

EVOLUTIONARY GAME THEORY AND EVO-DEVO DYNAMICS  
VON NEUMANN, LIFE  
AND EVOLUTION

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# John von Neumann是何许人也

- 电子计算机之父

EDVAC (1945) , 冯·诺依曼结构 (二进制、内存)

- 博弈论之父

与Oskar Morgenstern合著《博弈论和经济行为》 (1944)

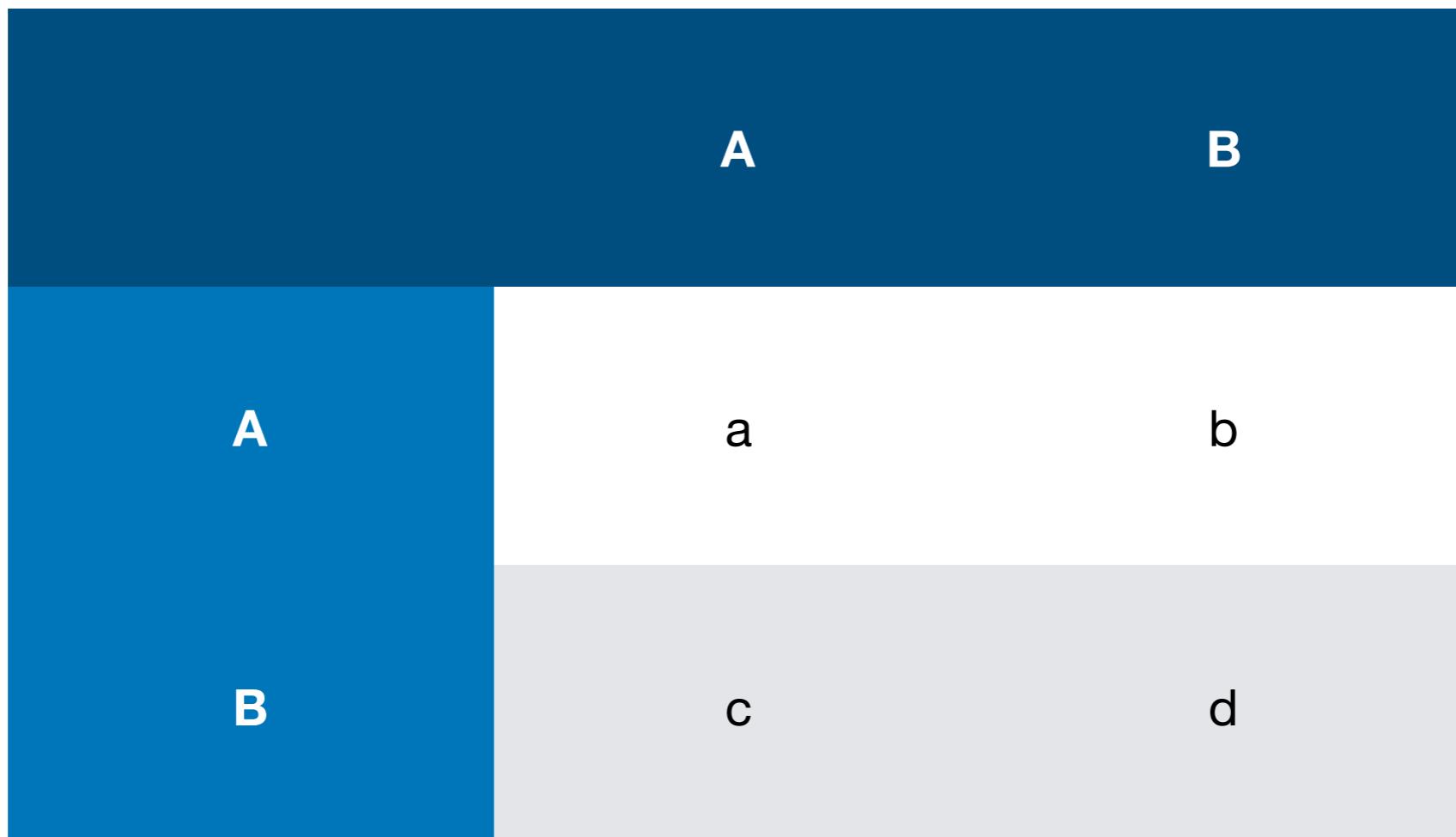
- 对基础数学、应用数学、量子力学以及曼哈顿计划等都作出大量杰出的贡献。

- 晚年研究自动机 (Automata) , 即能够进行自我复制的机器, 提出了“转录”和“翻译”的概念; 闲暇时曾用计算机对进化进行数值模拟。



(1903~1957)

# Game Theory



# Example1：夫妻打扫卫生



妻子的收益

	她打扫	她不打扫	总分
他打扫	10	4	14
他不打扫	2	0	2
总分	12	4	16

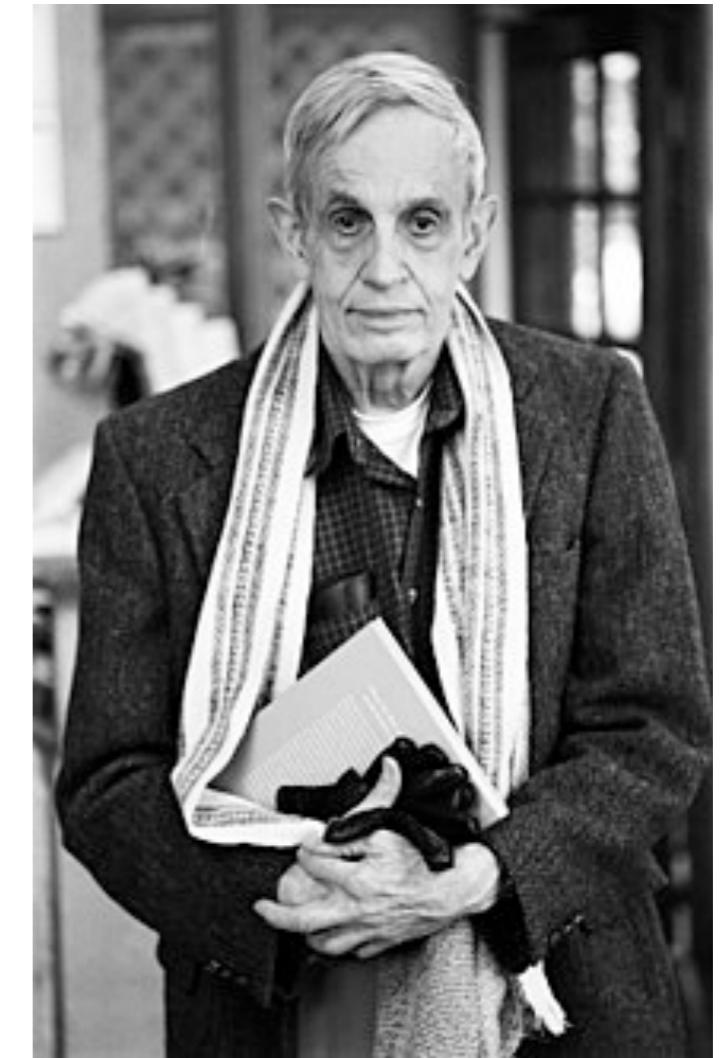
丈夫的收益

	她打扫	她不打扫	总分
他打扫	8	2	10
他不打扫	7	2	9
总分	15	4	19

# Nash Equilibrium

		A	B
A	A	a	b
	B	c	d

如果  $a > c$ , 那么 A 策略是纳什均衡;  
如果  $d > b$ , 那么 B 策略是纳什均衡。



John Forbes Nash Jr.  
(1928 – 2015)

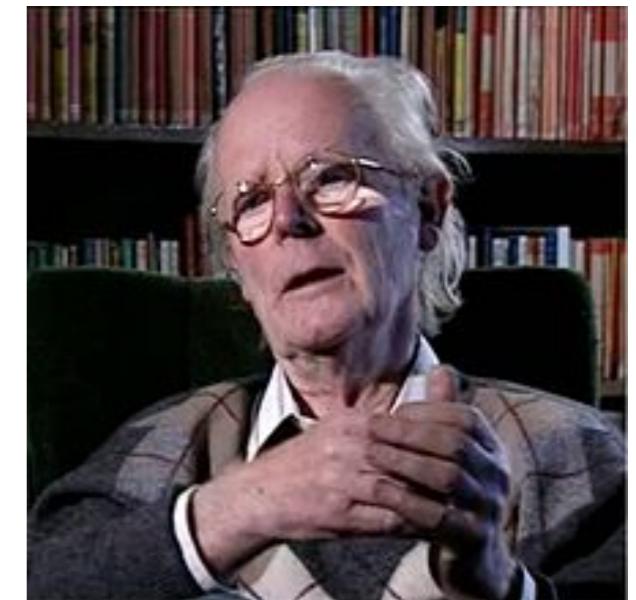
# Example2: 鹰鸽博弈 (斗争策略)

**win:  $b$  = benefit**

**lose:  $c$  = cost**

$b < c$

	鹰 	鸽 
鹰 	$(b-c)/2$	$b$
鸽 	0	$b/2$



J. Maynard Smith

(1920 - 2004)

ESS(进化稳定策略)

# Example3：求偶策略的博弈

		追求者的收益		被追求者的收益		
		Coy	Fast	Coy	Fast	
Faithful	Coy	15-10-3=2	15-10=5	Faithful	15-20-3=2	15-10=5
	Philander	0	15	Philander	0	15-20=-5

# prisoner's dilemma

	沉默 (合作)	认罪 (背叛)
沉默 (合作)	-1	-10
认罪 (背叛)	0	-7

# Five Rules for Cooperations:

## 1. Direct reciprocity(直接互惠)



Robert Trivers  
(1943~)

ALLD vs GRIM

		合作	背叛
合作	R	S	$T > R > P > S$ , 且 $R > (T+S)/2$
	T	P	
		GRIM	ALLD
GRIM	mR	$S + (m-1)P$	$mR > T + (m-1)P$
	$T + (m-1)P$	mP	

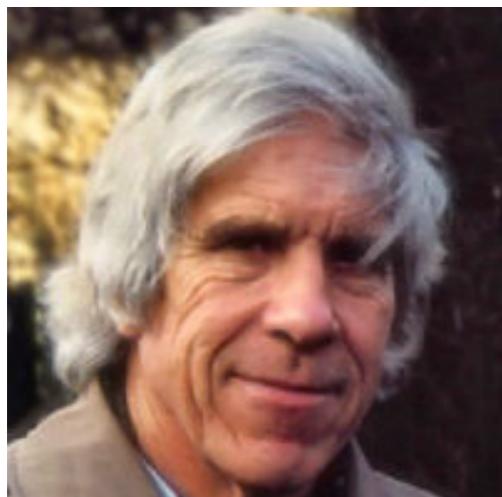
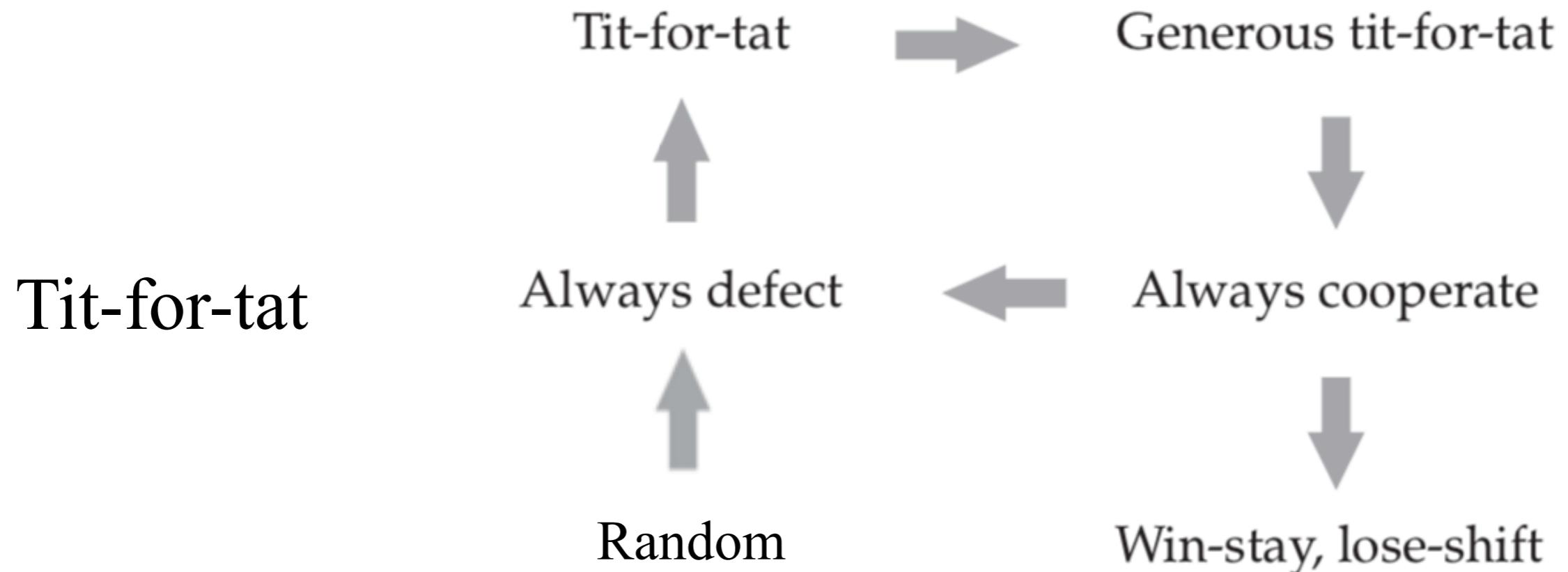
$m$ 代表博弈局数

$$mR > T + (m-1)P \longrightarrow m > (T-P)/(R-P) \longrightarrow w > c/b$$

w代表一局结束再来一局的概率  $m = 1/(1-w)$ , 令  $T = b$ 、  $R = b - c$ 、  $P = 0$  和  $S = -c$

# Five Rules for Cooperations:

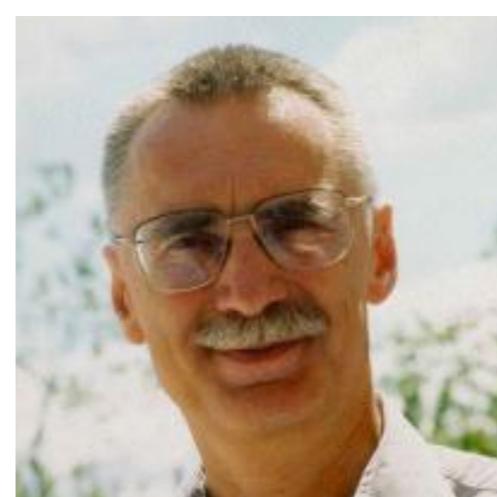
## 1. Direct reciprocity(直接互惠)



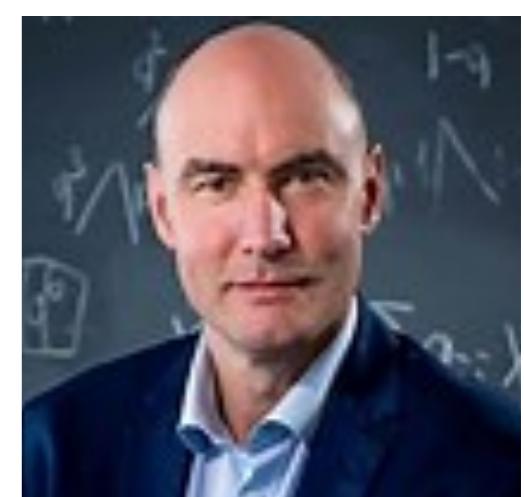
W. D. Hamilton



Robert Axelrod



Karl Sigmund



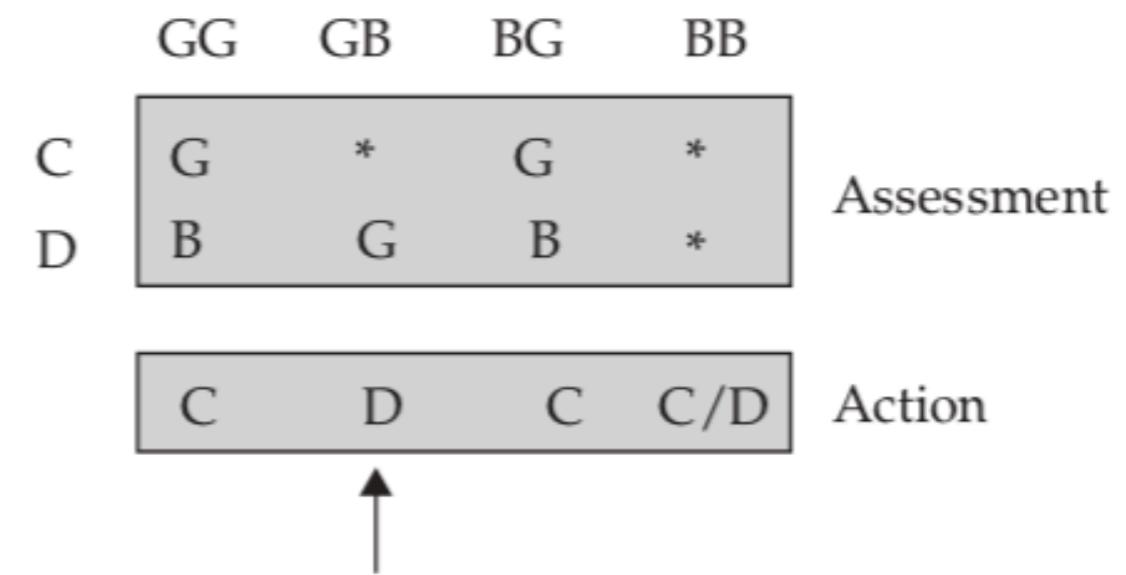
Martin Nowak

# Five Rules for Cooperations:

## 2. Indirect reciprocity(间接互惠)

Reputation of donor and recipient

	GG	GB	BG	BB	
C	G	G	G	G	Scoring
D	B	B	B	B	
	G	G	G	G	Standing
C	B	G	B	B	
	G	B	G	B	Judging
C	B	G	B	B	
	G	B	G	B	Shunning
D	B	B	B	B	
Reputation of donor after the action					



If a good donor meets a bad recipient, the donor must defect, and this action does not reduce his reputation.

\* can be set as G or B.

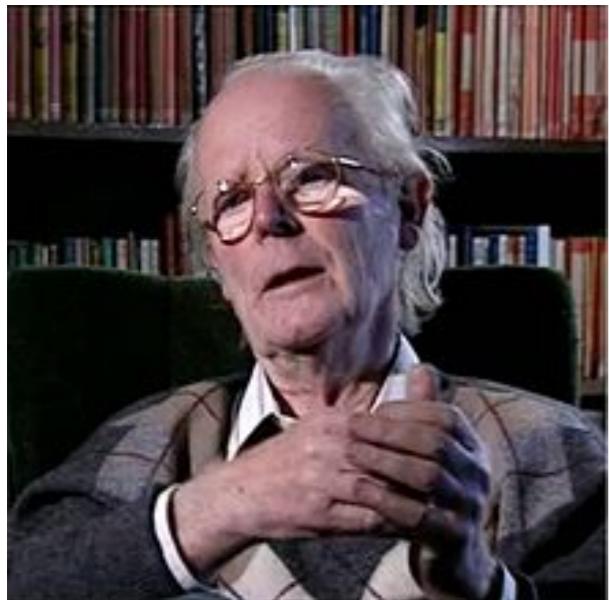
If a column in the assessment module is then the action must be C, otherwise D.

G  
B

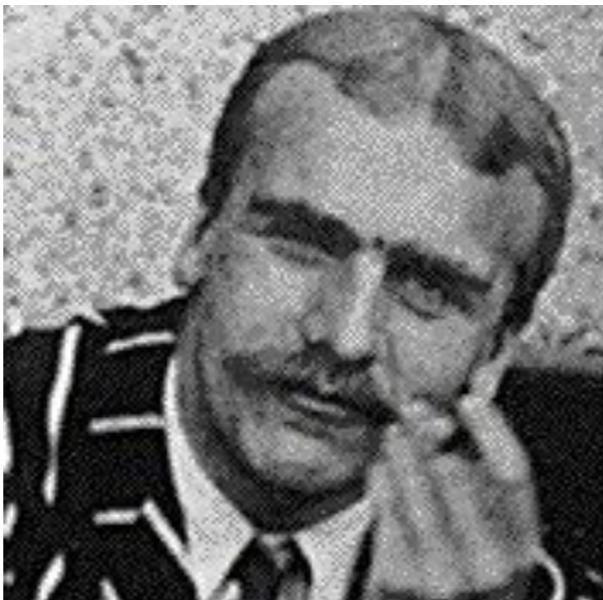
# Five Rules for Cooperations:

## 3. Kin Selection(亲缘选择)

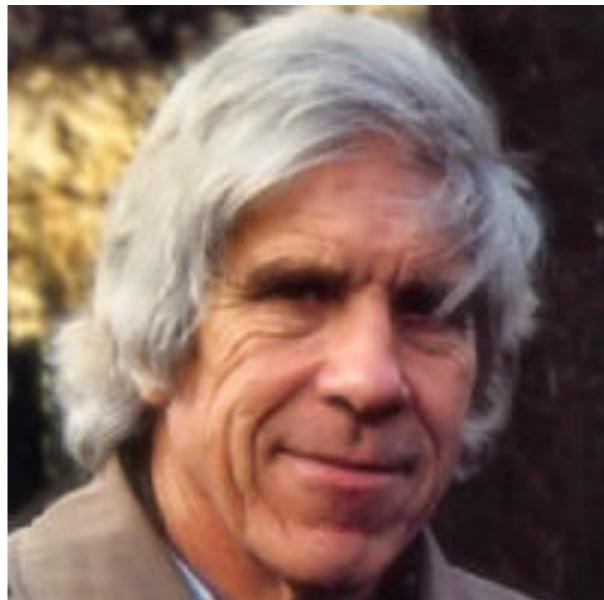
$$cost < r * benefit$$



J. Maynard Smith  
(1920 - 2004)



J. B. S. Haldane  
(1892 - 1964)



W. D. Hamilton  
(1936–2000)



George C. Williams  
(1926-2010)

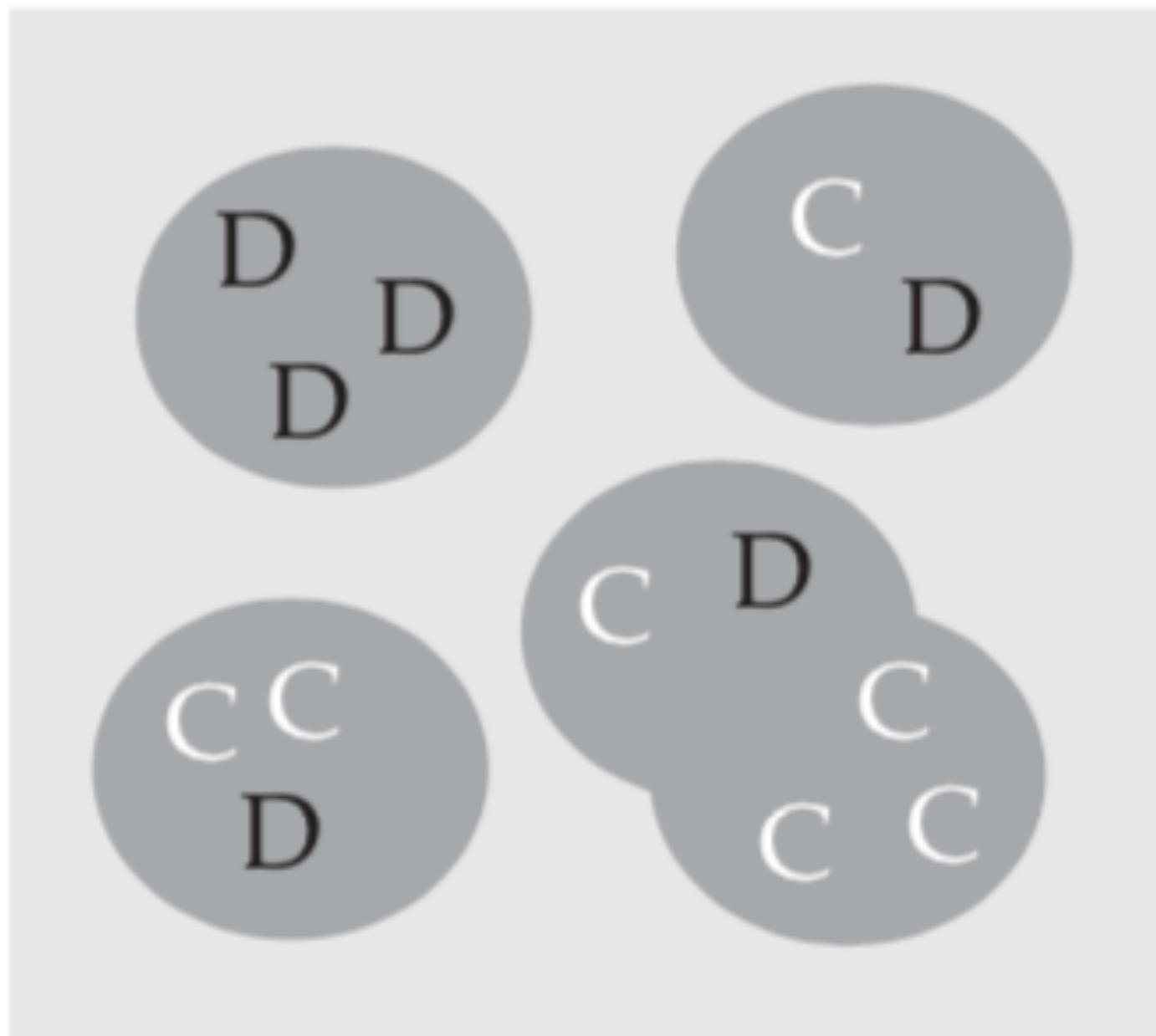
# Five Rules for Cooperations:

## 4. Group Selection



George C. Williams  
(1926-2010)

挑战



# Five Rules for Cooperations:

## 4. Group Selection

代	1+0.4	1	1.1+0.4	1.1	sum
0	$10*10*(10/200)=5$	$10-5=5$	$10*10*(190/200)=95$	$190-95=95$	200
1.0	7	5	142.5	104.5	259
1	$12*10*(12/259)=5.56$	$12-5.56=6.44$	$12*10*(247/259)=114.44$	$247-114.44=132.56$	259
2.0	7.784	6.44	171.66	145.816	331.7

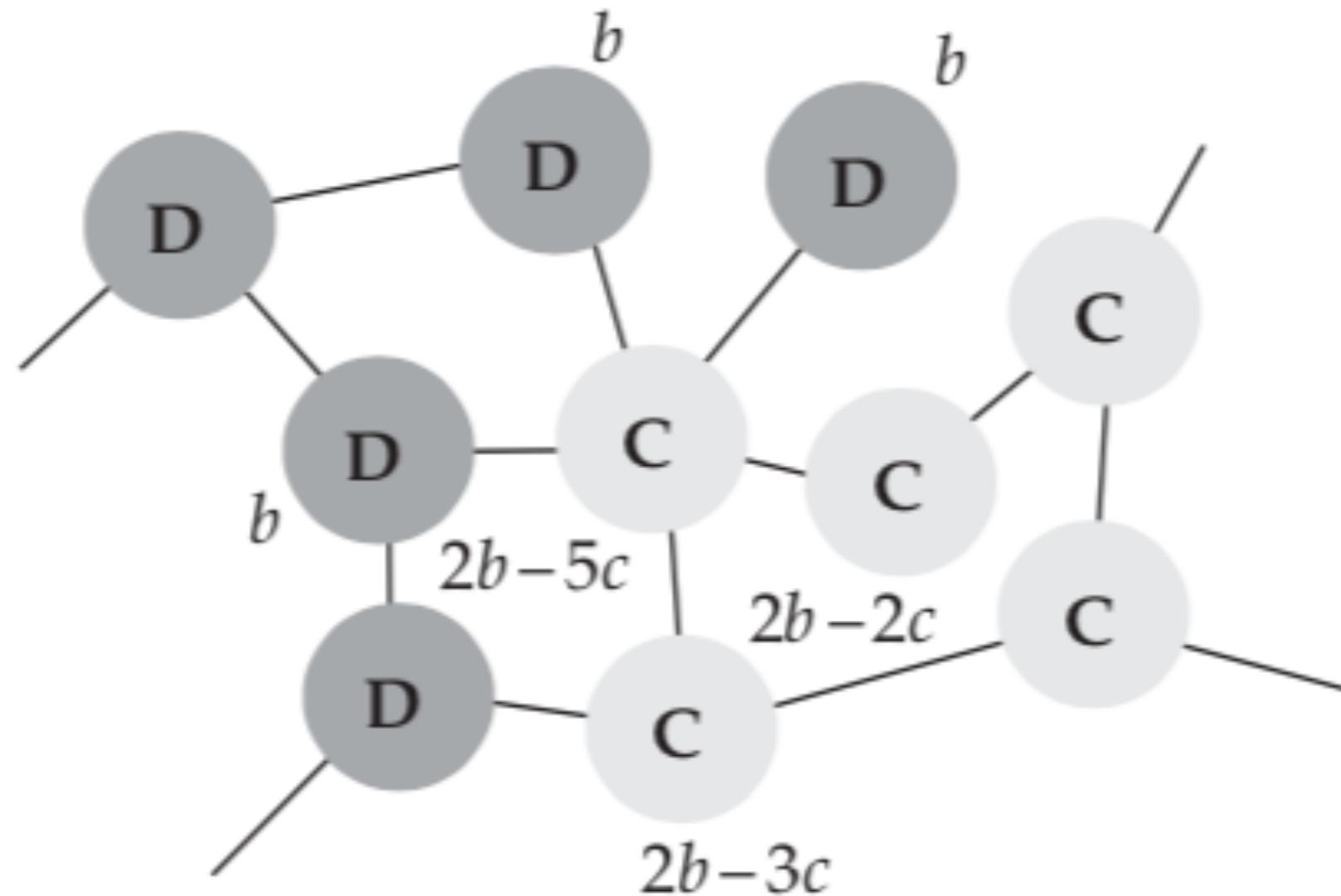
助他个体从5%降到4.6%再到4.2%      Simpson's paradox

代	1+0.4	1	1.1+0.4	1.1	B	sum
0	$10*10*(10/100)=10$	$10-10=0$	$10*10*(90/100)=90$	$90-90=0$	100	200
1.0	14	0	135	0	110	259
1	$14*10*(14/149)=13.15$	$14-13.15=0.85$	$14*10*(135/149)=126.85$	$135-126.85=8.15$	110	259
2.0	18.41	0.85	190.275	8.965	121	339.5

在Group A, 助他个体从10%降到9.4%再到8.7%；相对于总体，则是从5%升到5.4%再到5.6%

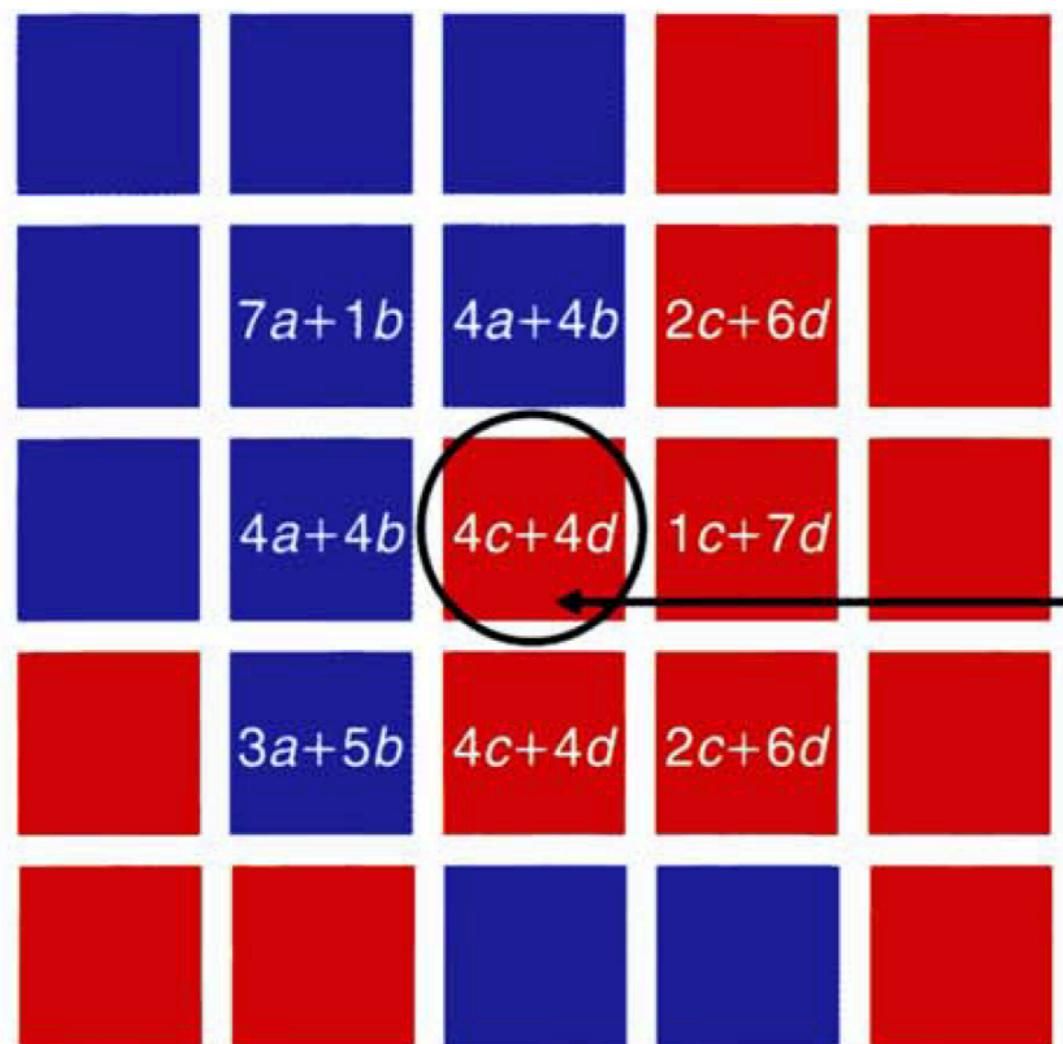
# Five Rules for Cooperations:

## 5. Graph Selection



# Spatial Games = Cellular Automata + Game Theory

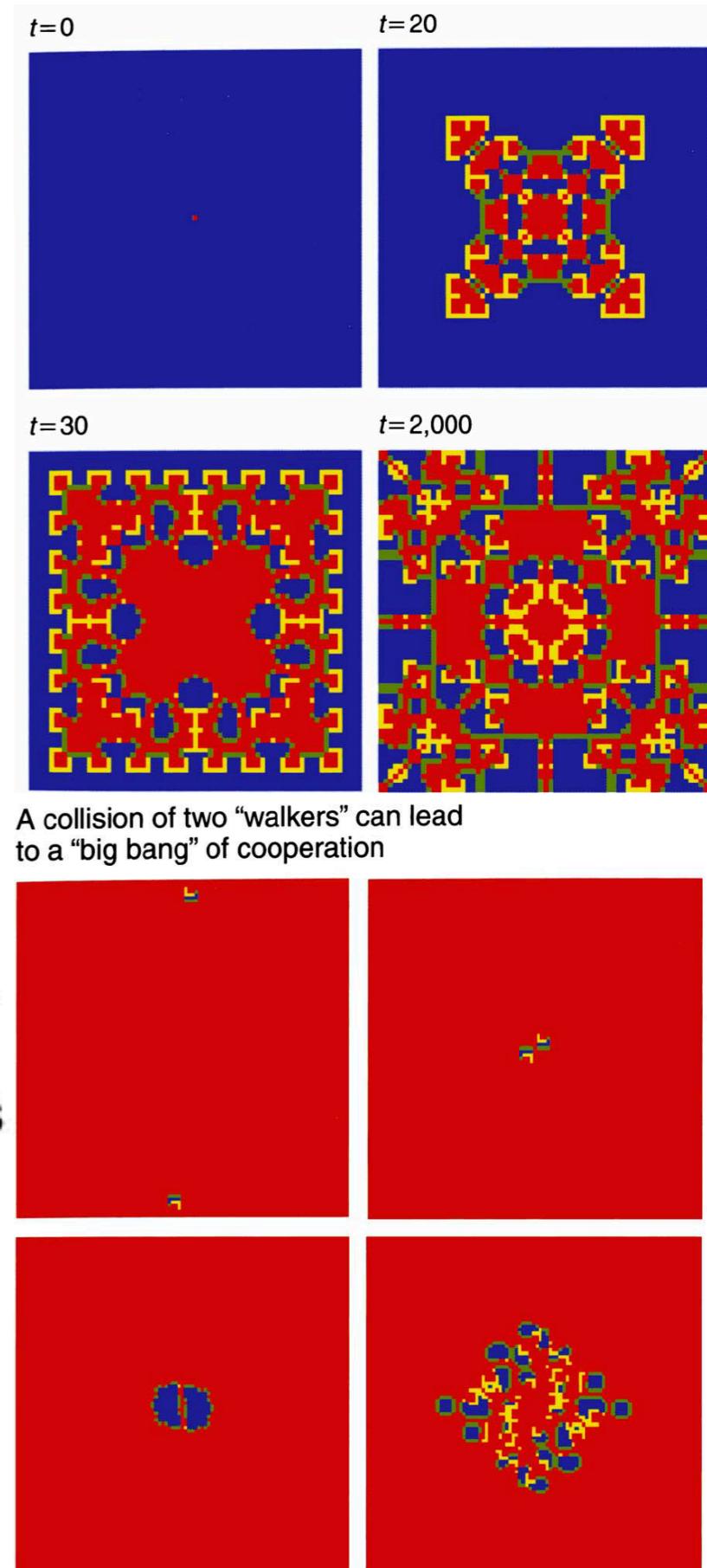
## Spatial games



Payoff matrix:

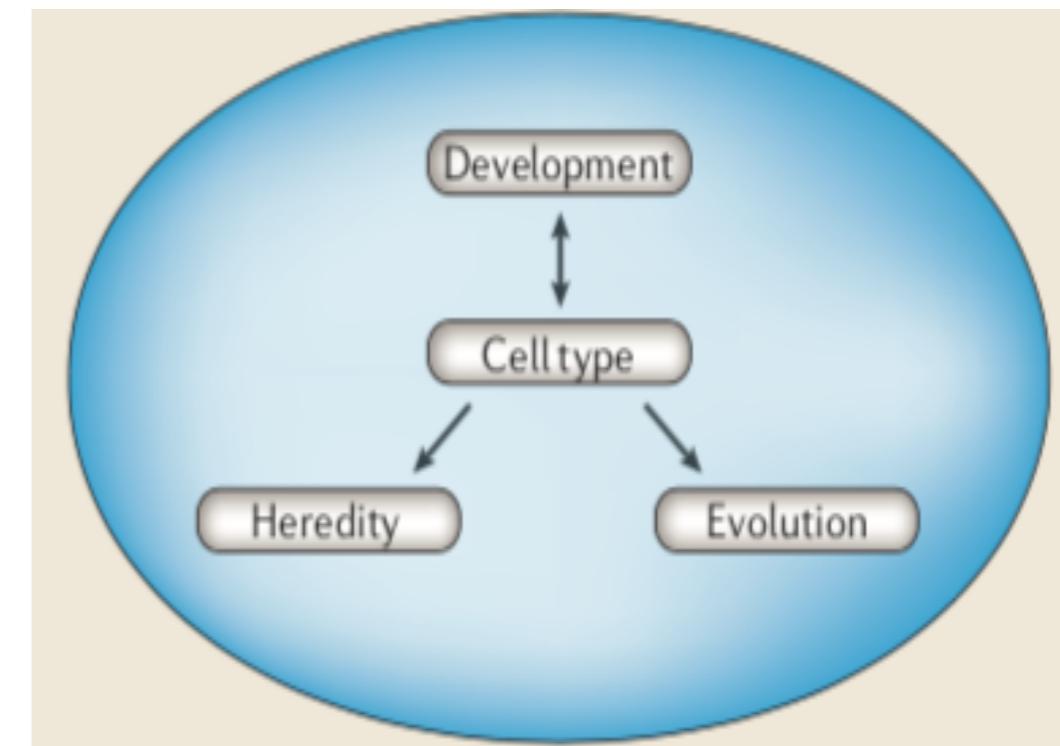
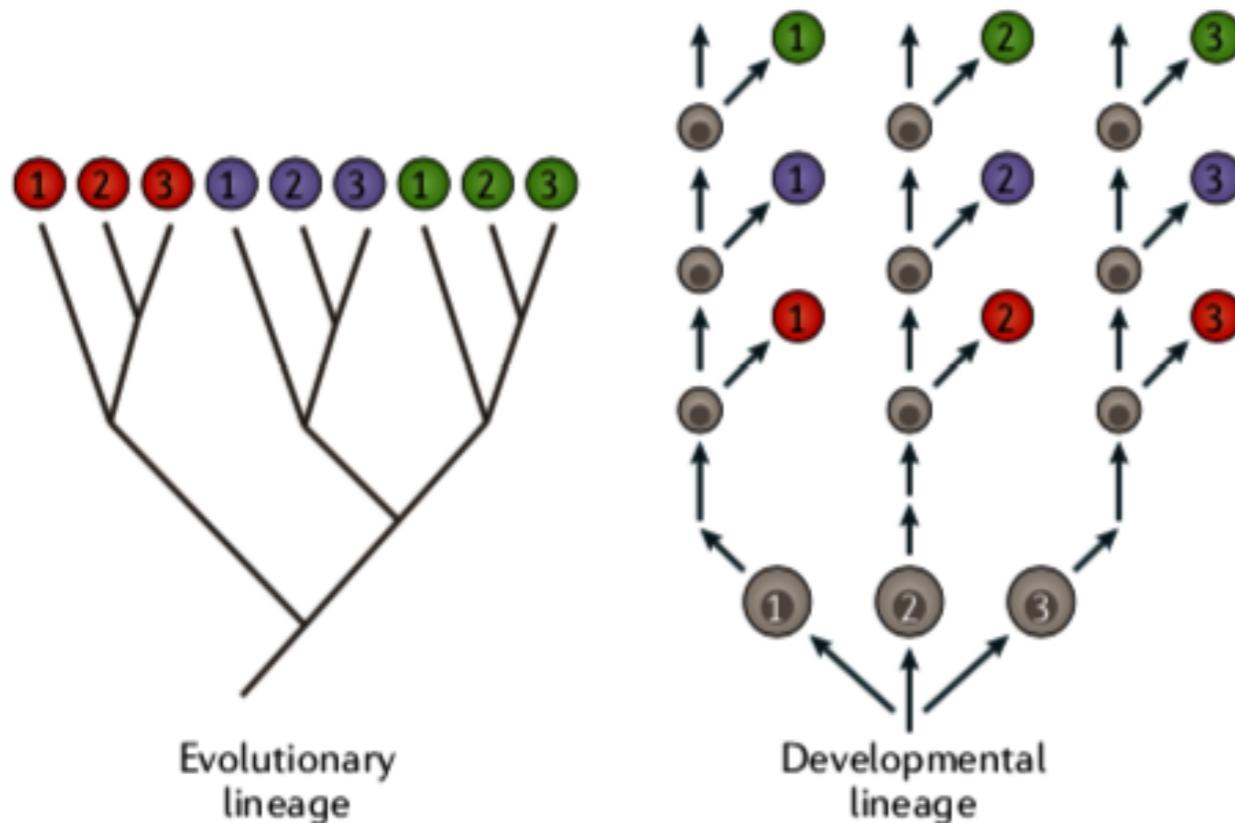
	<i>A</i>	<i>B</i>
<i>A</i>	<i>a</i>	<i>b</i>
<i>B</i>	<i>c</i>	<i>d</i>

The focal cell will be taken over by whoever has the highest payoff among the 8 neighbors and the cell itself

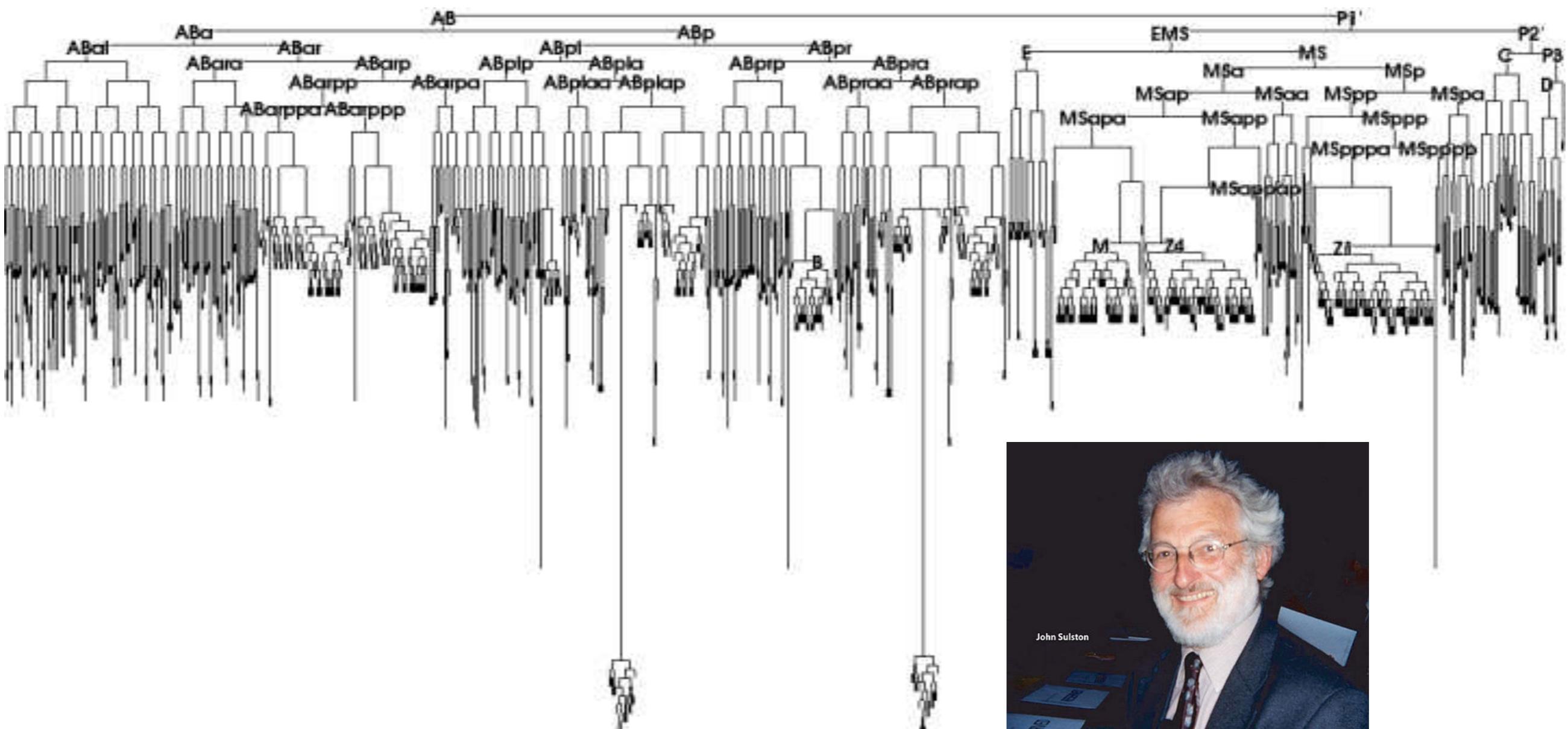


# What is the Cell Type?

**Cell Type Classification foundation:**  
**Molecular fingerprints,**  
**Cellular modules,**  
**Sister cell types,**  
**Gene expression level,**  
**etc.**



# The embryonic cell lineage of the nematode *C. elegans*

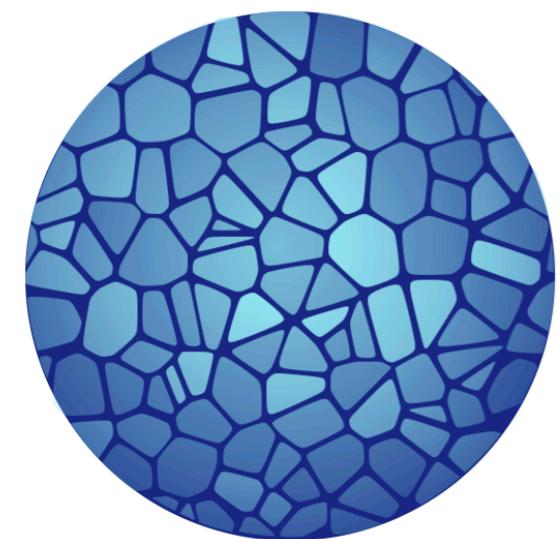


John Sulston  
(1942-2018)

# The Human Cell Lineage Flagship Initiative



Ehud Shapiro@Weizmann



HUMAN  
CELL  
ATLAS



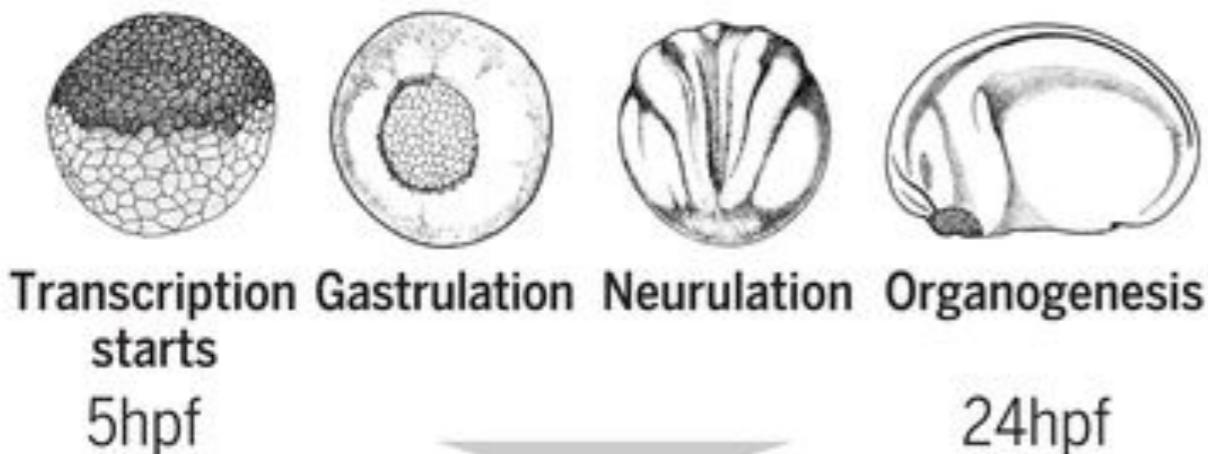
Aviv Regev@Broad



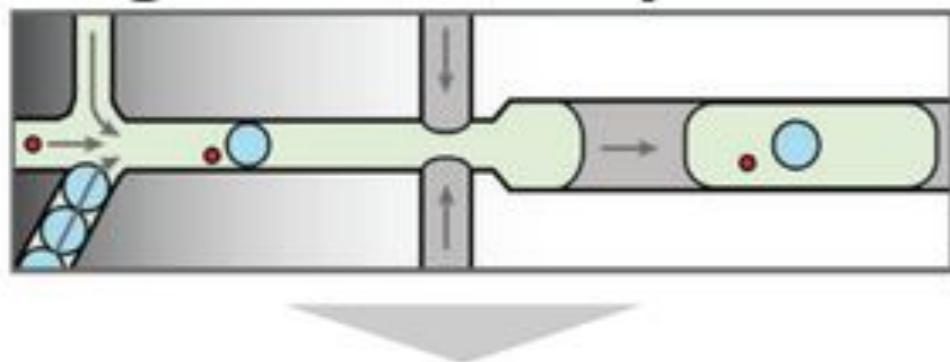
Sarah Teichmann@Sanger



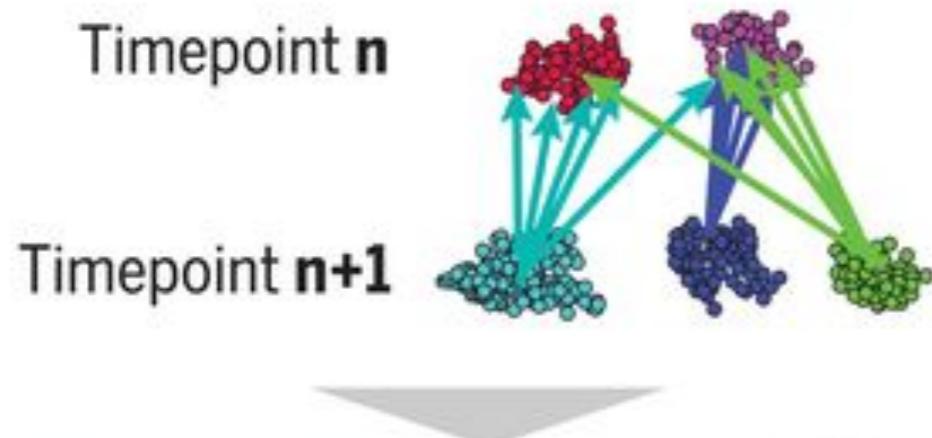
## Whole embryos at ten timepoints



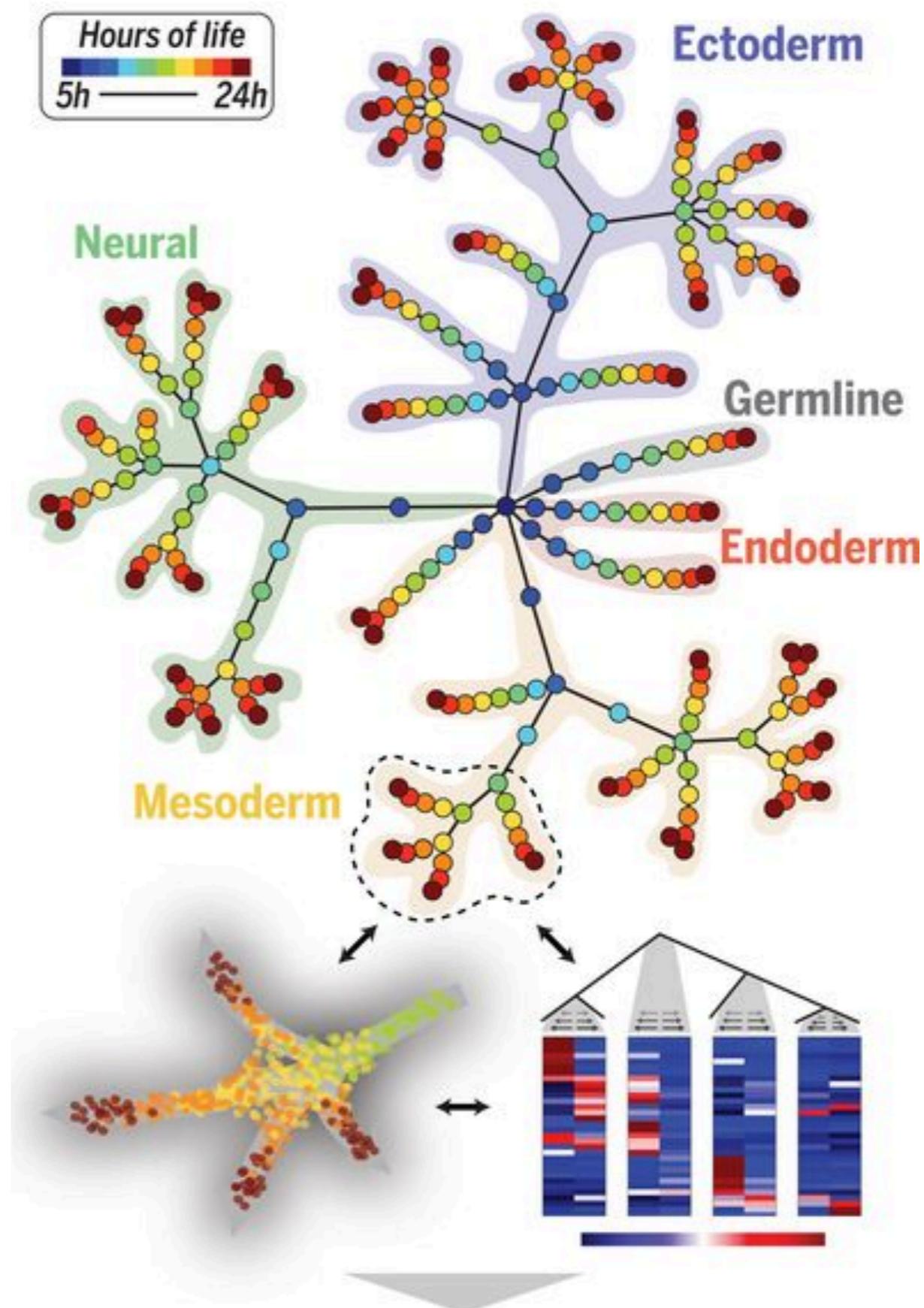
## Single cell transcriptomics



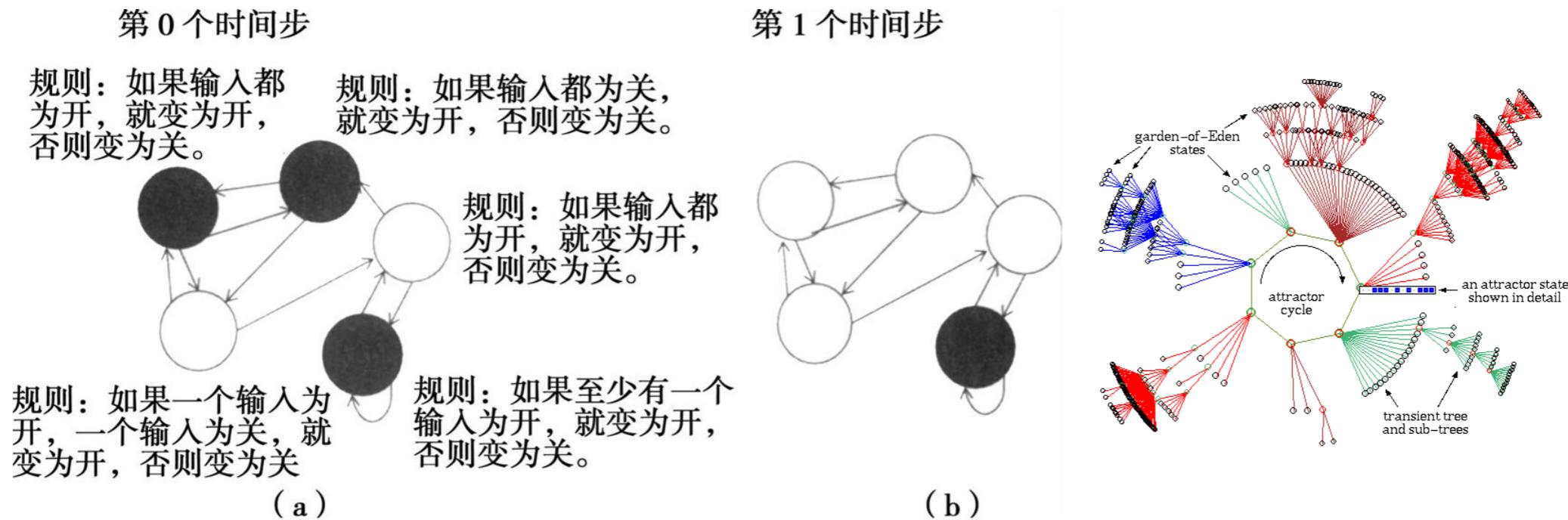
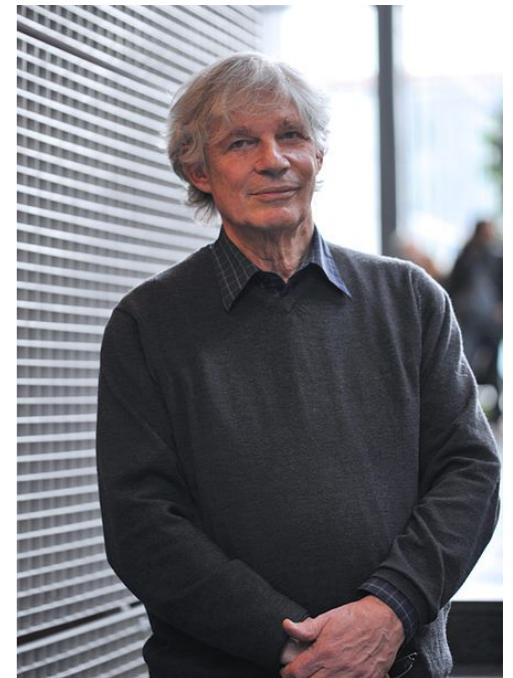
## Cell state linkage over time



## Cell state tree transcriptional dynamics



# Stuart Kauffman and Artificial Gene Regulatory Networks

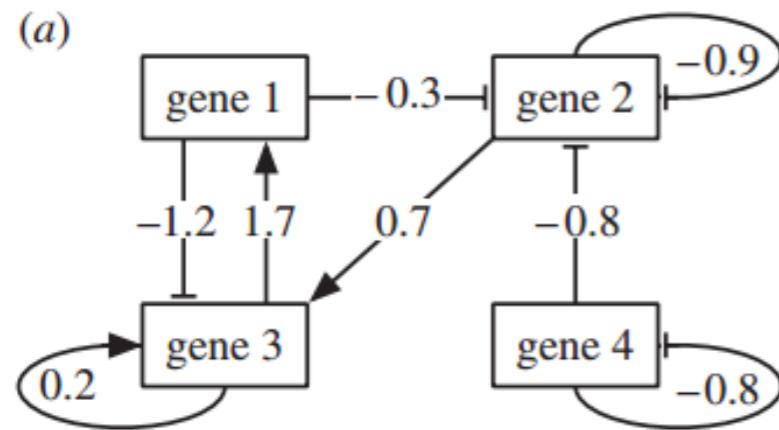


He used **random boolean networks**, proposing that **cell types** are dynamical **attractors** in gene regulatory networks and that cell **differentiation** can be understood as **transitions** between attractors, argued that **natural selection** is not necessary in genesis of complex life.

**Node** of net means a **gene**, **N** is the number of nodes; **Edge** of net means **gene interaction**, **K** is **half** the number of edges. When **K=2**, He found that the number of attractors (cell types) is approximately  $\sqrt{N}$ . So with the theory, number of types in Nematodes is nearly  $\sqrt{20470 + 1300} = 148$ , as human is  $\sqrt{21306 + 21856} = 208$

- Limitations:**
1. Binary states (boolean)
  2. Ignore expression level
  3. Discrete time simultaneously
  4. Ignore noises (mutation and uncertain bias from environment)

# A generative bias towards average complexity in artificial cell lineages



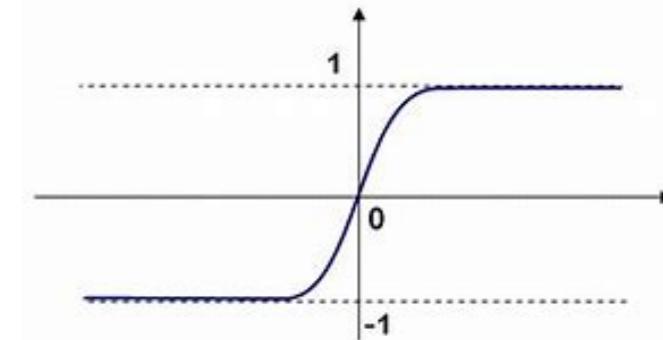
- Gene 1 is a **cell-cycle regulator**.
- If gene 1 is **ON**, the cell divides instantaneously, and gene 1 is turned **OFF** in both daughter cells.
- Gene 2 is a **asymmetric cell division** gene.
- Gene  $i$  is **ON** when  $0 < s_i(t) \leq 1$ , and **OFF** when  $-1 \leq s_i(t) < 0$ .
- The gene expression pattern  $\mathbf{S}(t)$

## Gene 2 Regulatory Rules

	Gene 1 is ON
Gene 2 is ON	Divide asymmetrically, $s_{2L}(t) = -1, s_{2R}(t) = s_2(t)$
Gene 2 is OFF	Divide symmetrically.

$$s_i(t+1) = f\left[\sum_{j=1}^N r_{ij} s_j(t)\right]$$

$$f(x) = 2/(1 + e^{-ax}) - 1$$



## Parameters:

- **R**, the **genotype (mutant** with random !0 element substitution )
- **S(0)**, the **epigenetic state**
- $D_{max}$  and  $t_{max}$  of **development**
- **N, K** and **Rules(General)**
- $a$  in the **sigmoidal filter function**

For example.

$$R = \begin{vmatrix} 0 & 0 & 1.7 & 0 \\ -0.3 & -0.9 & 0 & -0.8 \\ -1.2 & 0.7 & 0.2 & 0 \\ 0 & -0.8 & 0 & -0.8 \end{vmatrix}$$

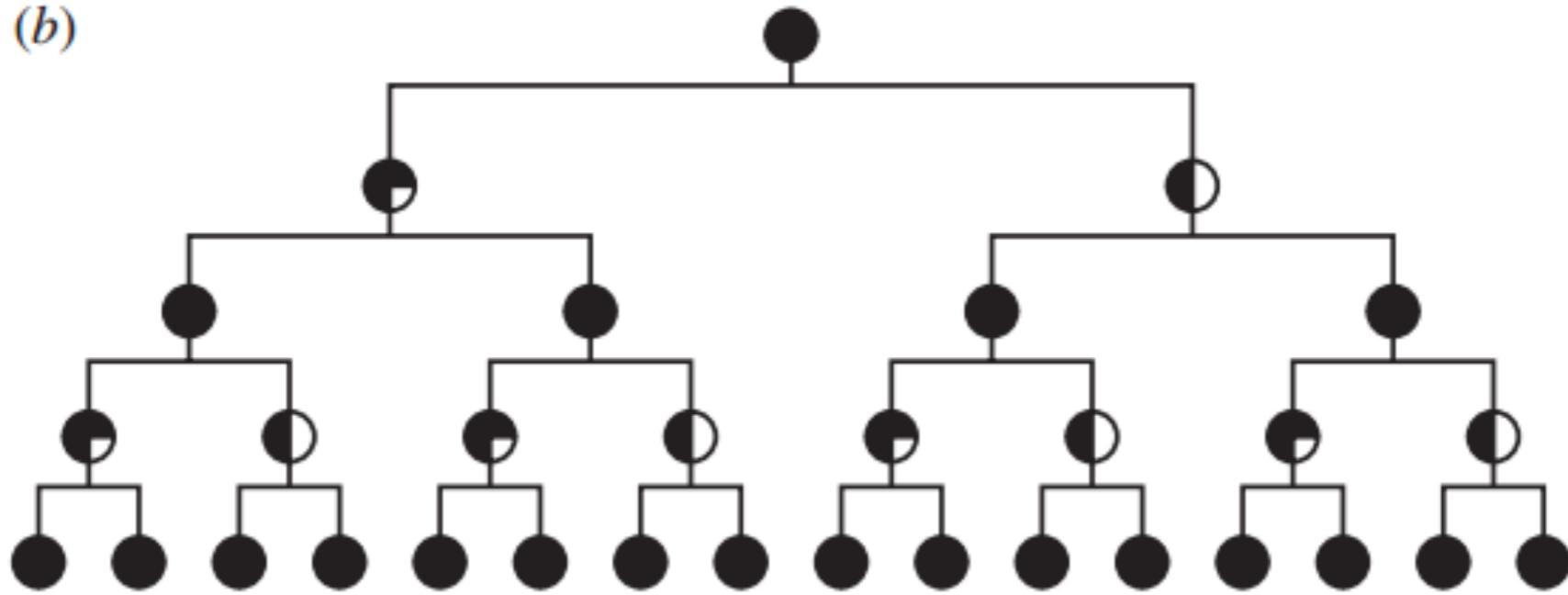
$$S(t) = \begin{vmatrix} 1 \\ 1 \\ 1 \\ 1 \end{vmatrix}$$

After **cell divide**, two daughter cells are born, which are  $S_L(t) = \begin{vmatrix} -1 \\ -1 \\ 1 \\ 1 \end{vmatrix}$  and  $S_R(t) = \begin{vmatrix} -1 \\ 1 \\ 1 \\ 1 \end{vmatrix}$

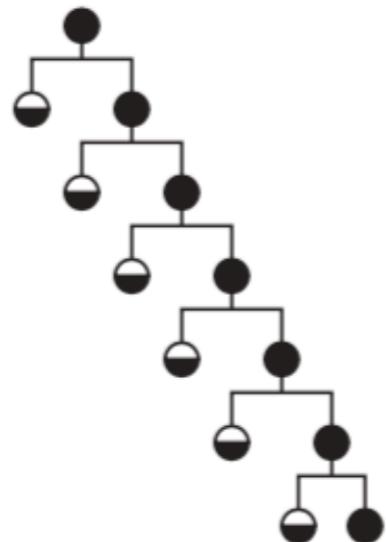
At time **t+1**,  $S_L(t+1) = f(R * S_L(t))$

# Artificial cell lineage Tree

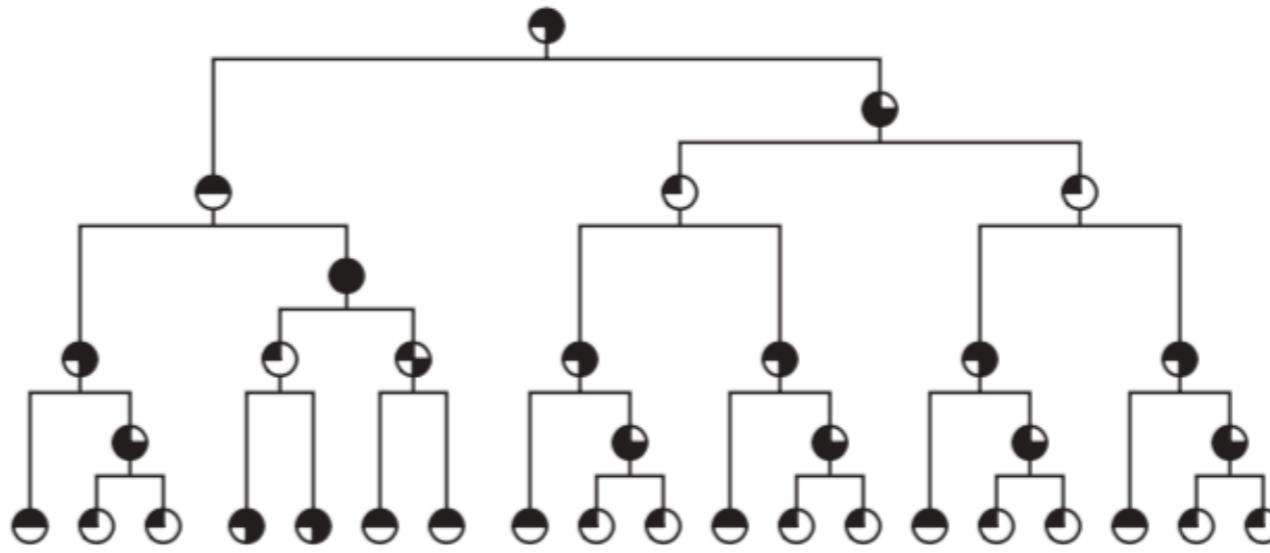
(b)



(c)



(d)



[gene 1] cell-cycle gene

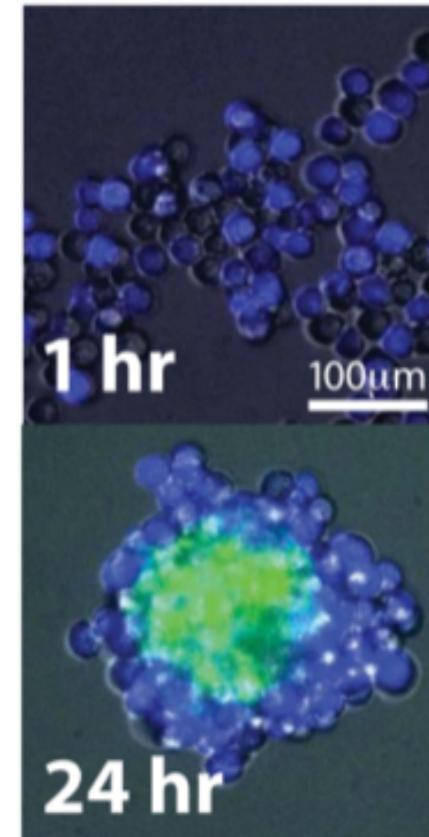
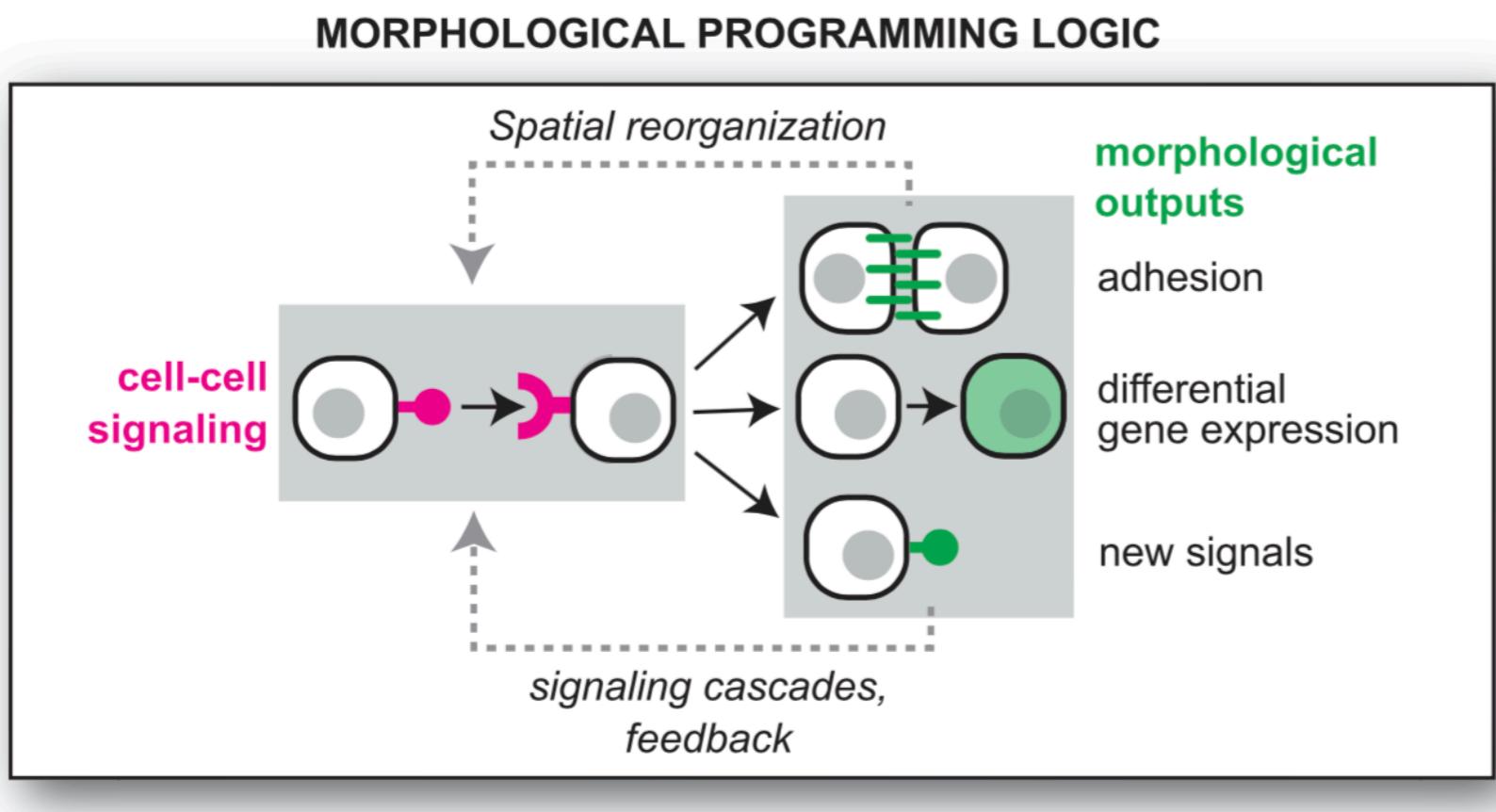
[gene 2] asymmetric division gene

[solid black shape] gene ON

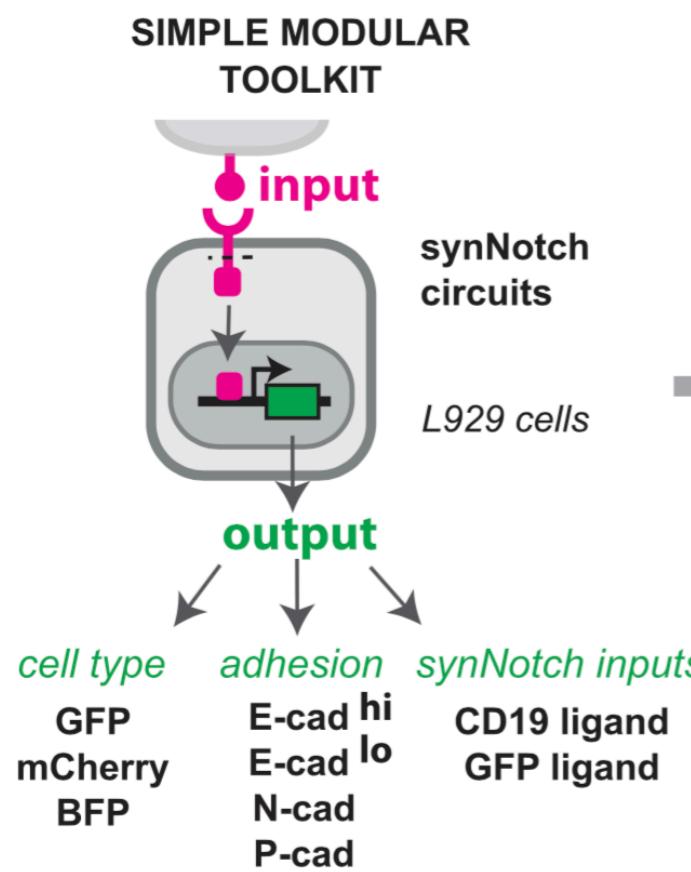
[white shape with black wedge] gene OFF

# Synthetic Notch Receptor System

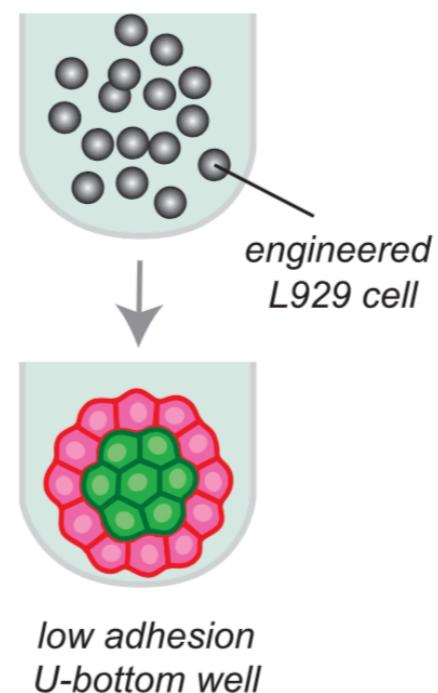
A



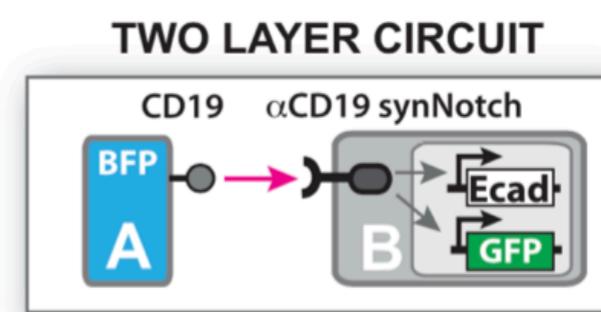
B



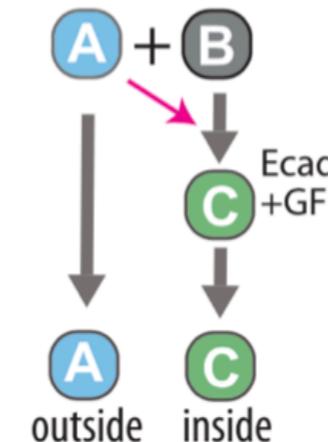
**TEST FOR SELF-ORGANIZATION**



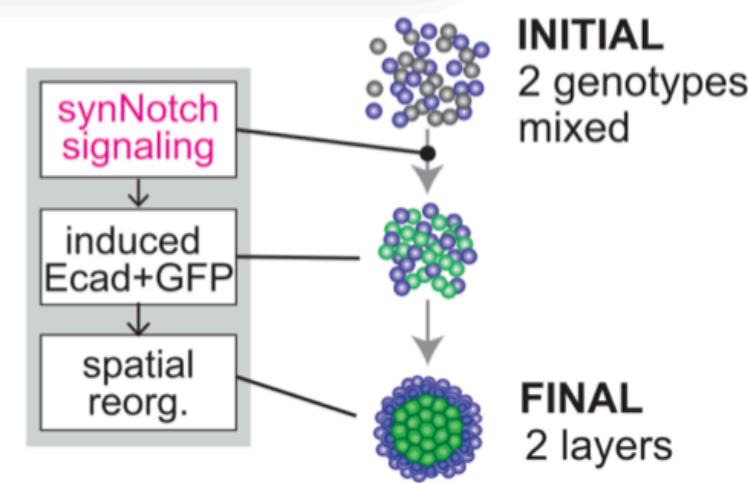
A



B



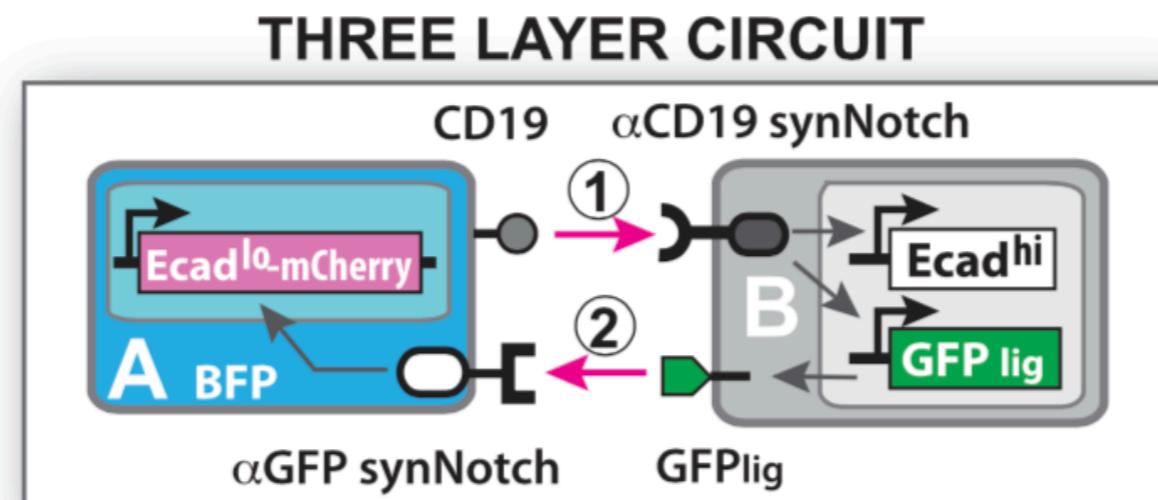
C



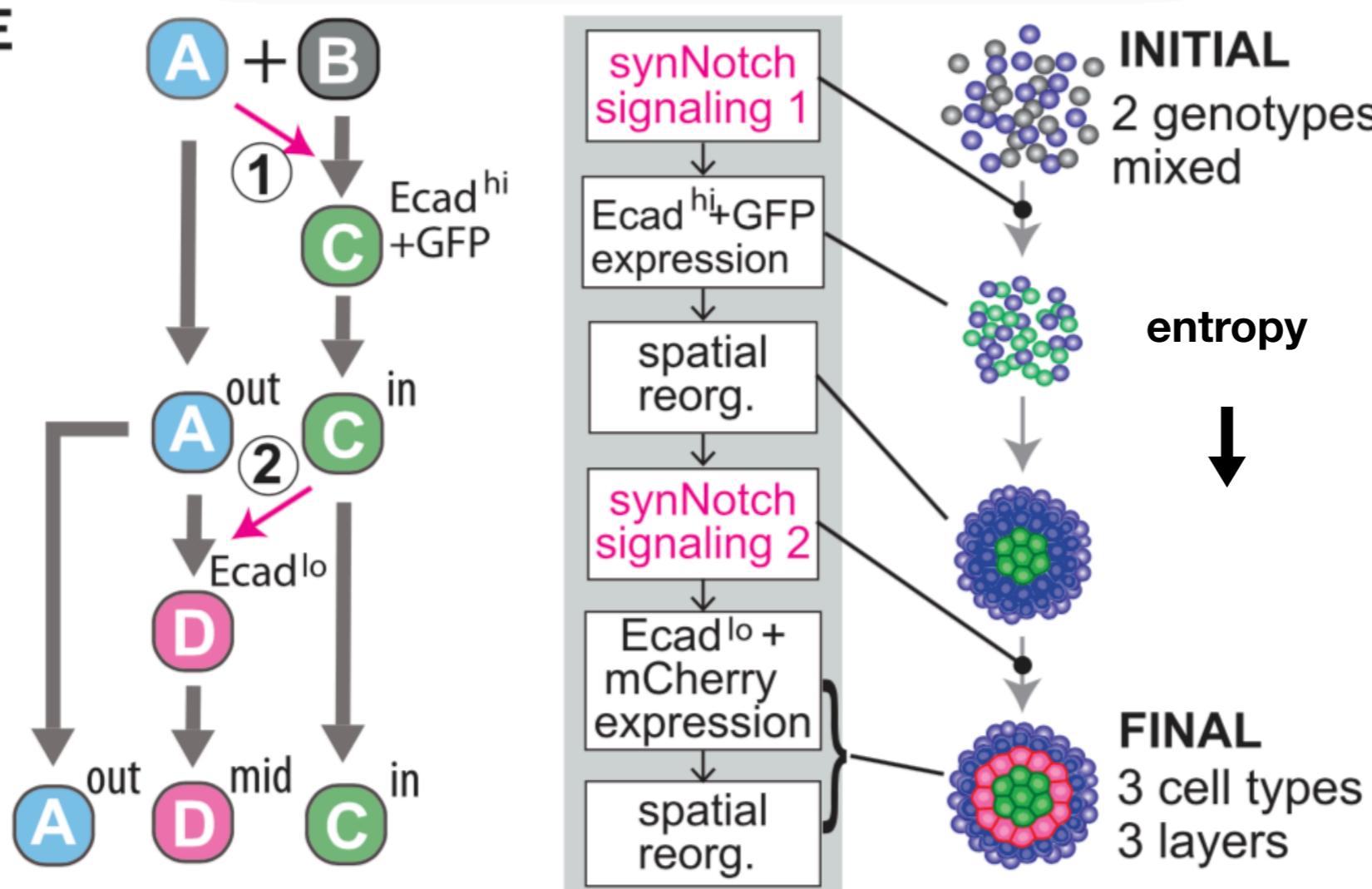
# Three-layer circuit

[cell A: CD19;  $\alpha$ GFP synNotch]  
 → [cell B:  $\alpha$ CD19 synNotch → Ecad<sup>hi</sup> + GFP<sub>lig</sub>]  
 → [cell A:  $\alpha$ GFP synNotch → Ecad<sup>lo</sup> + mCherry]

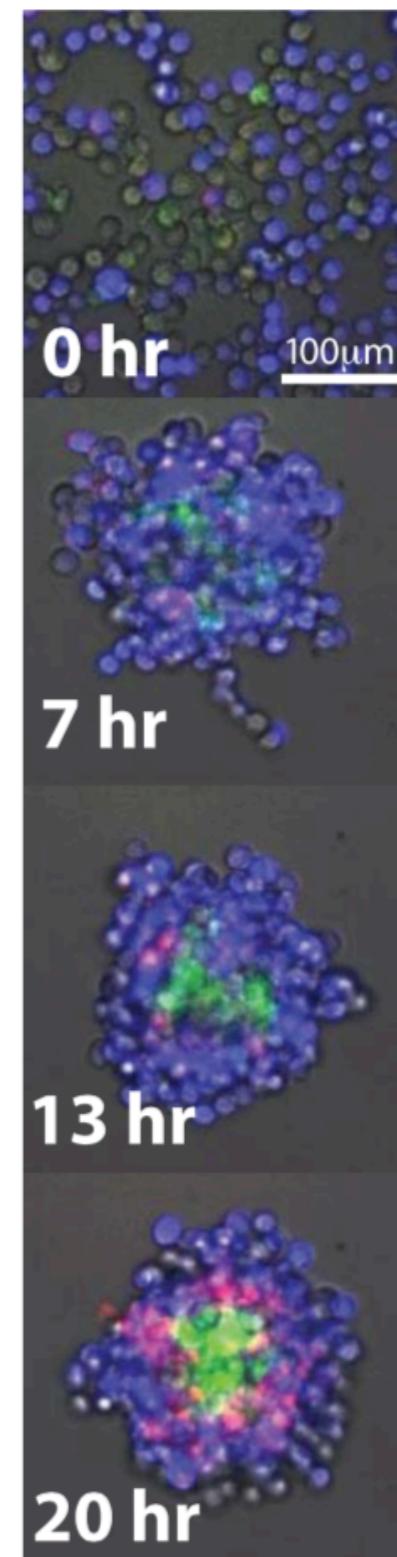
D



E

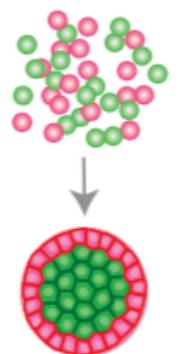
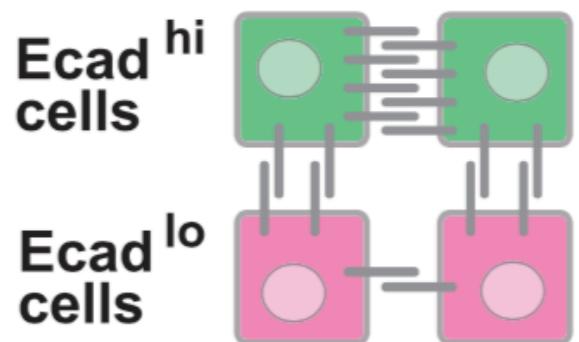


F

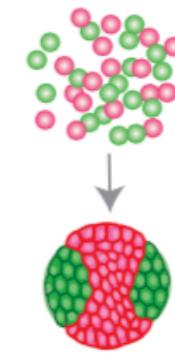
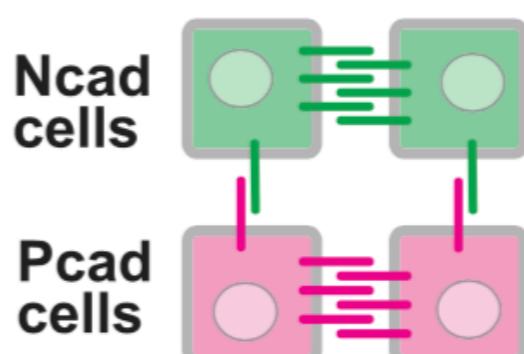


**A**

## DIFFERENTIALLY SORTING CADHERINS



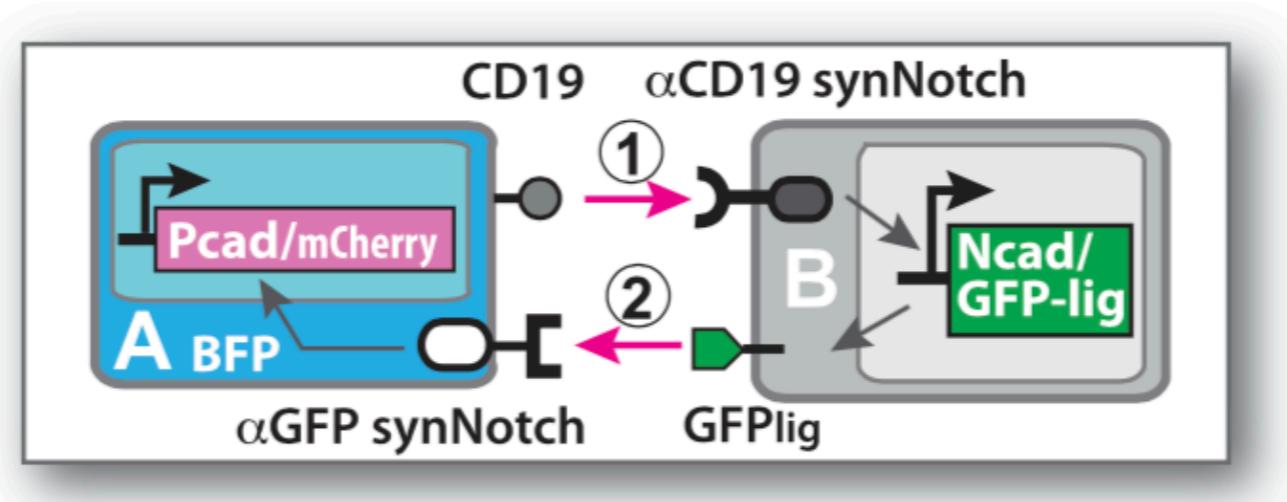
**Ecad<sup>hi</sup>:Ecad<sup>hi</sup> > Ecad<sup>hi</sup>:Ecad<sup>lo</sup> > Ecad<sup>lo</sup>:Ecad<sup>lo</sup>**



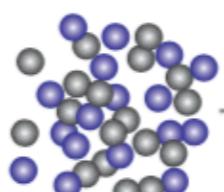
**Pcad : Pcad = Ncad : Ncad > Pcad : Ncad**

**B**

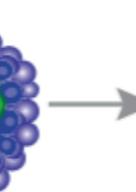
### THREE LAYER ASYMMETRIC CIRCUIT (I)



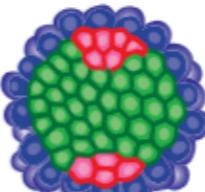
**INITIAL:**  
2 cell genotypes  
(mixed)



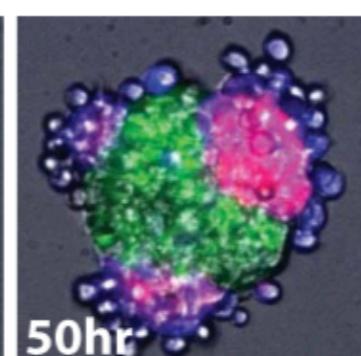
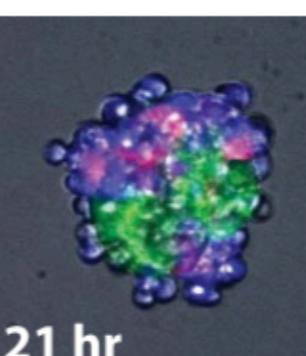
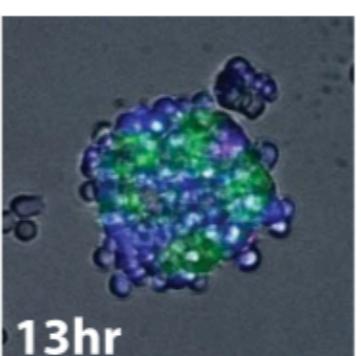
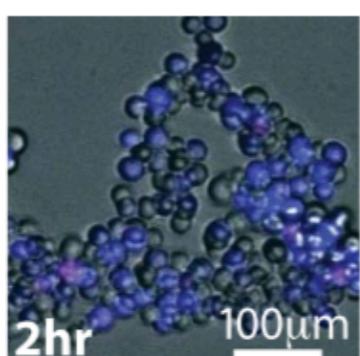
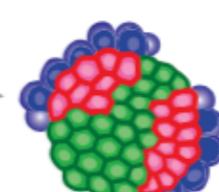
synNotch1 signaling      spatial reorg.



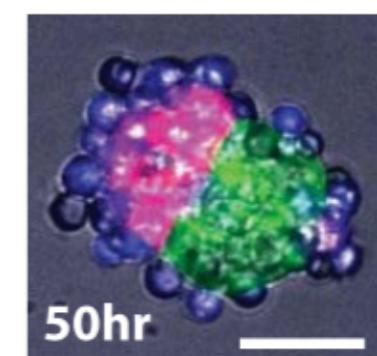
synNotch2 signaling      spatial reorg.



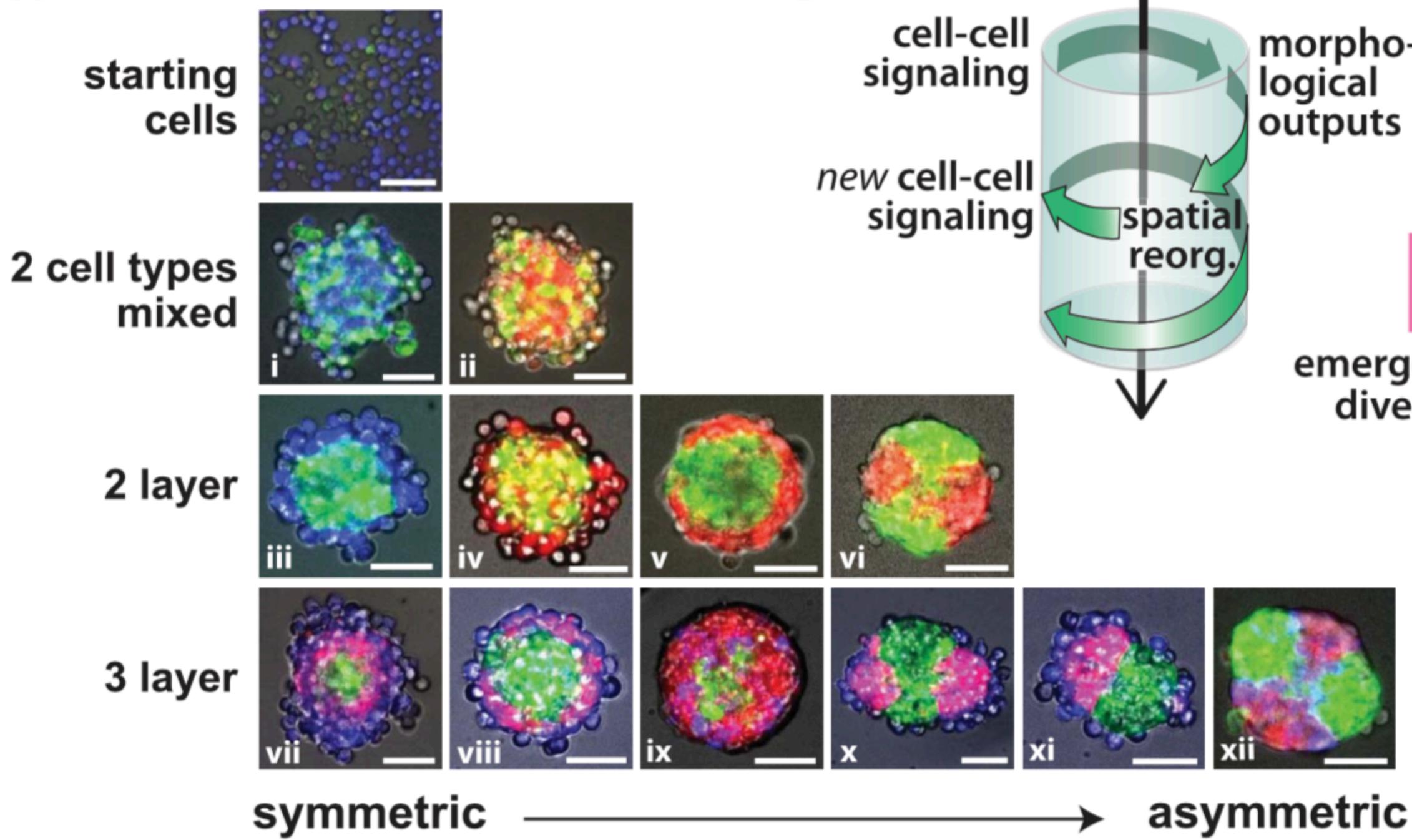
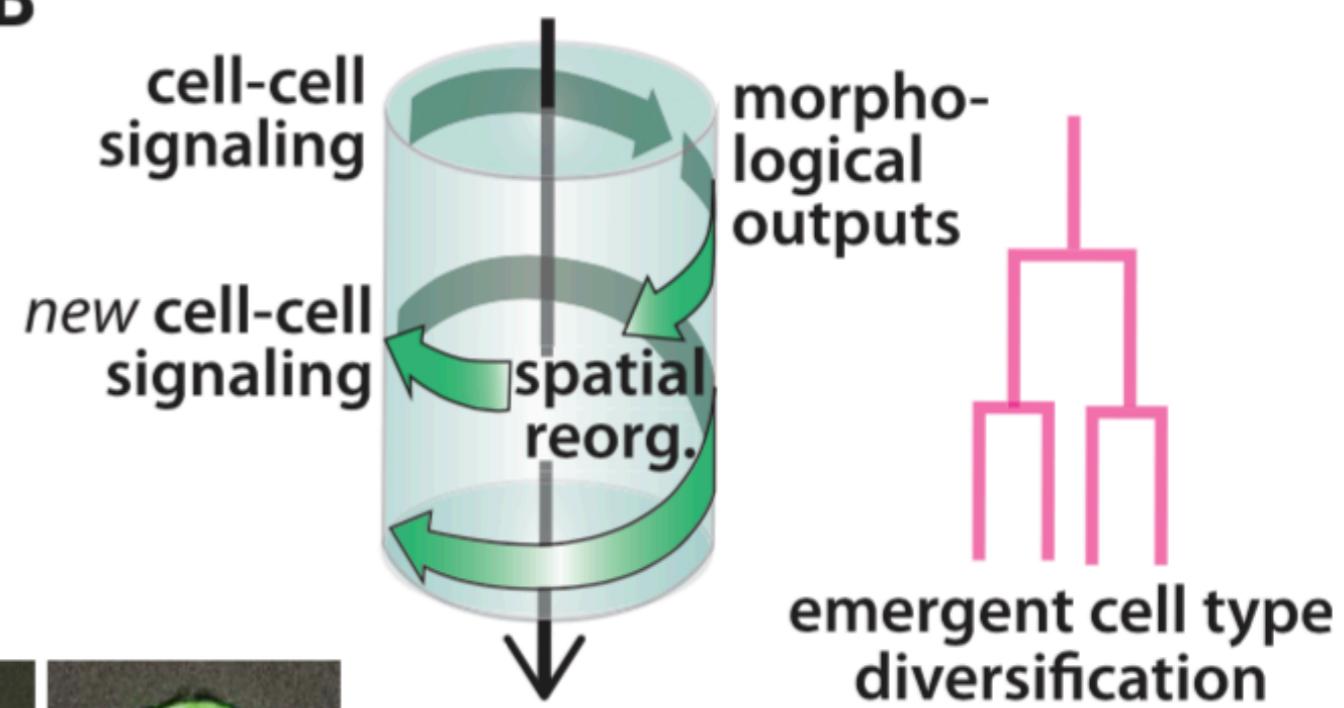
**FINAL:**  
asymmetric  
3 layer



start: 100 cells each



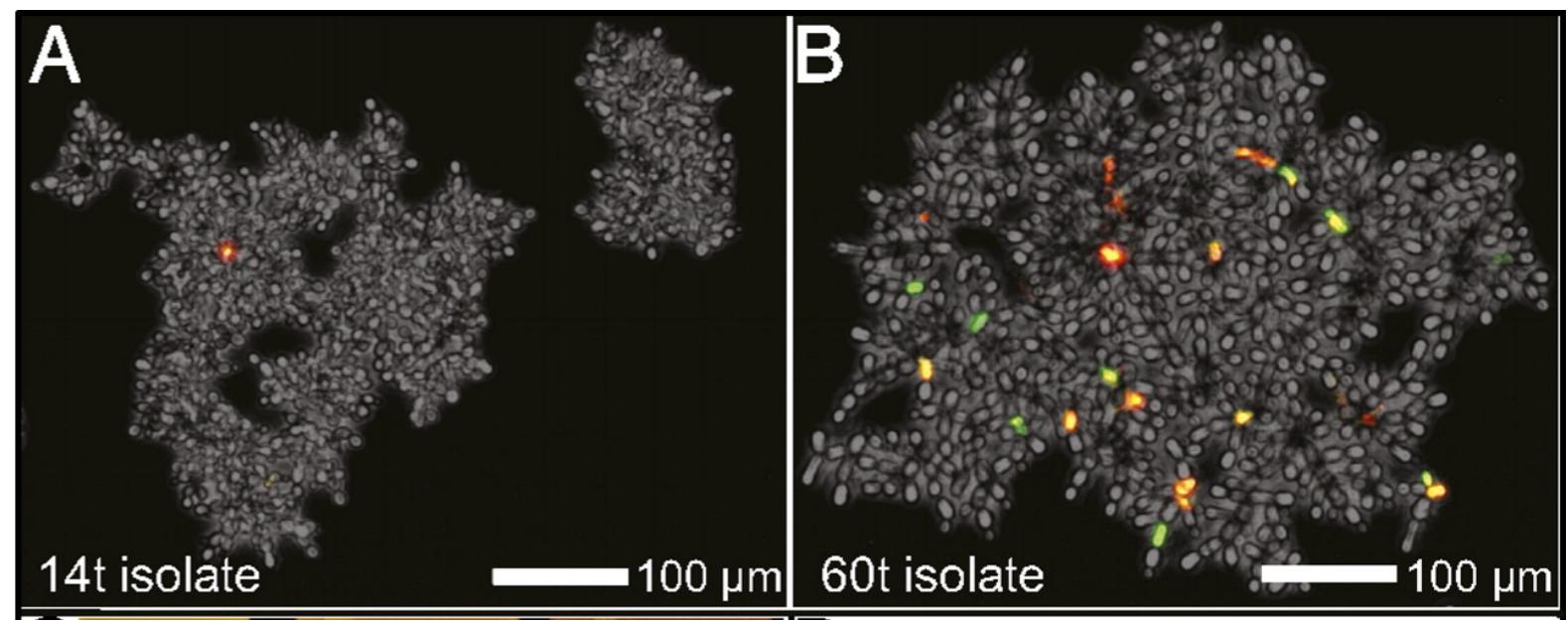
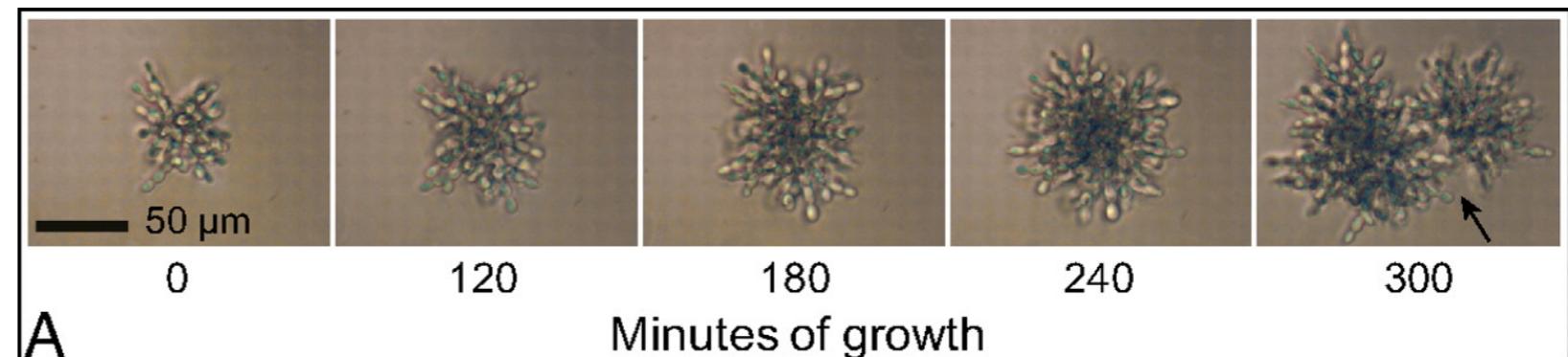
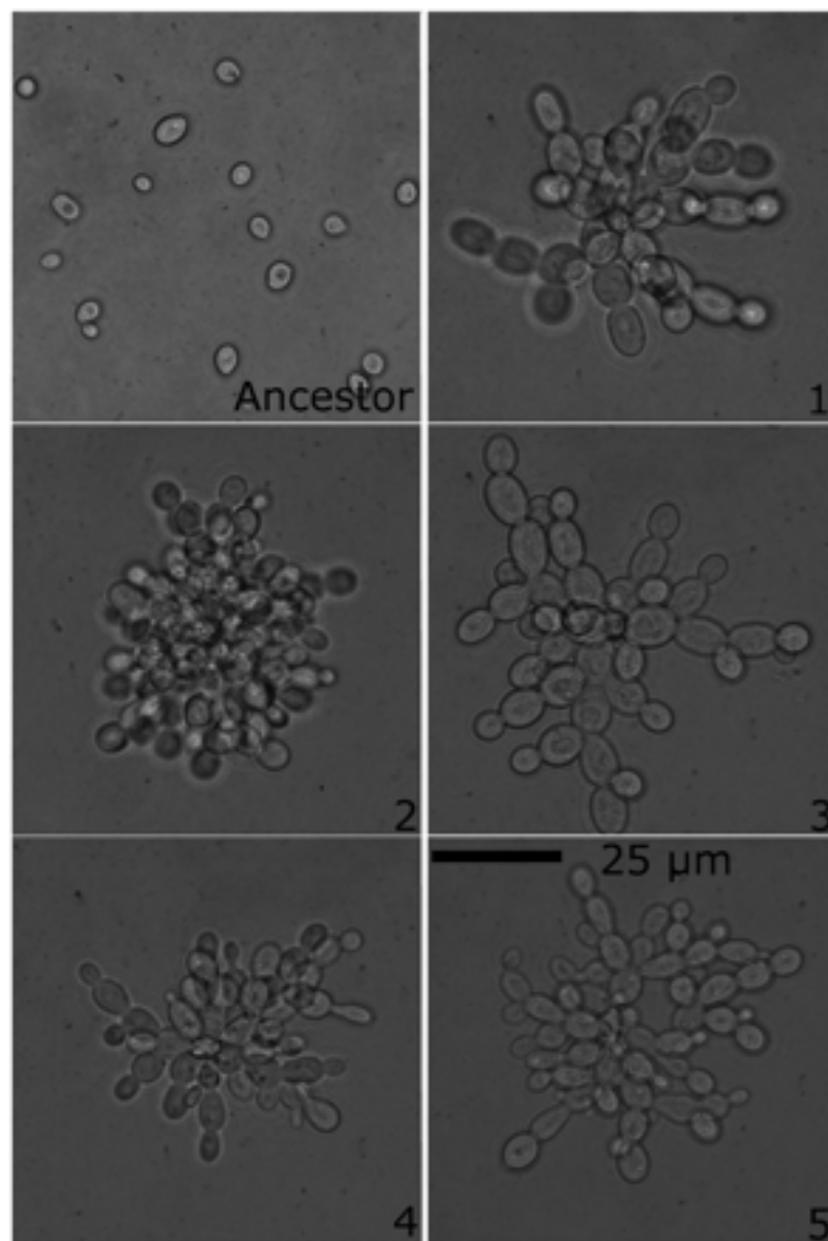
start: 30 cells each

**A****B**

# Experimental evolution of multicellularity

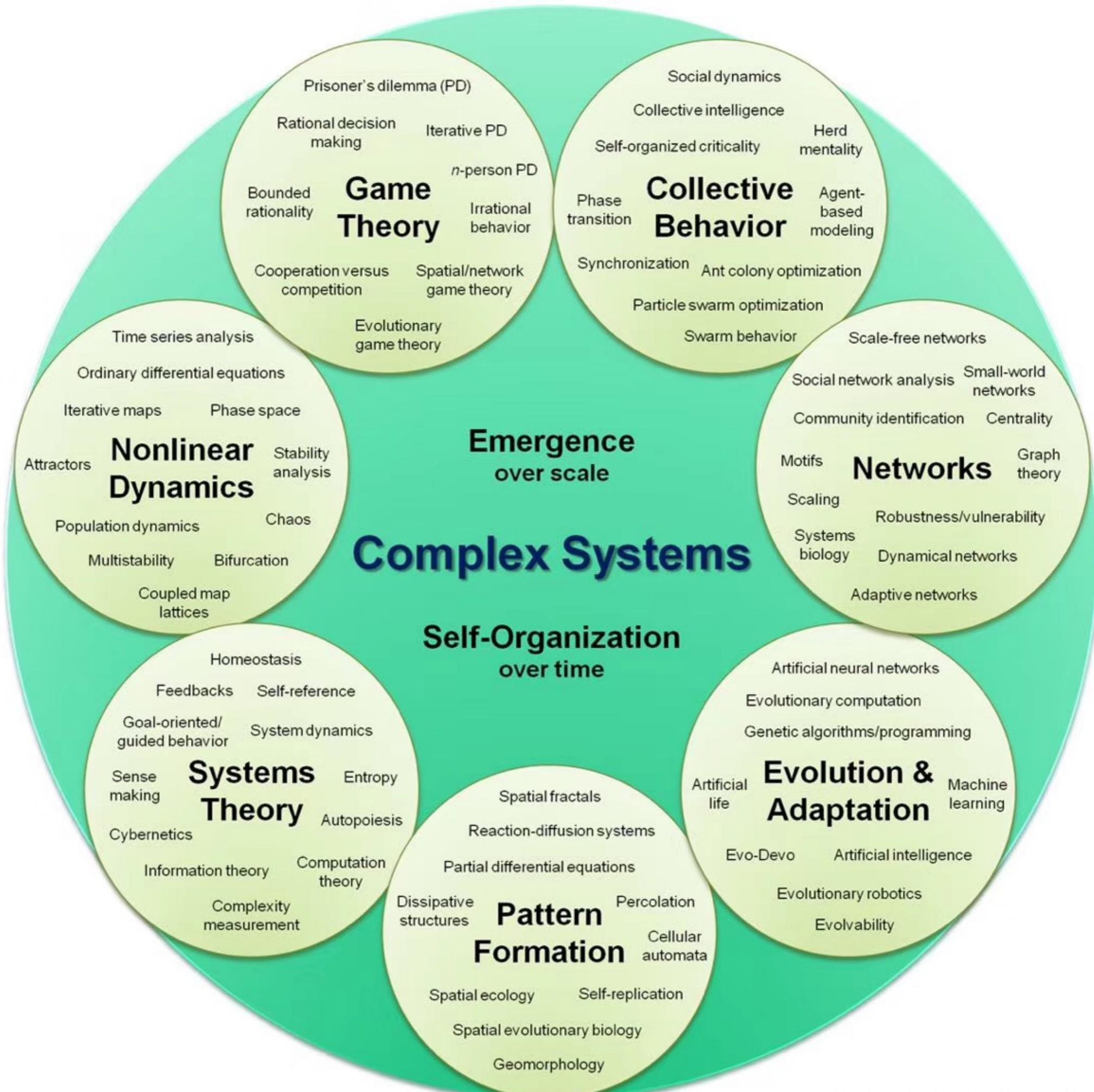
William C. Ratcliff, R. Ford Denison, Mark Borrello, and Michael Travisano

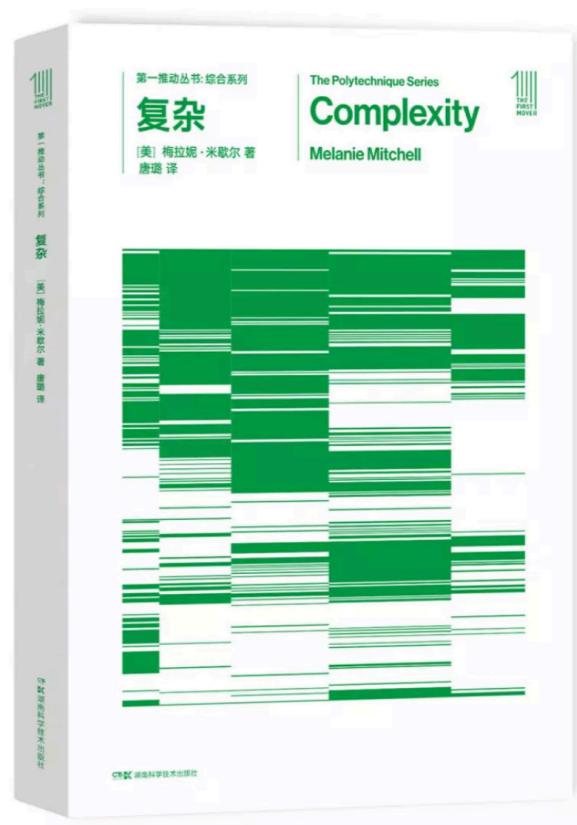
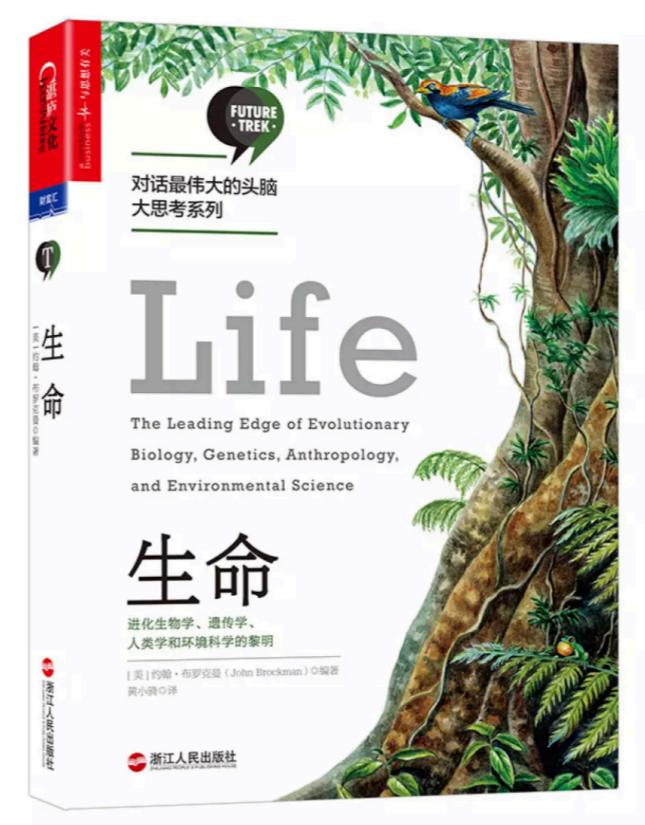
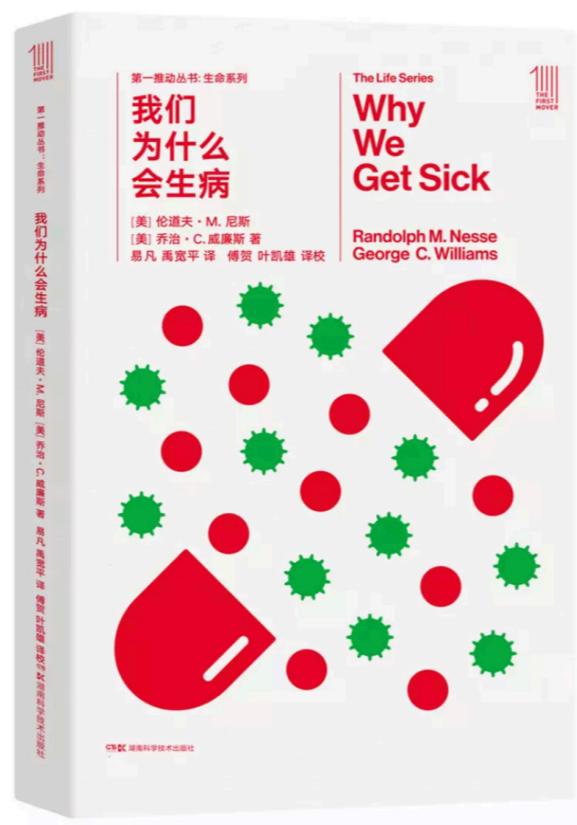
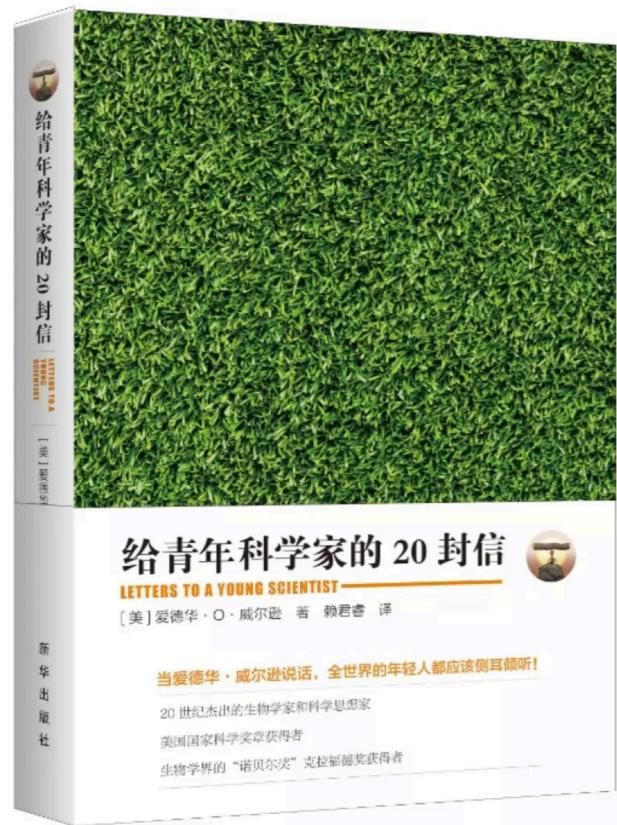
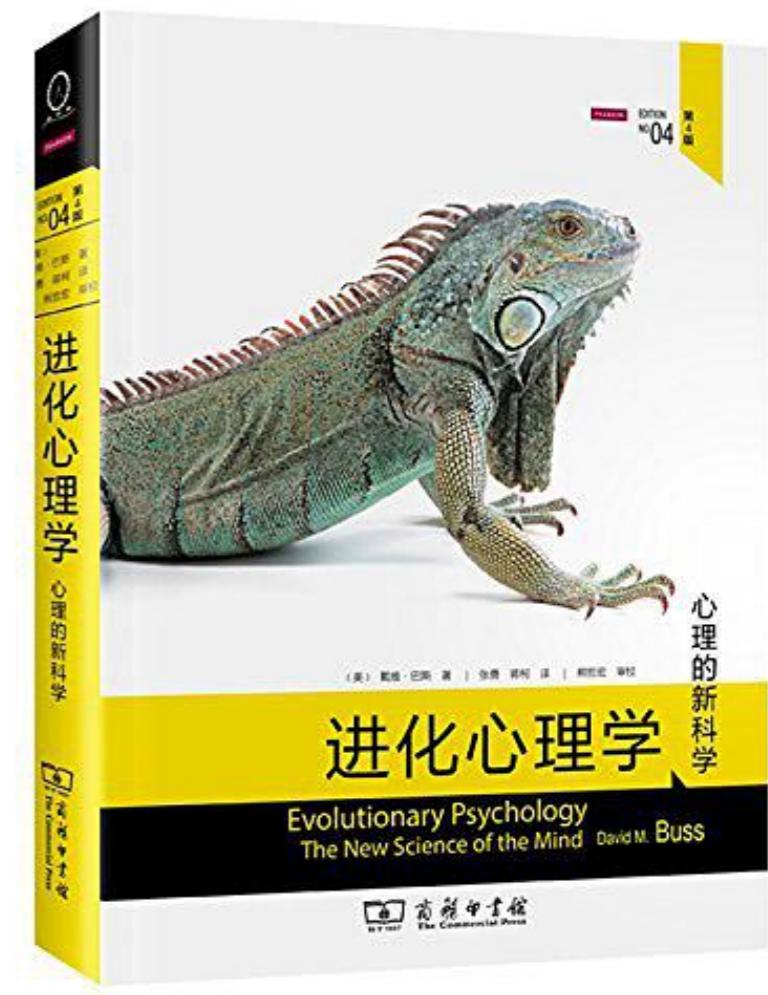
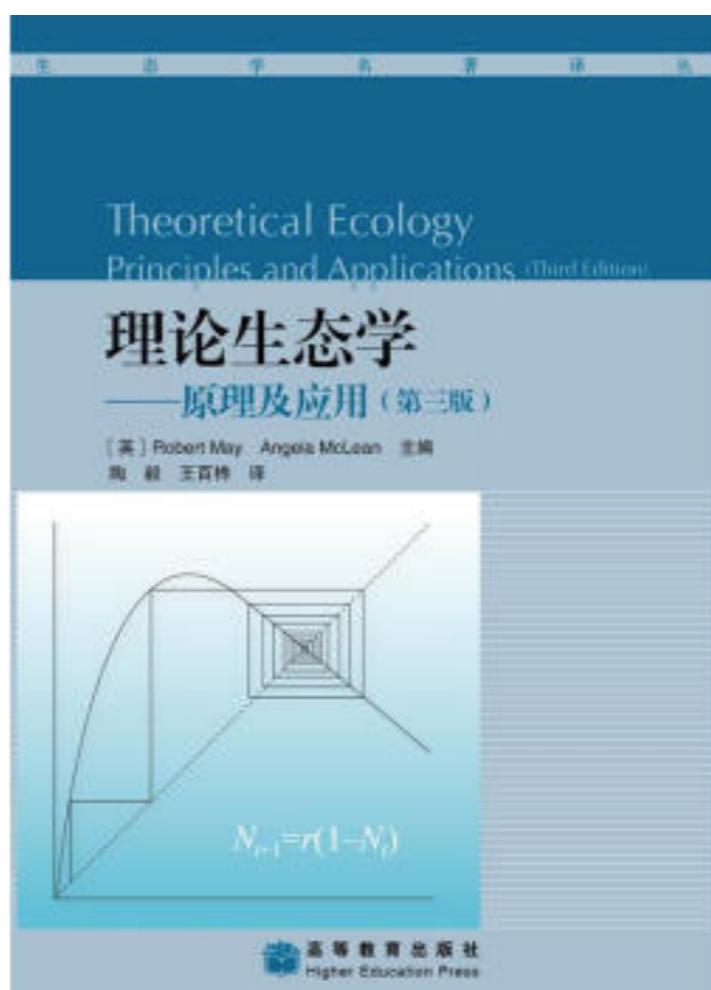
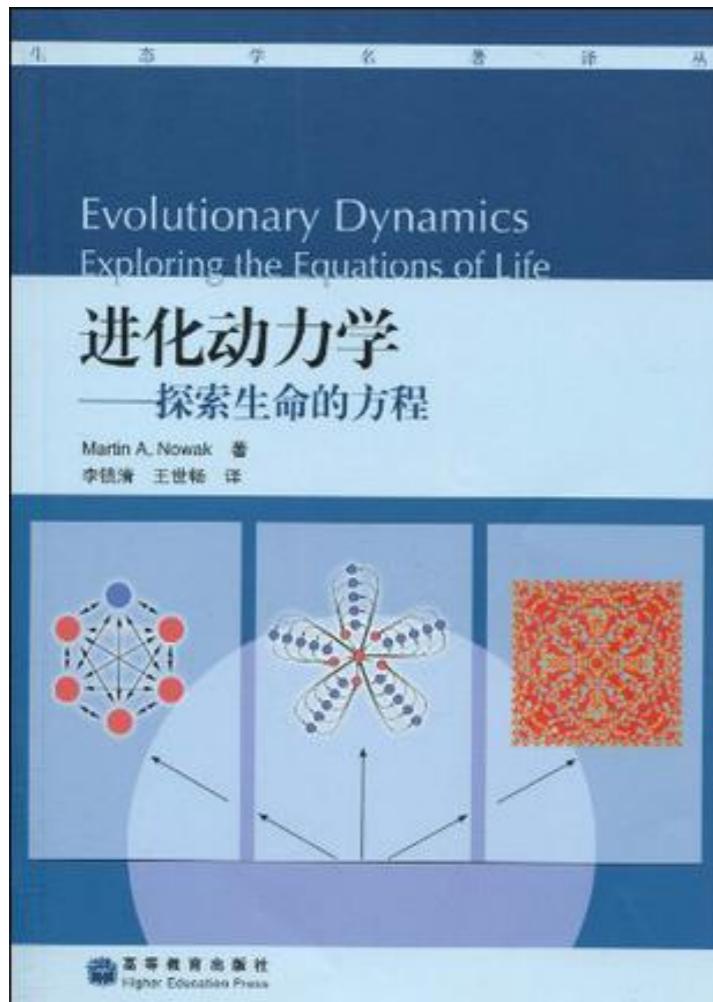
PNAS January 31, 2012 109 (5) 1595-1600; <https://doi.org/10.1073/pnas.1115323109>



# Complex Systems

## Self-Organization over time





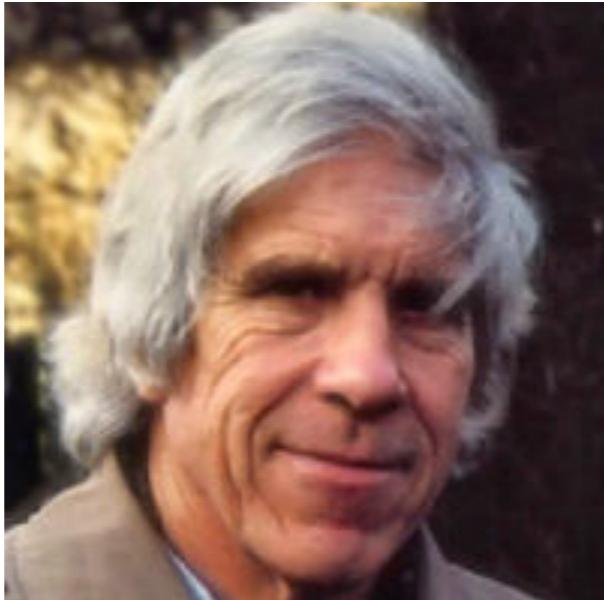
# Thanks



# How Populations Cohere: Evolution of Cooperation



Robert Axelrod  
(1943~)



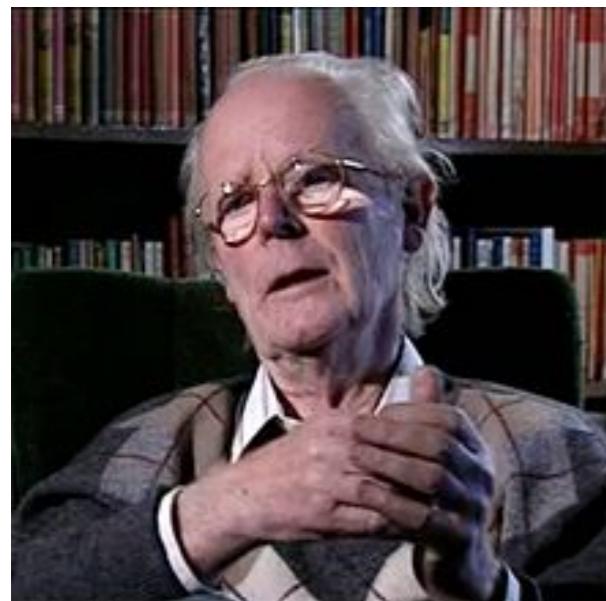
W. D. Hamilton  
(1936–2000)



George C. Williams  
(1926-2010)



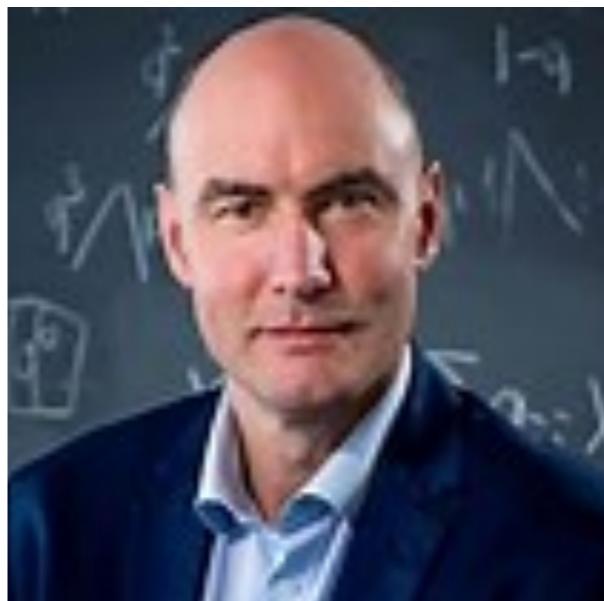
Robert Trivers  
(1943~)



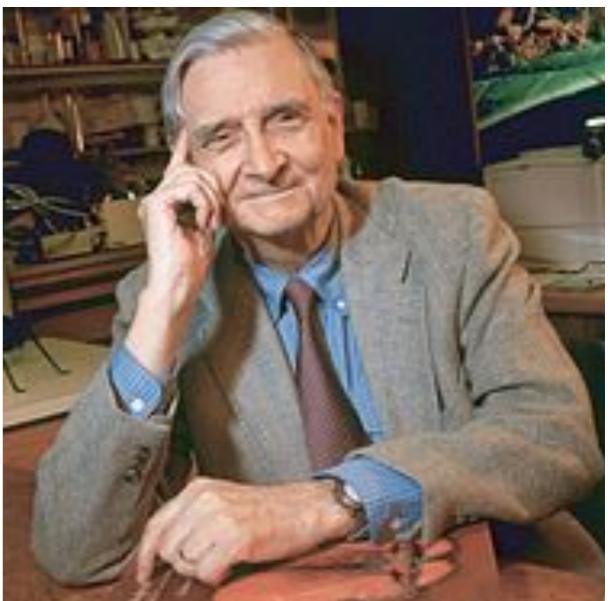
J. Maynard Smith  
(1920 - 2004)



Karl Sigmund  
(1945~)



Martin Nowak  
(1965~)



E. O. Wilson  
(1929~)