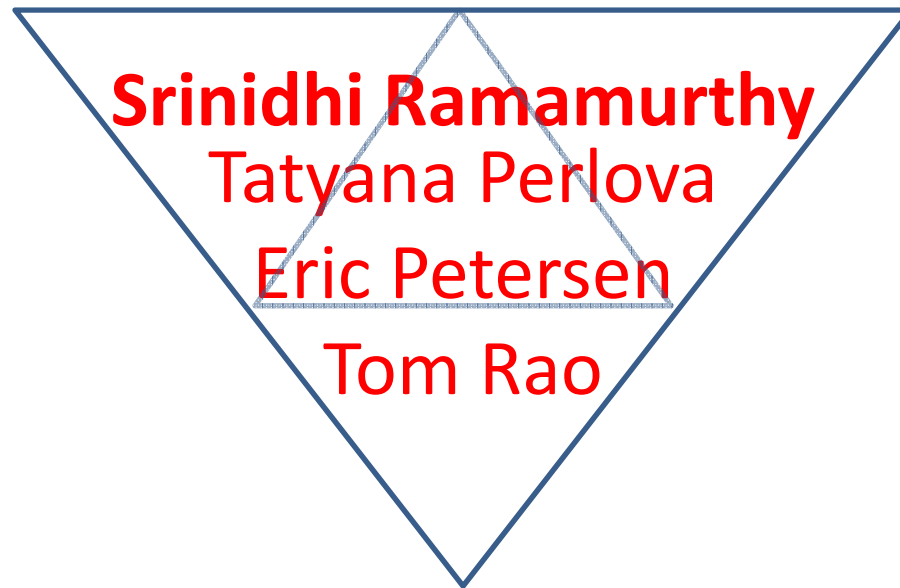


*Snowdrift game dynamics and facultative cheating in yeast*<sup>[1]</sup>

or

# To Steal or Not to Steal? That is the Question.



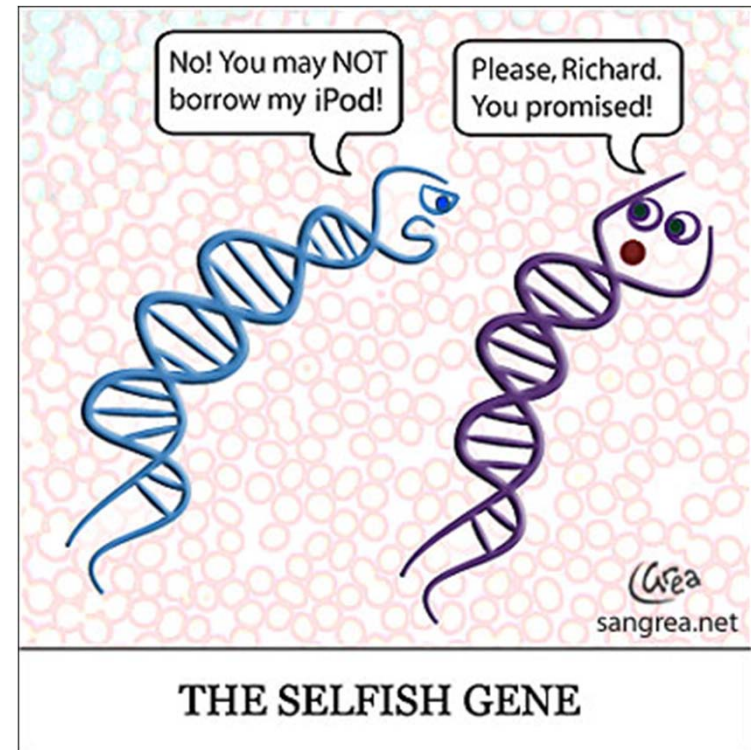
[1] Jeff Gore, Hyun Youk, Alexander van Oudenaarden,  
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yeast*. Nature. Vol. 459. May 2009. p253-256

# Outline

- Motivation. Selfish gene concept
- Game theory
- Biological background. Scheme of experiment
- Results
- Critique and citation report
- Conclusions

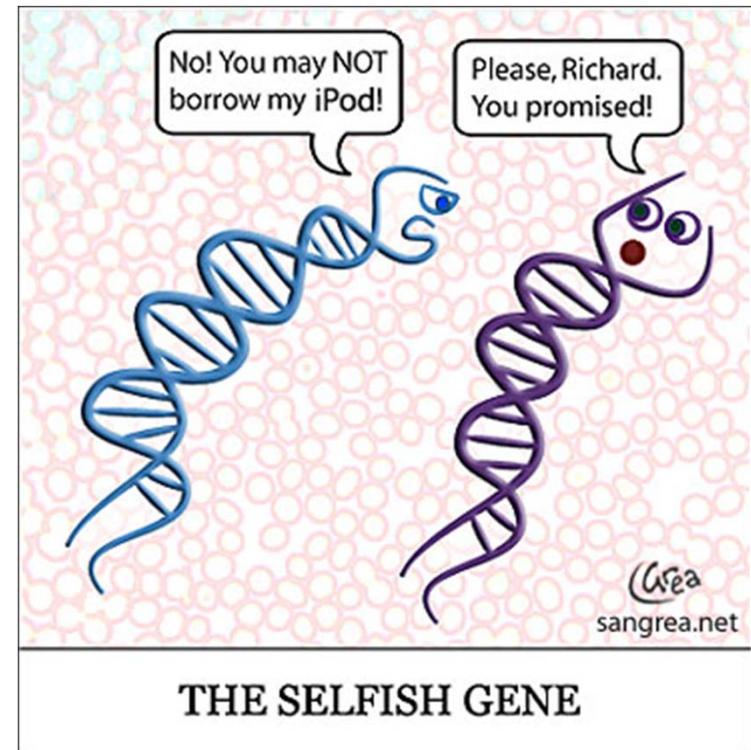
# Selfish Gene

- Natural selection— a fight to the death.
- Can the “selfish gene” lead to cooperation?



# Selfish Gene

- Natural selection— a fight to the death.
- Can the “selfish gene” lead to cooperation?
- Survival is not a zero-sum game.



# Why Yeast?

- Humans and animals – too complex



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- Simple “decisions” by yeast *genes*



# Why Yeast?

- Humans and animals – too complex
  - Simple “decisions” by yeast *genes*
- ↓
- More easily interpreted results!



# Game Theory



# Game Theory Rules

- 2 Players.

# Game Theory Rules

- 2 Players.
- Each decides to “cooperate” or “defect”.

# Game Theory Rules

- 2 Players.
- Each decides to “cooperate” or “defect”.
- Each is rewarded according to both decisions.

# Game Theory Rules



- Both players get large payoff.

# Game Theory Rules



- Both players get large payoff.



- Player **A** gets larger payoff than player **B**.

# Game Theory Rules



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# Mutual Beneficence

- First of three types of games.




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- First of three types of games.
- Each player benefits from any cooperation.



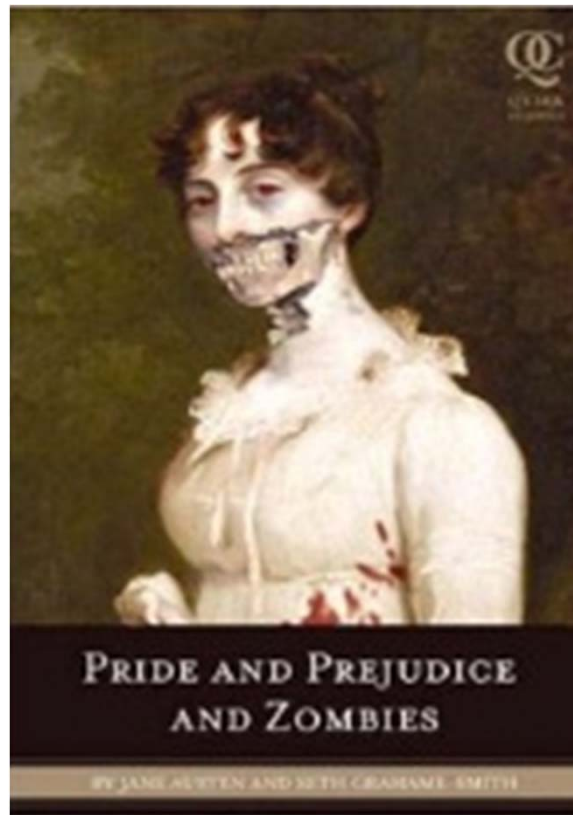
# Mutual Beneficence

- First of three types of games.
- Each player benefits from any cooperation.

	A "Co-op."	A "Defects"
B "Co-op."		
B "Defects"		

# Mutual Beneficence




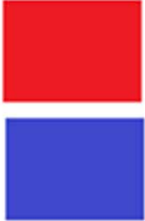
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<<http://www.zombiecommand.com/page/113/>>




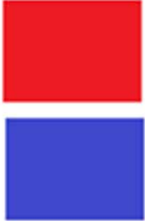
# Prisoners' Dilemma

- Best global outcome with both players cooperating.

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<[http://www.itsallaboutlappy.com/news1\\_07.htm](http://www.itsallaboutlappy.com/news1_07.htm)>




# Snowdrift Game (Chicken)

- Cooperation is beneficial, but costly.

	A "Co-op."	A "Defects"
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# Snowdrift Game (Chicken)

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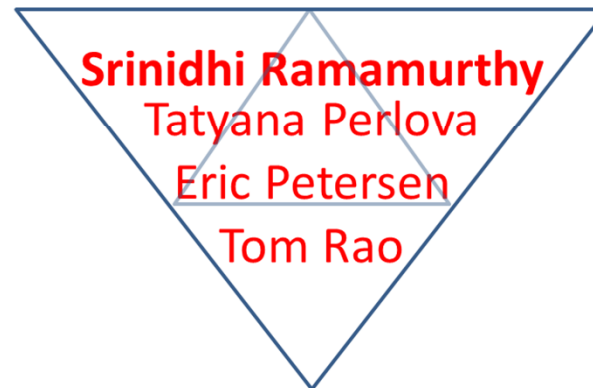
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Ramamurthy et. al. "Snowdrift Game Dynamics and Facultative Cheating in Yeast."  
Phys 596 Journal Club Presentation. 144 Loomis Lab of Physics, Urbana. 21 Oct. 2011.



# Biological Background


# Yeast as a model organism to study microbial cooperation



# Yeast

- Need Glucose

# Yeast

- Need Glucose
- Sucrose + Invertase  Glucose

# Yeast

- Need Glucose

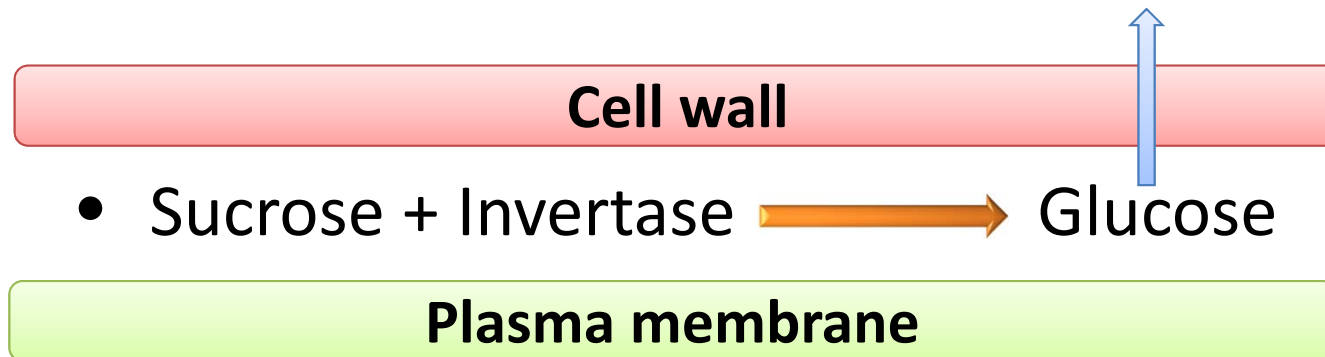
**Cell wall**

- Sucrose + Invertase  Glucose

**Plasma membrane**

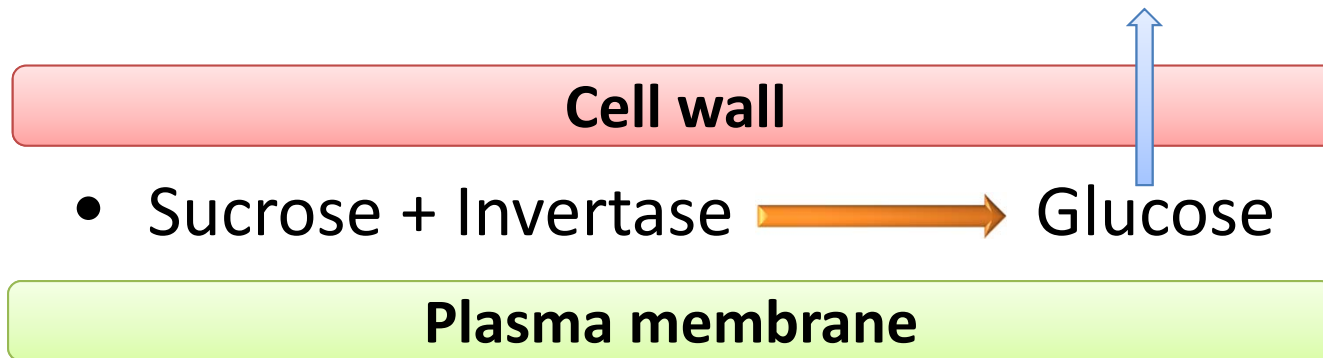
# Yeast

- Need Glucose



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- Sucrose + Invertase → Glucose

- **99% of created Glucose diffuses away**

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- Need Glucose
- Sucrose + Invertase  Glucose

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## **“Cheating”**

- Using Glucose produced by other cells  
*and*
- Not producing invertase

# Game

- Cooperation cost – invertase production
- Cooperation benefit – Glucose capture efficiency 1%



Constant parameters

# Can we vary cost of cooperation?

- Delete gene coding Histidine in the “Cooperator” strain

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- Decreasing [Histidine] will limit growth of “Cooperators”

# Can we vary cost of cooperation?

- Delete gene coding Histidine in the “Cooperator” strain



- Decreasing [Histidine] will limit growth of “Cooperators”



- Effective increase of cooperation cost

# “Cooperator” and “Cheater” Yeast strains

## “Cooperators”

- Produce Invertase
- Cannot produce Histidine
- Express YFP



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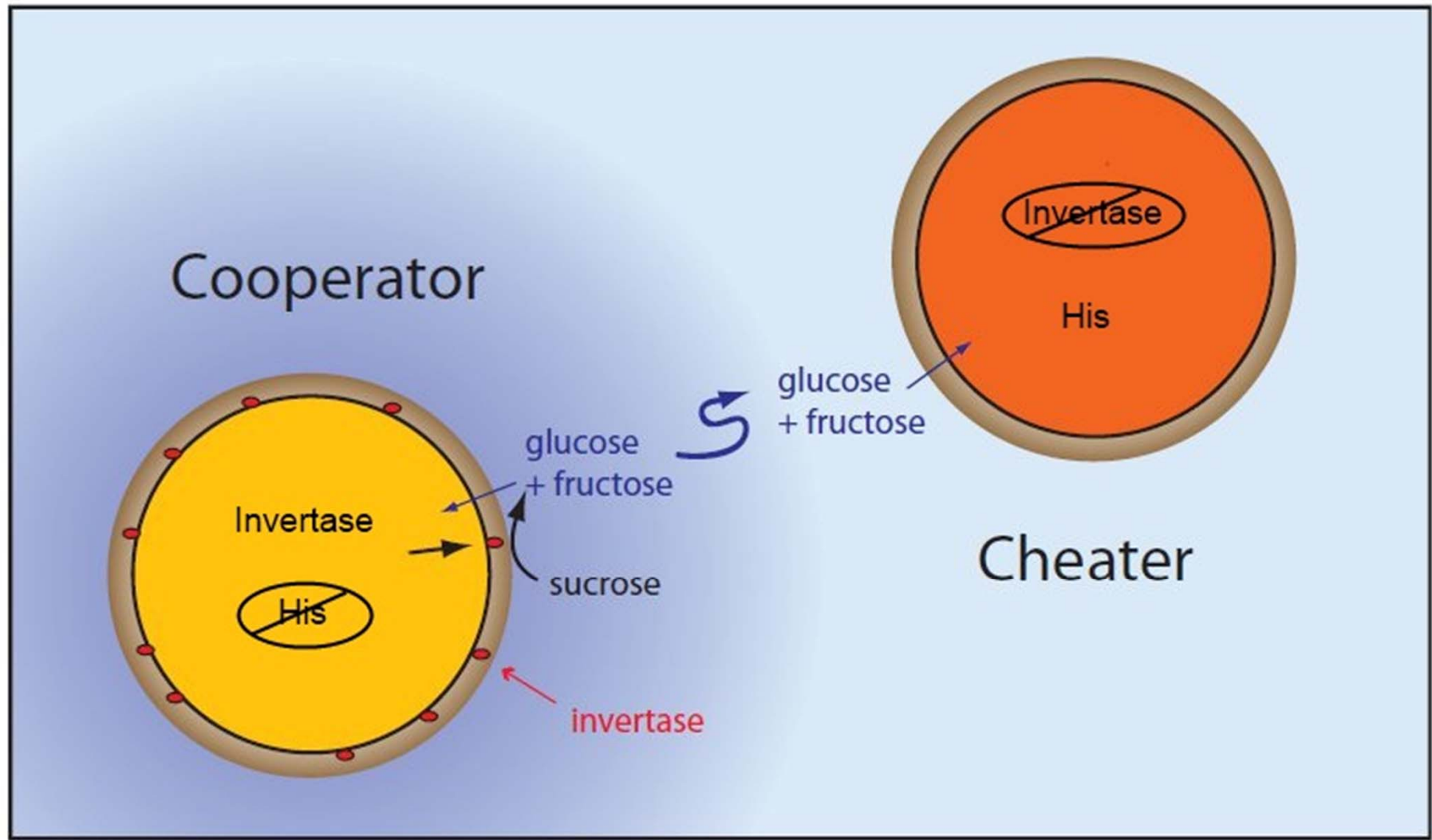


## “Cheaters”

- Do not produce Invertase
- Can produce Histidine
- Express Tdtomato



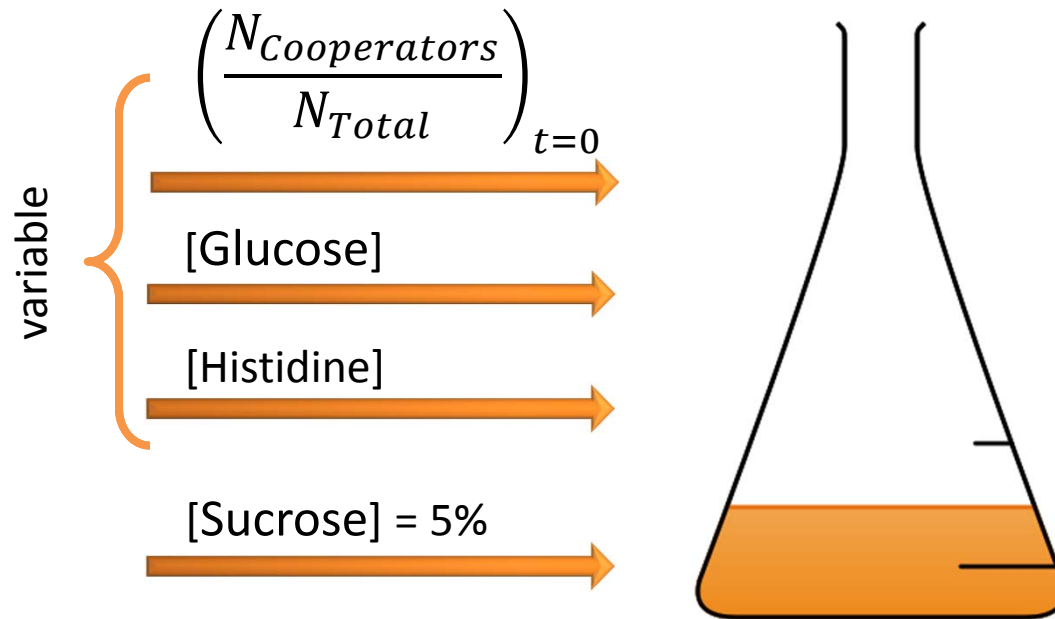
# “Cooperator” and “Cheater” Yeast strains



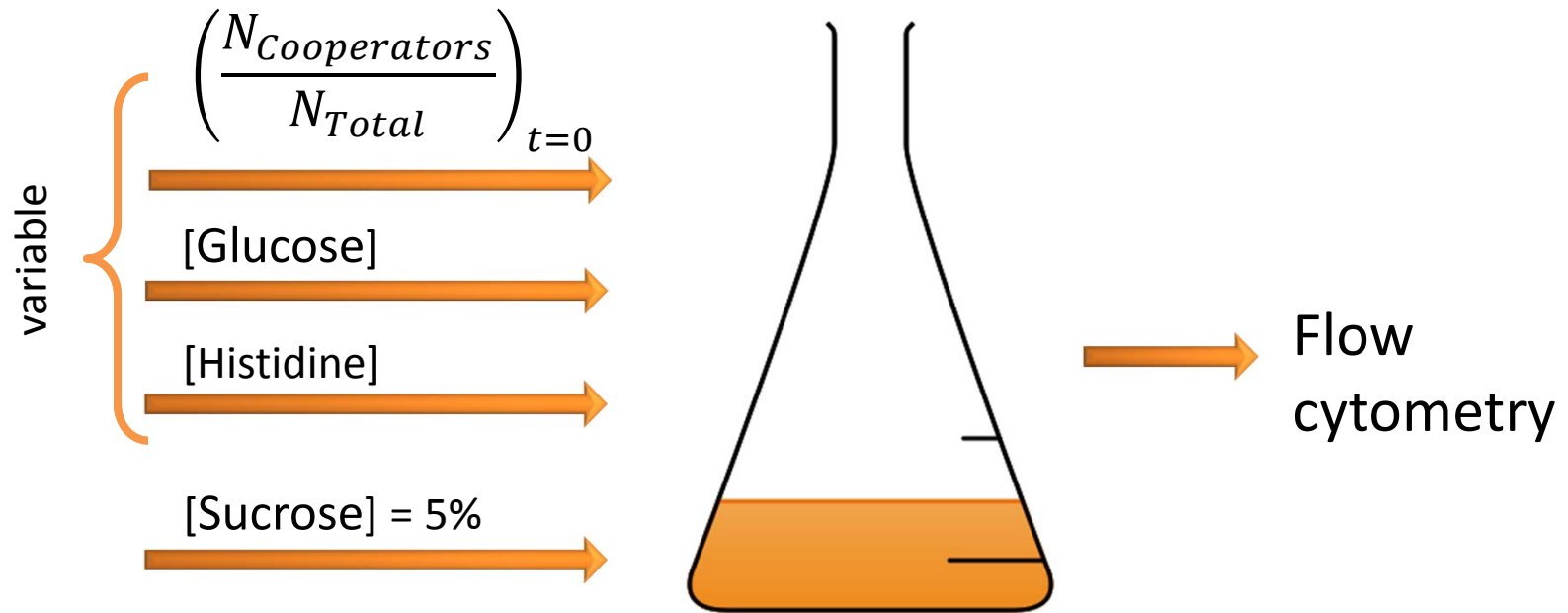
Adapted from J. Gore et al, Nature. Vol. 459. May 2009. p 253-256



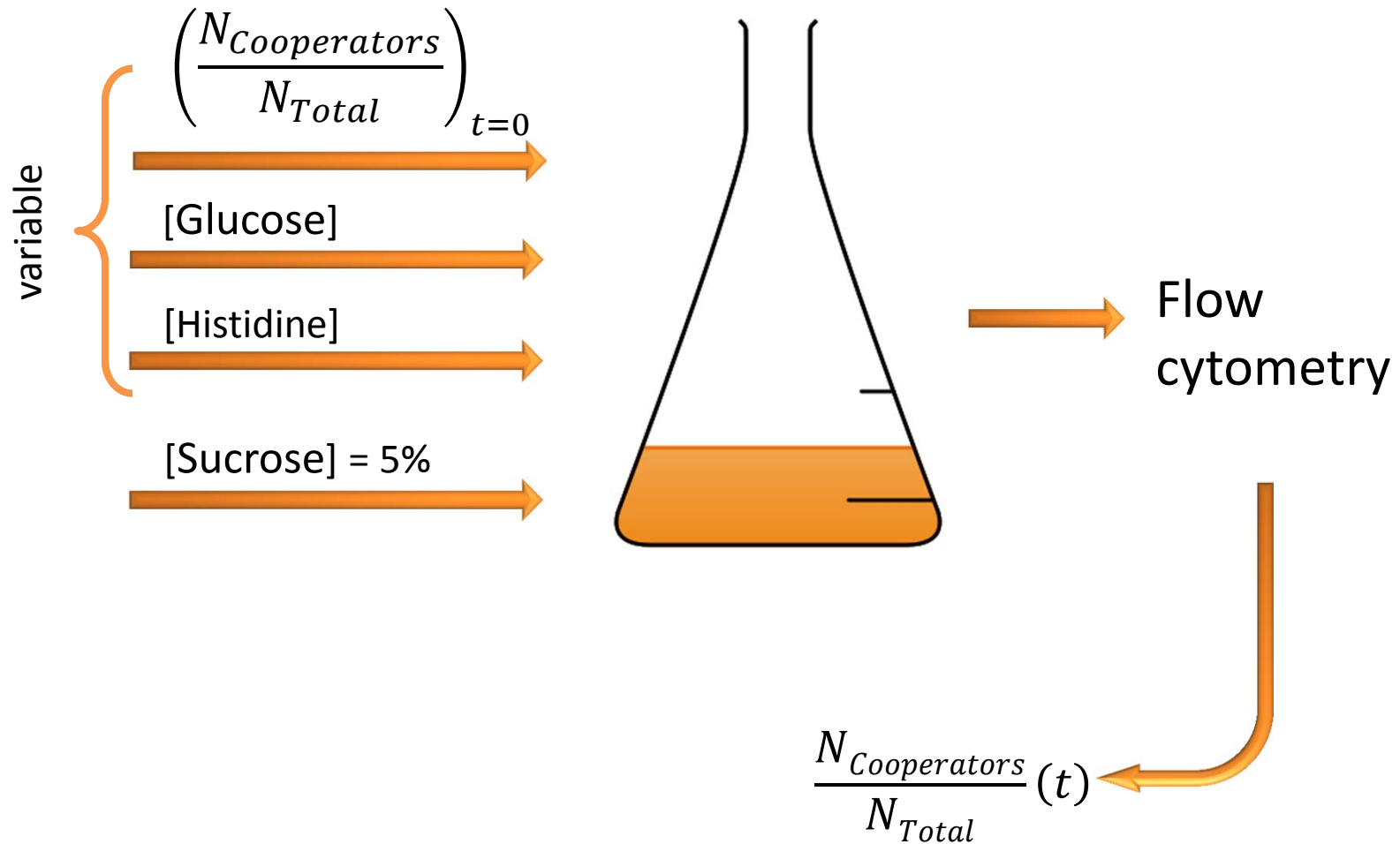
# Scheme of the experiment



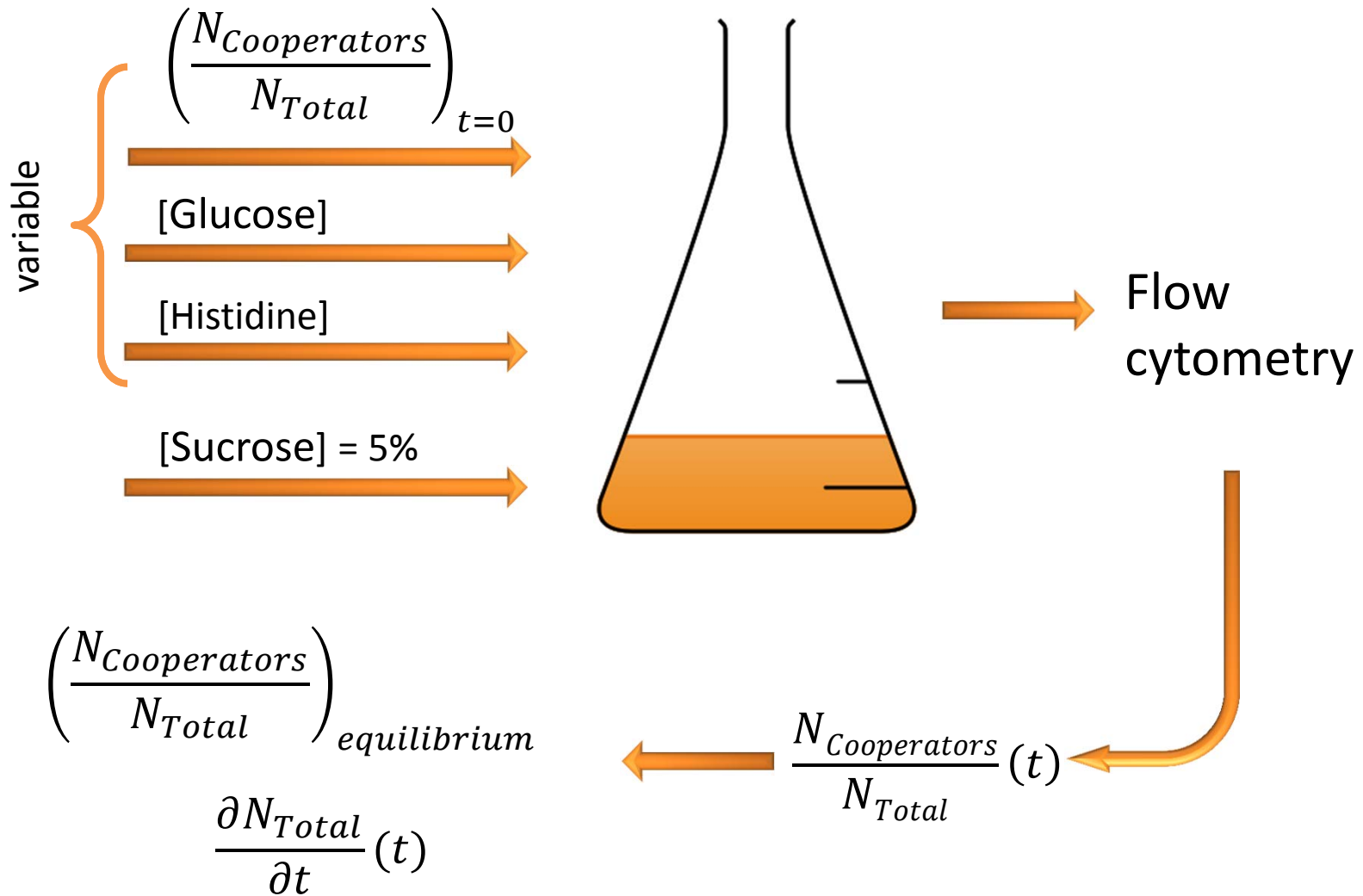
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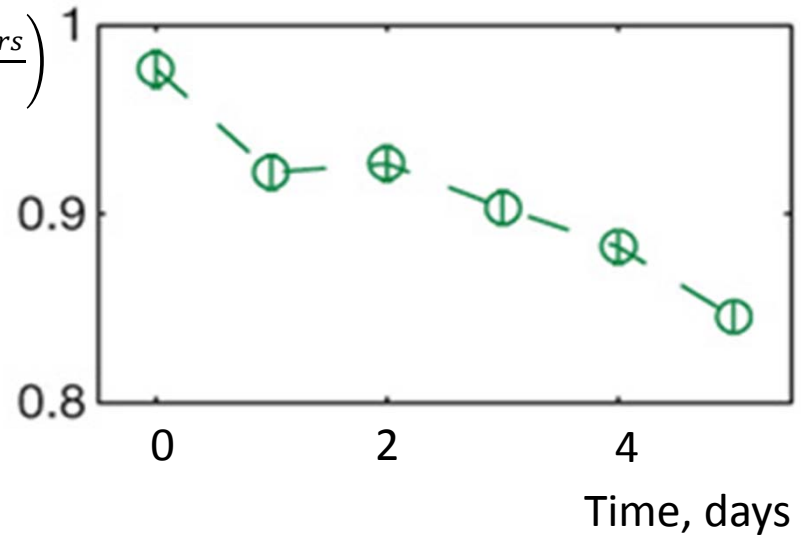
# Scheme of the experiment



# Results

# Uncommon Strategies Win!

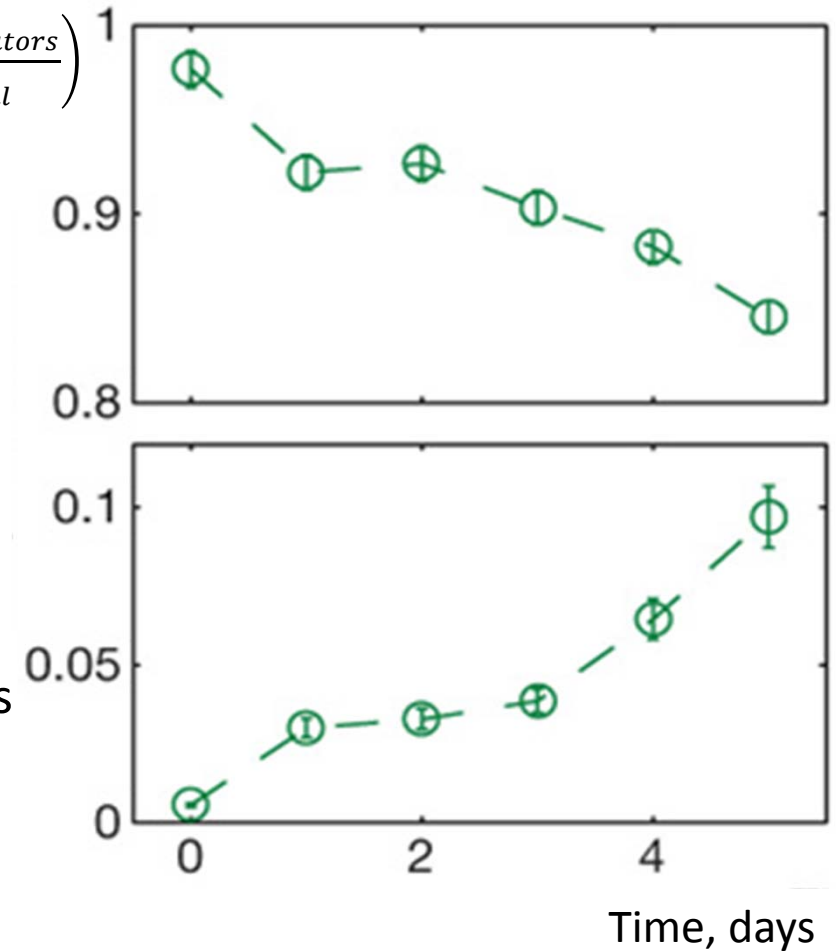
- Large  $\left(\frac{N_{Cooperators}}{N_{Total}}\right)_{t=0}$   increase in cheaters



# Uncommon Strategies Win!

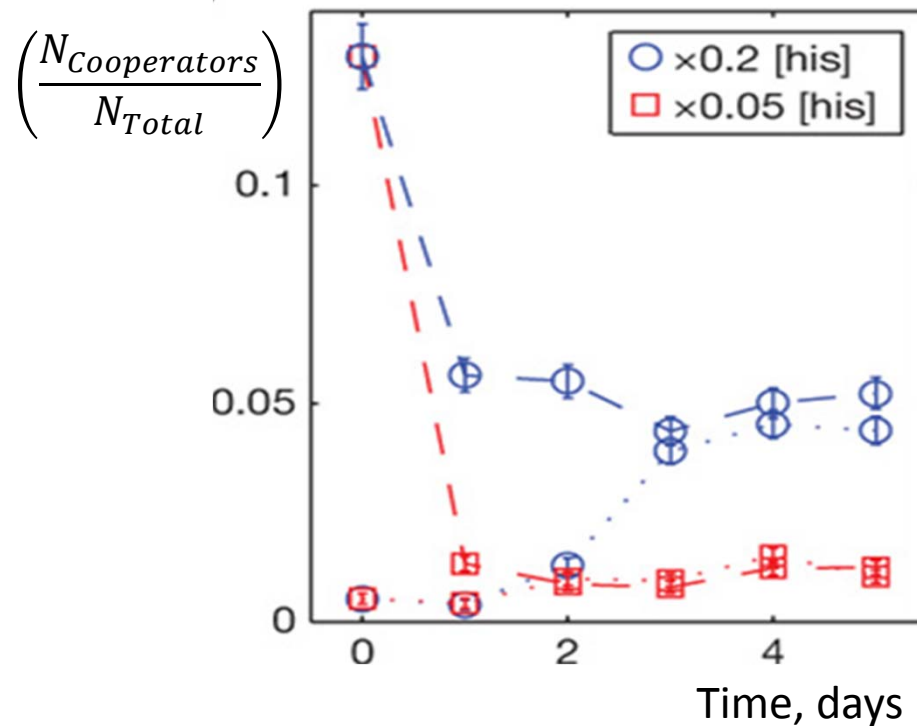
- Large  $\left(\frac{N_{Cooperators}}{N_{Total}}\right)_{t=0}$   $\rightarrow$  increase in cheaters

- Small  $\left(\frac{N_{Cooperators}}{N_{Total}}\right)_{t=0}$   $\rightarrow$  increase in cooperators



# It's a Snowdrift Game!

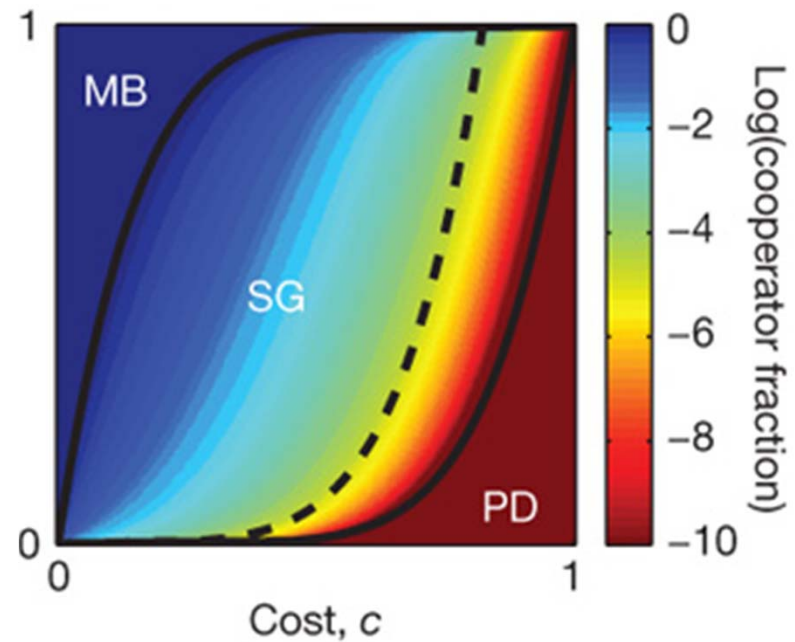
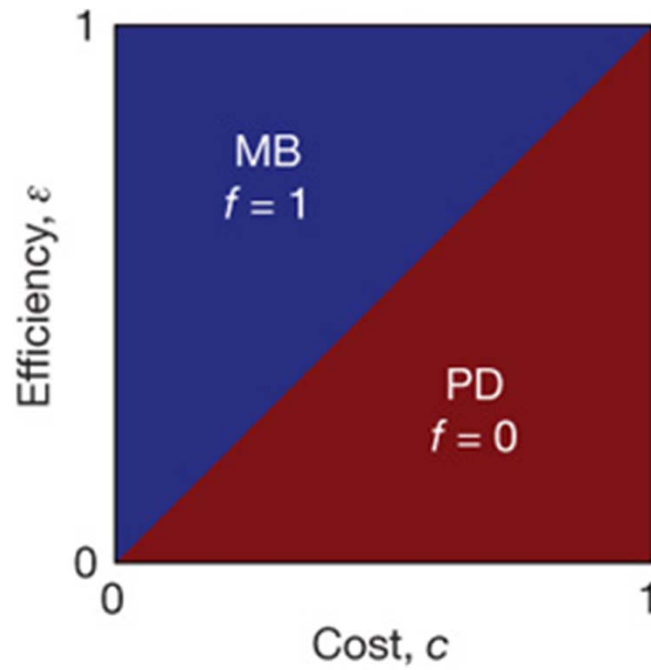
- Steady state is only dependent on [His] - cost of cooperation
- Existence of cooperation in steady state implies it's a snowdrift game





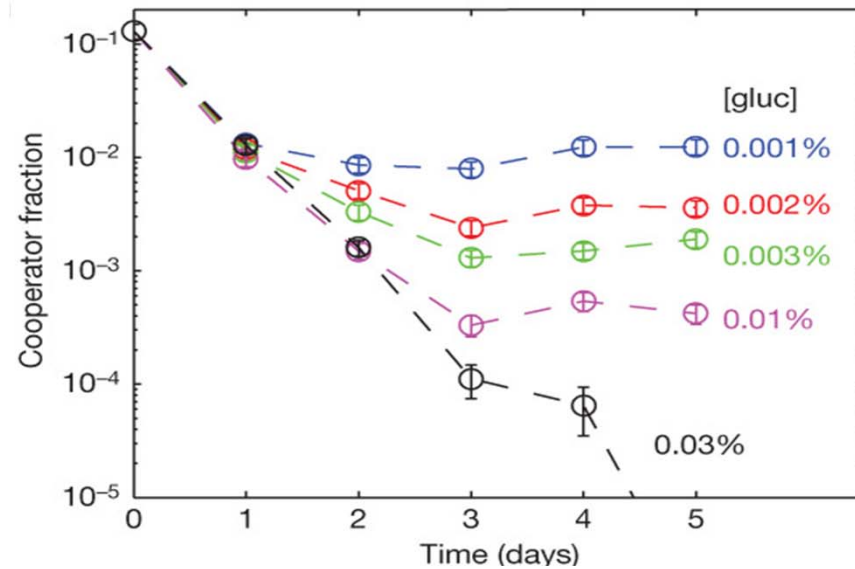
# Linear model doesn't work!

- A linear model  $\longrightarrow$  No snowdrift game.
- We need nonlinearity.



# More food less growth?

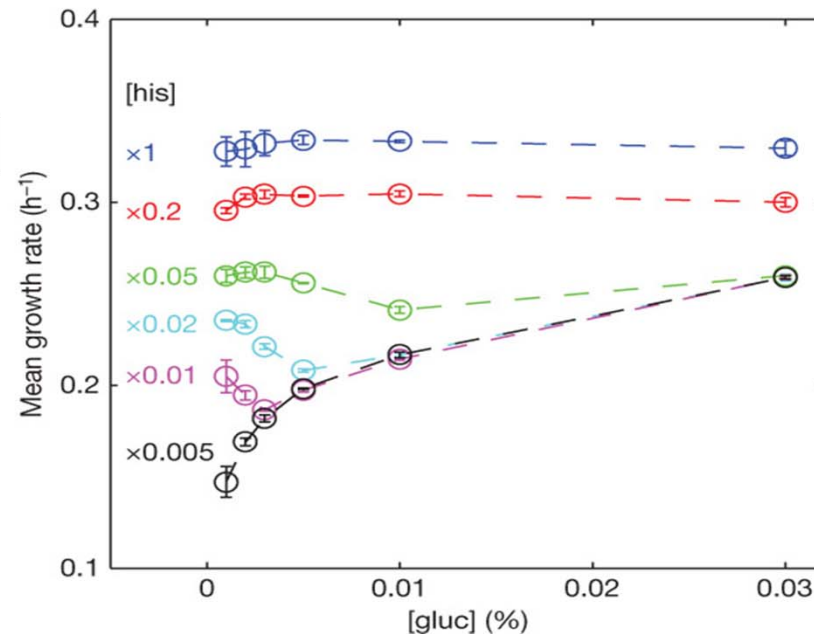
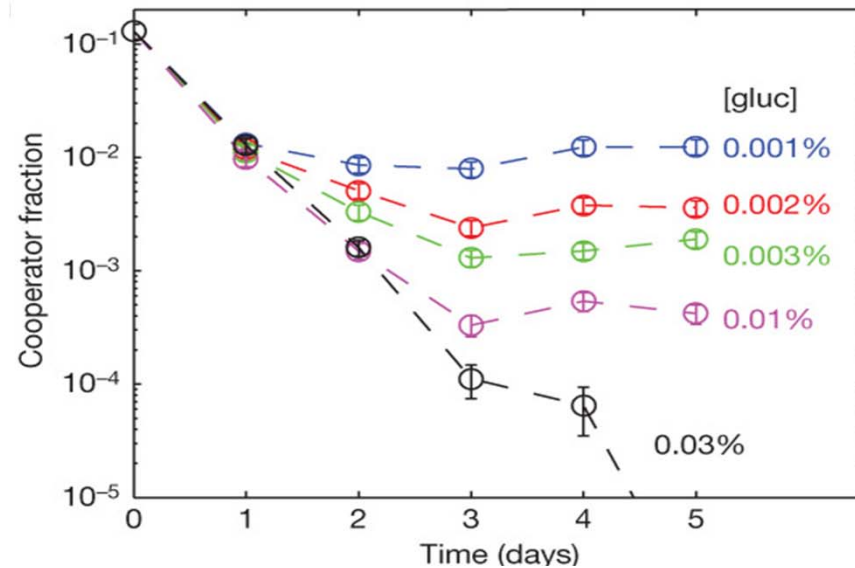
- Increasing [glucose] reduces cooperator fraction



[gluc] (%)

# More food less growth?

- Increasing [glucose] reduces cooperator fraction
- ↓
- Less growth as [glucose] is increased for large enough [histidine]

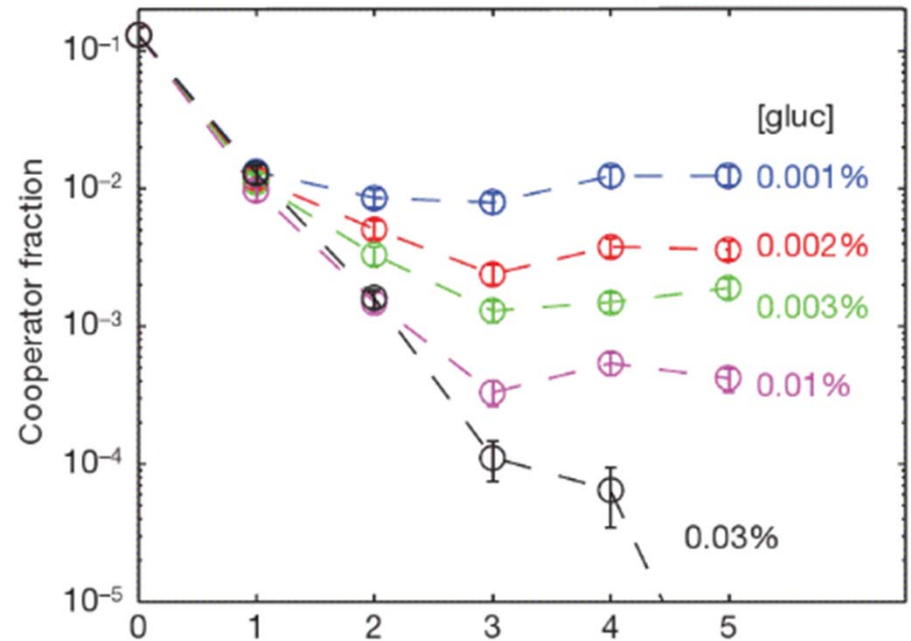


# Critique and Citation Report

# (Minor) Scientific Deficiencies

Fig. 3.a.

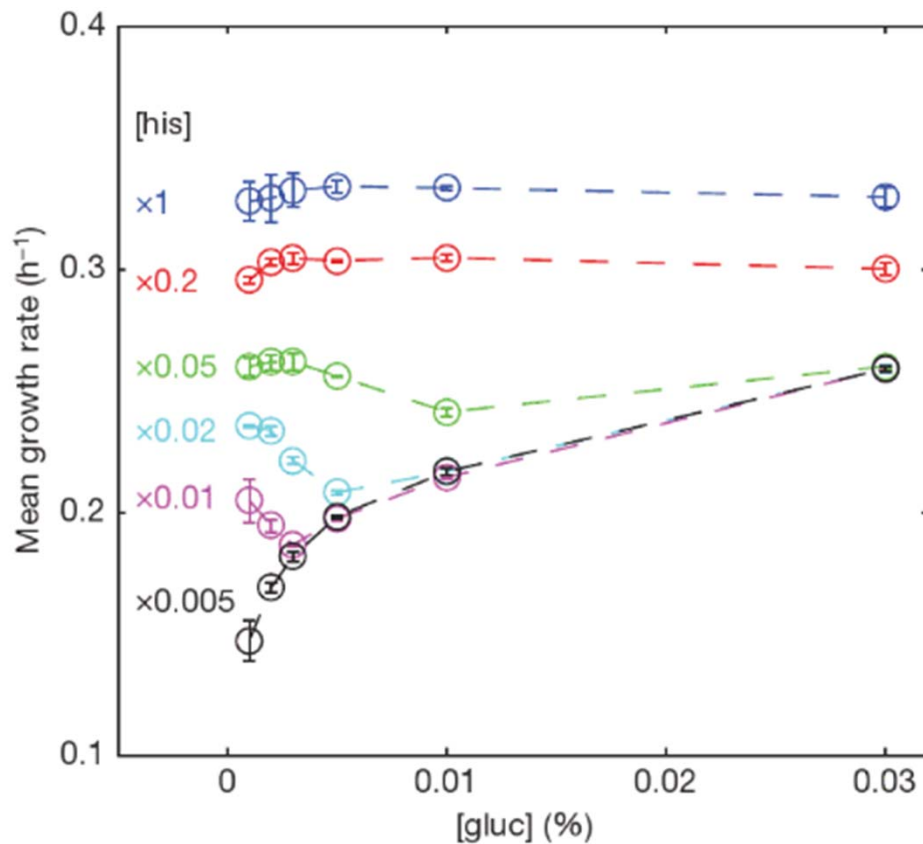
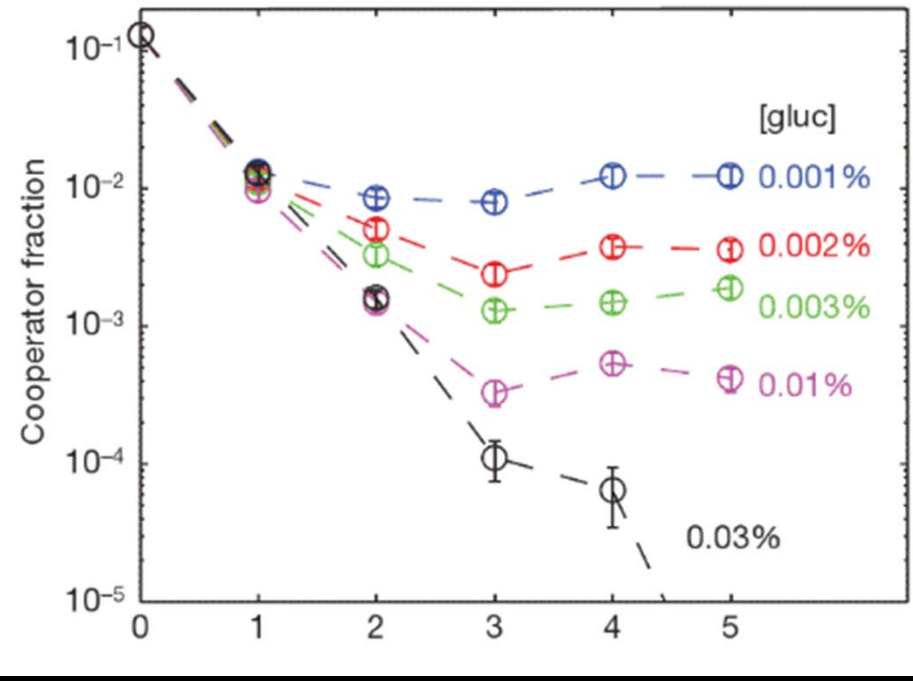
Error bars only significant at  $\sim 1\sigma$   
No Quantitative Statistics



# (Minor) Scientific Deficiencies

Fig. 3.a.

Error bars only significant at  $\sim 1\sigma$   
No Quantitative Statistics



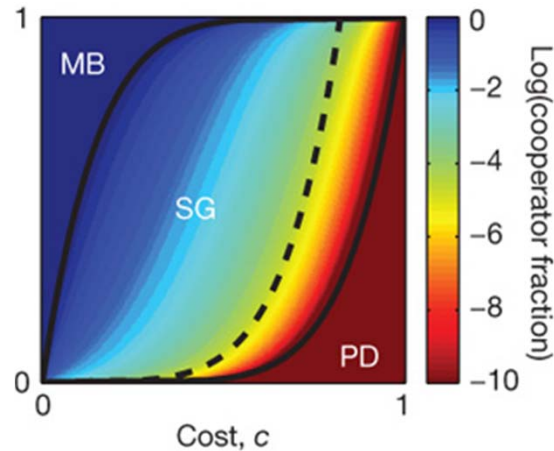
Gap in data

No Quantitative Statistics

Fig. 3.c

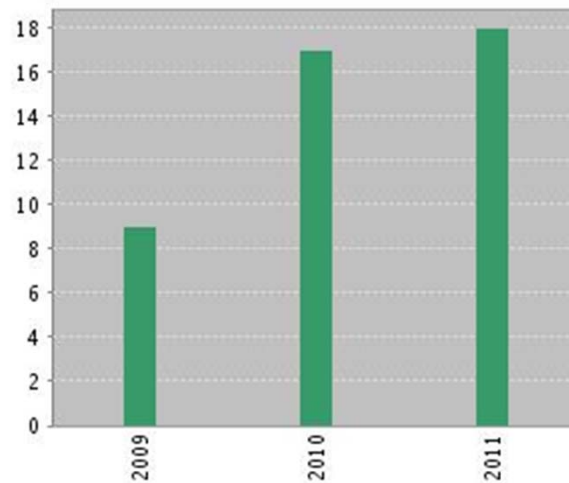
# Critique

- Clear explanation of fitted model not presented.
- Different data points could've been distinguished better.
- MB and PD are not demonstrated.



# Citation report

Paper was cited 44 times since its publication in 2009





# Positive Impact

OPEN ACCESS Freely available online

PLOS BIOLOGY

## Sucrose Utilization in Budding Yeast as a Model for the Origin of Undifferentiated Multicellularity

John H. Koschwanez<sup>1,2\*</sup>, Kevin R. Foster<sup>1,3,4</sup>, Andrew W. Murray<sup>1,2</sup>

**1** FAS Center for Systems Biology, Harvard University, Cambridge, Massachusetts, United States of America, **2** Department of Molecular and Cellular Biology, Harvard University, Cambridge, Massachusetts, United States of America, **3** Department of Zoology, University of Oxford, Oxford, United Kingdom, **4** Oxford Center for Integrative Systems Biology, University of Oxford, Oxford, United Kingdom

### Abstract

We use the budding yeast, *Saccharomyces cerevisiae*, to investigate one model for the initial emergence of multicellularity: the formation of multicellular aggregates as a result of incomplete cell separation. We combine simulations with experiments to show how the use of secreted public goods favors the formation of multicellular aggregates. Yeast cells can cooperate by secreting invertase, an enzyme that digests sucrose into monosaccharides, and many wild isolates are multicellular because cell walls remain attached to each other after the cells divide. We manipulate invertase secretion and cell attachment, and show that multicellular clumps have two advantages over single cells: they grow under conditions where single cells cannot and they compete better against cheaters, cells that do not make invertase. We propose that the prior use of public goods led to selection for the incomplete cell separation that first produced multicellularity.

# Conclusions

- Clear example of snowdrift game in coexistence of both strains.
- Both strategies survive.
- Hint towards Multicellularity?

# Questions





# **The Eh-Team**

# Game Type Comparison

Mutual Beneficence:

$$C > W > L > D$$

Prisoner's Dilemma:

$$C > W > D > L$$

Snow Drift:

$$W > C > L > D$$

	A "Co-op."	A "Defects"
B "Co-op."	(C,C)	(W,L)
B "Defects"	(L,W)	(D,D)

## Backup slide #1

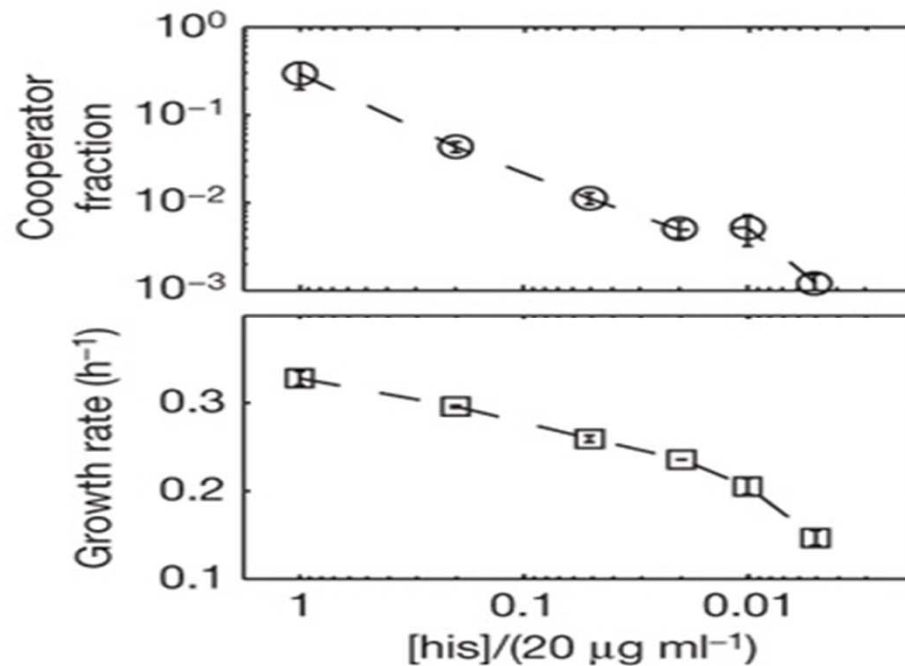
# Yeast as a model organism to study microbial cooperation

- Simplest eucaryote
- Short generation time – 1.25-2 h
- Easy to culture
- Well studied – genome is sequenced
- Developed genetic techniques

# Histidine, Cooperation, and Growth rate



- Less histidine => less cooperation (more cheaters)
- Less histidine => slower growth rate



# Modeling the Game. Linear model

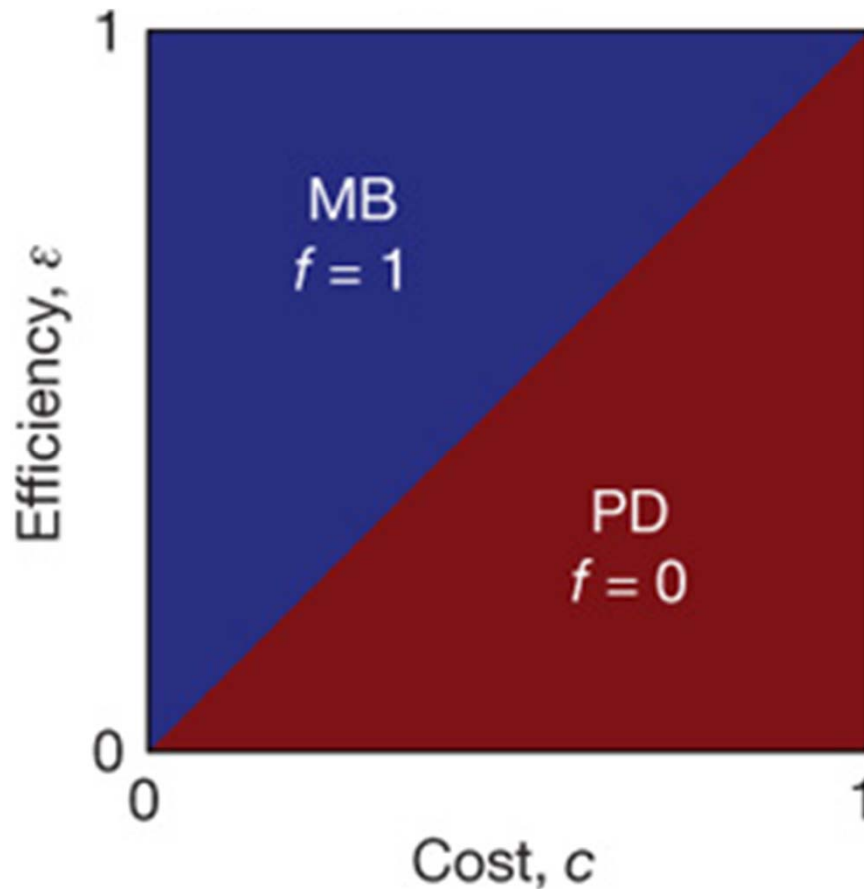
If  $P_D$  and  $P_C$  are linear with  $\varepsilon$  and  $c$ :

$$P_D = f(1 - \varepsilon)$$

$$P_C = \varepsilon + f(1 - \varepsilon) - c$$



No snowdrift  
game



$P_D$  - defector growth rate  
 $P_C$  - cooperator growth rate  
 $\varepsilon$  - glucose capture efficiency  
 $c$  - cooperation cost  
 $f$  - cooperator fraction



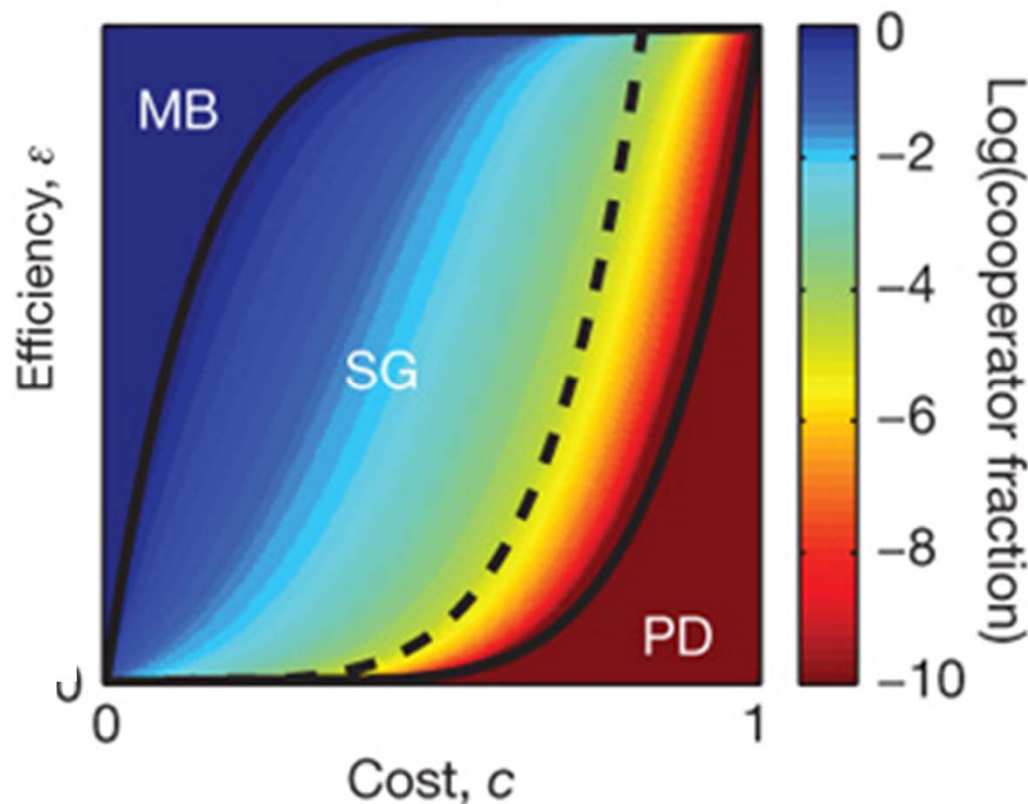
# Modeling the Game. Nonlinear model

If  $P_D$  and  $P_C$  are nonlinear with  $\varepsilon$  and  $c$ :

$$P_D = [f(1 - \varepsilon)]^\alpha$$

$$P_C = [\varepsilon + f(1 - \varepsilon)]^\alpha - c$$

→ Snowdrift game



$$\alpha \in [0.15, 0.1]$$

$P_D$  - defector growth rate

$P_C$  - cooperator growth rate

$\varepsilon$  - glucose capture efficiency

$c$  - cooperation cost

$f$  - cooperator fraction