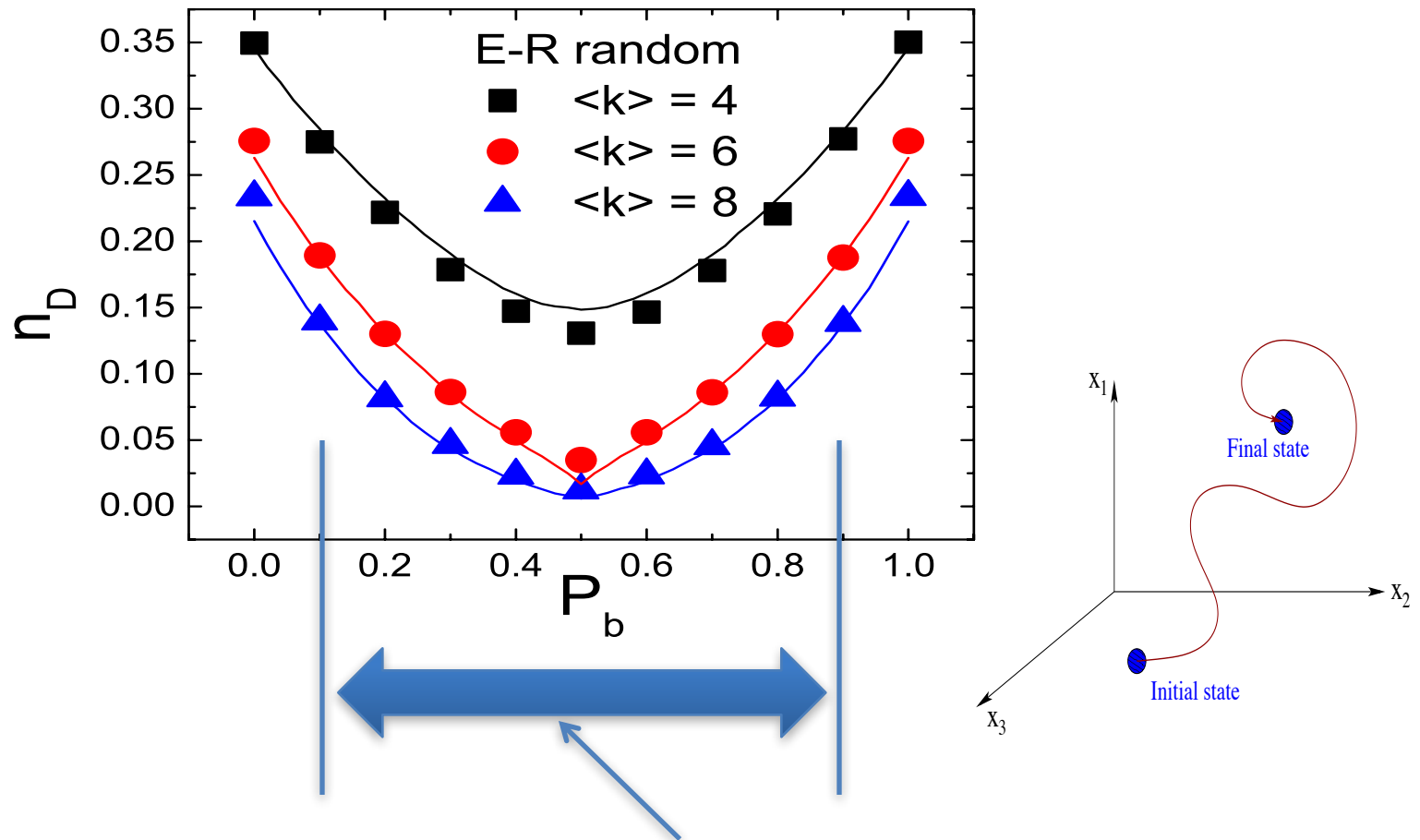
$$\mathbf{H}(T_f) \equiv \exp(-\mathbf{A}T_f) \cdot \mathbf{W}_{T_f} \cdot \exp(-\mathbf{A}^T T_f)$$

Normalized energy cost

$$E(T_f) \equiv \varepsilon(T_f) / \|\mathbf{x}_0\|^2 = \frac{\mathbf{x}_0^T \cdot \mathbf{H}^{-1} \cdot \mathbf{x}_0}{\mathbf{x}_0^T \cdot \mathbf{x}_0}$$

W. J. Rugh, *Linear System Theory* (2<sup>nd</sup> ed.)  
(Prentice-Hall, NJ, 1996)

# Is Control Physically Achievable?



**Our finding: High probability of divergence in required energy to achieve control**

# Physical Controllability

$\varepsilon$  – measurement error or computer roundoff

Consider linear equation:  $W \cdot X = Y$

$C_W$  - condition number of  $W$

Say  $e_x = 10^{-k}$  - accuracy of solution of  $X$

Then  $e_x \geq C_W \cdot \varepsilon$  (Strang, *Linear Algebra and Its Applications*, AP, 1976)

$$\Rightarrow C_W \leq e_x / \varepsilon \equiv \bar{C}_W$$

$\Rightarrow$  A linear system can be physically controlled with accuracy  $e_x$  only for

$$C_W \leq \bar{C}_W$$

Physical controllability can be characterized by

$P(\bar{C}_W)$  - probability that a network with its conditional number less than  $\bar{C}_W$

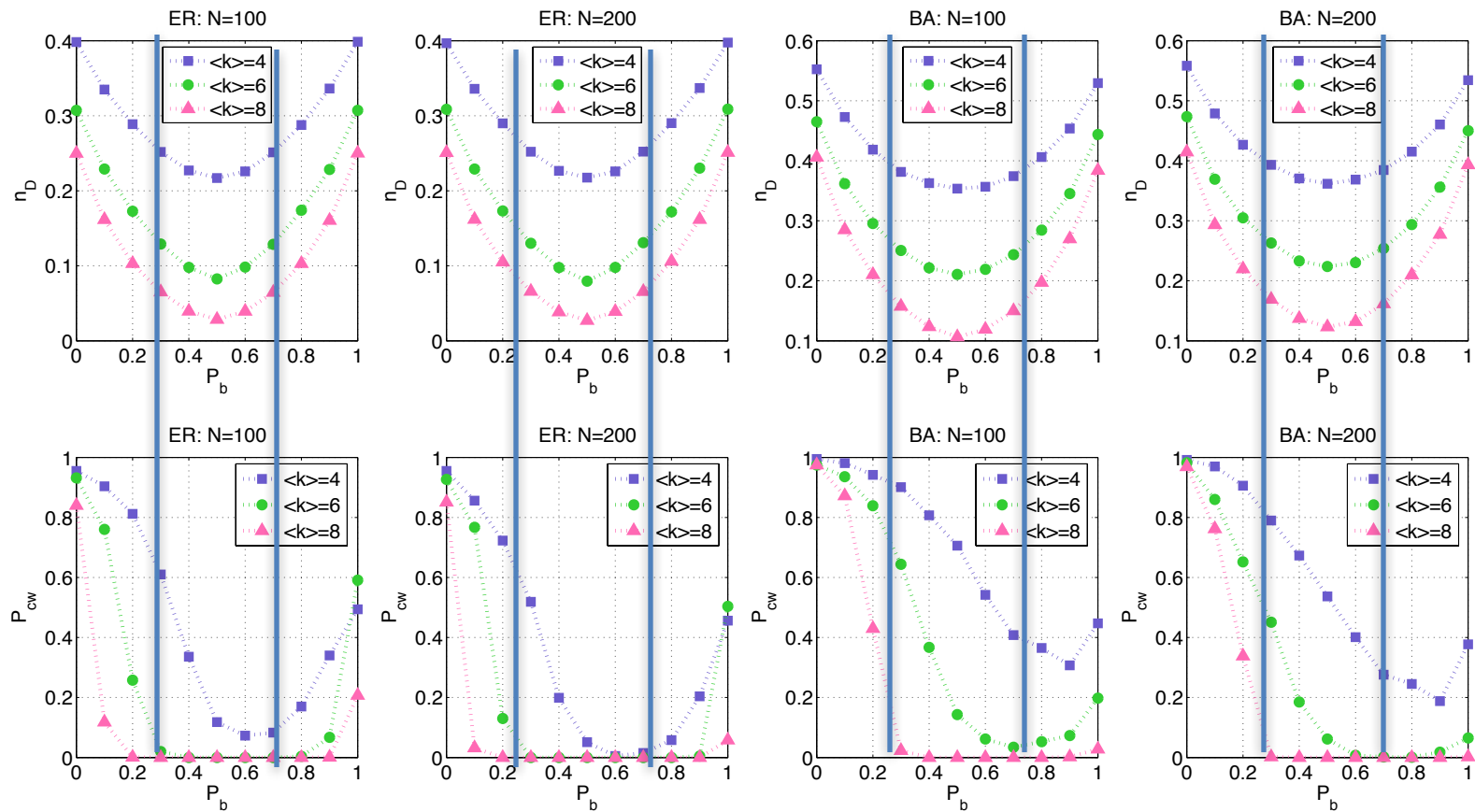
$P(\bar{C}_W) < \approx 1$  - network is physically controllable

$P(\bar{C}_W) \approx 0$  - network is physically uncontrollable

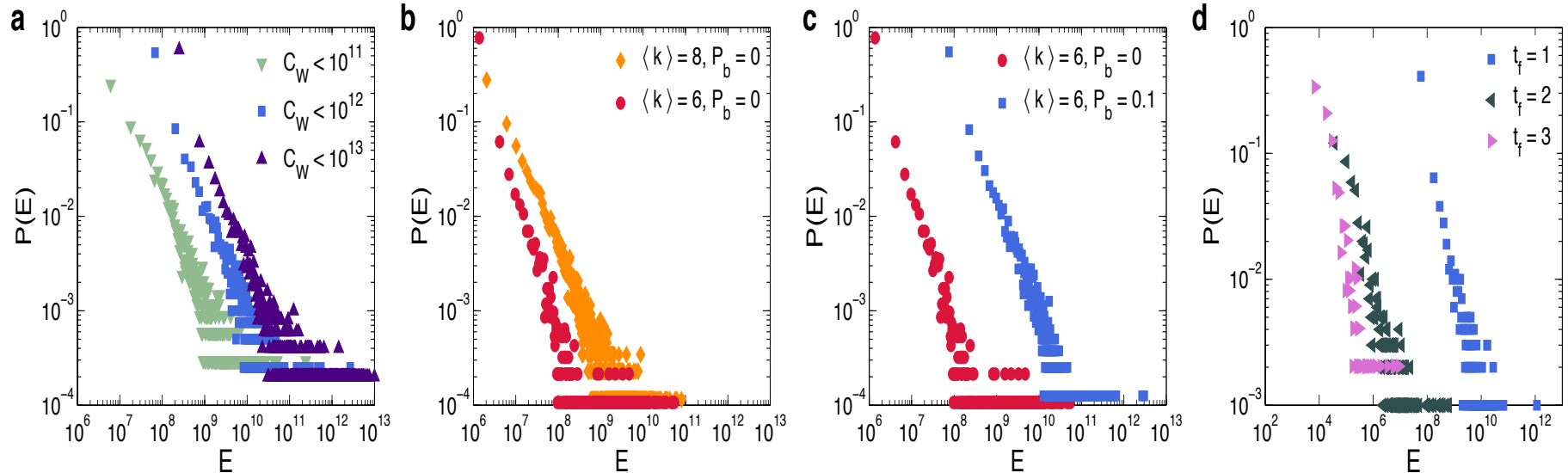
L.-Z. Wang, Y.-Z. Chen, W.-X. Wang, and Y.-C. Lai, “Physical controllability of complex networks,” *SREP* 7, 40198 (2017).



# Structural versus Physical Controllability



# Energy Scaling for Physically Controllable Networks

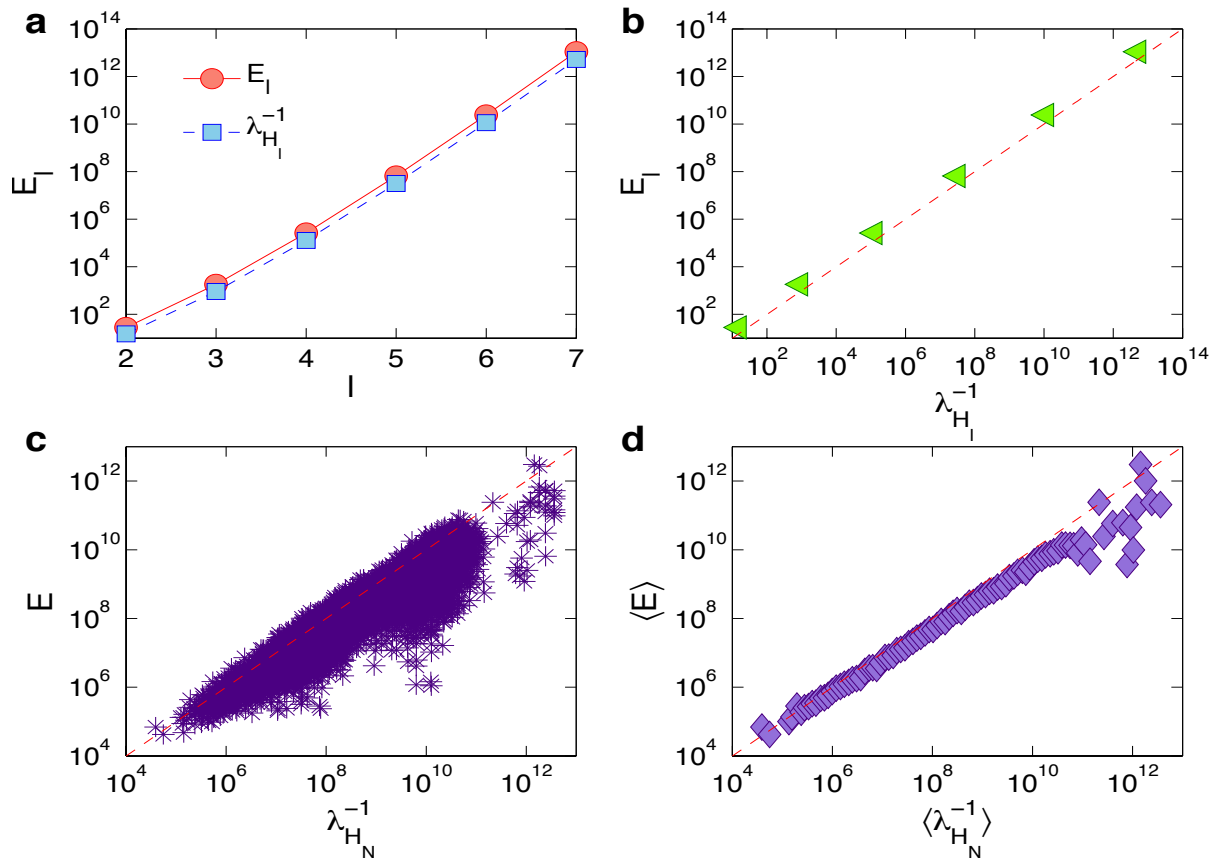


$$P(E) \propto E^{-\alpha}$$

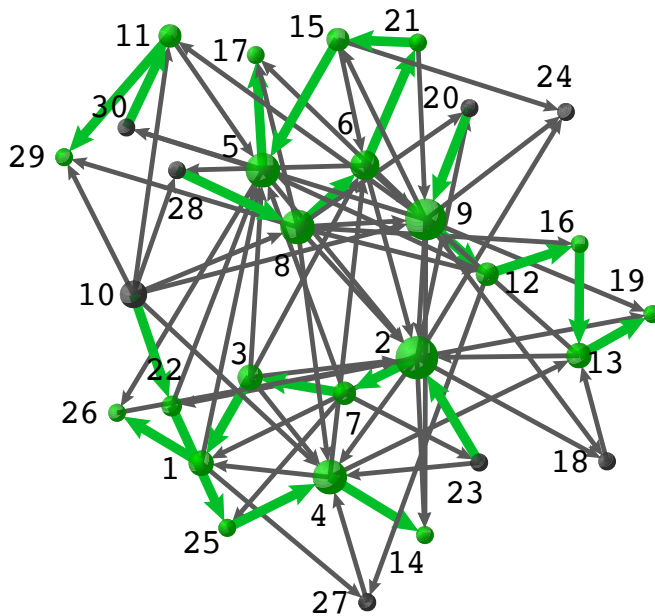
**There are networks that require an enormous amount of energy to be controlled!**

# Control Energy: One-Dimensional Chain versus Random Networks

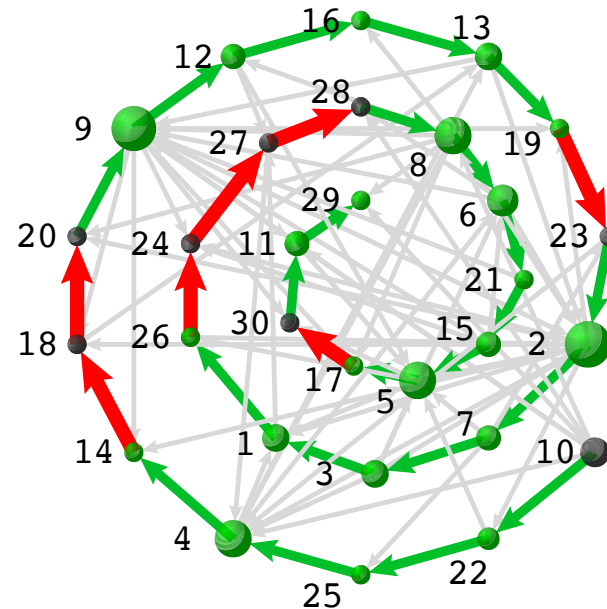
One-dimensional chain of length  $l$  :  $E \equiv \lambda_H^{-1}$   
(can be derived analytically)



# Maximum Matching – An Example



(a)



(b)

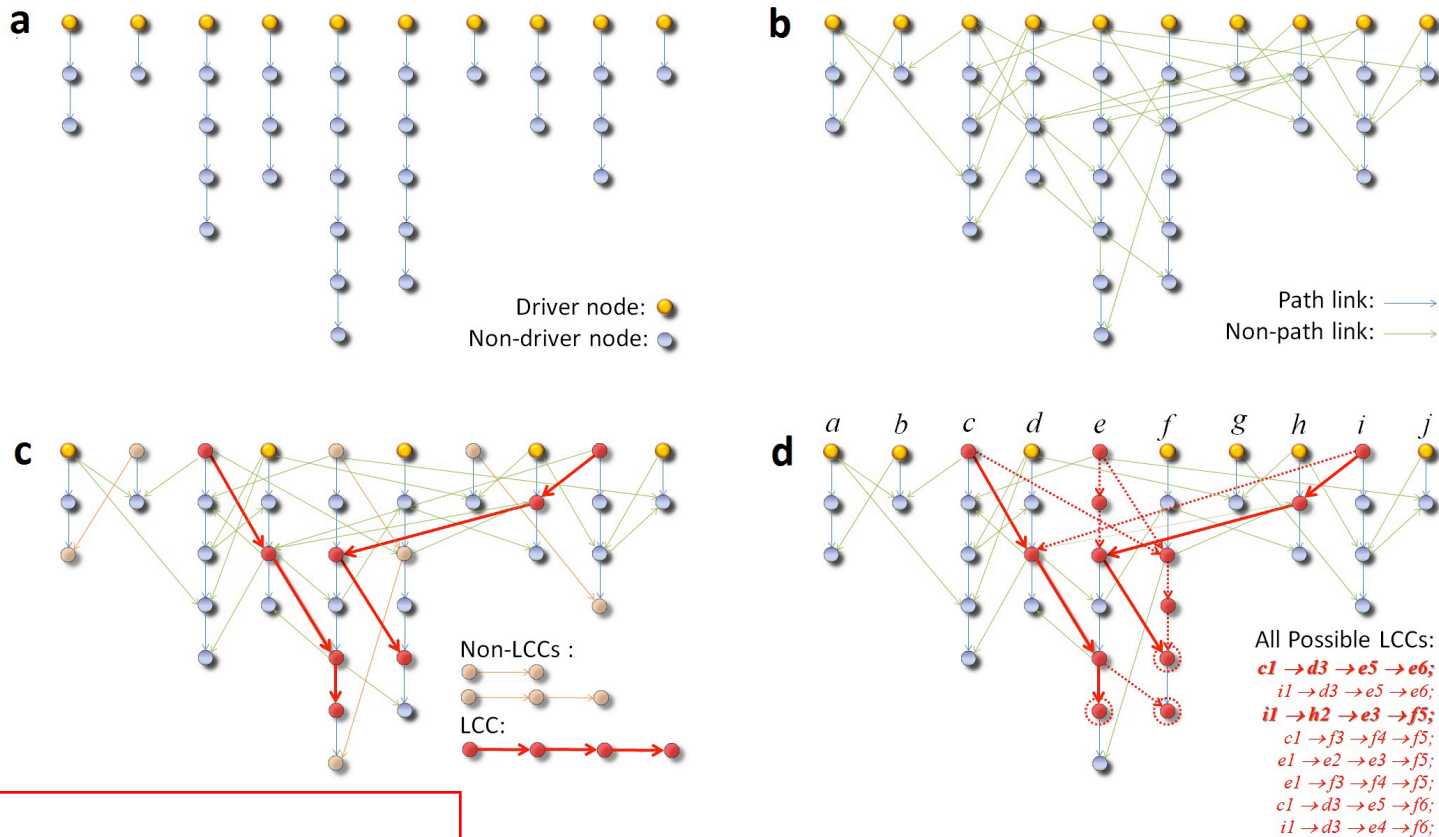
Green edges – maximum matching

Green nodes – matched nodes

Gray nodes – unmatched nodes – control nodes

Red edges – added edges to realize perfect matching

# Elements for Power-Law Energy Scaling – Longest Control Chains (LCCs)



$$E \approx m \cdot E_L$$

$E_L$  - Energy required to control an LCC  
 $m$  - # of LCCs of identical length (degeneracy)

# Power-Law Energy Scaling - Theory

Control diameter  $D_C$  = length of LCC

Distribution of  $D_C$  :  $P(D_C) \propto e^{-b \cdot D_C}$

Exponential dependence of  $E_L$  on  $D_C$

$$E_L \propto e^{\beta \cdot D_C}$$

$$\Rightarrow P(E_L) \propto E_L^{-(1+b/\beta)}$$

$E \approx m \cdot E_L \Rightarrow$  Cumulative distribution of  $E$

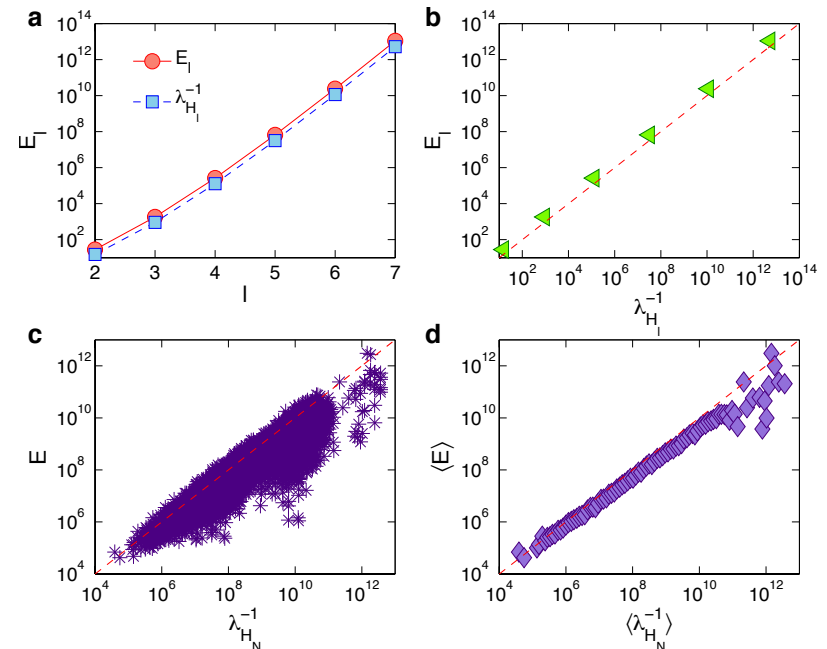
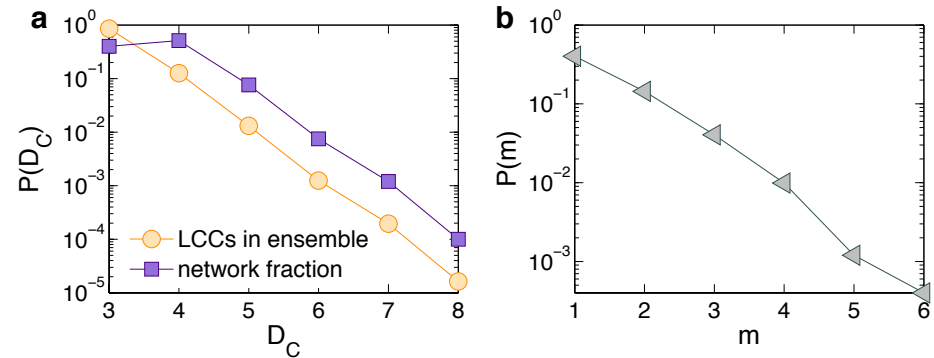
$$F(E) = P(m \cdot E_L < E) =$$

$$\int_0^{\infty} \left[ \int_0^{E/E_L} P(E_L, m) \cdot dm \right] dE_L$$

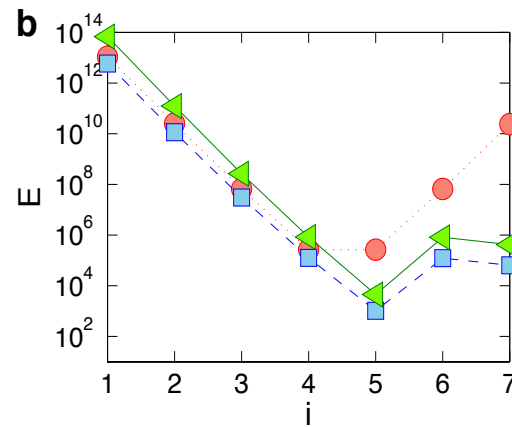
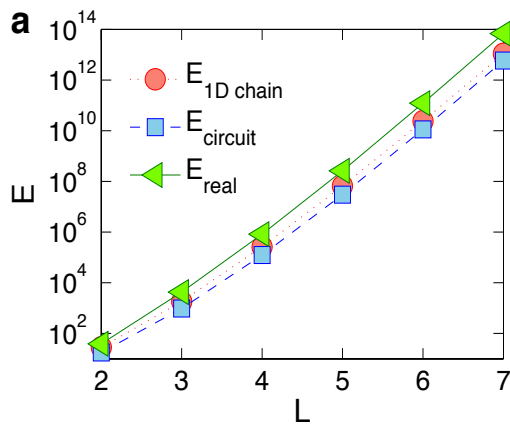
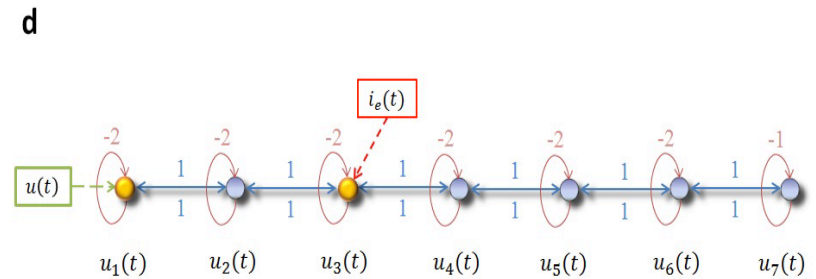
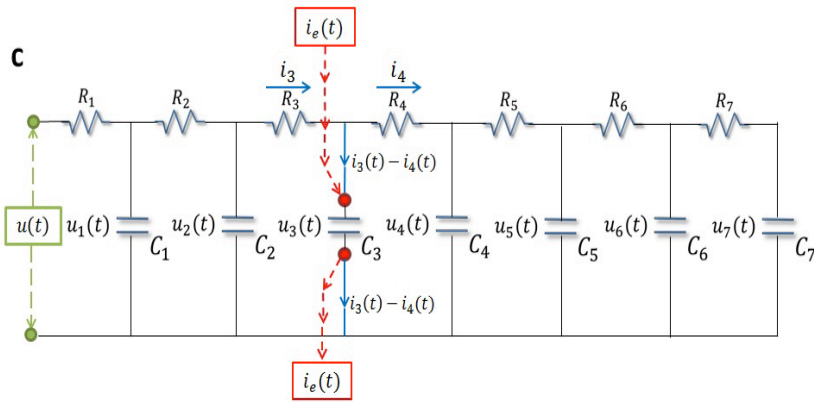
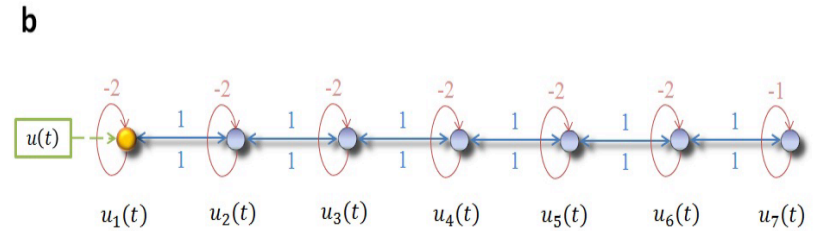
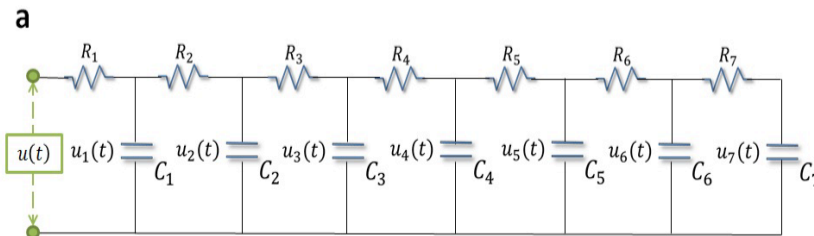
$$\approx \int_0^{\infty} P(E_L) \left[ \int_0^{E/E_L} P(m) dm \right] dE_L$$

$$P(m) \propto e^{-gm}$$

$$\text{Finally } P(E) = \frac{dF(E)}{dE} \propto E^{-(1+b/\beta)}$$



# Energy Reduction in a Linear Circuit Network



Y.-Z. Chen, L.-Z. Wang, W.-X. Wang, and Y.-C. Lai, "Energy scaling and reduction in controlling complex networks," *Royal Society Open Science* **3**, 160064 (2016).

# Nonlinear Dynamical Systems 101

Nonlinear dynamical system:

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}),$$

where  $\mathbf{f}(\mathbf{x})$  is a nonlinear vector function of  $\mathbf{x}$  which cannot be written in the form  $\mathbf{A} \cdot \mathbf{x}$ .

Example from mechanics: particle motion in a 1D potential field with the potential function

$$V(x) = \frac{x^2}{2} - \frac{x^4}{4}$$

Local minima or maxima:

$$\frac{dV}{dx} = x - x^3 = 0 \rightarrow x = 0, \pm 1$$

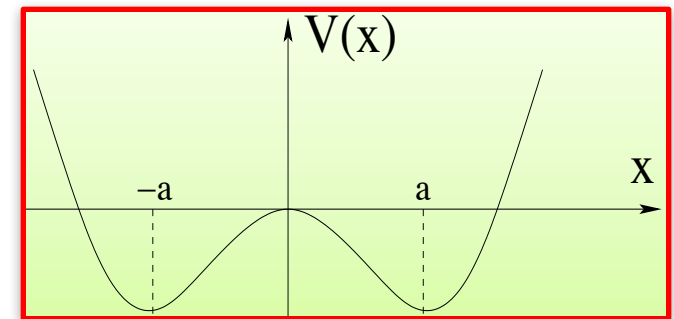
Newton's equation of motion (assuming unit mass)

$$\frac{dv}{dt} = -\alpha v - \frac{dV}{dx} = -\alpha v - x + x^3$$

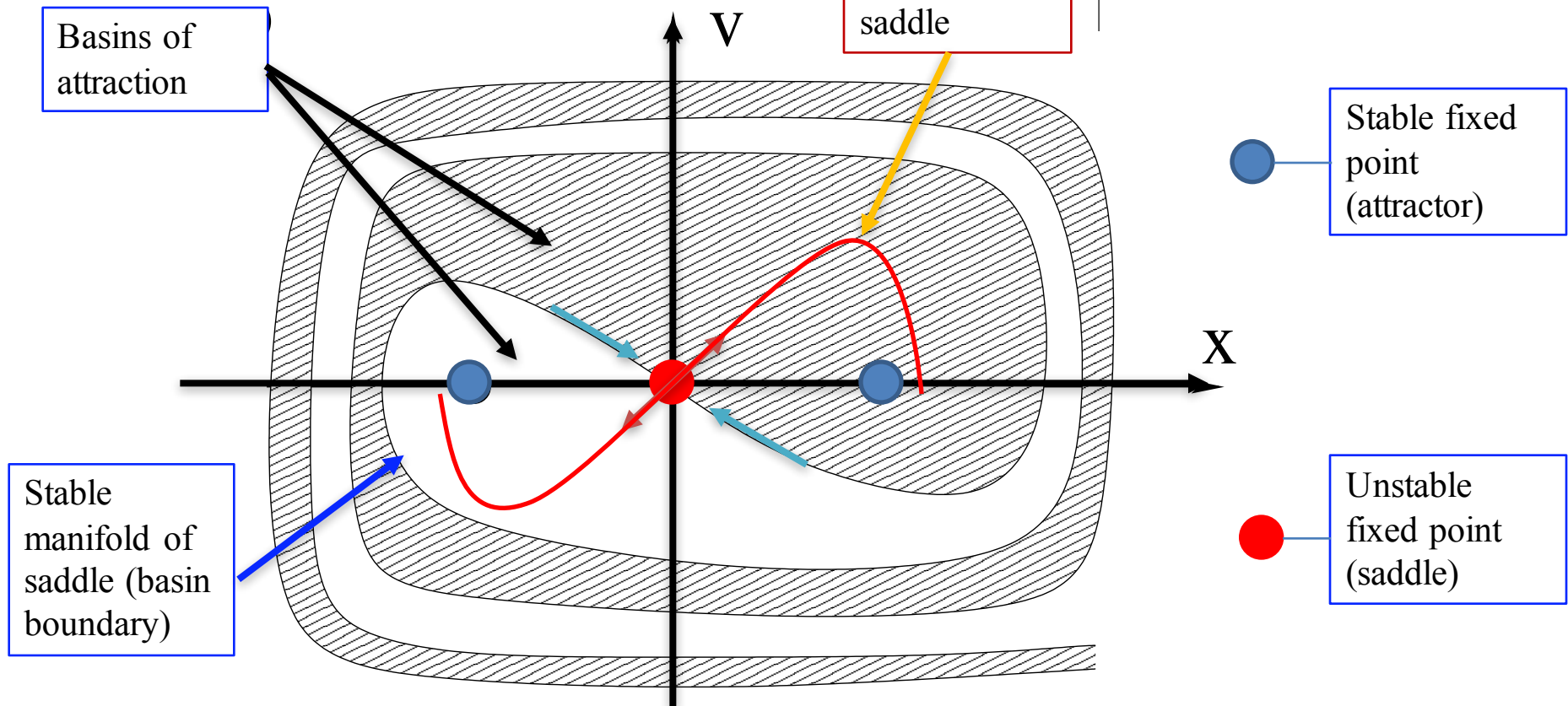
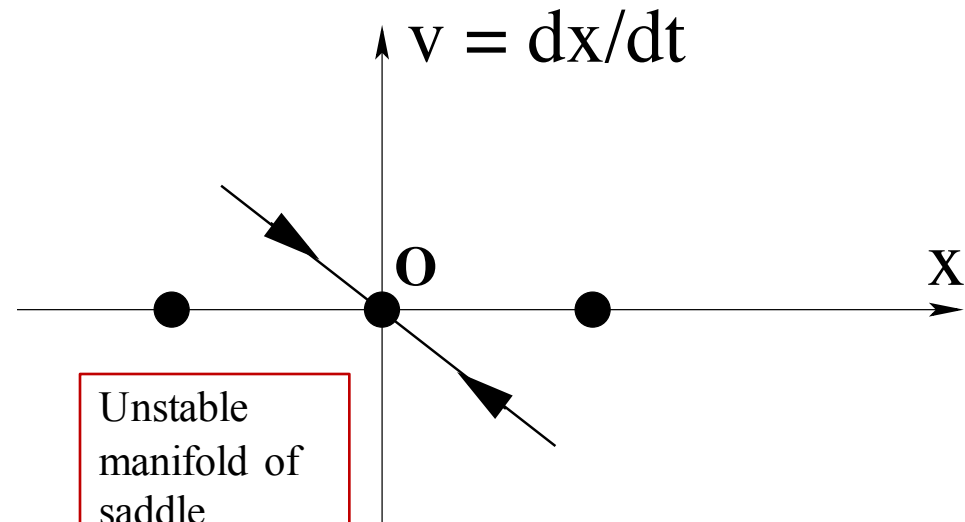
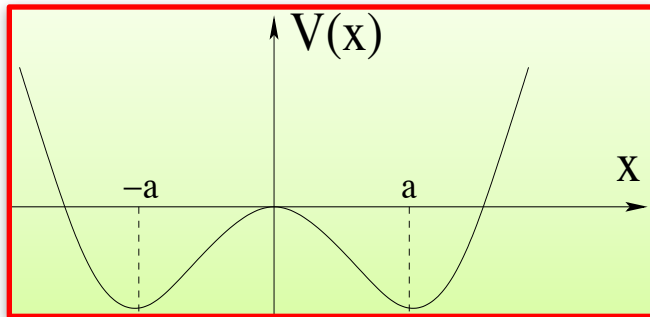
where  $\alpha > 0$  is the friction coefficient.

Letting  $x_1(t) \equiv x(t)$  and  $x_2(t) \equiv v(t)$ , one has

$$\begin{aligned} \frac{dx_1}{dt} &= x_2 \\ \frac{dx_2}{dt} &= -\alpha x_2 - x_1 + x_1^3 \end{aligned}$$







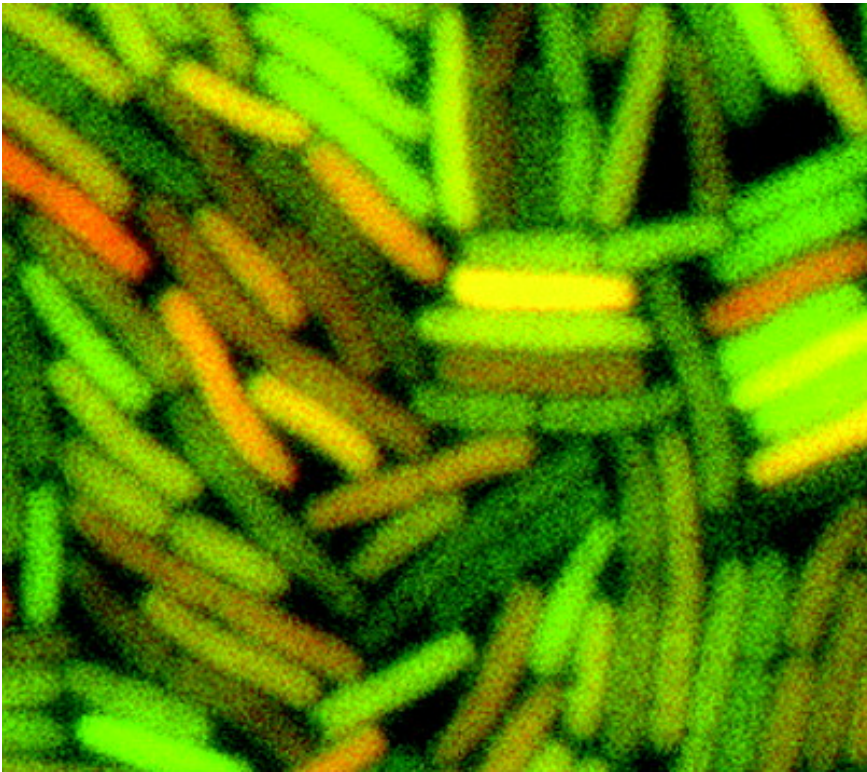
# Synthetic Biology



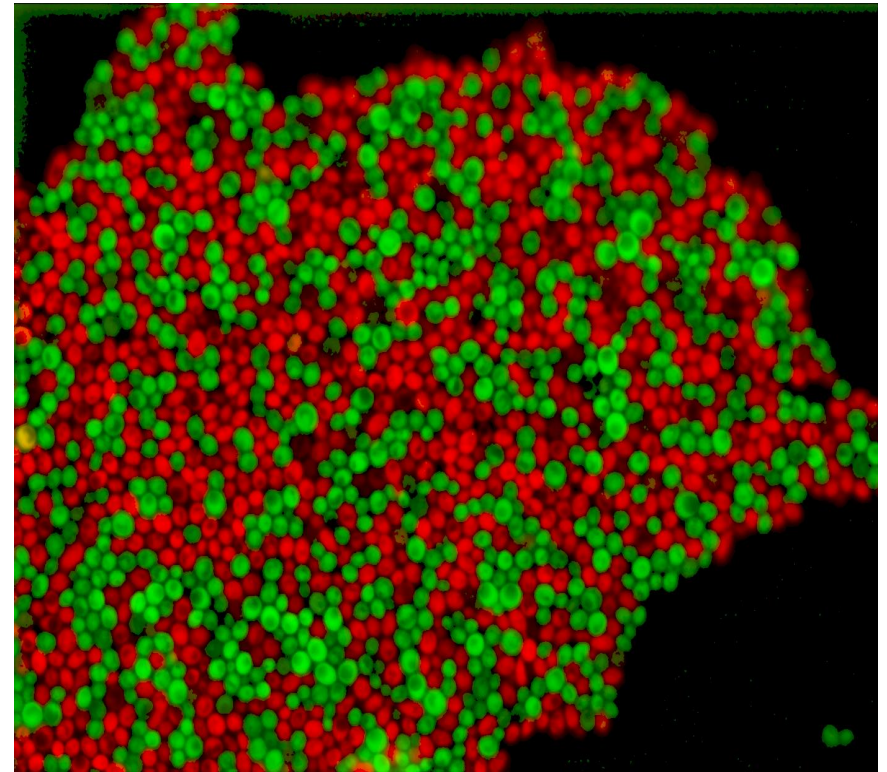
- **Synthetic Biology** applies engineering principles to build controllable and predictable cellular networks and behaviors
- **Biotech applications:** bio-energy, vaccines, petrochemical substitutes, etc.

# Cell Fates

Cell-cell variability studied using synthetic gene networks



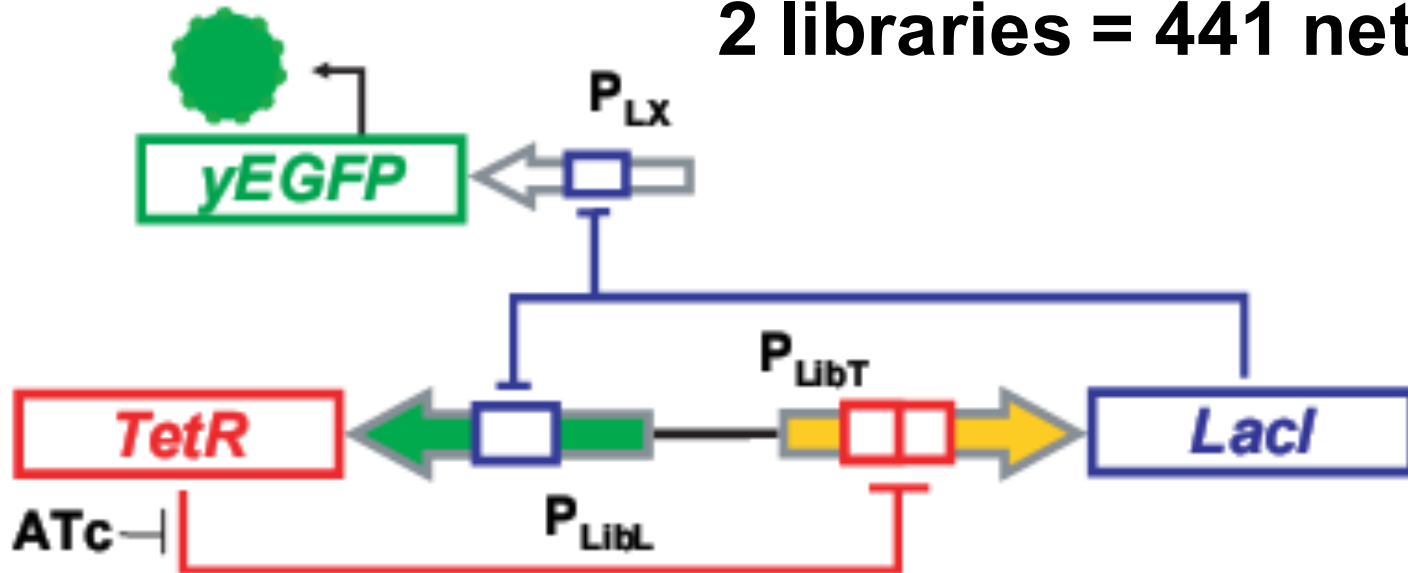
Elowitz *et al*, 2002



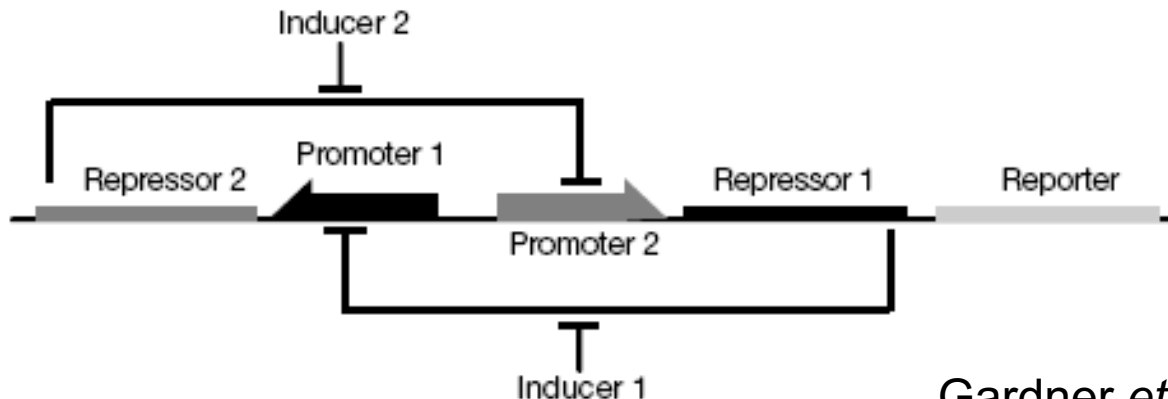
Wu *et al*, 2013

# Yeast Toggle Switch

2 libraries = 441 networks



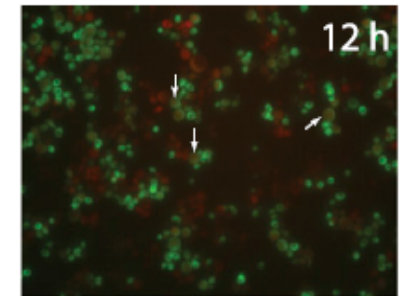
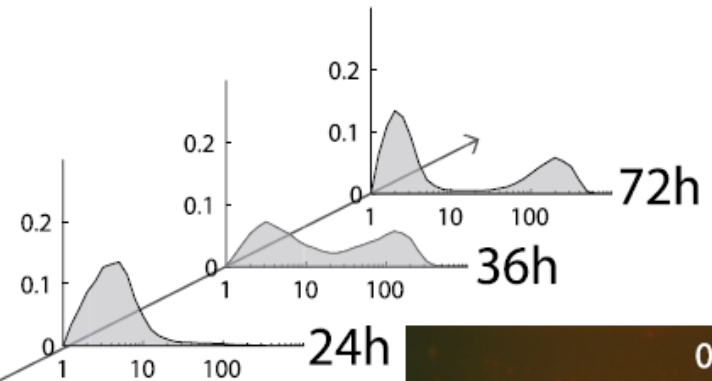
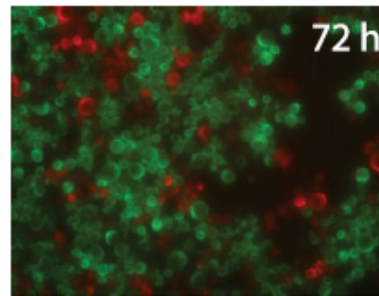
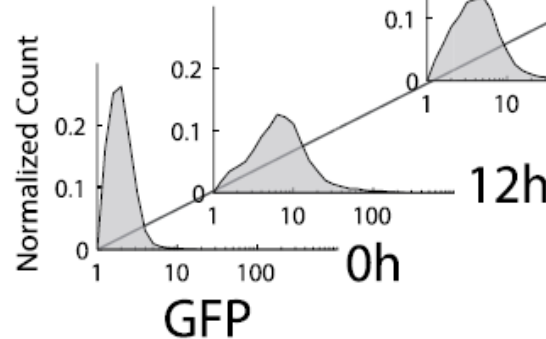
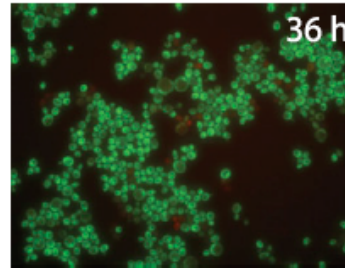
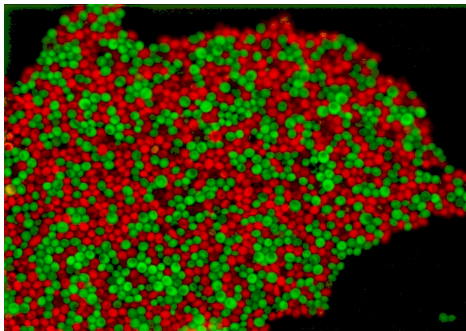
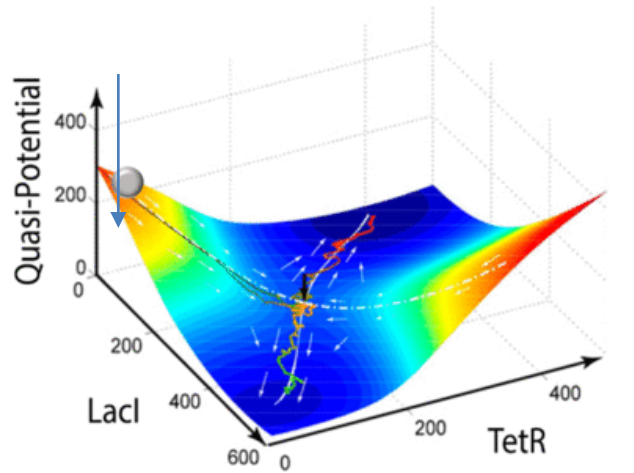
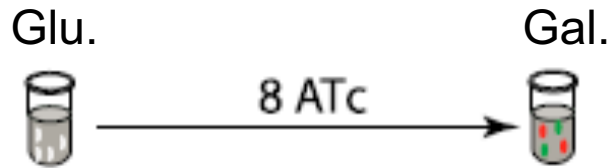
Ellis & Wang *et al*,  
Nature Biotech, 2009



Gardner *et al*, Nature, 2000



# Experimental Result: Multistability



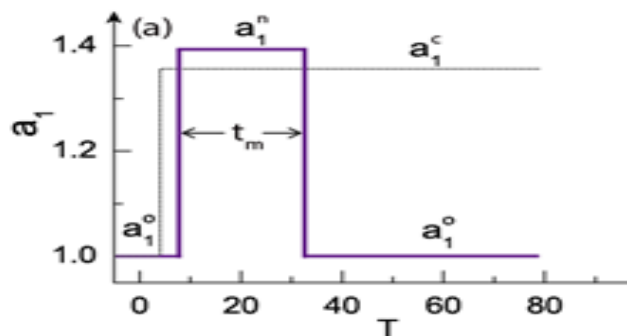
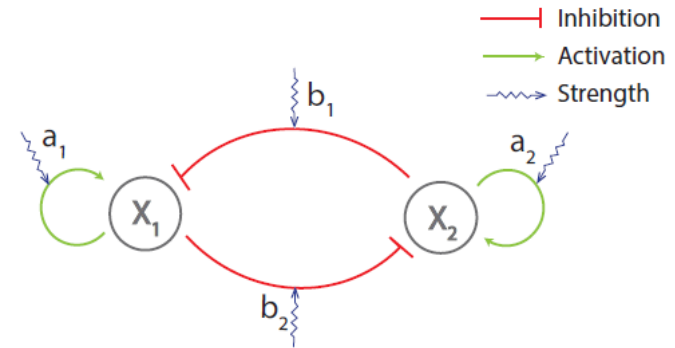
- M. Wu, R.-Q. Su, X.-H. Li, T. Ellis, Y.-C. Lai, and X. Wang, "Engineering of regulated stochastic cell fate determination," *PNAS* **110**, 10610-10615 (2013).
- F.-Q. Wu, R.-Q. Su, Y.-C. Lai, and X. Wang, "Engineering of a synthetic quadrastable gene network to approach Waddington landscape and cell fate determination," *eLIFE* **6**, e23701 (2017).

# Gene Regulatory Networks

- Directed connections between nodes:
  - Inhibition or excitation
- Coupling strengths can be adjusted by, e.g., application of drugs
- Only stable steady states can be observed.

How to drive the system from an initial attractor *to a desirable attractor* by changing some *experimentally accessible parameters* ?

Applying temporal perturbations to parameters  $a_1$ ,  $a_2$ ,  $b_1$  or  $b_2$



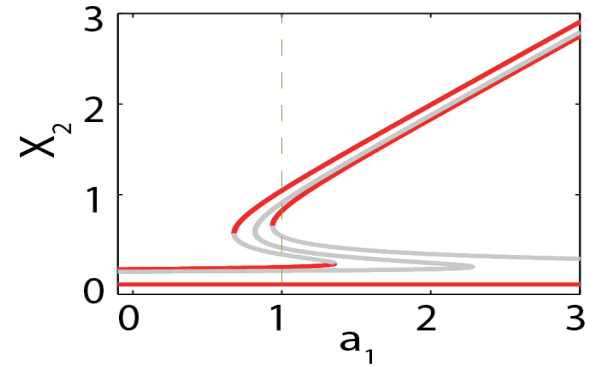
$$\begin{aligned} \dot{x}_1 &= a_1 \cdot \frac{x_1^n}{s^n + x_1^n} + b_1 \cdot \frac{s^n}{s^n + x_2^n} - k \cdot x_1 \\ \dot{x}_2 &= a_2 \cdot \frac{x_2^n}{s^n + x_2^n} + b_2 \cdot \frac{s^n}{s^n + x_1^n} - k \cdot x_2 \end{aligned}$$

# How Control is Done

$$\dot{x}_1 = a_1 \cdot \frac{x_1^n}{s^n + x_1^n} + b_1 \cdot \frac{s^n}{s^n + x_2^n} - k \cdot x_1$$

$$\dot{x}_2 = a_2 \cdot \frac{x_2^n}{s^n + x_2^n} + b_2 \cdot \frac{s^n}{s^n + x_1^n} - k \cdot x_2$$

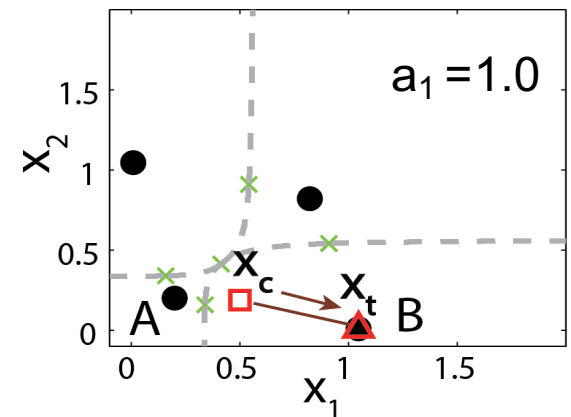
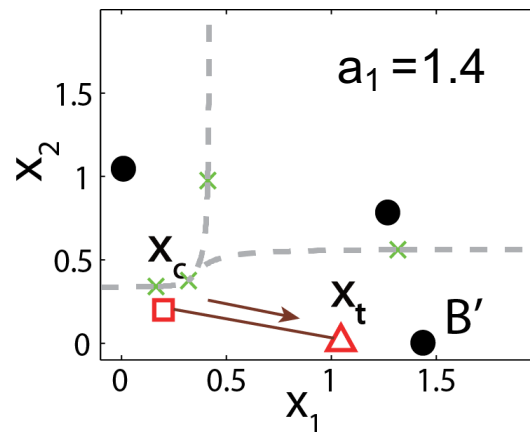
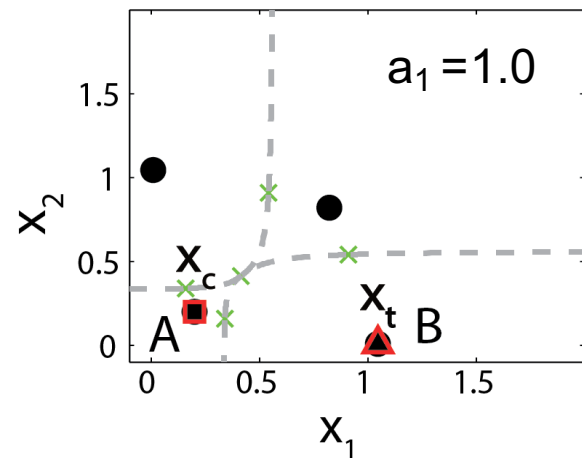
$$a_2=1; \quad b_1, b_2=0.2, \quad k=1.1, \quad s=0.5, \quad n=4$$



4 attractors

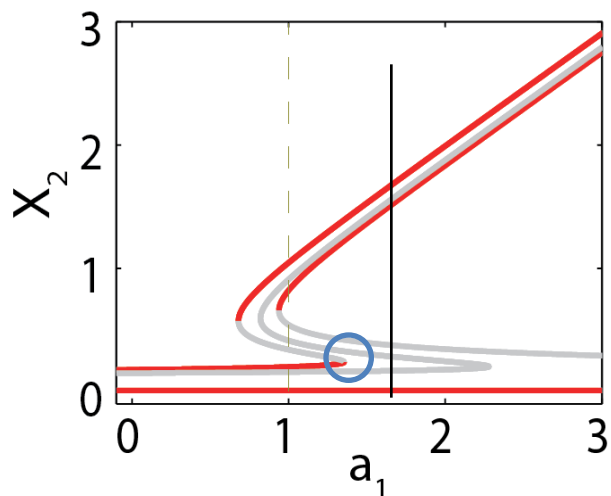
Basin of original attractor **A** is absorbed into that of attractor **B**

When system is in basin of attractor **B**, remove perturbation to  $a_1$



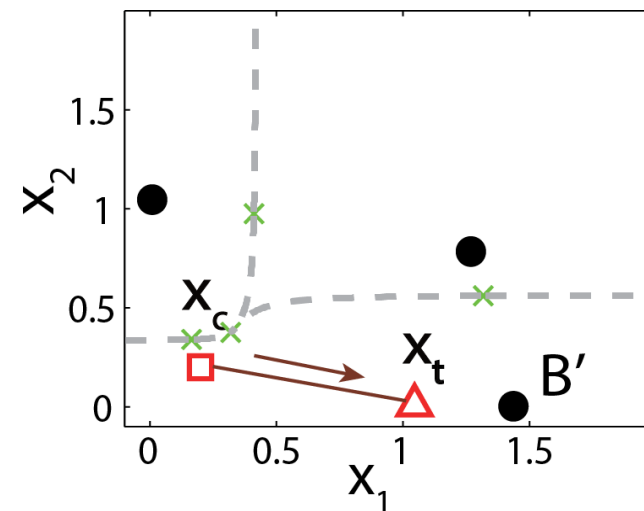
# Control Strength and Duration

How large is the required parameter perturbation?



Parameter  $a_1$  has to pass a critical point, say,  $a_1 > 1.36$

How long should the perturbation be maintained?

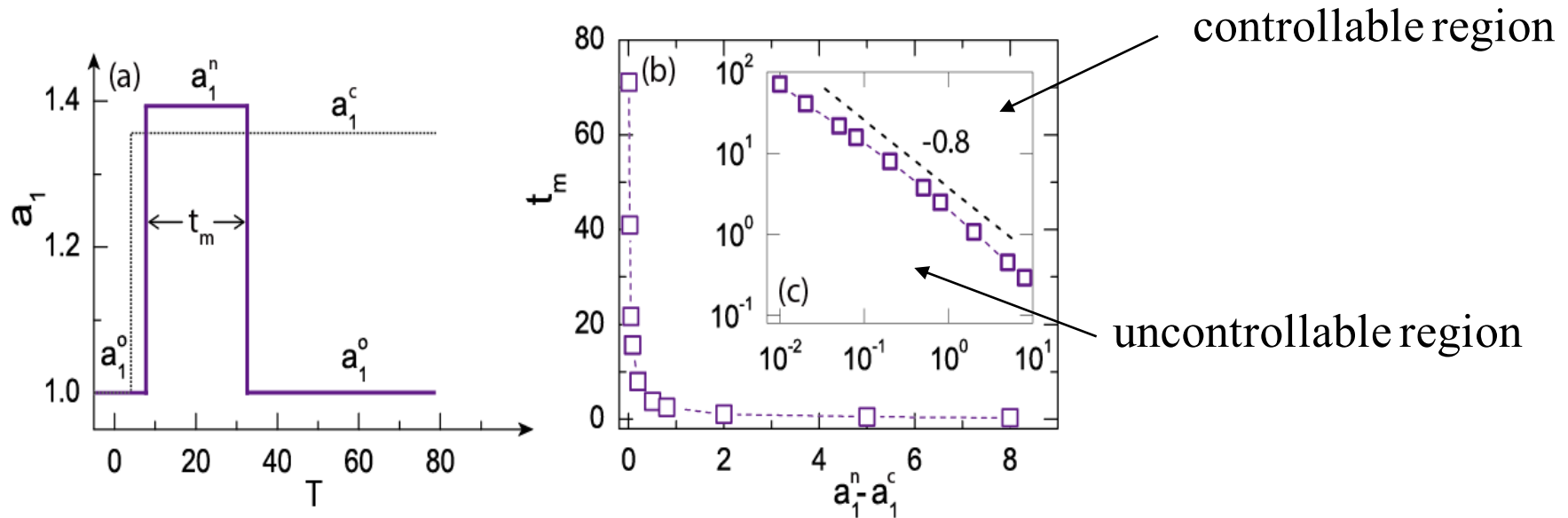


Perturbation has to stay “on” until  $x_t$  crosses basin boundary



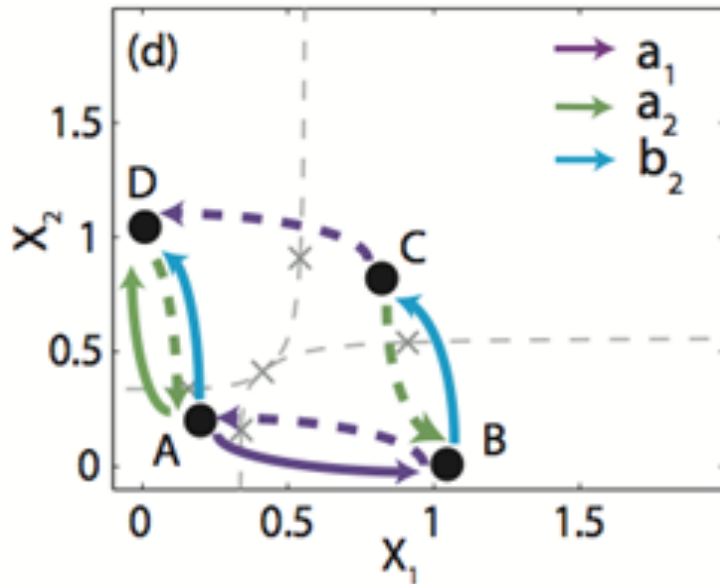
# Scaling between Control Strength and Duration

Minimal control duration  $t_m$  versus perturbation to  $a_1$



Insofar as the combination of  $[a_1, t_m]$  is in the controllable region, the system can be driven to the desirable attractor

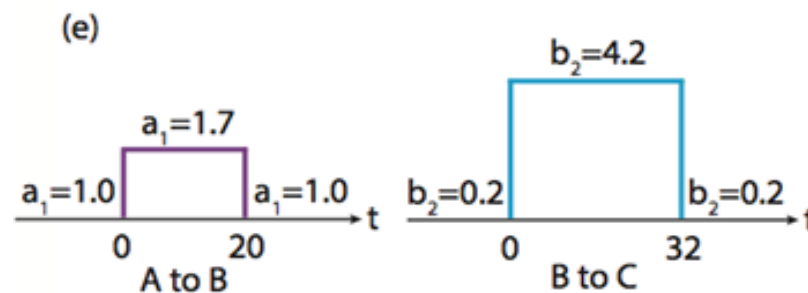
# Attractor Network



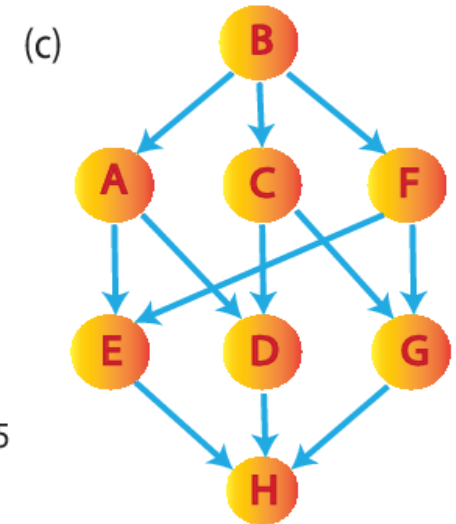
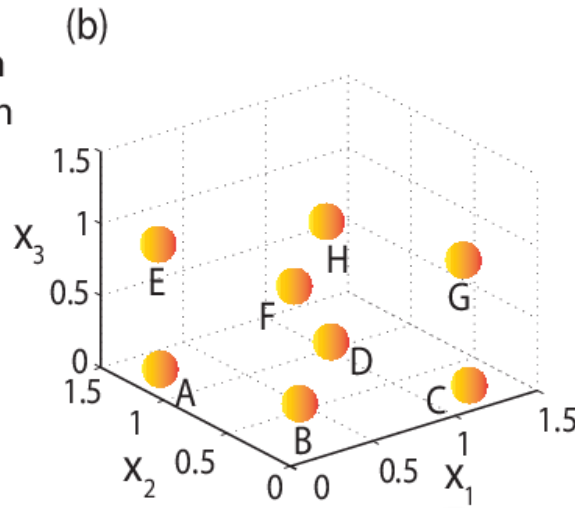
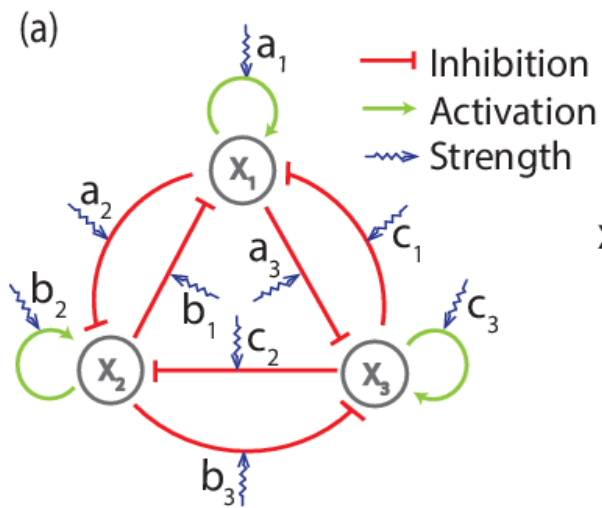
Each node in the attractor network represents one attractor. If perturbation of any accessible parameter can drive the system from attractor **A** to attractor **B**, we say there is a directed link from **A** to **B**.

Y.-C. Lai, "Controlling complex, nonlinear dynamical networks," *Nat. Sci. Rev.* **1**, 339-341 (2014).

If the attractor network is strongly connected, we can drive the system from any undesirable attractor to a desirable one, e.g., from A to C:



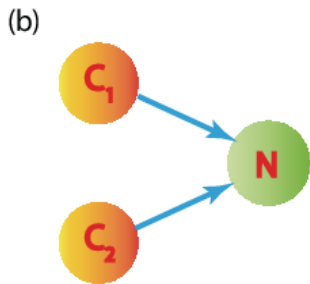
# A Three-Gene Network



$$\begin{aligned} \dot{x}_1 &= a_1 \cdot \frac{x_1^n}{s^n + x_1^n} + b_1 \cdot \frac{s^n}{s^n + x_2^n} + c_1 \cdot \frac{s^n}{s^n + x_3^n} - k \cdot x_1 \\ \dot{x}_2 &= a_2 \cdot \frac{s^n}{s^n + x_1^n} + b_2 \cdot \frac{x_2^n}{s^n + x_2^n} + c_2 \cdot \frac{s^n}{s^n + x_3^n} - k \cdot x_2 \\ \dot{x}_3 &= a_3 \cdot \frac{s^n}{s^n + x_1^n} + b_3 \cdot \frac{s^n}{s^n + x_2^n} + c_3 \cdot \frac{x_3^n}{s^n + x_3^n} - k \cdot x_3 \end{aligned}$$

Eight attractors

Attractor network

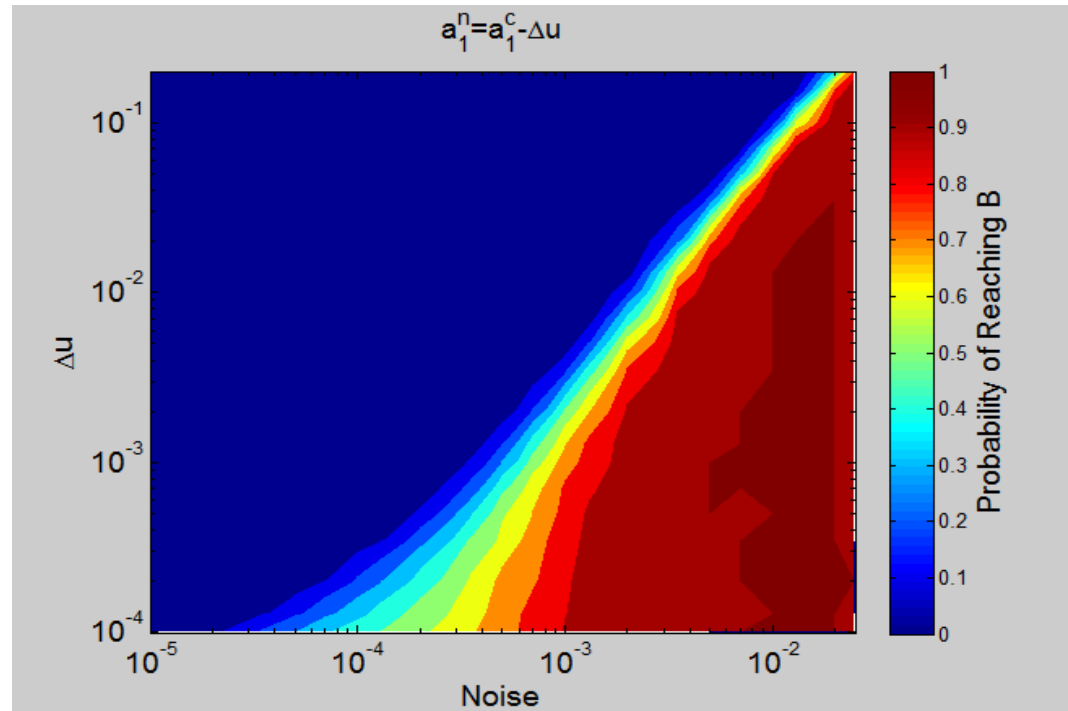


- R. Zhang, M. V. Shah, J. Yang, S. B. Nyland, X. Liu, J. K. Yun, and T. P. Loughran. Network model of survival signaling in large granular lymphocyte leukemia. *PNAS*, **105**:16308–16313, 2008.
- A. Saadatpour, R.-S. Wang, A. Liao, X. Liu, T. P. Loughran, I. Albert, and R. Albert. Dynamical and structural analysis of a t cell survival network identifies novel candidate therapeutic targets for large granular lymphocyte leukemia. *PloS Comp. Biol.*, **7**:e1002267, 2011.

# Controllability of Nonlinear Networks

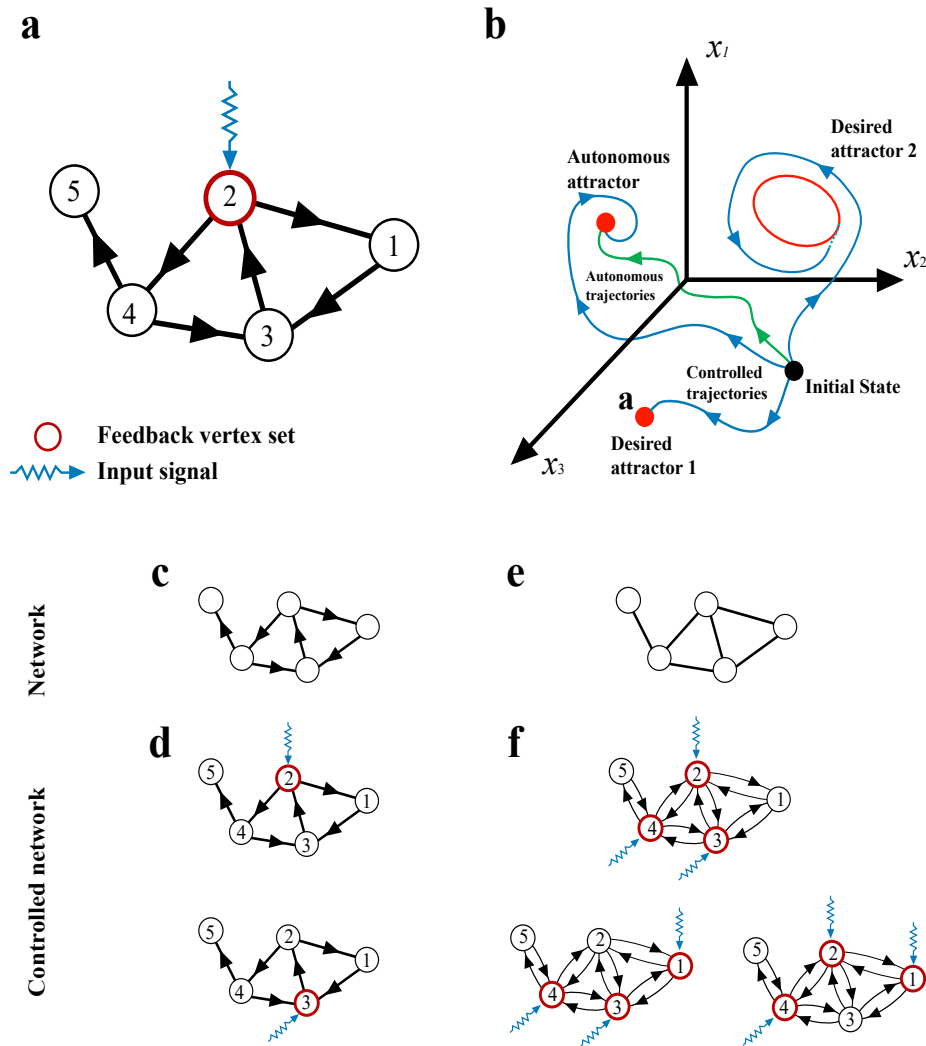
- Controllability of a nonlinear networks can be determined by the properties of its attractor network: The stronger the attractor network is connected, the more controllable the original network

- Noise-enhanced controllability



L.-Z. Wang, R.-Q. Su, Z.-G. Huang, X. Wang, W.-X. Wang, C. Grebogi, and Y.-C. Lai, "A geometrical approach to control and controllability of complex nonlinear dynamical networks," *Nat. Commun.* **7**, 11323 (2016).

# FVS Based Control (Ongoing)



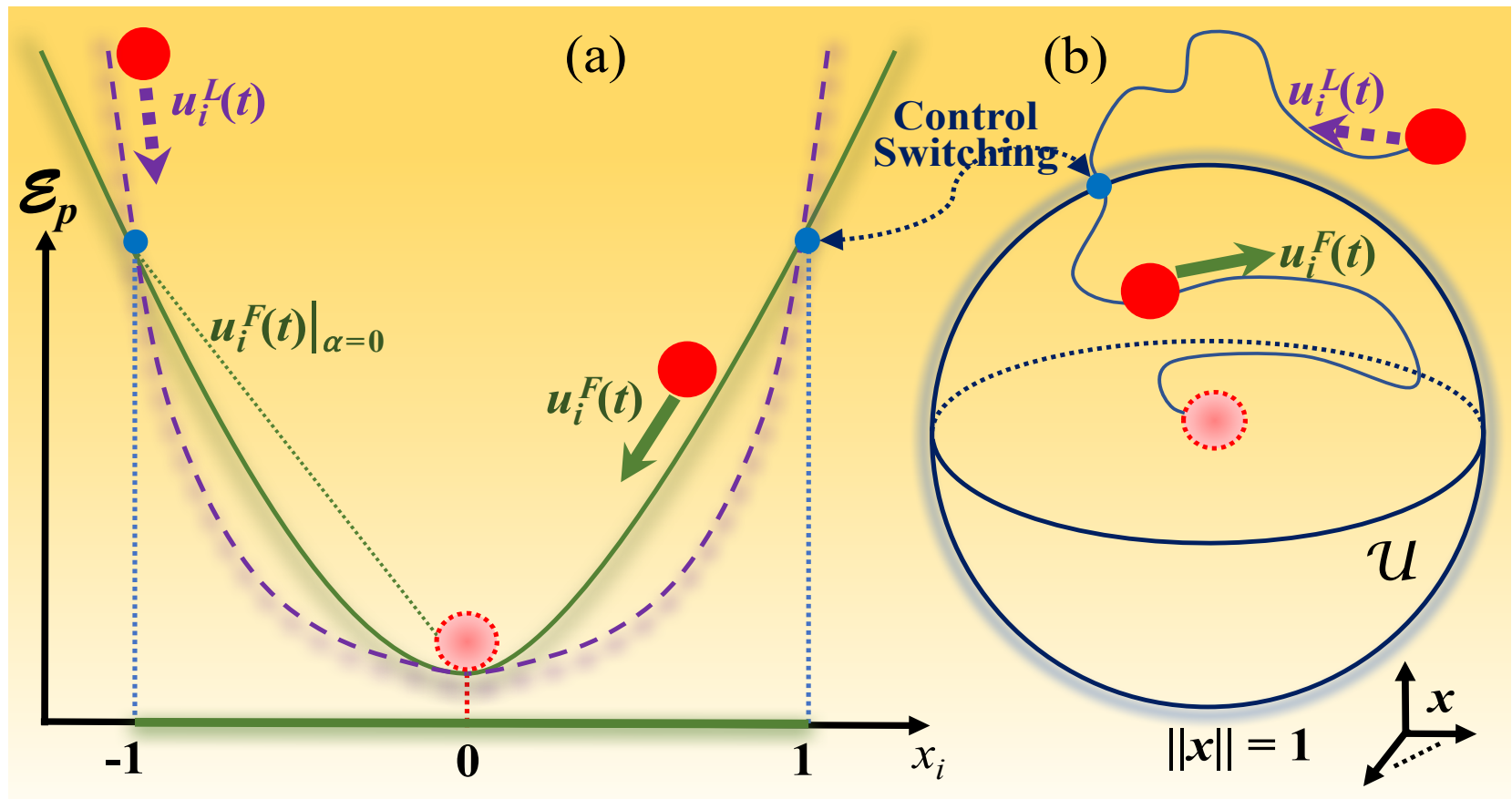
FVS (Feedback Vertex Set):

- A. Mochizuki et al., 2013
- H.-J. Zhou, 2013

Joint work with Beijing Normal colleagues:

Z.-S. Shen, W.-X. Wang, H.-J. Zhou, Z.-Y. Gao, A. Mochizuki, and Y.-C. Lai, “Control paradigm for nonlinear dynamical networks,” preprint (2017).

# Closed-Loop Control of Complex Nonlinear Dynamical Networks



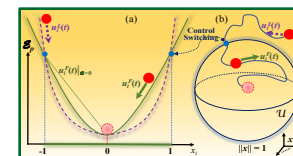
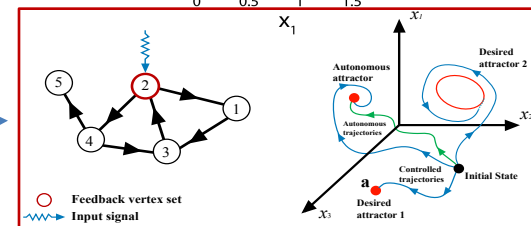
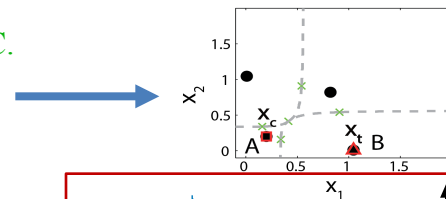
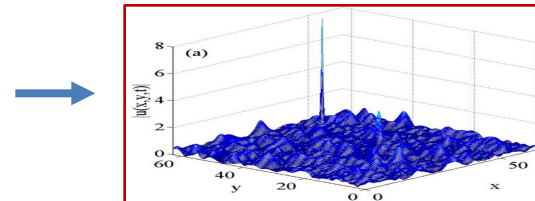
Joint work with Fudan colleagues:

Y.-Z. Sun, S.-Y. Leng, Y.-C. Lai, C. Grebogi, and W. Lin, *Phys. Rev. Lett.* **119**, 198301 (2017)

# Take Home Message: Controlling Nonlinear Networks - DIVERSITY

1. Lack of a general mathematical control/controlability framework
2. Extremely **diverse** nonlinear dynamical behaviors require a diverse array of control methodologies:

- Controlling collective dynamics, e.g., Y.-Z. Chen, Z.-G. Huang, and Y.-C. Lai, "Controlling extreme events on complex networks," *SREP* **4**, 6121 (2014)
- Controlling destinations (attractors), e.g., L.-Z. Wang, R.-Q. Su, Z.-G. Huang, X. Wang, W.-X. Wang, C. Grebogi, and Y.-C. Lai, "A geometrical approach to control and controllability of complex nonlinear dynamical networks," *Nat. Commun.* **7**, 11323 (2016).
- Control principle based on feedback vertex set – ongoing work
- Closed-loop control, Y.-Z. Sun, S.-Y. Leng, Y.-C. Lai, C. Grebogi, and W. Lin, *Phys. Reve. Lett.* **119**, 198301 (2017)



- Predicting and controlling tipping point in complex mutualistic networks
1. J.-J. Jiang, Z.-G. Huang, T. P. Seager, W. Lin, C. Grebogi, A. Hastings and Y.-C. Lai, *PNAS (Plus)*, published online on 1/8/2018.
  2. J.-J. Jiang, A. Hastings, and Y.-C. Lai, "Controlling tipping point in complex systems," preprint (2017)

