CEPLAS
Cluster of Excellence on Plant Sciences

HEINRICH HEINE
UNIVERSITÄT DÜSSELDORF

Mathematical models of plant energy metabolism

Towards synthetic starch

Oliver Ebenhöh

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www.accliphot.eu

Bordeaux, 2.10.2015

Institute for Quantitative and Theoretical Biology

Internet: http://qtb.hhu.de

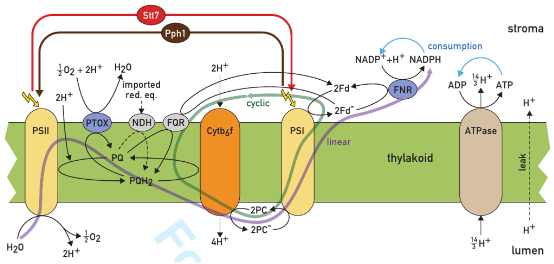
Public wiki: http://wiki.hhu.de/

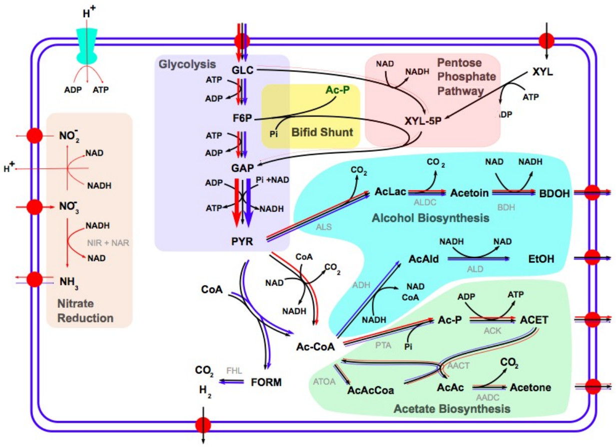
Software & Models: http://github.com/QTB-HHU

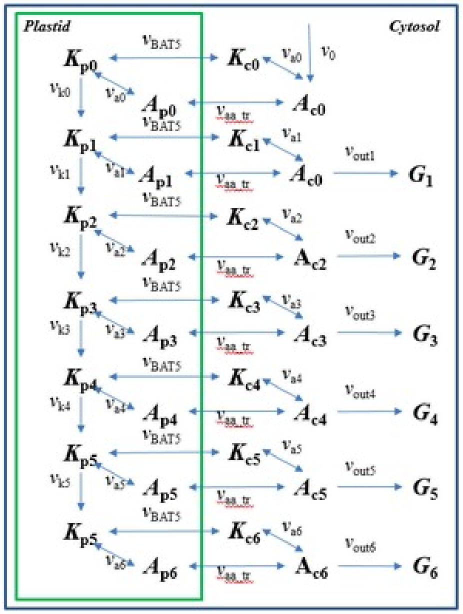
@qtbduesseldorf

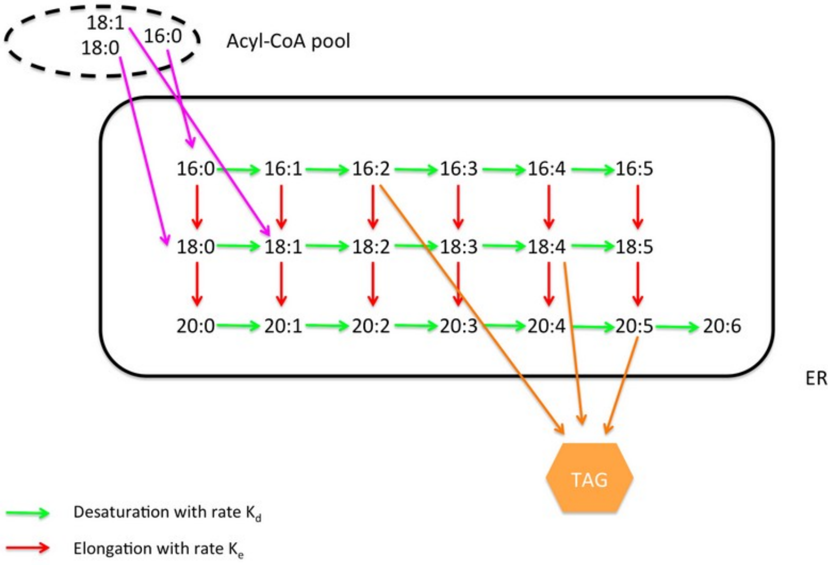
Ongoing research projects:

- Acclimation of Photosynthesis
- Starch metabolism
- Lipid production in microalgae
- Secondary metabolism in plants
- Plant/Algae-microbe interactions
- Evolution of metabolism
- Biotechnological applications









Why do we need mathematical models?

- Simplified representation of reality
- Reduction to the essentials

“Simplicity is the ultimate sophistication”

(Leonardo da Vinci)

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⇨ Models help to discover general principles!

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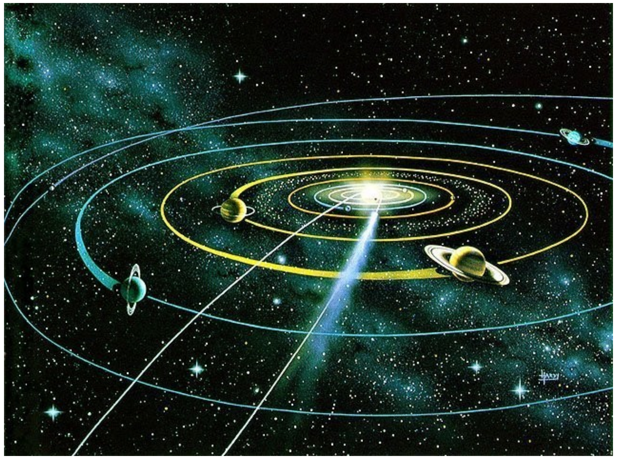
Example from physics:

$$\boxed{\vec{F} = m \cdot \vec{a}}$$

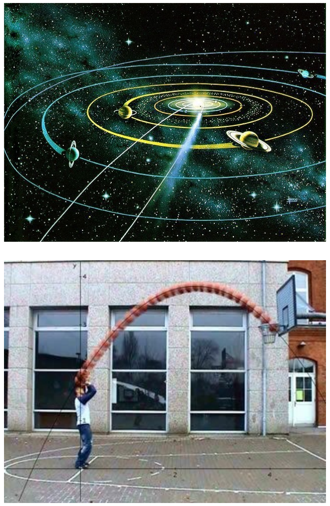


www.thehungryandfoolish.com

www.hh.schule.de

www.welt.de

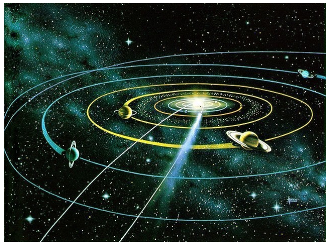
How does one find principles (theory building)?



???

$$\boxed{\vec{F}=m\cdot\vec{a}}$$

How does one find principles (theory building)?



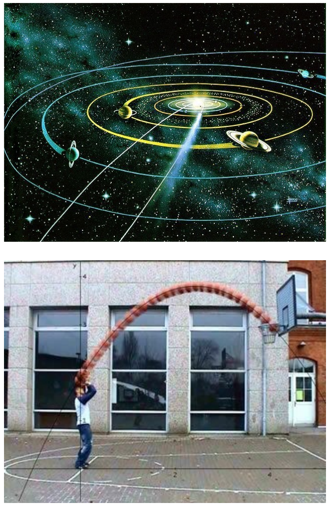
$$\boxed{\vec{F} = m \cdot \vec{a}}$$

???

Intuition

Every model is a small step on this path

How does one find principles (theory building)?



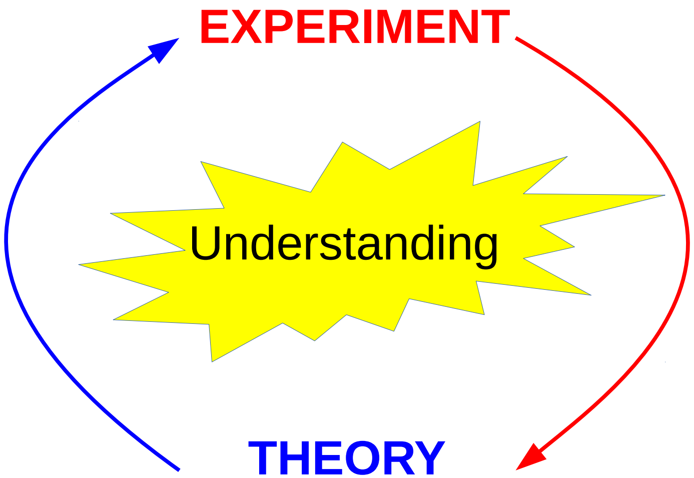
$$\boxed{\vec{F}=m\cdot\vec{a}}$$

Intuition

???

Every model is a small step on this path

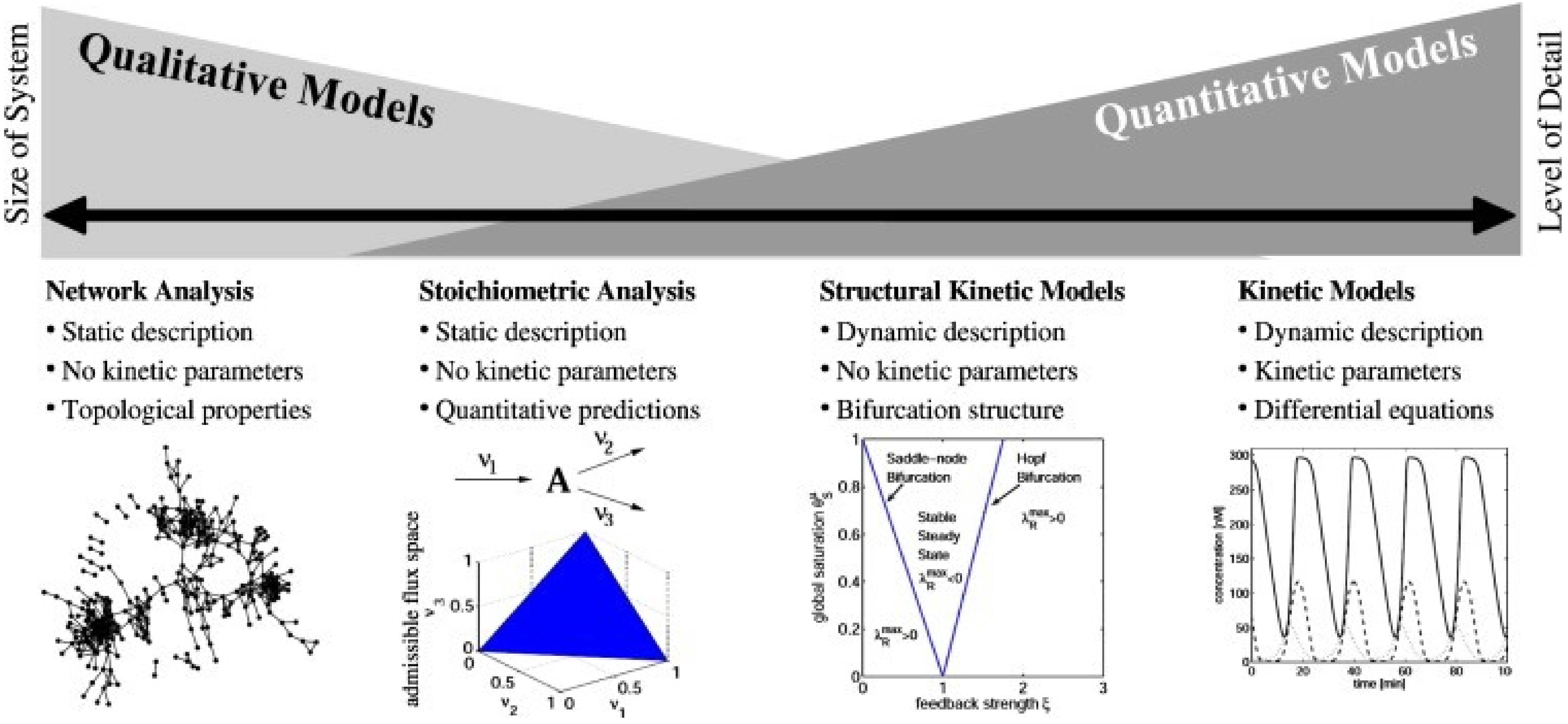
- Model predictions / new hypotheses
- Suggestions for new experiments
- Improvement of experimental design



- Initial model formulation
- Confirmation / falsification of predictions
- New model assumptions

The Systems biology principle

Modelling techniques - overview



Network Analysis
- Static description
- No kinetic parameters
- Topological properties

Stoichiometric Analysis
- Static description
- No kinetic parameters
- Quantitative predictions

Structural Kinetic Models
- Dynamic description
- No kinetic parameters
- Bifurcation structure

Kinetic Models
- Dynamic description
- Kinetic parameters
- Differential equations

(Steuer, 2007)

Starch – half of the calories in the human diet


1


2


3


7


8


4


5


6

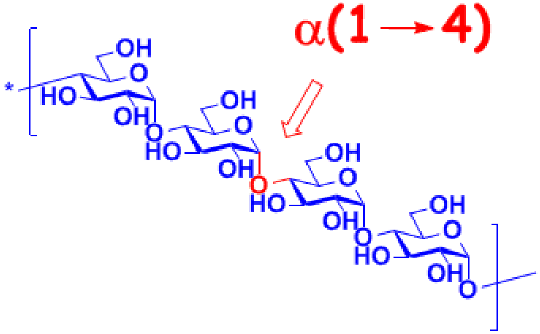
pictures from:

1 – cropsforthefuture.org / commons.wikimedia.org (Author: NusHub)
2 – nutr130.wikispaces.com
3 – nutr130.wikispaces.com
4 – newworldencyclopedia.org
5 – freefoodfotos.com
6 – commons.wikimedia.org (Author: KATORISI)
7 – mappingignorace.org (Sanjeev Gupta / EPA)
8 – commons.wikimedia.org (Author: P. Brundel)

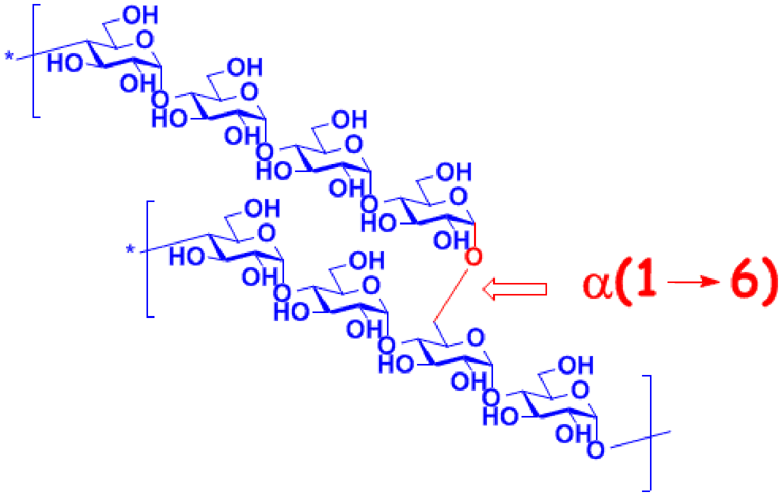
What is starch?

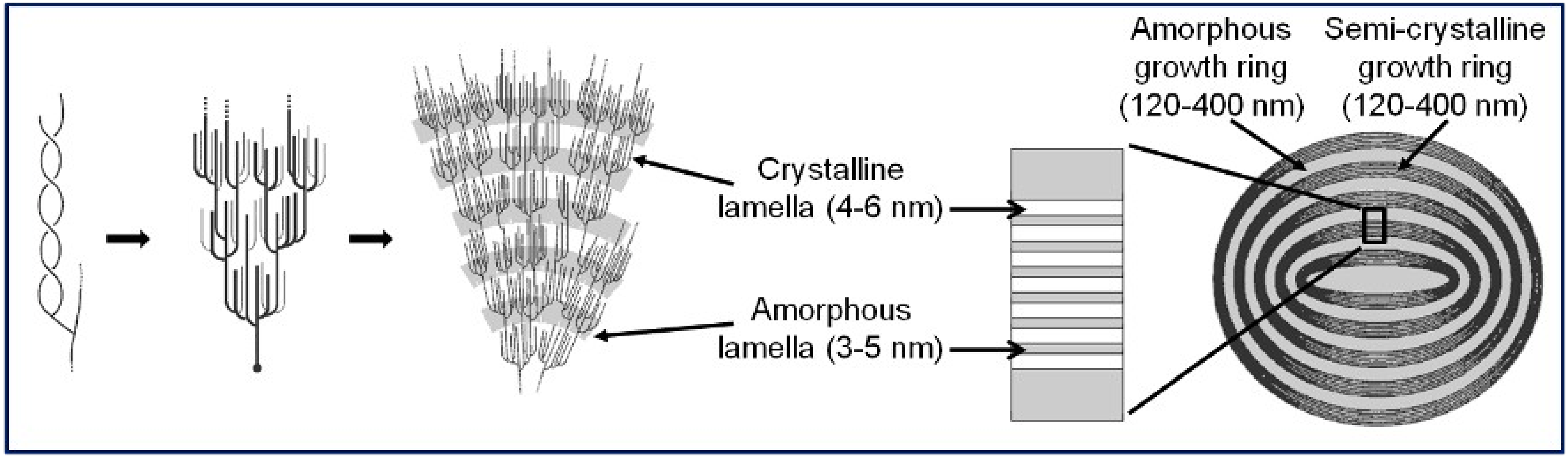
The structure of a starch granule

Amylose
(MW 32,000-113,000)

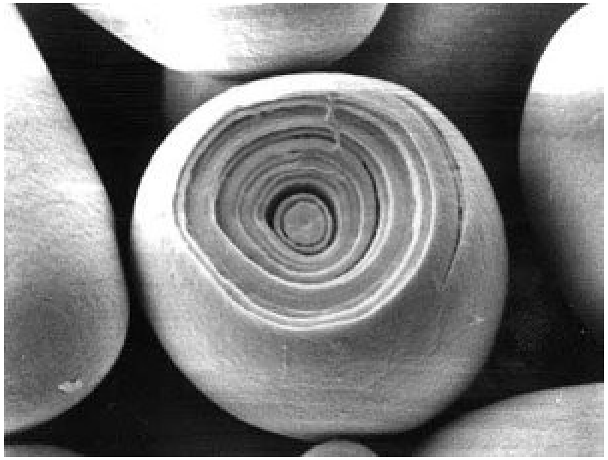


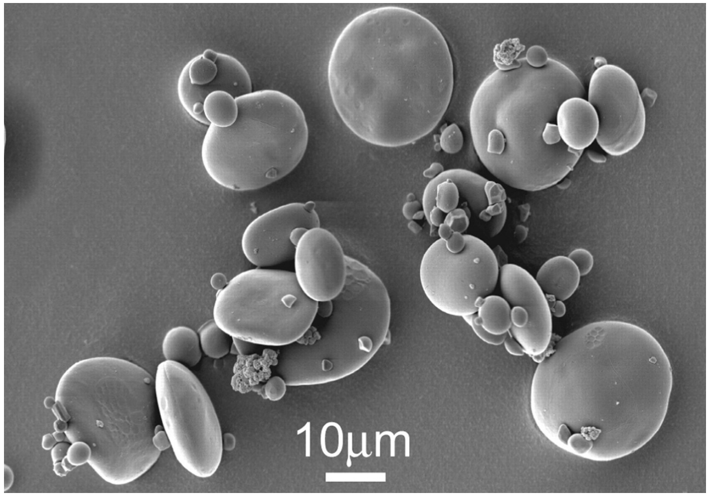
Amylopectin
(MW 10^7-10^9)

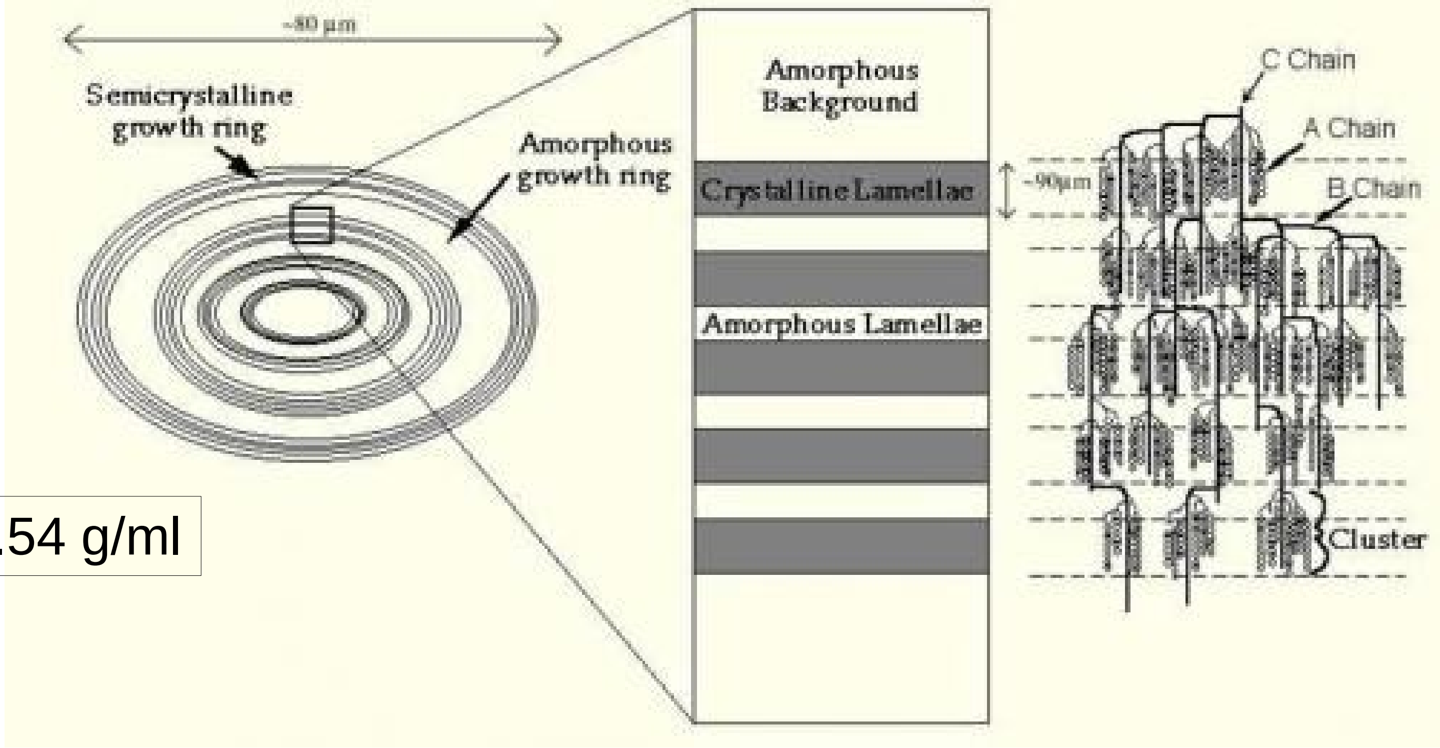




Why starch?







Density: 1.54 g/ml

The structure of starch allows for an extremely high energy storage density

Why starch?

Alternatives?

	energy content (kJ/g)
Carbohydrates	17
Lipids	38
Proteins	17
Alcohol	30

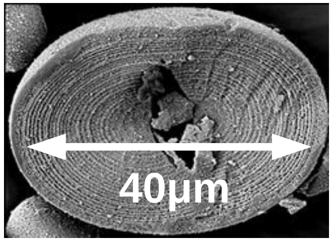
We (animals and fungi) predominantly use glycogen

big molecule (up to 10 MDa)

Possible advantages of starch

- low osmolarity
- large size
- high density

still small compared to starch



$3\cdot10^{10}$ Da!!!

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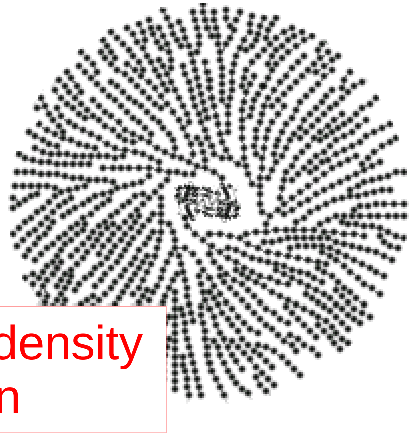

trade-off between storage density
and rapid mobilization

big molecule (up to 10 MDa)

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- low osmolarity
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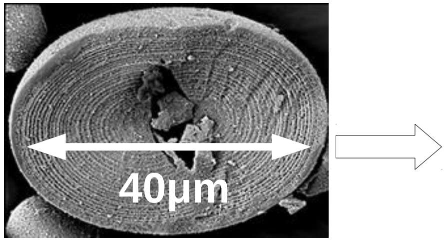
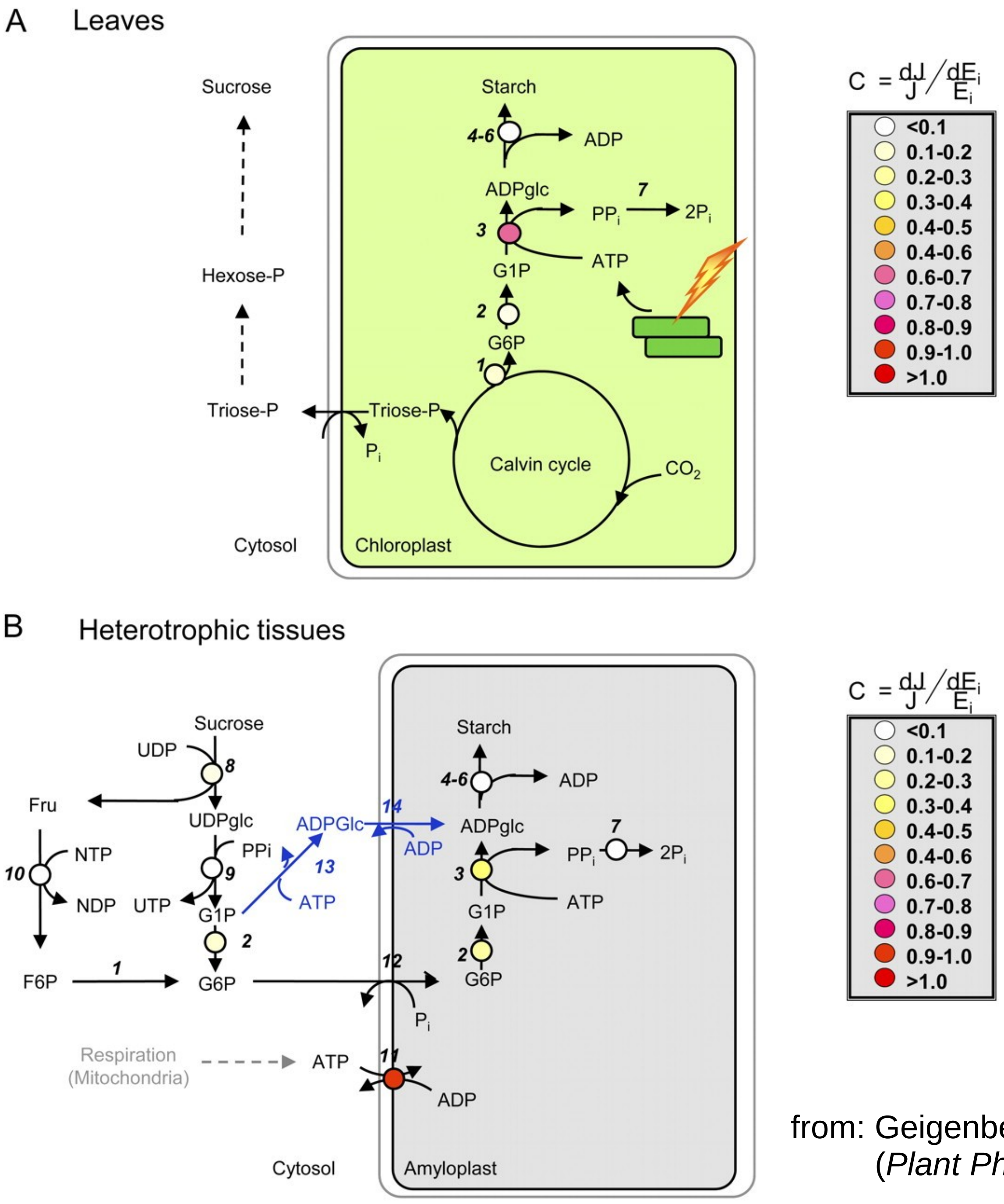


$3 \cdot 10^{10}$ Da!!!

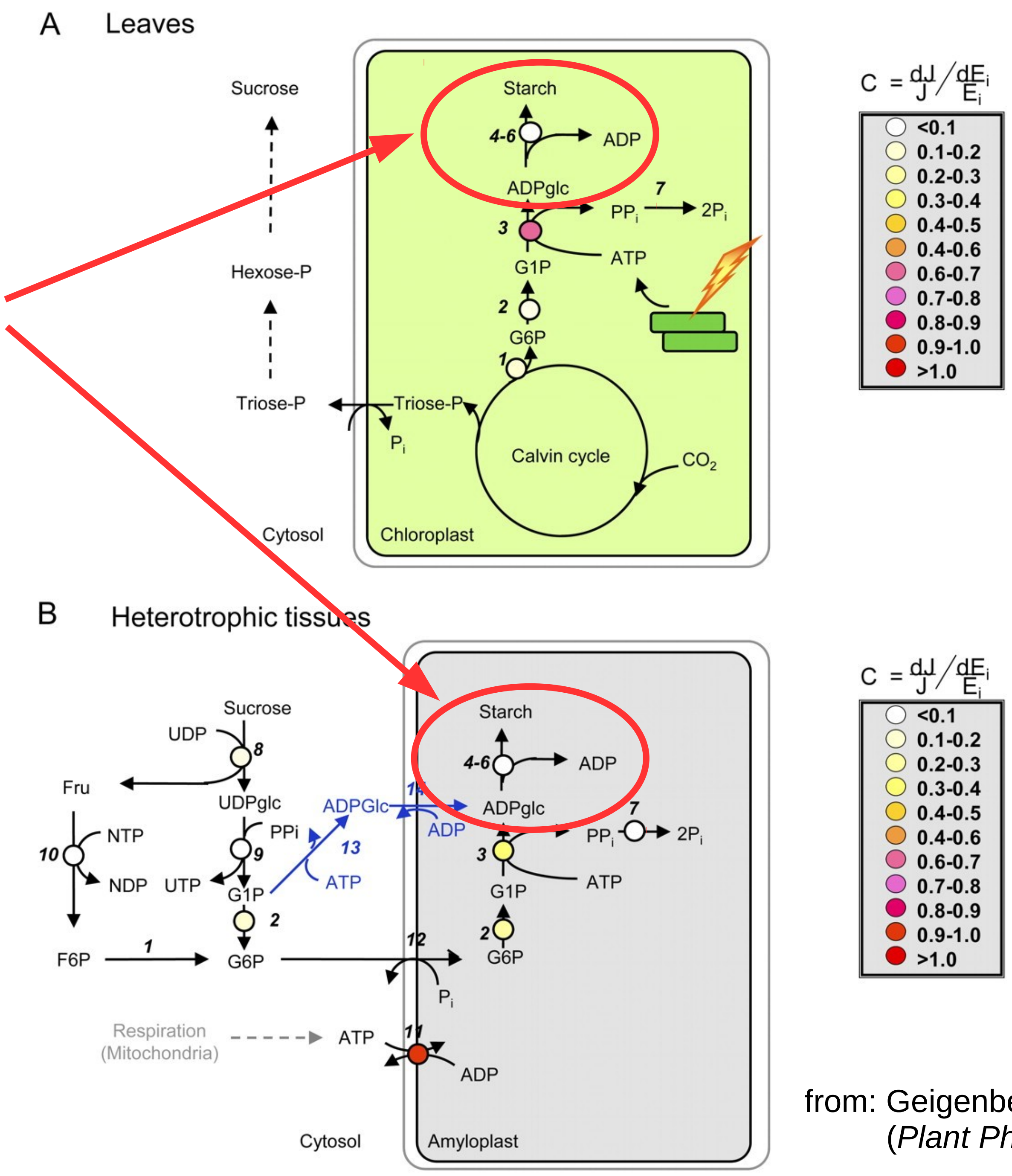
optimised for storage density,
slower deployment

How is starch made?



from: Geigenberger 2011
(*Plant Phys*)

How is starch made?



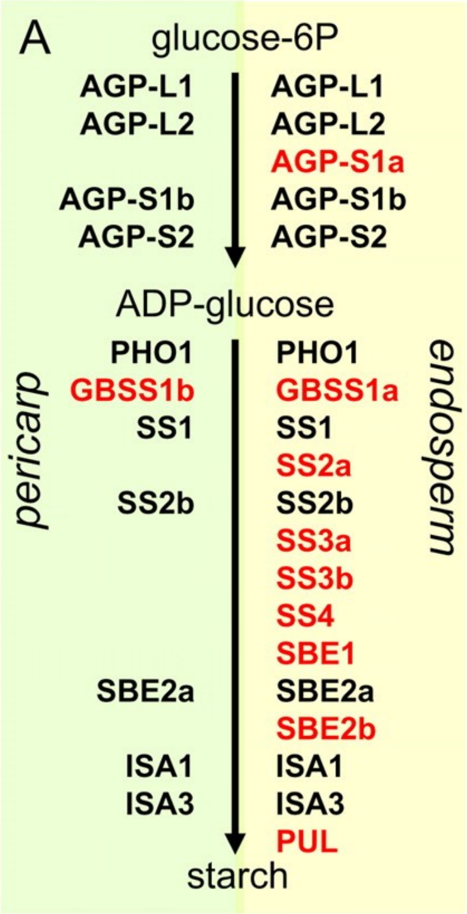
What's behind these?

from: Geigenberger 2011 (*Plant Phys*)

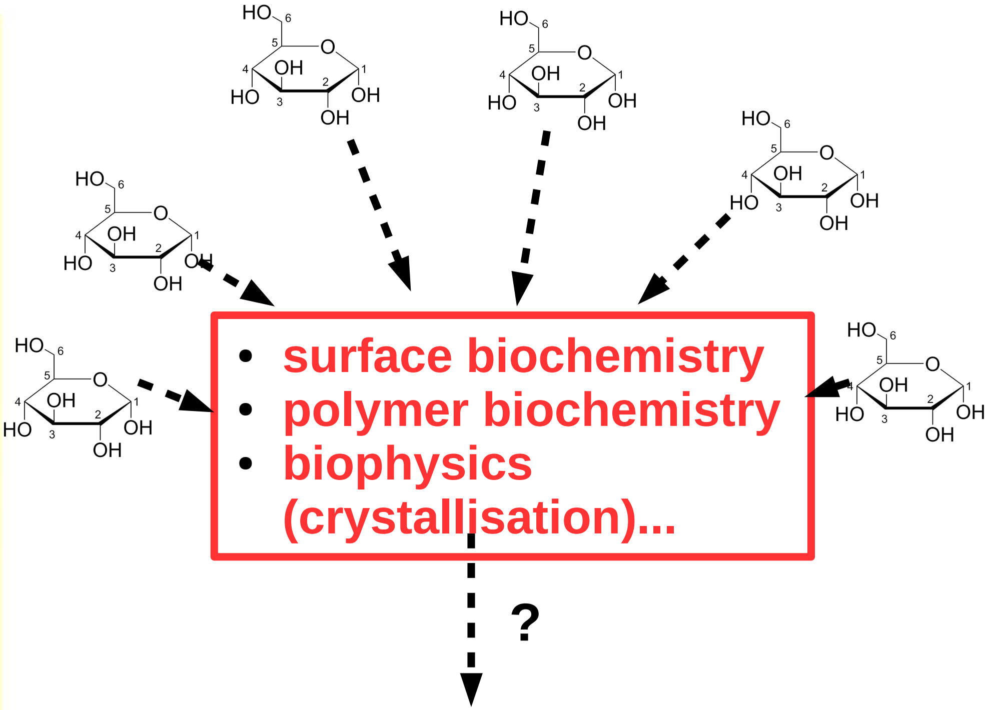
How is starch made?

Many different processes play together!

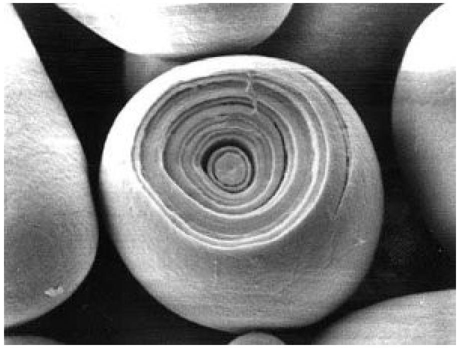
- starch synthases
- branching enzymes
- phosphorylases
- isoamylases



(Radchuk et al, 2009)



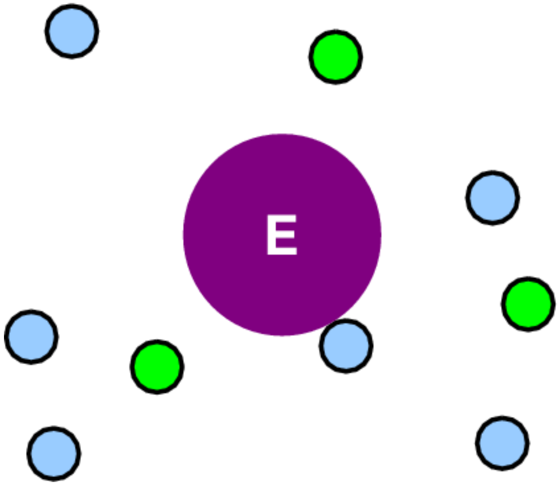
- surface biochemistry
- polymer biochemistry
- biophysics (crystallisation)...



1. Surface-active enzymes

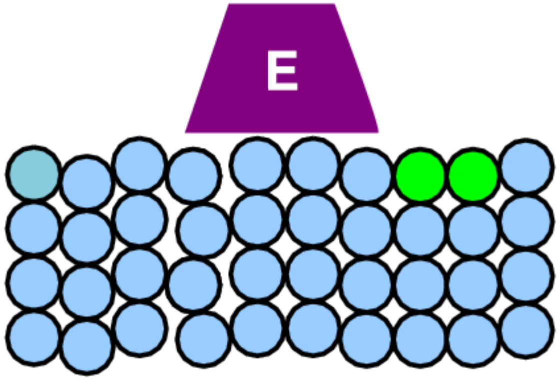
Rate laws for surfactive enzymes

dissolved substrate



$$v=\frac{V_{\max}S}{K_M+S}$$

aggregated substrate
(with interfacial reaction space)



$$v=f(?)$$

Rate laws for surfactive enzymes

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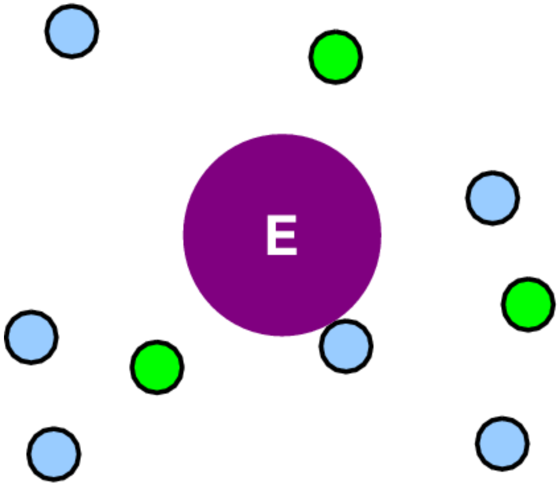

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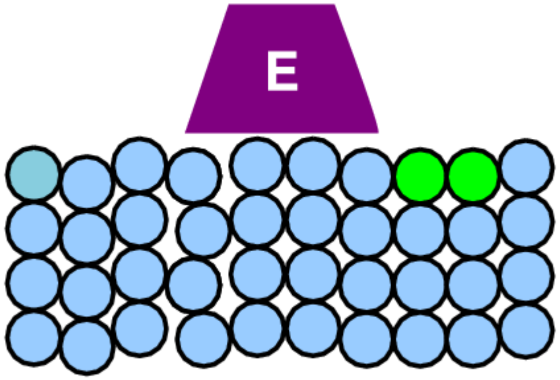

$$v=f(?)$$

Reaction space confined to 2D!

Rate laws for surfactive enzymes

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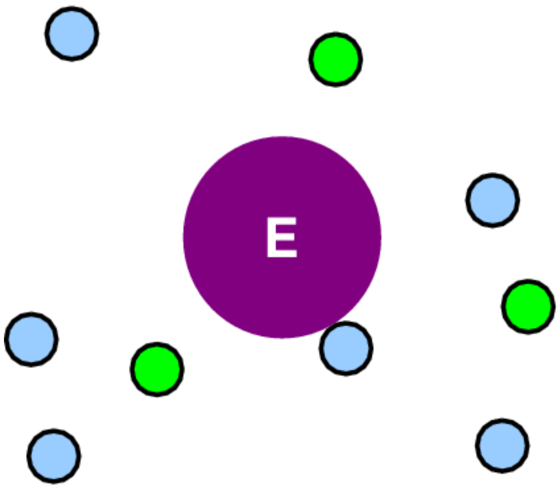
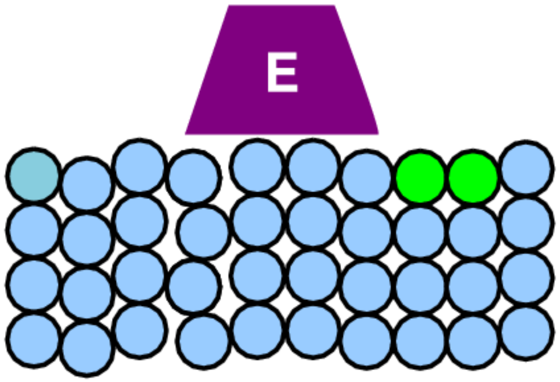


$$v = \frac{V_{\max} S}{K_M + S}$$

aggregated substrate (with interfacial reaction space)



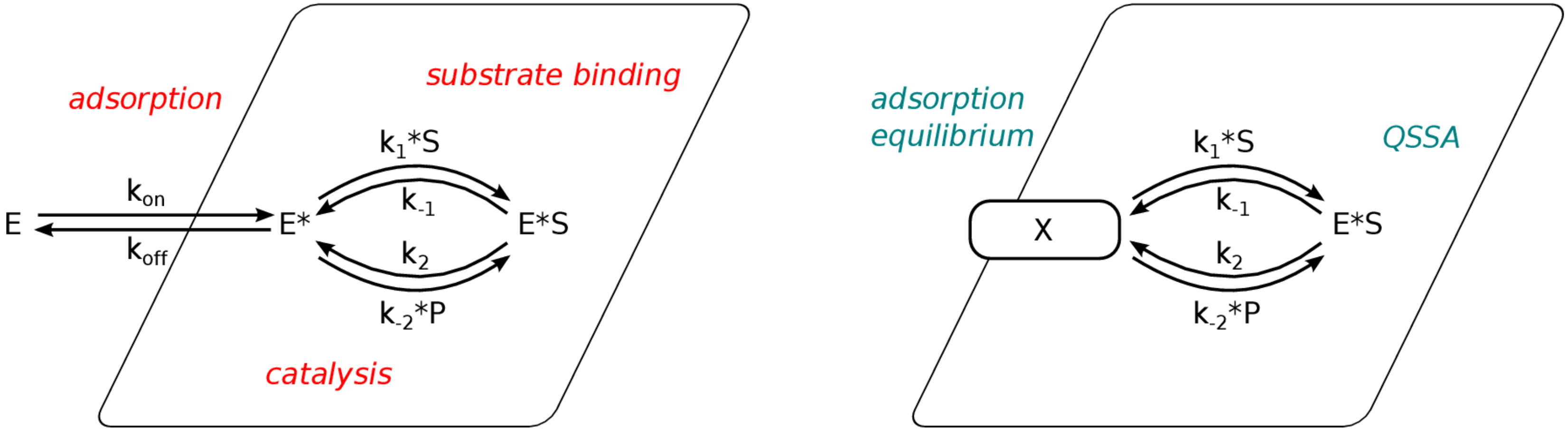
$$v = f(?)$$

Reaction space confined to 2D!

⇨ Implications! - Fundamental differences to the classical case in solution:

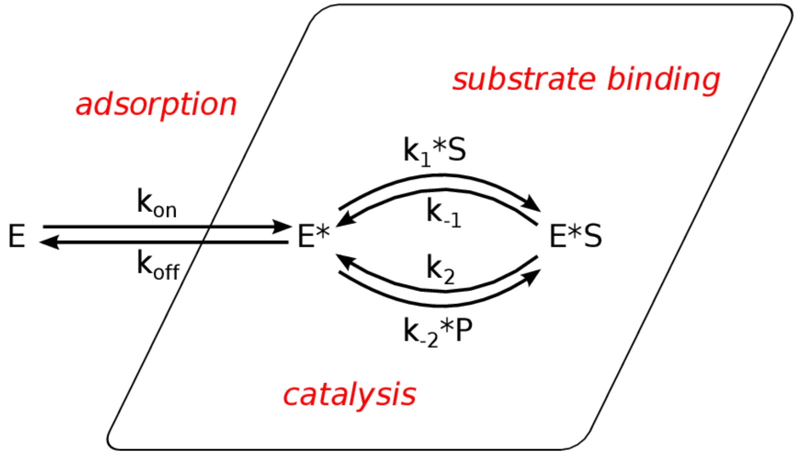
- Relative activity dependent on enzyme concentration (jamming)
- Rate not independent on presence of other enzyme species! (competition)

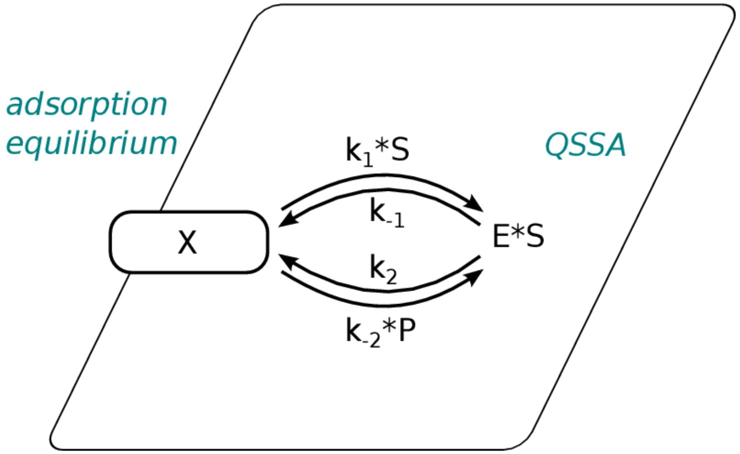
Derivation of a generic surfactive rate-law



Kartal and Ebenhöh (2013) FEBS Letters – centenary issue commemorating Michaelis-Menten 'Kinetik der Invertinwirkung'

Derivation of a generic surfactive rate-law





$$v = \frac{k_\mathrm{A} a_\mathrm{s} \Phi_\mathrm{eq} [M][E_0](k_\mathrm{S}\langle *S\rangle - k_\mathrm{P}\langle *P\rangle)}{1 + k_\mathrm{A} a_\mathrm{s} \Phi_\mathrm{eq}[M]\left(1 + \frac{\langle *S\rangle}{K_\mathrm{mS}} + \frac{\langle *P\rangle}{K_\mathrm{mP}}\right)} = \frac{V_\mathrm{M}^\mathrm{app}\frac{[M]}{K_\mathrm{mM}^\mathrm{app}}}{1 + \frac{[M]}{K_\mathrm{mM}^\mathrm{app}}}$$

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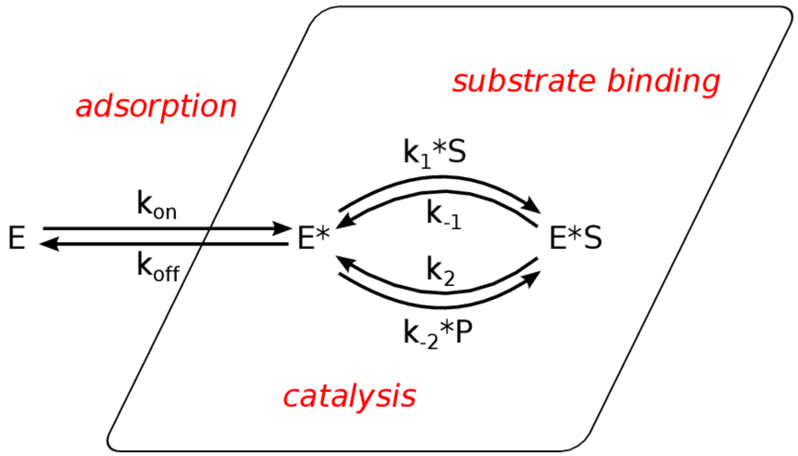

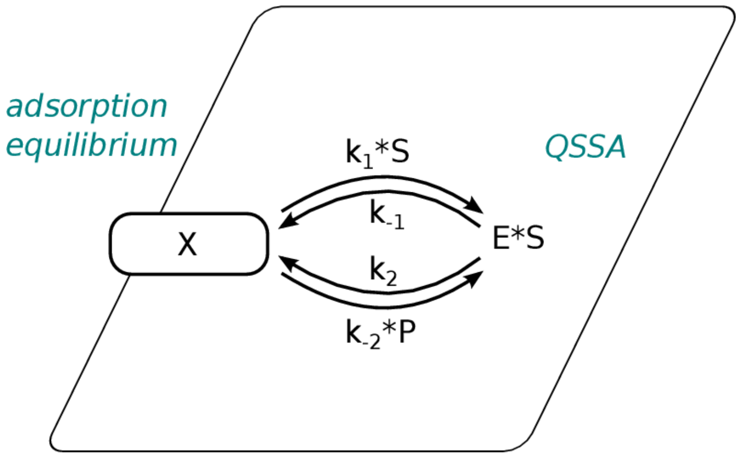

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specific surface area

available area function

“few big objects behave different to many small objects”

“many enzymes (also others) jam the surface”

Kartal and Ebenhöh (2013) FEBS Letters – centenary issue commemorating Michaelis-Menten 'Kinetik der Invertinwirkung'

The adsorption equilibrium

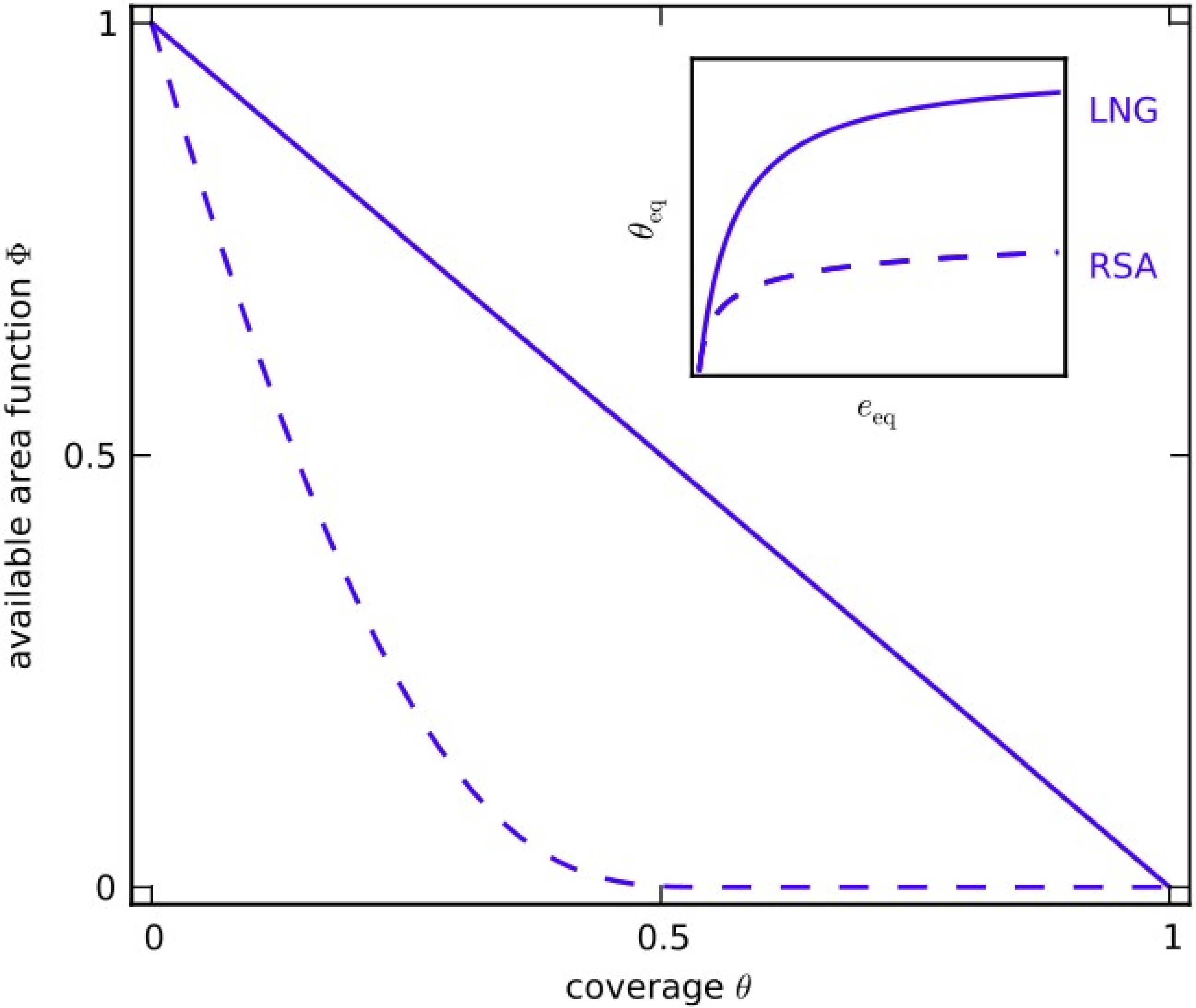
Adsorption rate:

$$r_a \propto c(E)\cdot\Phi$$

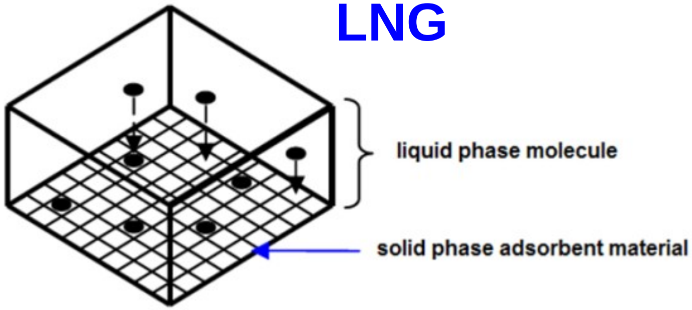
Desorption rate:

$$r_d \propto \theta$$

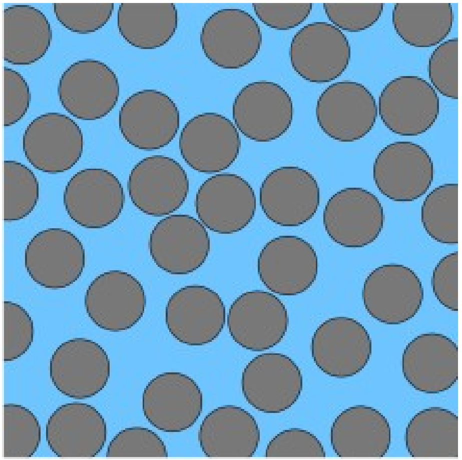
Other adsorption models can give quite different results:



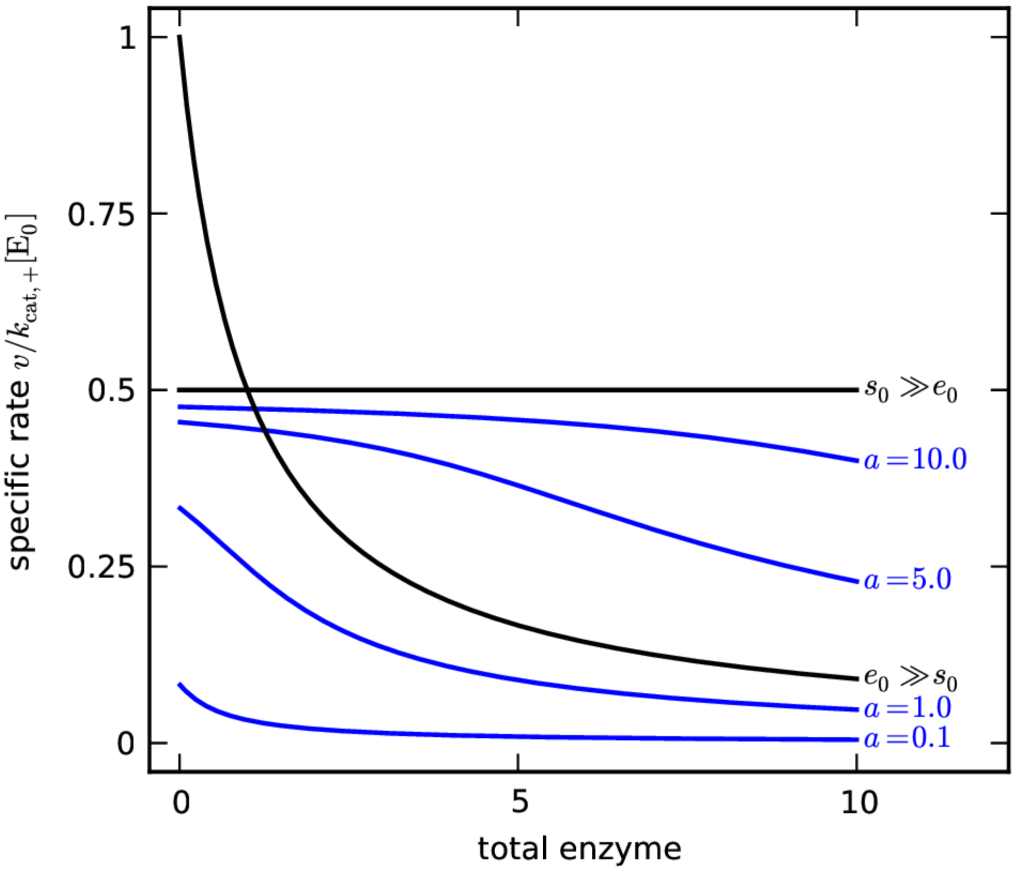
LNG

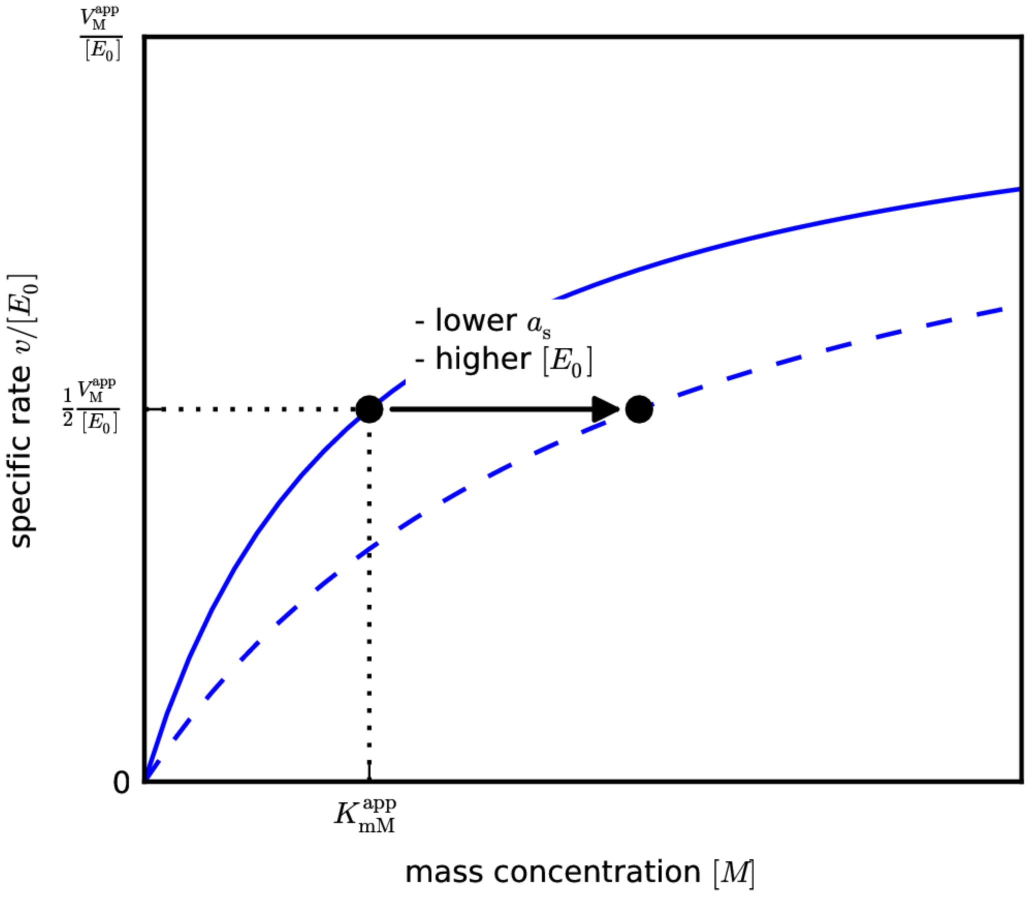


RSA



Consequences for experimental design

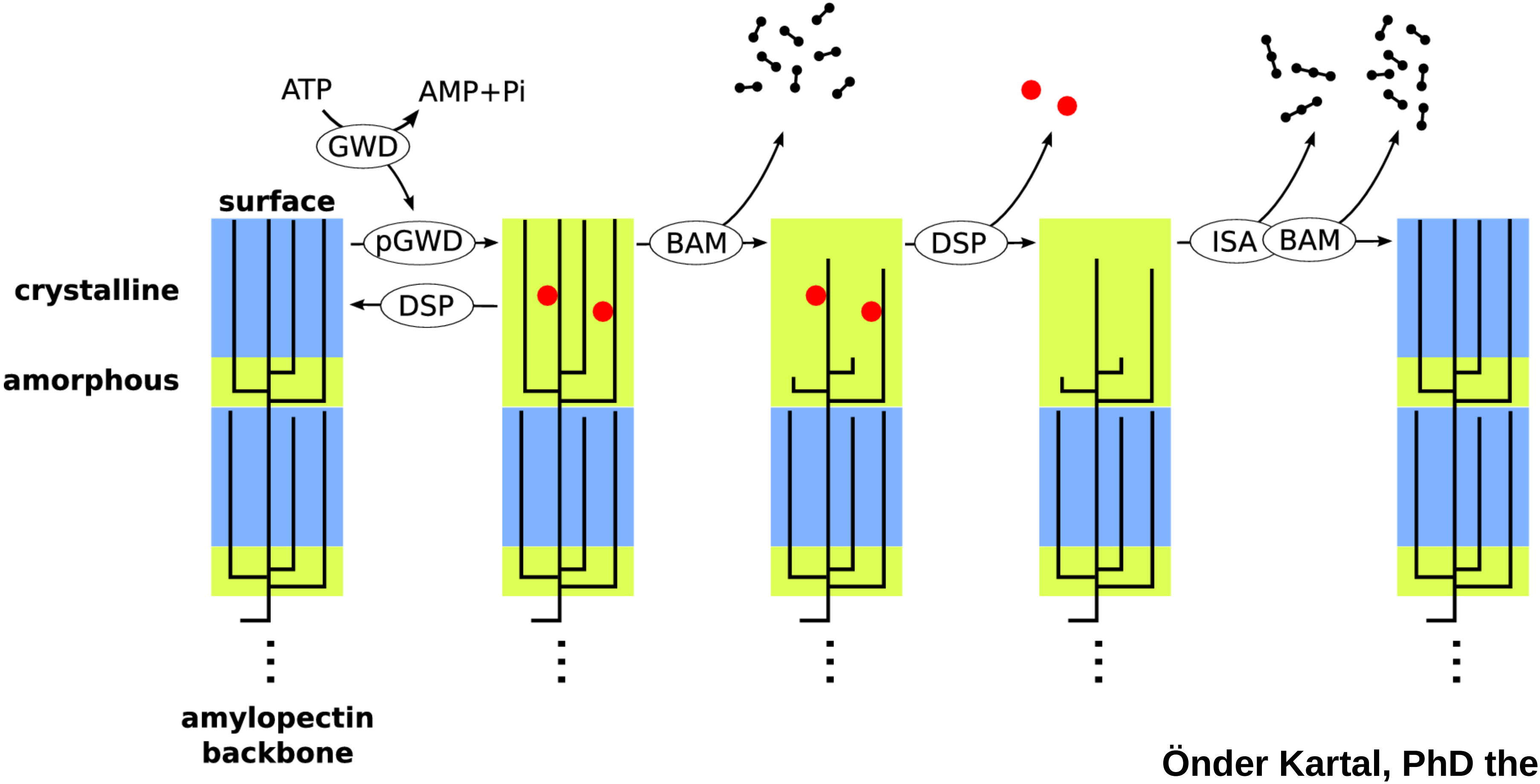




mass alone is insufficient!

⇨ **Define Experimental Standard Conditions for surface-active enzymes!**

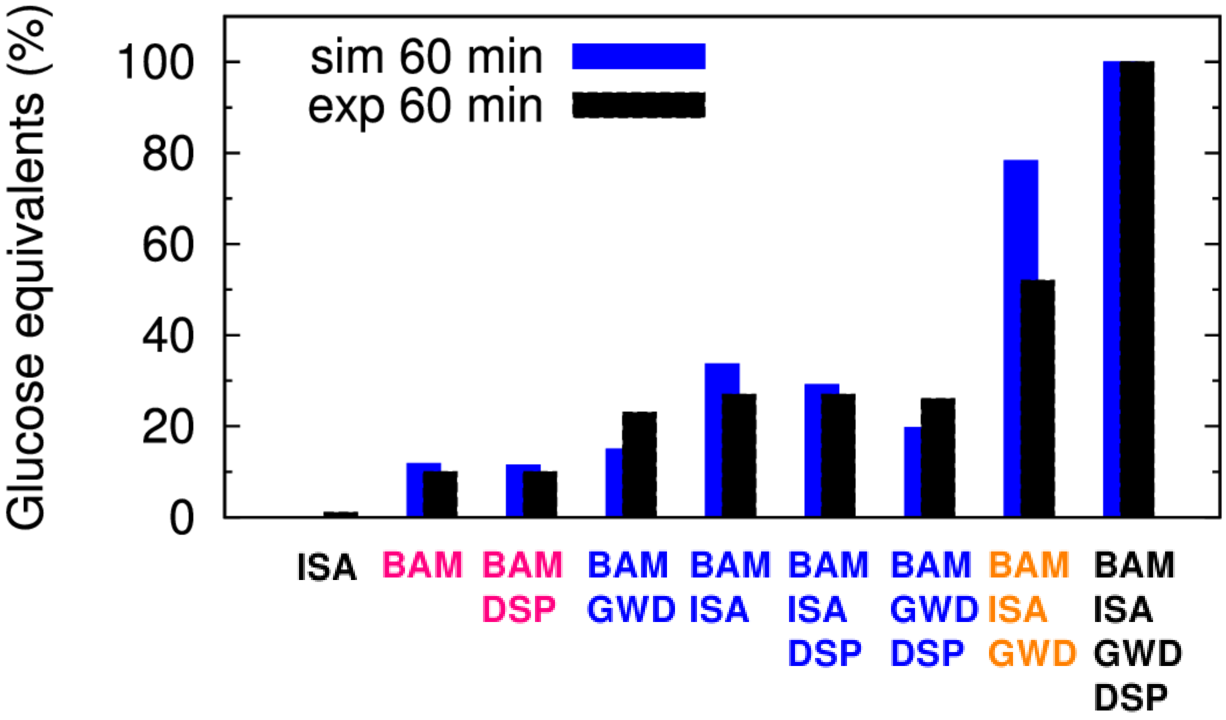
A kinetic model of starch surface attack

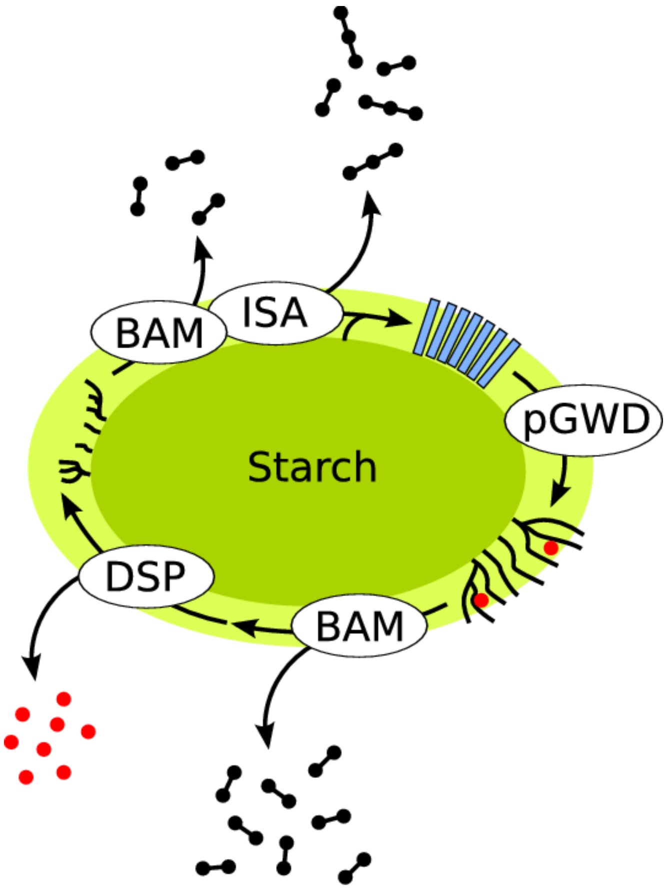


Önder Kartal, PhD thesis

- Disruption of crystalline surface by phosphorylation allows access for BAM and ISA
- Dephosphorylation by DSP enables further degradation

Simulations compared to experiment



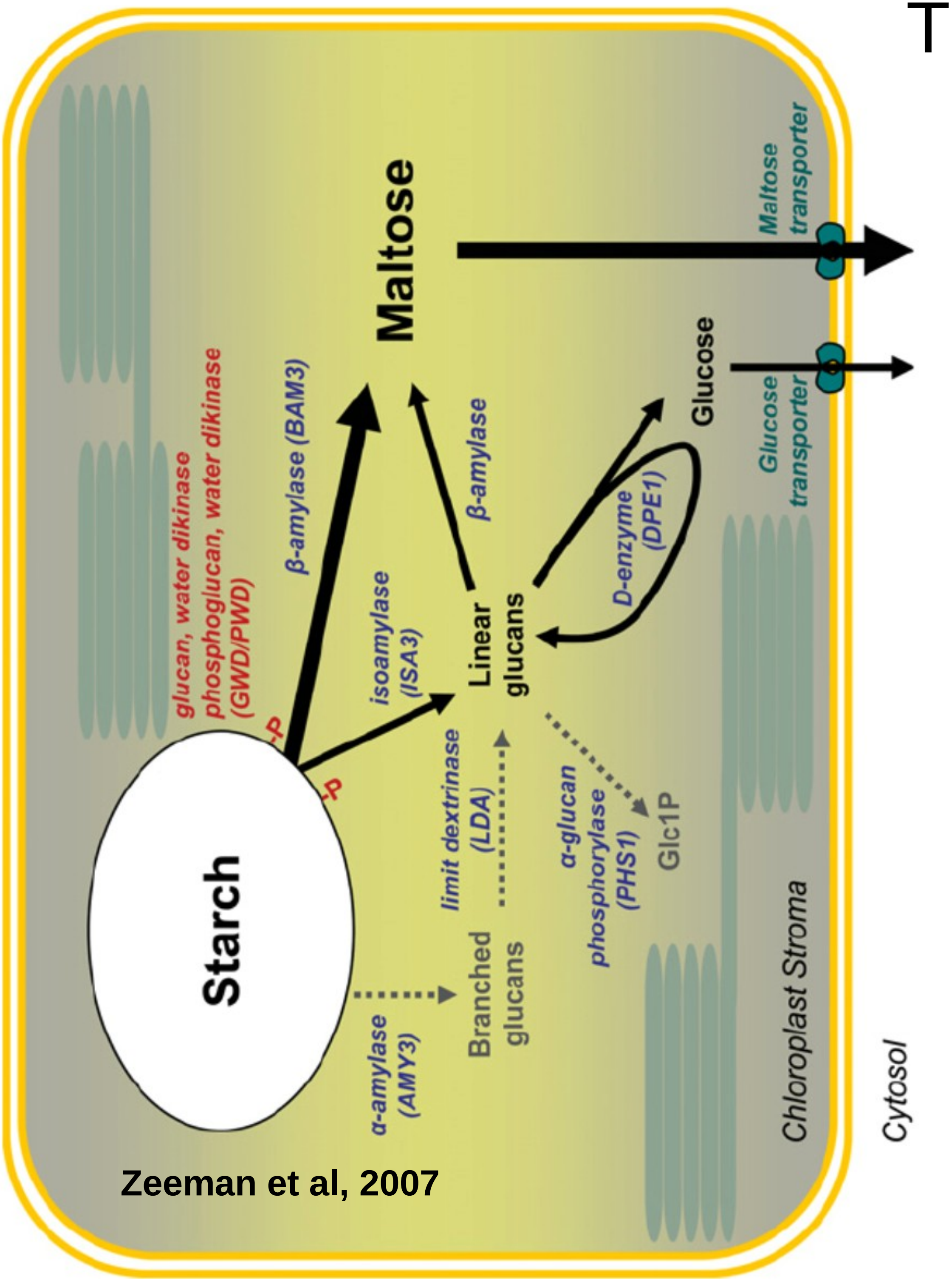


Good agreement with data from Kötting et al (2009) *Plant Cell*

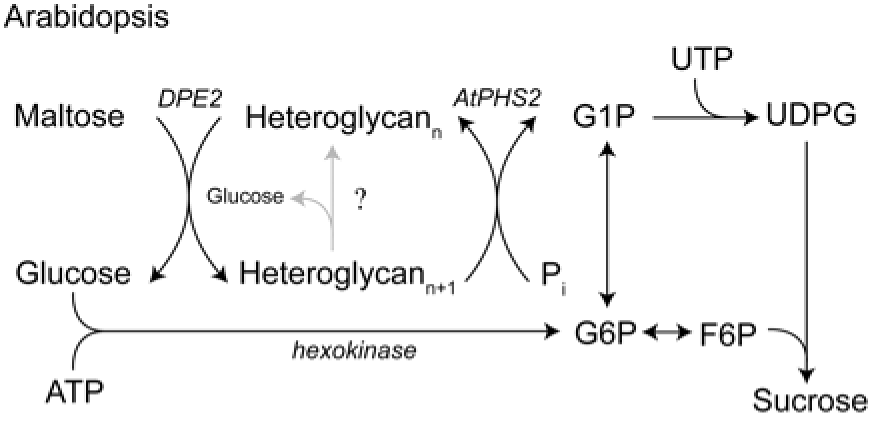
But: only one time point!

2. Polymer Biochemistry

The starch breakdown pathway

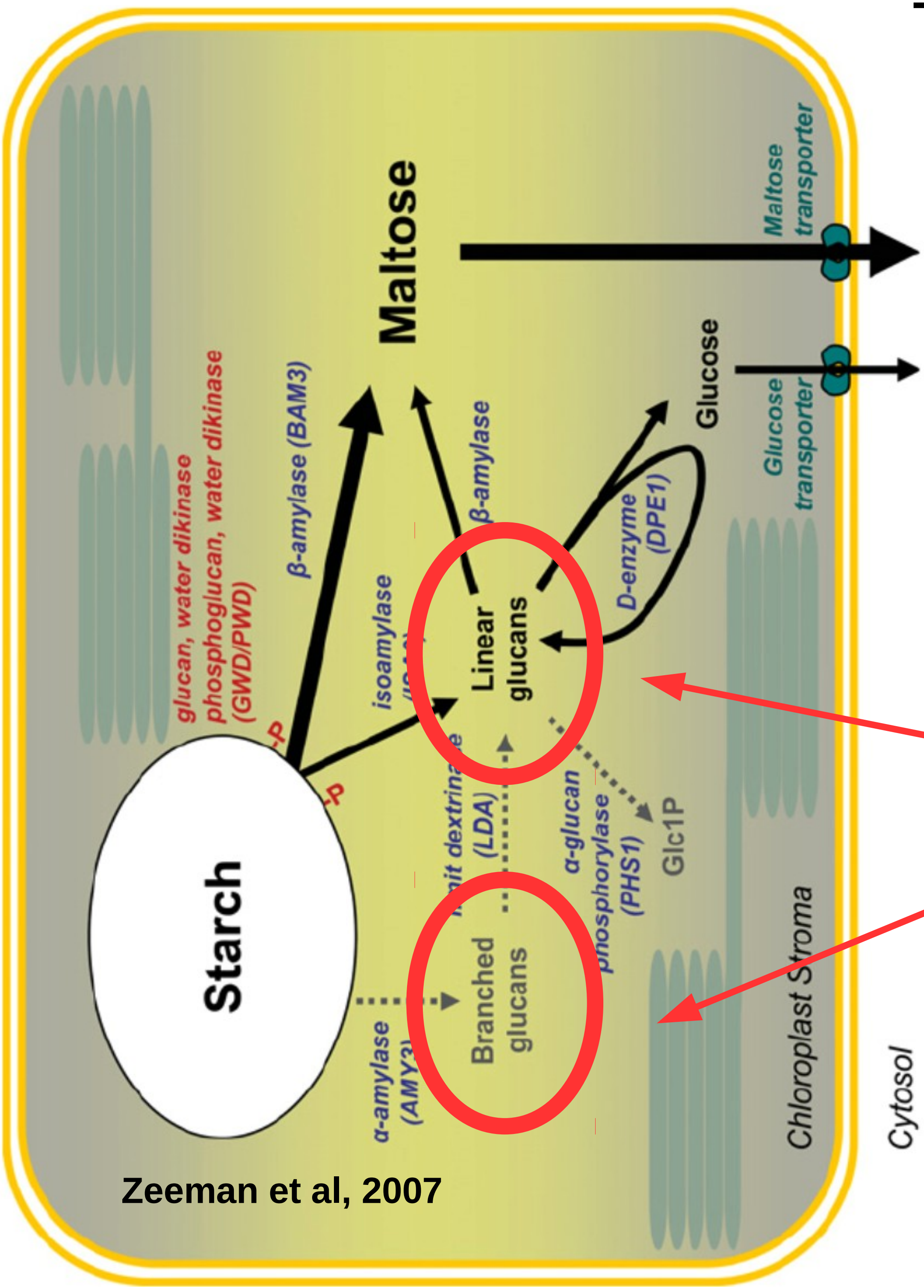


Zeeman et al, 2007

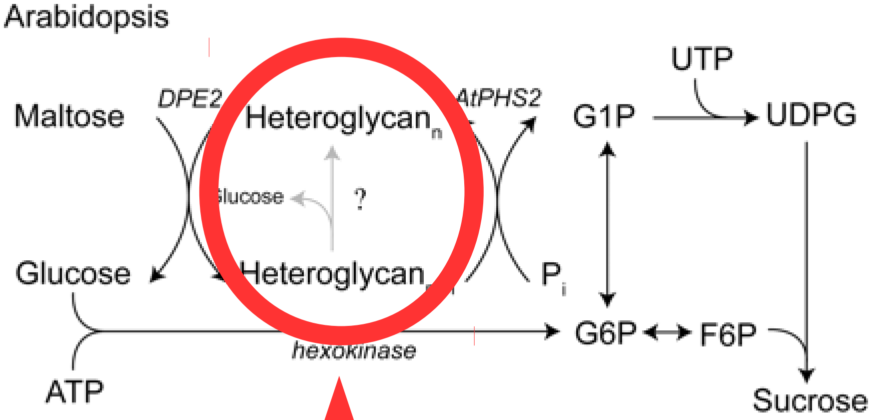


Lu et al, 2006

The starch breakdown pathway



Zeeman et al, 2007



Lu et al, 2006

GLUCAN POLYMERS

DPE1: $G_n + G_m \leftrightarrow G_{n-q} + G_{m+q}, q = 1,2,3$

DPE2: $G_n + G_m \leftrightarrow G_{n-1} + G_{m+1}, n \neq 3, m \neq 2$

PHS2: $P_i + G_n \leftrightarrow G1P + G_{n-1}$

… and many more

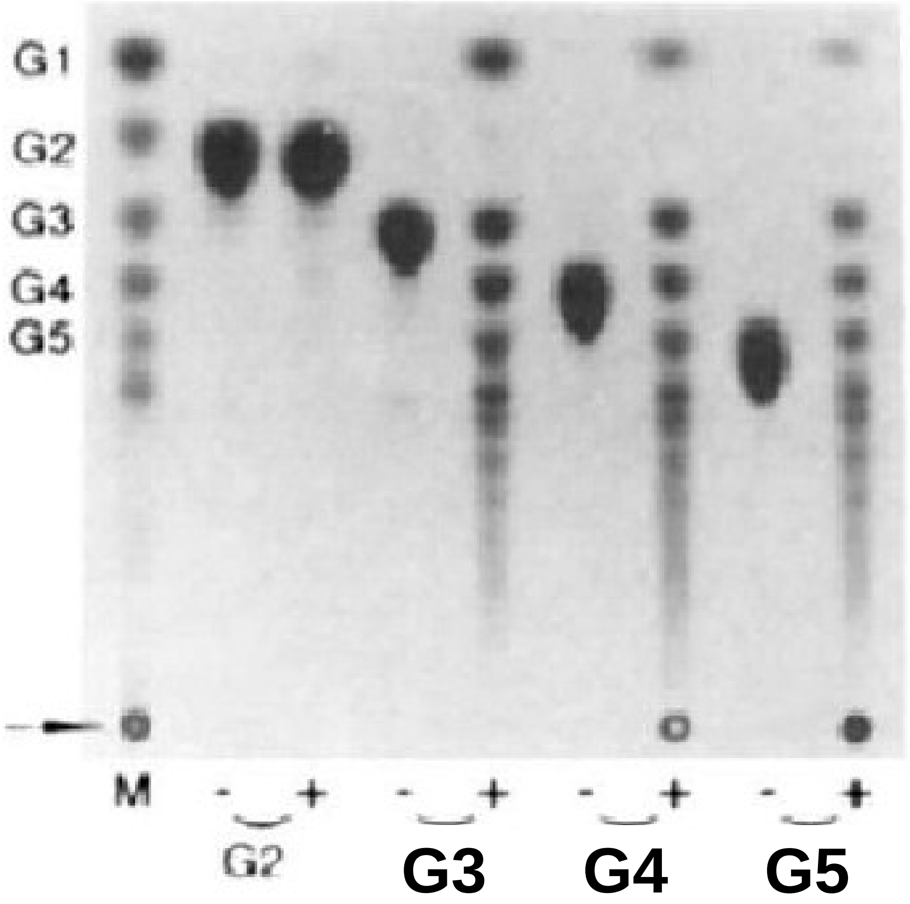
Disproportionating enzymes (D-enzymes)

DPE1

EC: 2.4.1.25

Main function in starch degradation: $G_3 + G_3 \longrightarrow G_5 + G_1$

But general reaction: $G_n + G_m \longleftrightarrow G_{n-q} + G_{m+q}, q = (1,)2,3$



DPE1 produces a set of glucans of different length in *in vitro* assays.

(Takaha et al., JBC 1993)

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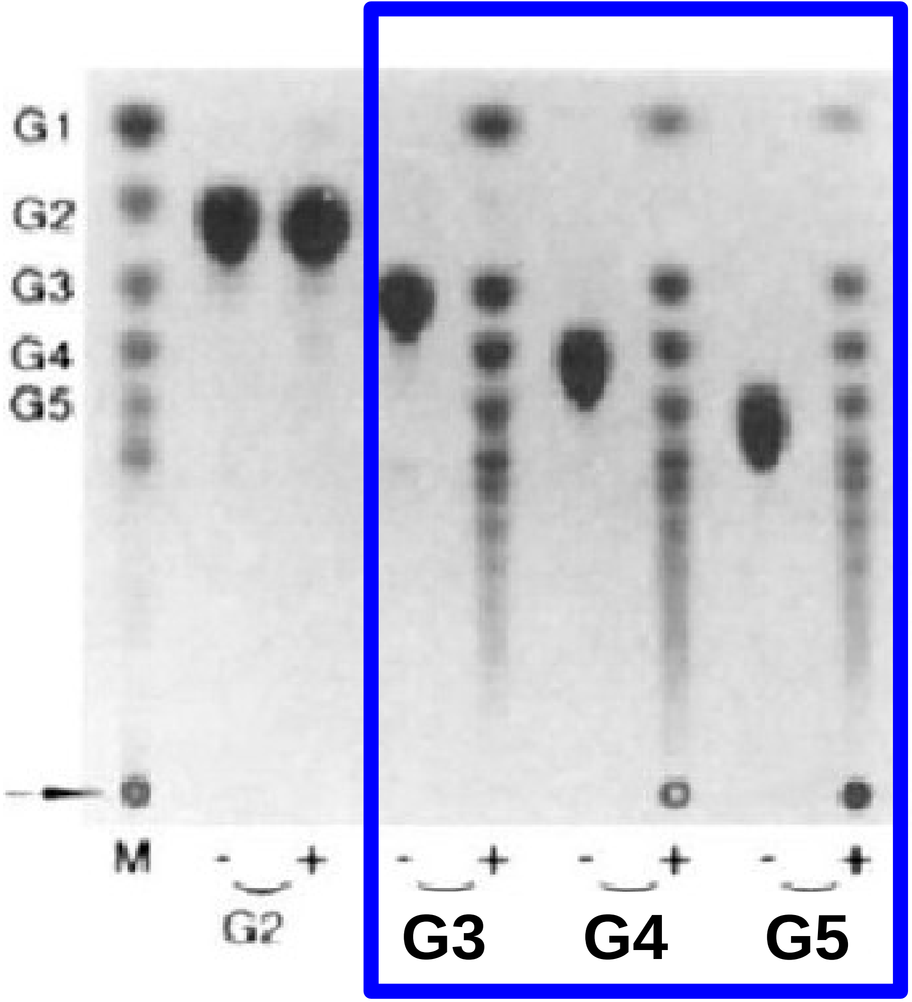

(*Takaha et al., JBC 1993*)

DPE1 produces a set of glucans of different length in *in vitro* assays.

Equilibrium distribution depends on initial conditions!

K_{eq}???

Disproportionating enzymes (D-enzymes)

DPE1

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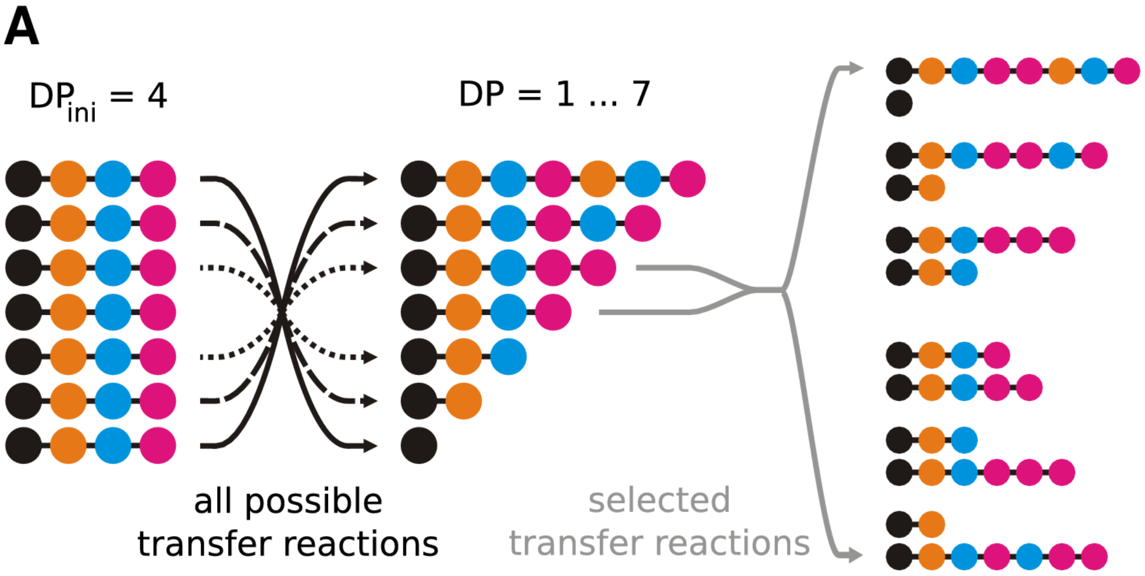
Disproportionating Enzyme randomises DPs



transfers glucosyl residues from one glucan to another: $G_n + G_m \longleftrightarrow G_{n-q} + G_{m+q}$

reaction must proceed towards a smaller Gibbs free energy : $\Delta G = \Delta H - T\Delta S < 0$

energy neutral (enthalpy of α-1,4-bond hydrolysis independent on position): $\Delta H = 0$

(Goldberg et al, 1992)

⇨ DPE1 maximises the entropy of the polydisperse reactant mixture

Polydisperse mixtures as statistical ensembles

x_i : molar fraction of glucans with length *i*
corresponds to occupation number of state *i*

The distribution $\{x_i\}$ fully characterises the polydisperse reactant mixture

The entropy of the statistical ensemble is $S = -\sum x_k \ln x_k$

<u>Equilibrium is determined by maximal entropy:</u>

$$S = -\sum x_k \ln x_k \to \max!$$

Maximum entropy principle under constraint that #bonds and #molecules is conserved!

conservation of #molecules: $\sum x_k = 1$

conservation of #bonds: $\sum k \cdot x_k = b$

determined by initially applied mixture of maltodextrins

Entropic approach

Solution using Lagrangian multipliers: Necessary conditions are given by

$$\frac{\partial L}{\partial x_k}=0 \quad \text{with} \quad L(x_k;\alpha,\beta)=\sum_k x_k \ln(x_k)+\alpha\left(\sum_k x_k-1\right)+\beta\left(\sum_k k\cdot x_k-b\right)$$

$$\Leftrightarrow \quad \ln(x_k)+1+\alpha+k\beta=0 \quad \text{for all} \quad k$$

Entropic approach

Solution using Lagrangian multipliers: Necessary conditions are given by

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$$\Leftrightarrow \quad \ln(x_k)+1+\alpha+k\beta=0 \quad \text{for all} \quad k$$

$$\Rightarrow \quad \boxed{x_k=\frac{1}{Z}e^{-k\beta}} \quad \text{with} \quad Z=\sum_k e^{-k\beta}$$

Entropic approach

Solution using Lagrangian multipliers: Necessary conditions are given by

$$\frac{\partial L}{\partial x_k} = 0 \quad \text{with} \quad L(x_k;\alpha,\beta) = \sum_k x_k \ln(x_k) + \alpha\left(\sum_k x_k - 1\right) + \beta\left(\sum_k k \cdot x_k - b\right)$$

$$\Leftrightarrow \quad \ln(x_k) + 1 + \alpha + k\beta = 0 \quad \text{for all} \quad k$$

$$\Rightarrow \quad \boxed{x_k = \frac{1}{Z} e^{-k\beta}} \quad \text{with} \quad Z = \sum_k e^{-k\beta}$$

Analogy to statistical physics! $\left(\text{There, } \beta = \frac{1}{k_B \cdot T}\right)$

Entropic approach

Solution using Lagrangian multipliers: Necessary conditions are given by

$$\frac{\partial L}{\partial x_k}=0 \quad \text{with} \quad L(x_k;\alpha,\beta)=\sum_k x_k \ln(x_k)+\alpha\left(\sum_k x_k-1\right)+\beta\left(\sum_k k\cdot x_k-b\right)$$

$$\Leftrightarrow \quad \ln(x_k)+1+\alpha+k\beta=0 \quad \text{for all} \quad k$$

$$\Rightarrow \quad \boxed{x_k=\frac{1}{Z}e^{-k\beta}} \quad \text{with} \quad Z=\sum_k e^{-k\beta}$$

Analogy to statistical physics! $\left(\text{There}, \beta \ = \ \frac{1}{k_B\cdot T}\right)$

Calculation of *β*: $-\frac{1}{Z}\frac{\partial Z}{\partial \beta} \ = \ b \ \Leftrightarrow \ \beta \ = \ \ln\frac{b+1}{b}$

Entropic approach

Solution using Lagrangian multipliers: Necessary conditions are given by

$$\frac{\partial L}{\partial x_k}=0 \quad \text{with} \quad L(x_k;\alpha,\beta)=\sum_k x_k \ln(x_k)+\alpha\left(\sum_k x_k-1\right)+\beta\left(\sum_k k\cdot x_k-b\right)$$

$$\Leftrightarrow \quad \ln(x_k)+1+\alpha+k\beta=0 \quad \text{for all} \quad k$$

$$\Rightarrow \quad \boxed{x_k=\frac{1}{Z}e^{-k\beta}} \quad \text{with} \quad Z=\sum_k e^{-k\beta}$$

Analogy to statistical physics! $\left(\text{There}, \beta = \frac{1}{k_B\cdot T}\right)$

Calculation of β: $-\frac{1}{Z}\frac{\partial Z}{\partial \beta} = b \;\Leftrightarrow\; \beta = \ln\frac{b+1}{b}$

Maximal entropy in equilibrium: $S_{max} = (b+1)\ln(b+1)-b\ln b$

Entropic approach

$$S = -\sum x_k \ln x_k \rightarrow \max!$$

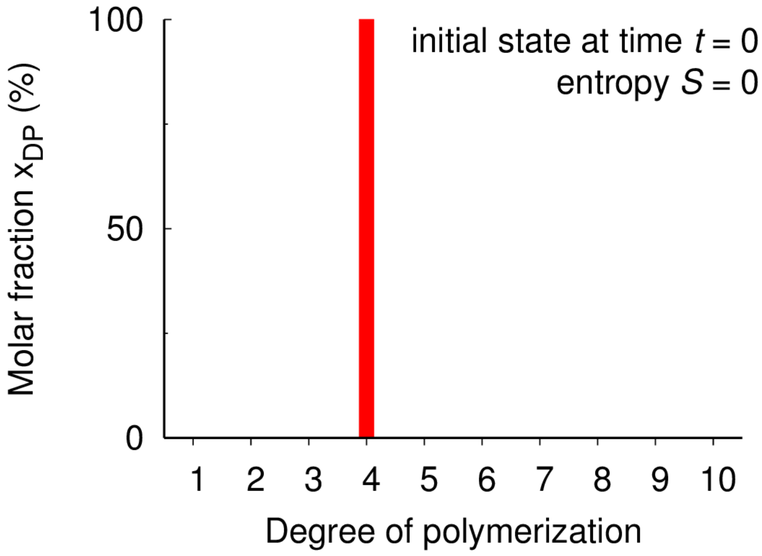
conservation of #molecules: $\sum x_k = 1$

conservation of #bonds: $\sum k \cdot x_k = \mathrm{DP}_{\mathrm{ini}} - 1$

implies

$$x_i = \frac{1}{Z} e^{-\beta E_i}, \quad \beta = \ln \frac{\mathrm{DP}_{\mathrm{ini}}}{\mathrm{DP}_{\mathrm{ini}} - 1}$$

predicts



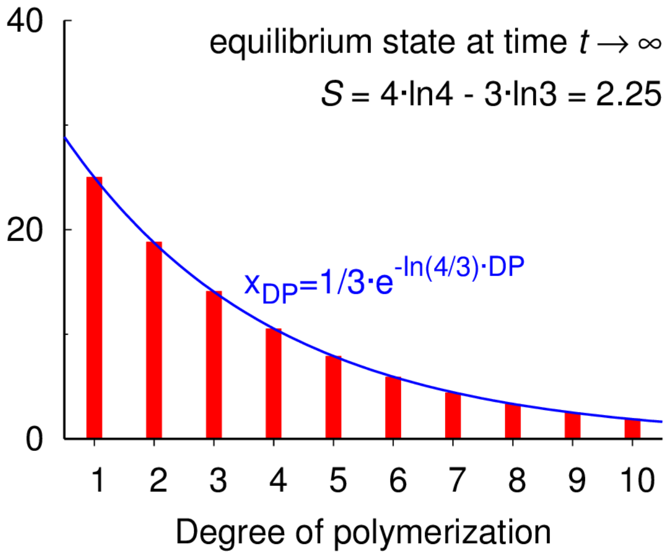
initial state at time $t = 0$

entropy $S = 0$

DPE1 action

$$G_n + G_m \longleftrightarrow G_{n-q} + G_{m+q}$$

with q = 1,2,3



equilibrium state at time $t \to \infty$

$S = 4\cdot\ln 4 - 3\cdot\ln 3 = 2.25$

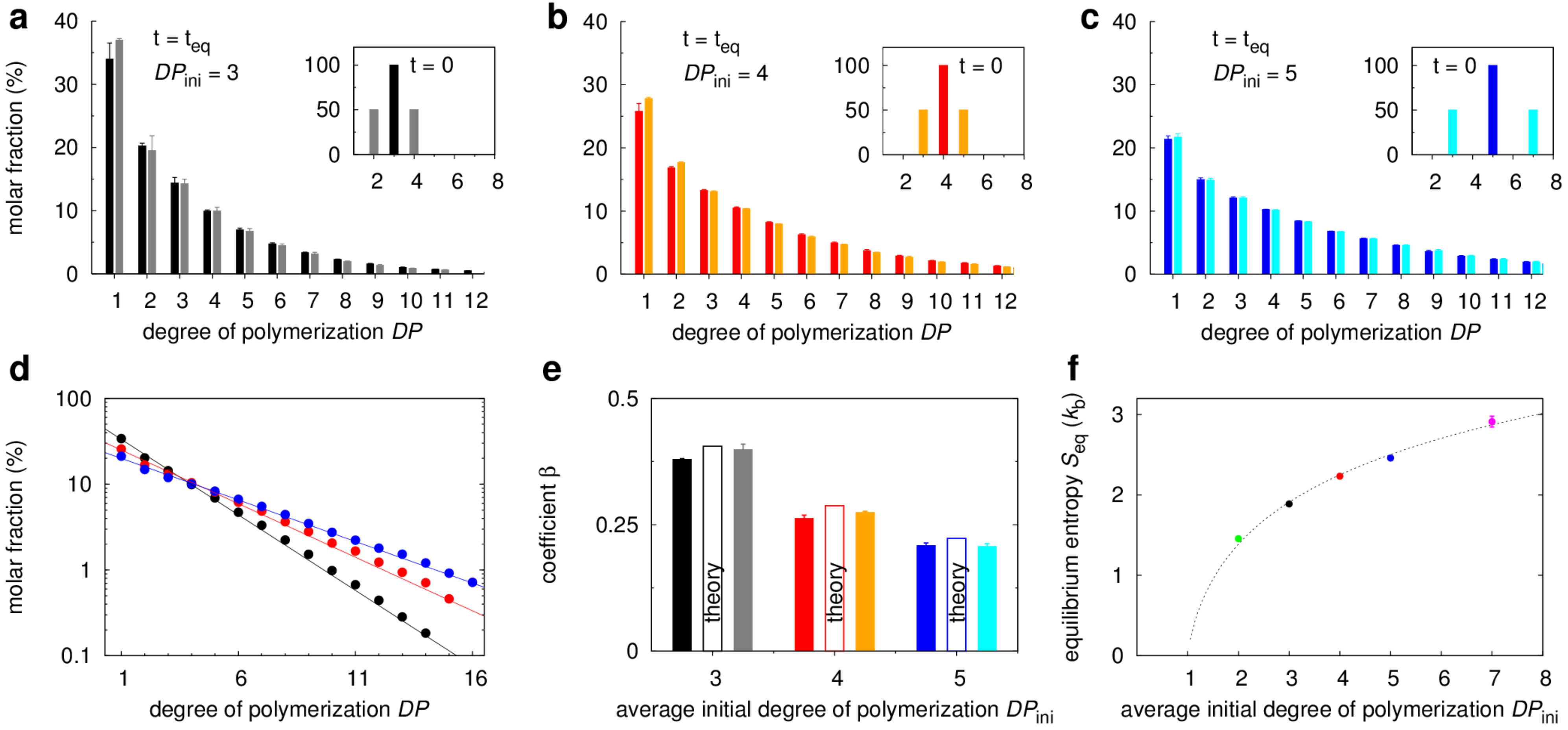
$x_{DP} = 1/3 \cdot e^{-\ln(4/3)\cdot DP}$

An instance of the 2nd law of TD!

DPE1 is entropy driven

Experiments with Martin Steup, University of Potsdam

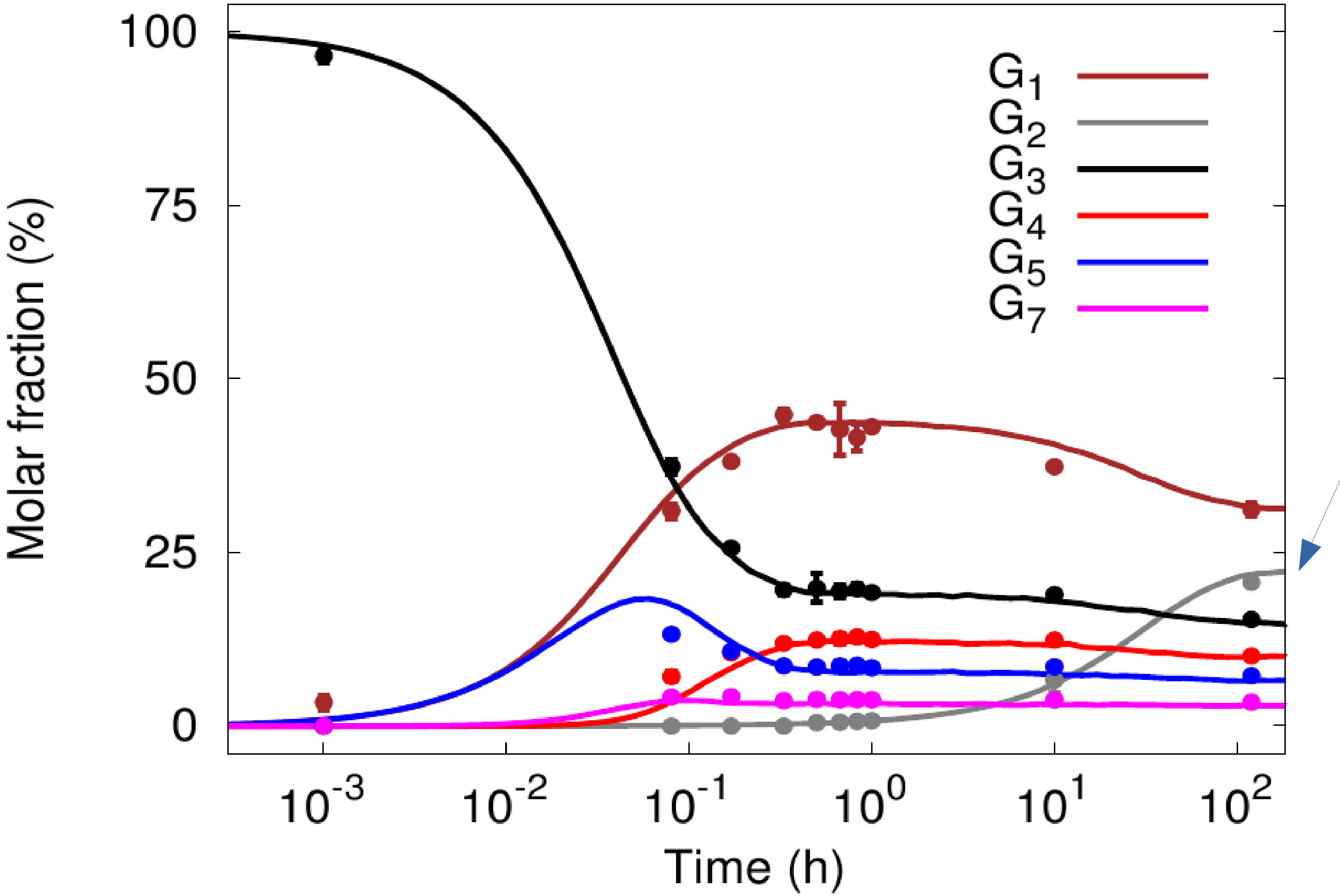
method: capillary electrophoresis



β is a generalisation of the equilibrium constant for polydisperse mixtures

(Kartal et al, 2011, Mol Syst Biol)

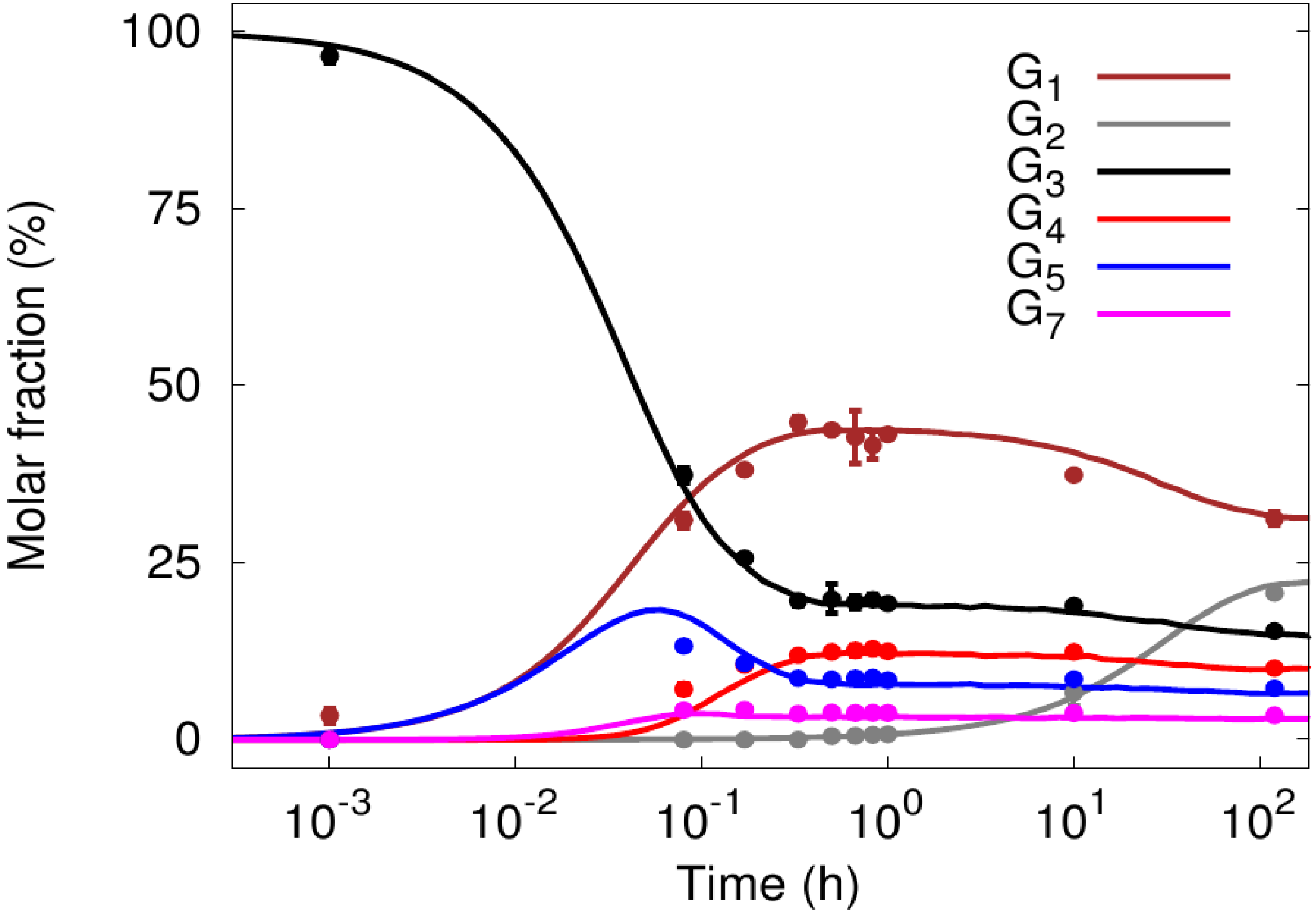
The dynamics of DPE1



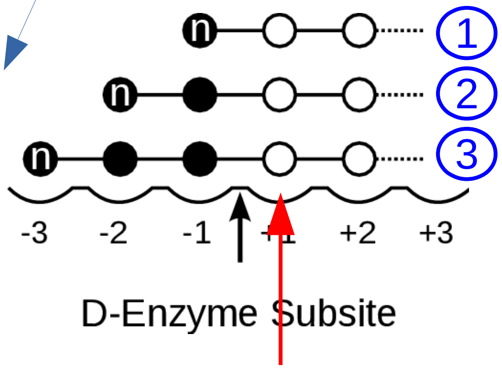
maltose is formed late

Two time scales!

The dynamics of DPE1



maltose is formed late



subsite +1 repellent (binding of G2 unlikely)

Two time scales!

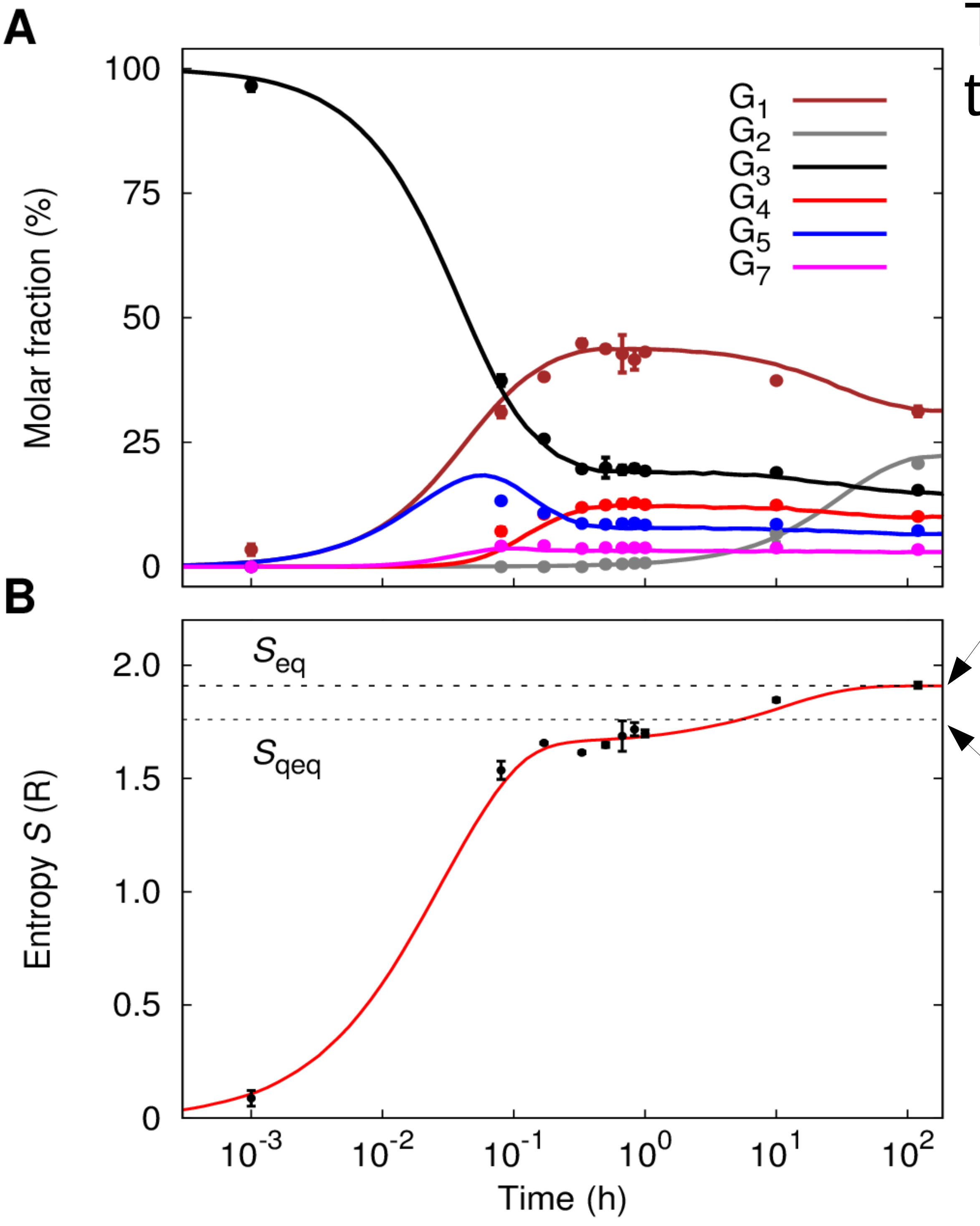
The simulations used 3 parameters:

- maximal turnover
- affinity for positional isomer 1
- affinities for positional isomers 2 and 3

kinetic characterisation

ratio 1:800

This system allows to follow the entropy *experimentally*!



“true” equilibrium

(calculated as previously)

“quasi” equilibrium

(calculated with the same approach but omitting maltose from the statistical ensemble)

Theory is also confirmed by DPE2

DPE2 vs DPE1

- transfers single glucosyl residues
- G2 only used as donor
- G3 only used as acceptor

Generic reaction catalysed:

$$G_n + G_1 \longleftrightarrow G_{n-1} + G_2$$

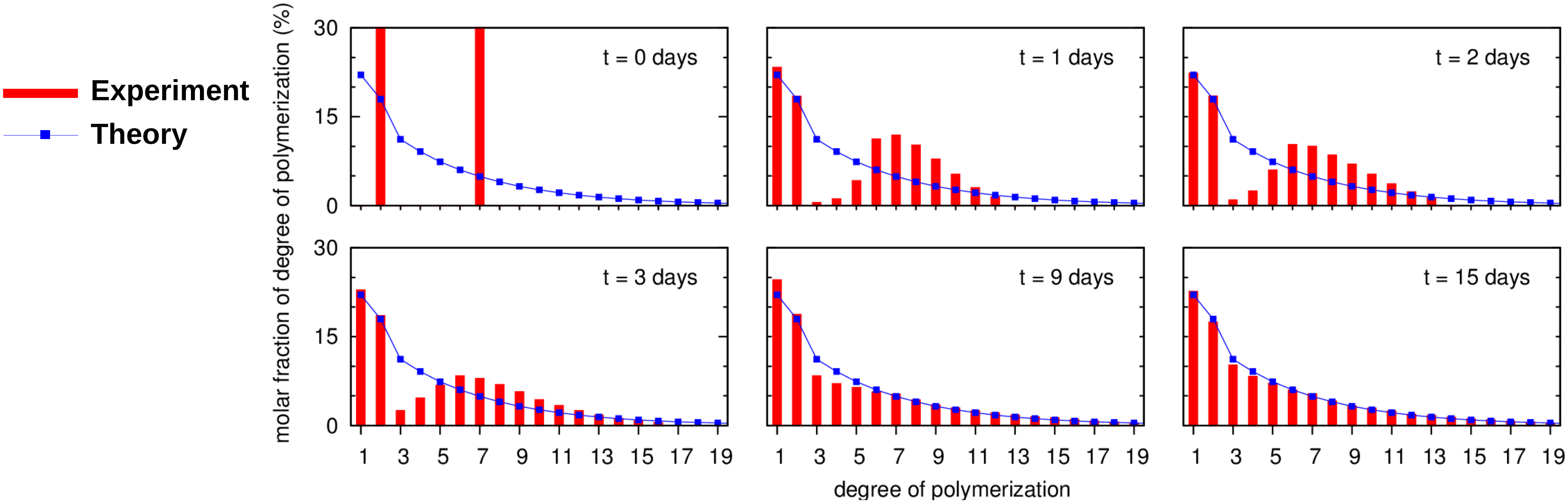
Entropic principle:

$$S = -\sum_k x_k \ln x_k \to \max$$

with one additional side constraint

$$x_1 + x_2 = m = \text{const.} \quad \left(\text{and} \sum x_k = 1 ; \sum k \cdot x_k = b\right)$$

$$\Rightarrow \quad x_i = \frac{1}{Z} e^{-\beta E_i} \quad \text{for} \quad i \geqslant 3 \quad \text{where } \beta \text{ fulfils} \quad b - 2(1-m) = m \cdot \frac{e^{-\beta}}{1+e^{-\beta}} + (1-m) \cdot \frac{e^{-\beta}}{1-e^{-\beta}}$$

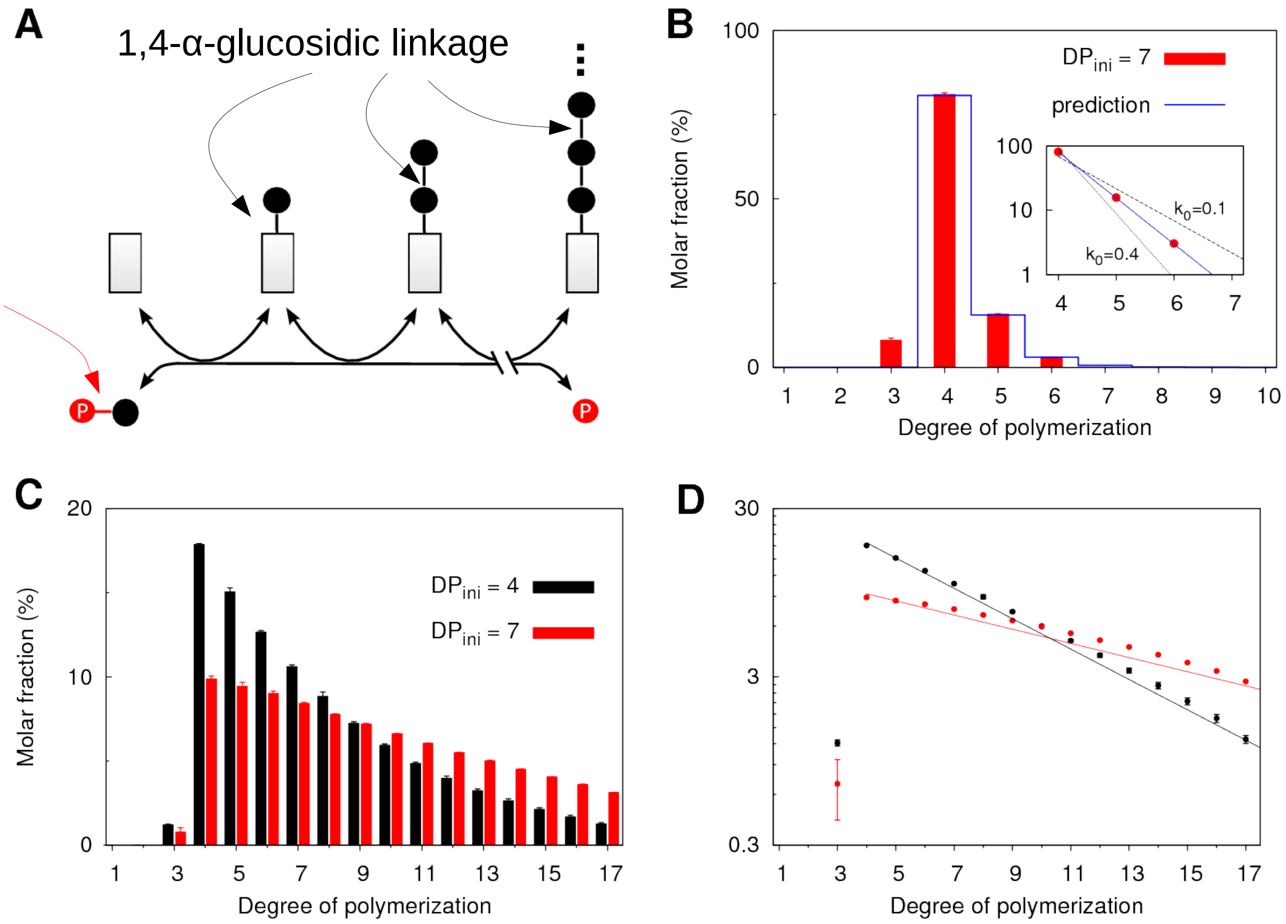


Generalisation to non-zero enthalpy changes

Phosphorylase (cPho):

$$P_i + G_n \longleftrightarrow G1P + G_{n-1}$$

$$\Delta H \neq 0!$$



Generalisation by including energetic and entropic contributions:

$$G = G^f - T \cdot S_{mix} \rightarrow \min!$$

Gibbs energy of formation

mixing entropy:

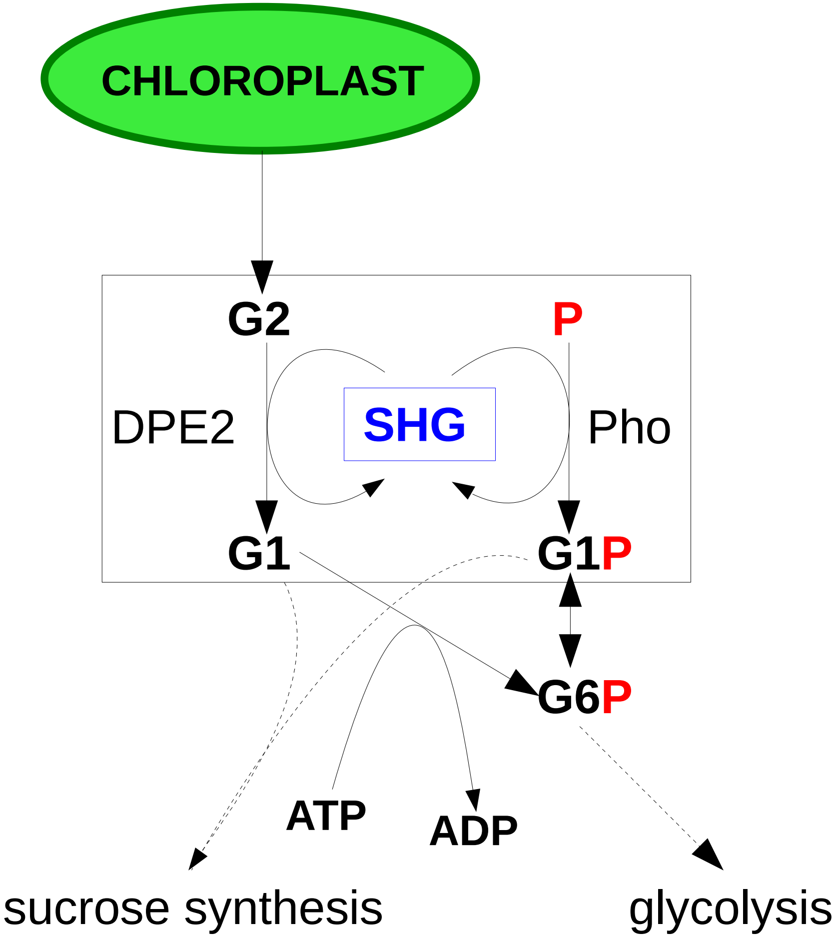
$$S_{mix} = -R \sum x_k \ln x_k$$

<u>Prediction</u>: Similar pattern as for DPE2

Experimentally confirmed.

(Kartal et al, Supp to MSB 2011; Ebenhöh et al, Proc 5th ESCEC 2013)

What is the role of the SHG pool?

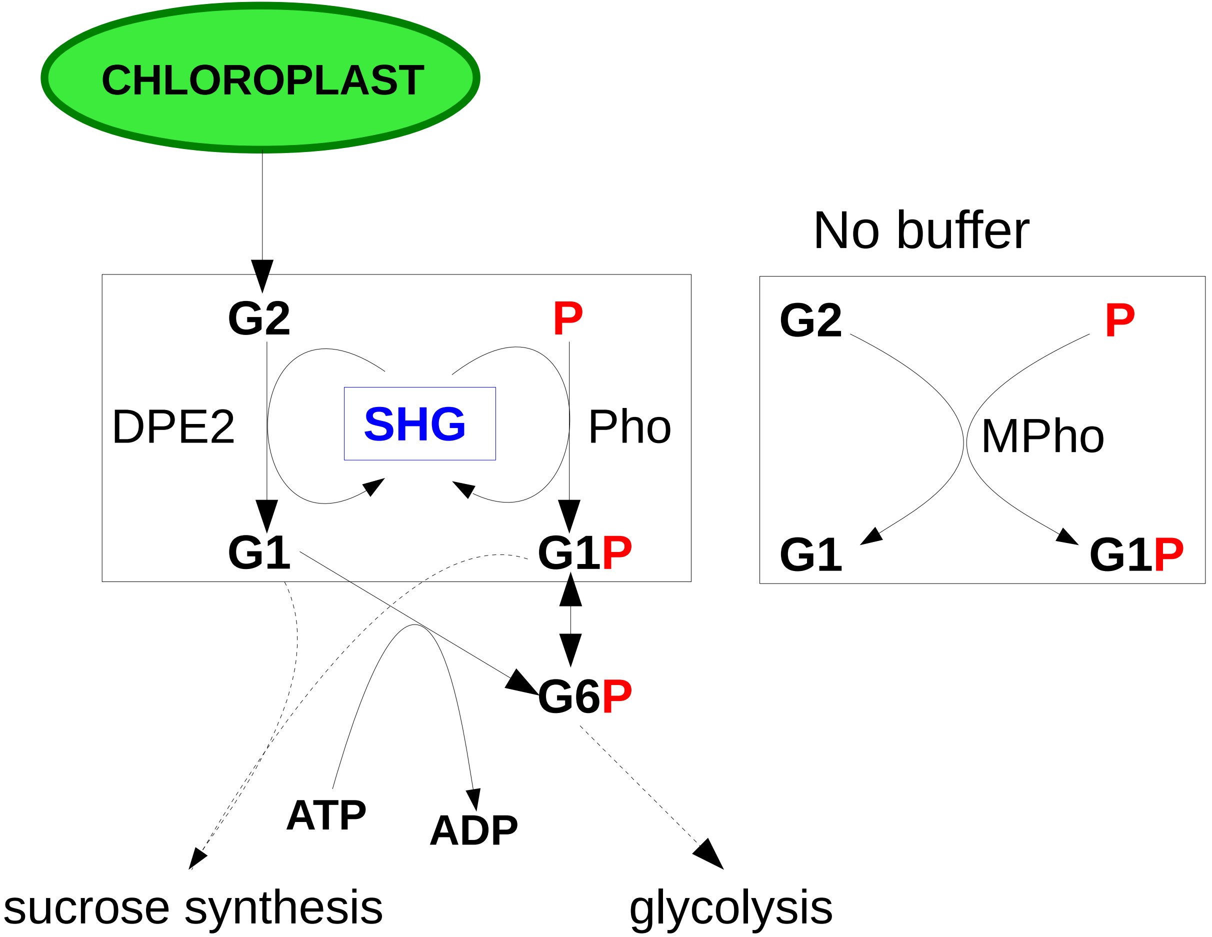


Two 'entropic' enzymes mediate the turnover of a polydisperse pool

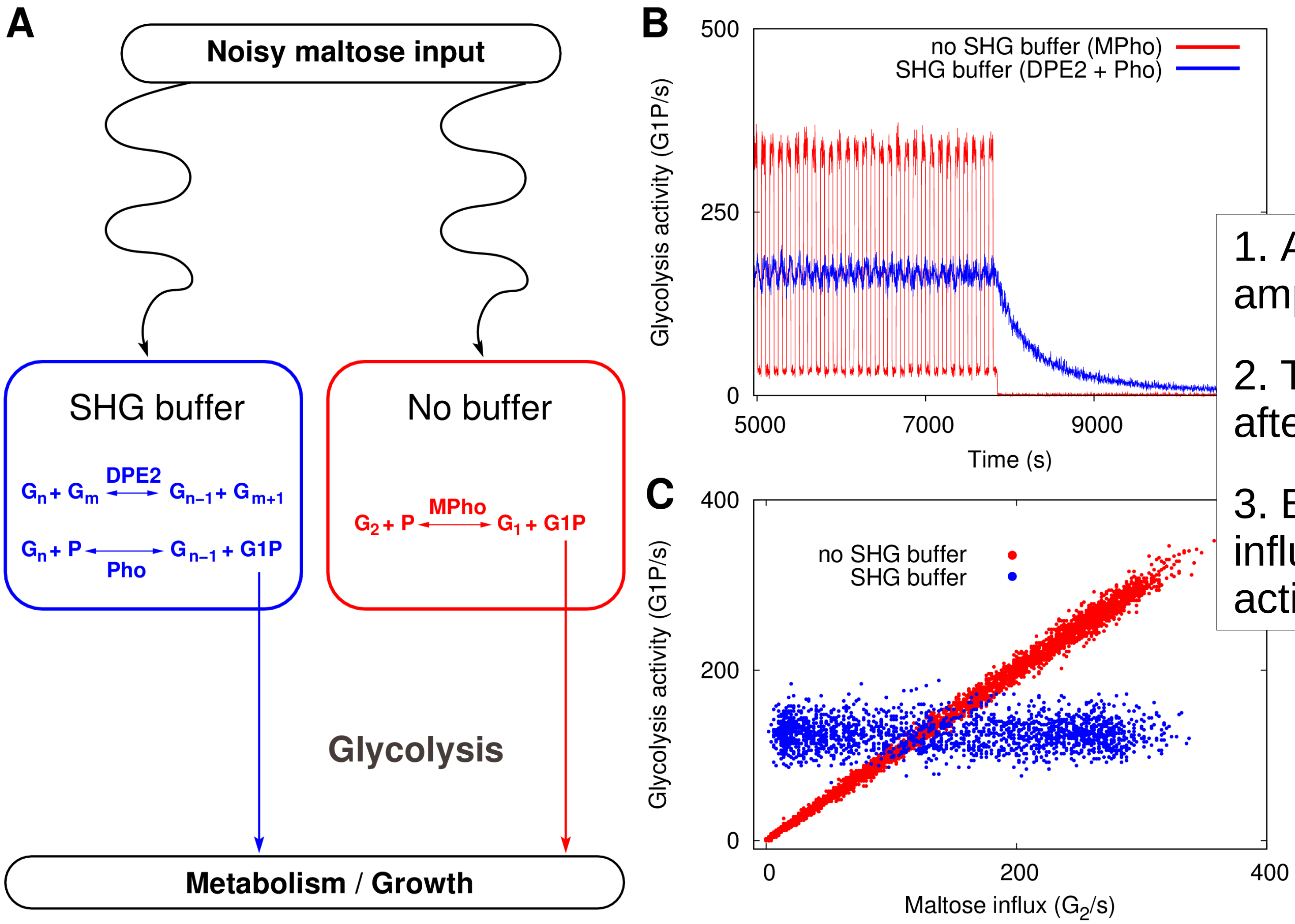
What is the advantage over other hypothetical systems?

What is the role of the SHG pool?

Comparison with alternative



Polydisperse SHG pools increases robustness *in vivo*

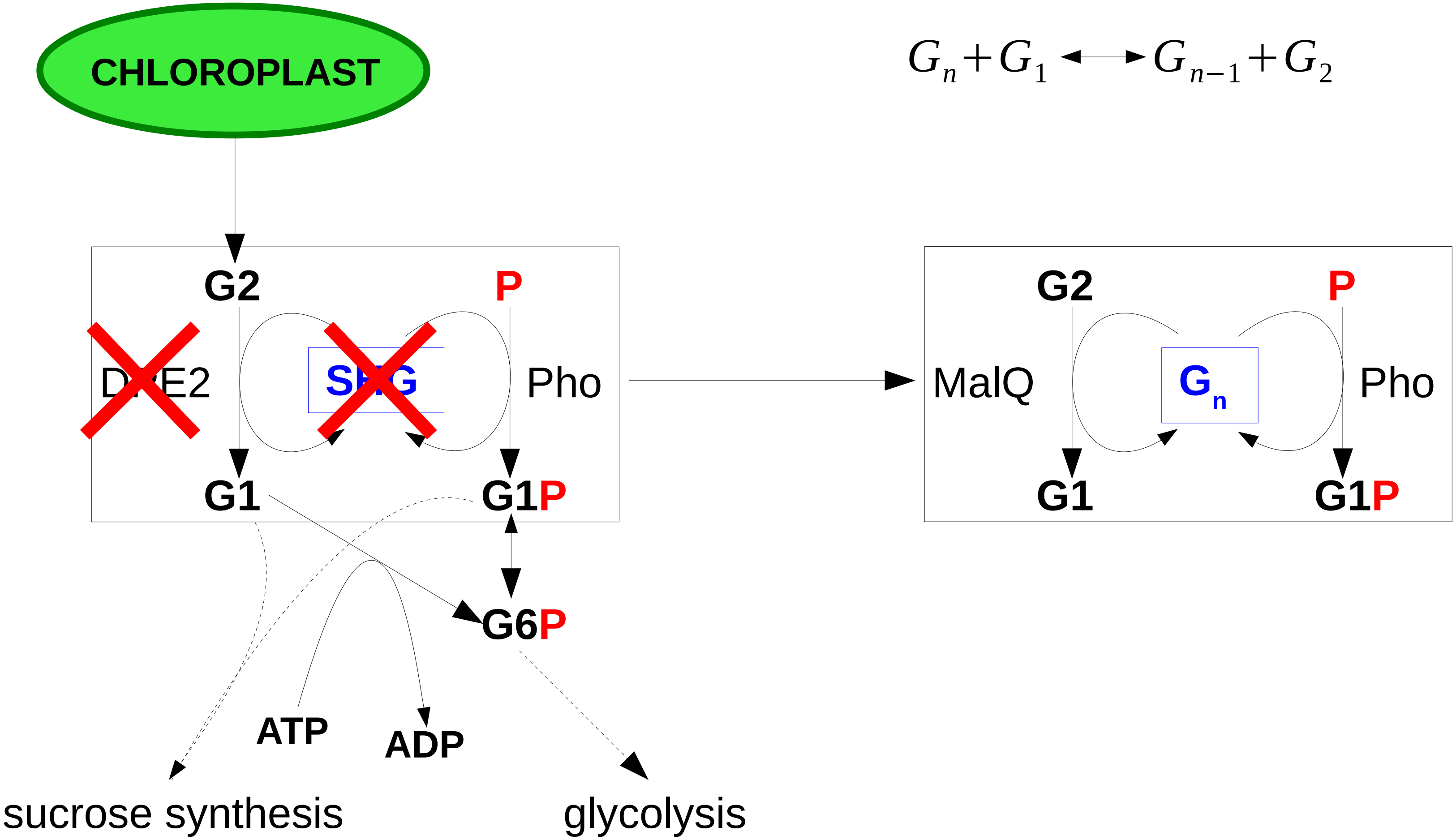


1. Attenuation of fluctuation amplitude (low-pass filter)
2. Transient support of activity after drop of maltose influx
3. Buffering large variations in influx to provide robust output activity

Replacing DPE2 by MalQ

MalQ does the same as DPE2, but does not use SHG

$$G_n + G_1 \longleftrightarrow G_{n-1} + G_2$$



Simulating MalQ in vitro kinetics

In vitro system: MalQ + HXK

$$G_n + G_m \longleftrightarrow G_{n-q} + G_{m+q}$$

$$G_1 \longrightarrow \emptyset$$

Incubation with G_2 only!

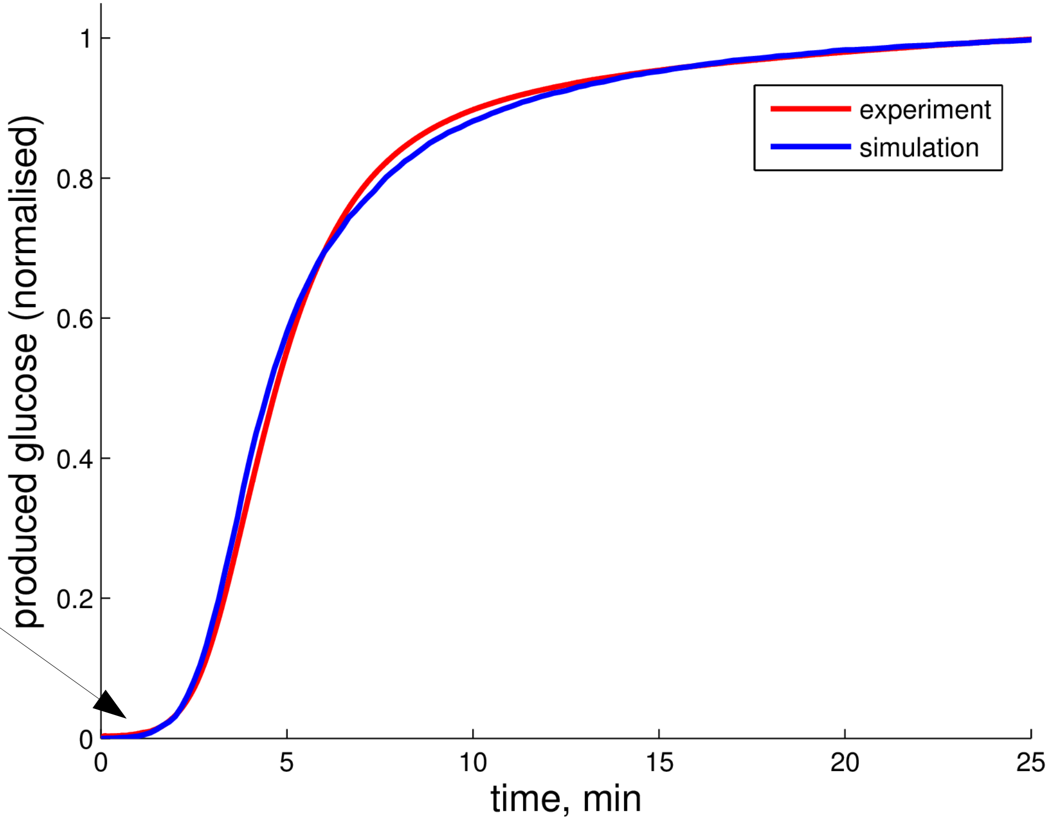
(maltose never acts as acceptor)

should not work...

A generalised ping-pong:

$$G_n + E_k \longrightarrow G_{n-q} + E_{k+q}$$ donor half-reaction

$$G_n + E_k \longrightarrow G_{n+q} + E_{k-q}$$ acceptor half-reaction



delayed start presumably due to enzyme-bound glucose residues

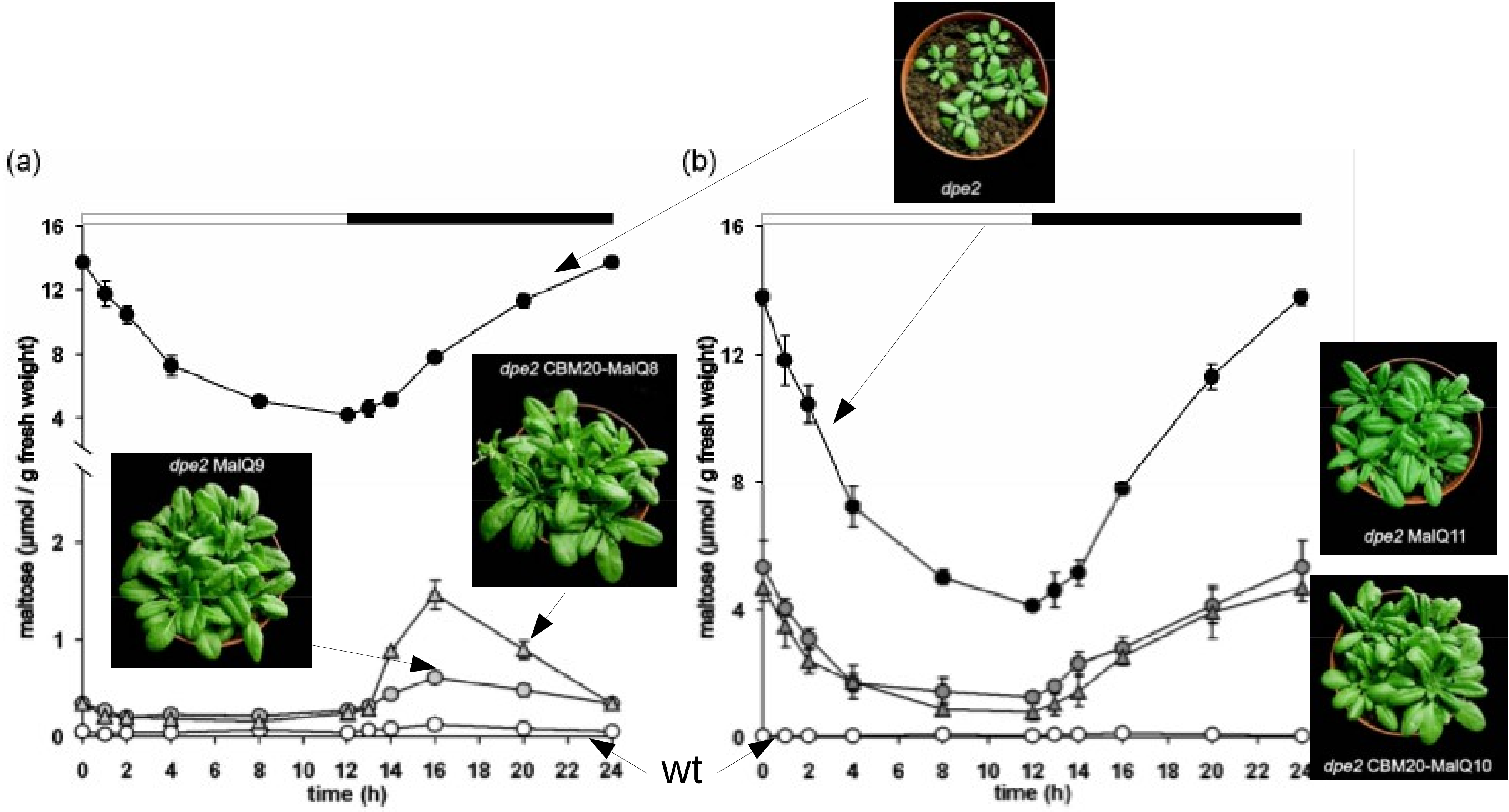
Ruzanski et al, JBC 2013

Moderate growth phenotype

(Julia Smirnova, PhD thesis; Ruzanski et al, JBC 2013)

complemented plants grow OK!

Maltose turnover

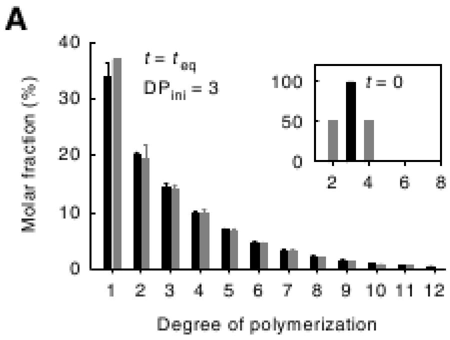


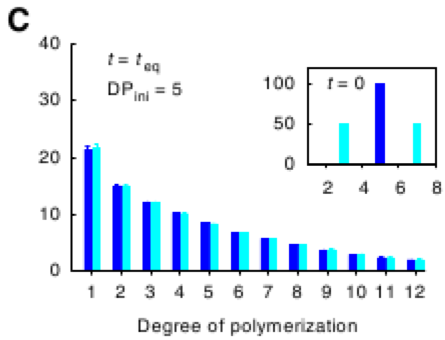
Where else do find entropic enzymes?

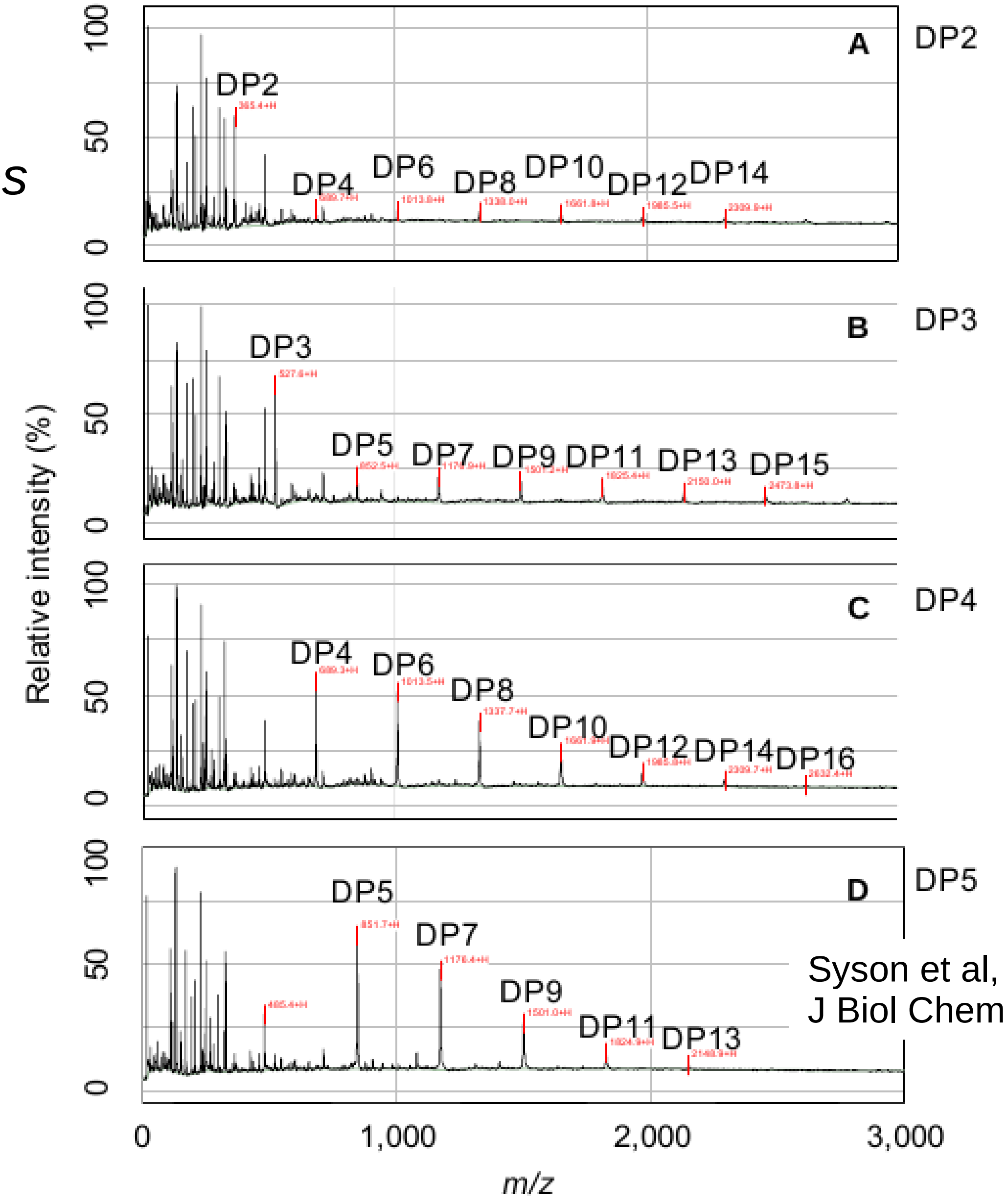
...for example

Maltosyltransferases in *Streptomyces*

“Acceptor specificity” can be explained by entropic principles







Syson et al, 2011, J Biol Chem

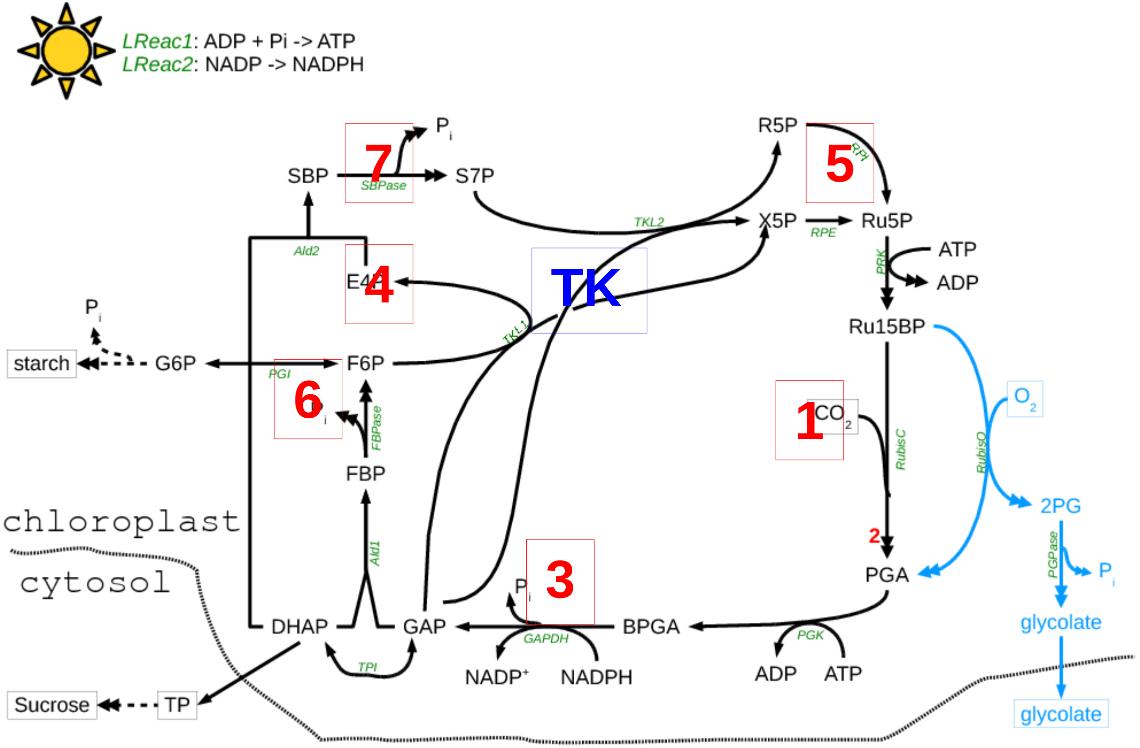
Where else do find entropic enzymes?

...or even in central metabolism?

Transketolase? $K_n + A_m \Leftrightarrow A_{n-2} + K_{m+2}$

Why only *n*=5,6,7 und *m*=3,4,5?
Why should there be no octuloses
nonuloses...?

Calvin cycle



Where else do find entropic enzymes?

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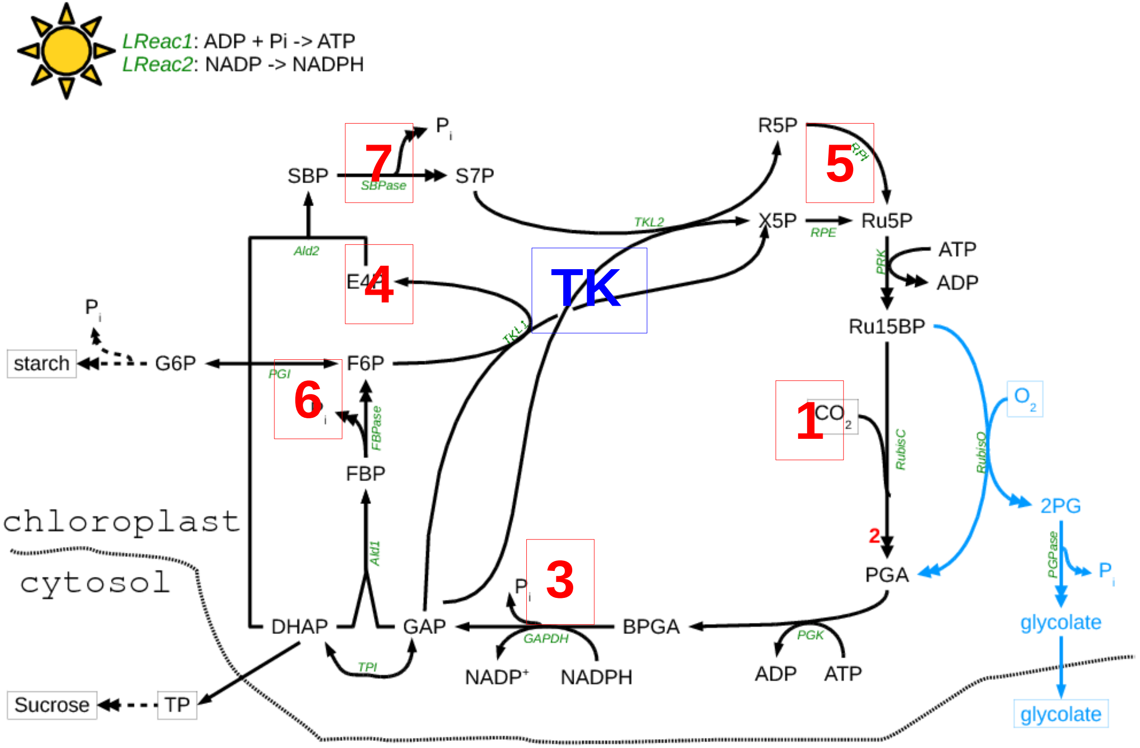
Calvin cycle

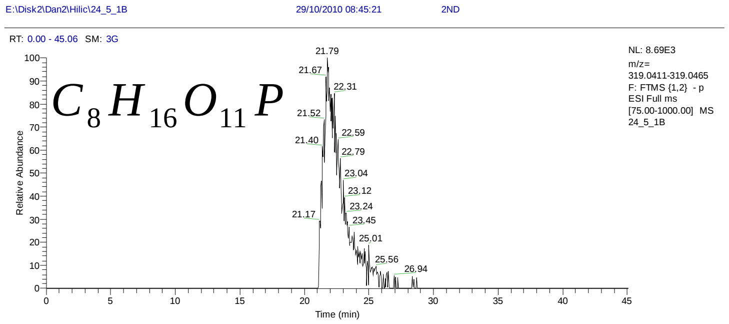


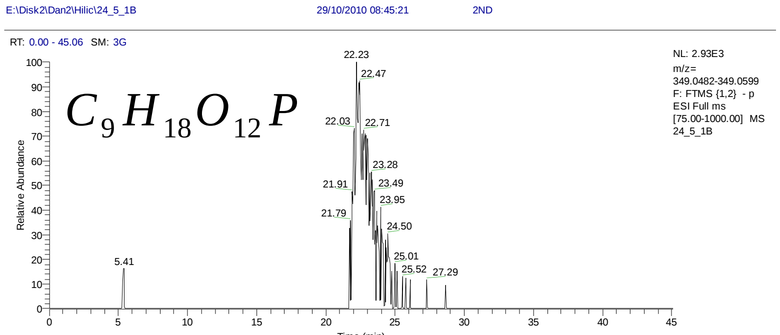
Transketolase? $K_n + A_m \Leftrightarrow A_{n-2} + K_{m+2}$

Why only *n*=5,6,7 und *m*=3,4,5?
Why should there be no octuloses nonuloses...?

The masses exist as 'unknown'

(C. Frezza, Glasgow, unpublished)


$C_8H_{16}O_{11}P$


$C_9H_{18}O_{12}P$

Calvin cycle energetics

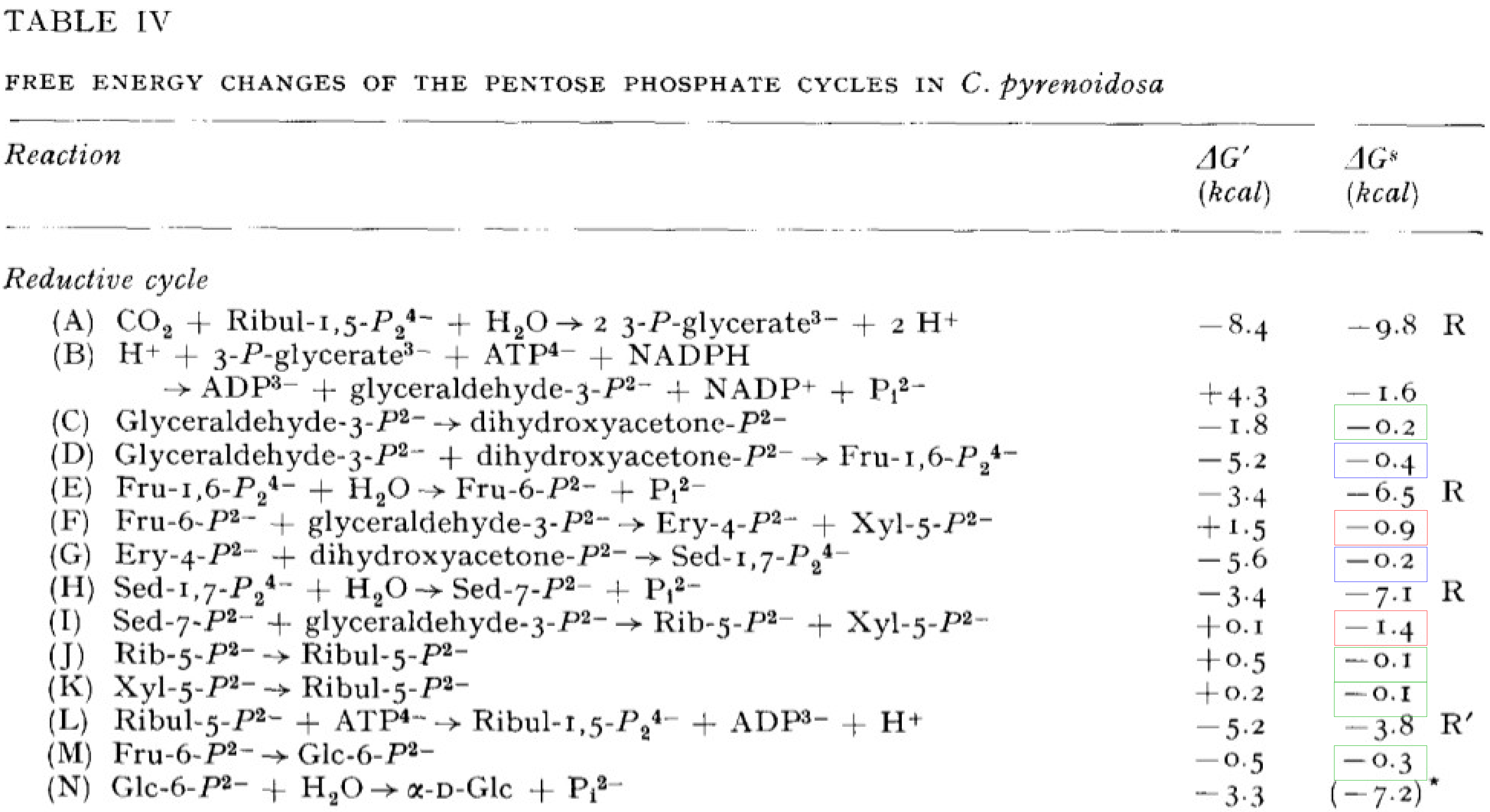


TABLE IV

FREE ENERGY CHANGES OF THE PENTOSE PHOSPHATE CYCLES IN *C. pyrenoidosa*

Reaction	$\Delta G'$ (*kcal*)	ΔG^s (*kcal*)		
Reductive cycle				
(A) CO_2 + Ribul-1,5-P_2^{4-} + H_2O → 2 3-*P*-glycerate^{3-} + 2 H^+	−8.4	−9.8	R	
(B) H^+ + 3-*P*-glycerate^{3-} + ATP^{4-} + NADPH → ADP^{3-} + glyceraldehyde-3-P^{2-} + $NADP^+$ + P_i^{2-}	+4.3	−1.6		
(C) Glyceraldehyde-3-P^{2-} → dihydroxyacetone-P^{2-}	−1.8	−0.2		**Iso**
(D) Glyceraldehyde-3-P^{2-} + dihydroxyacetone-P^{2-} → Fru-1,6-P_2^{4-}	−5.2	−0.4		**Ald**
(E) Fru-1,6-P_2^{4-} + H_2O → Fru-6-P^{2-} + P_i^{2-}	−3.4	−6.5	R	
(F) Fru-6-P^{2-} + glyceraldehyde-3-P^{2-} → Ery-4-P^{2-} + Xyl-5-P^{2-}	+1.5	−0.9		**TK**
(G) Ery-4-P^{2-} + dihydroxyacetone-P^{2-} → Sed-1,7-P_2^{4-}	−5.6	−0.2		**Ald**
(H) Sed-1,7-P_2^{4-} + H_2O → Sed-7-P^{2-} + P_i^{2-}	−3.4	−7.1	R	
(I) Sed-7-P^{2-} + glyceraldehyde-3-P^{2-} → Rib-5-P^{2-} + Xyl-5-P^{2-}	+0.1	−1.4		**TK**
(J) Rib-5-P^{2-} → Ribul-5-P^{2-}	+0.5	−0.1		**Iso**
(K) Xyl-5-P^{2-} → Ribul-5-P^{2-}	+0.2	−0.1		**Iso**
(L) Ribul-5-P^{2-} + ATP^{4-} → Ribul-1,5-P_2^{4-} + ADP^{3-} + H^+	−5.2	−3.8	R′	
(M) Fru-6-P^{2-} → Glc-6-P^{2-}	−0.5	−0.3		**Iso**
(N) Glc-6-P^{2-} + H_2O → α-D-Glc + P_i^{2-}	−3.3	(−7.2)*		

(Bassham and Krause, BBA 1969)

All 'close to equilibrium' reactions *shuffle*

Food for thoughts

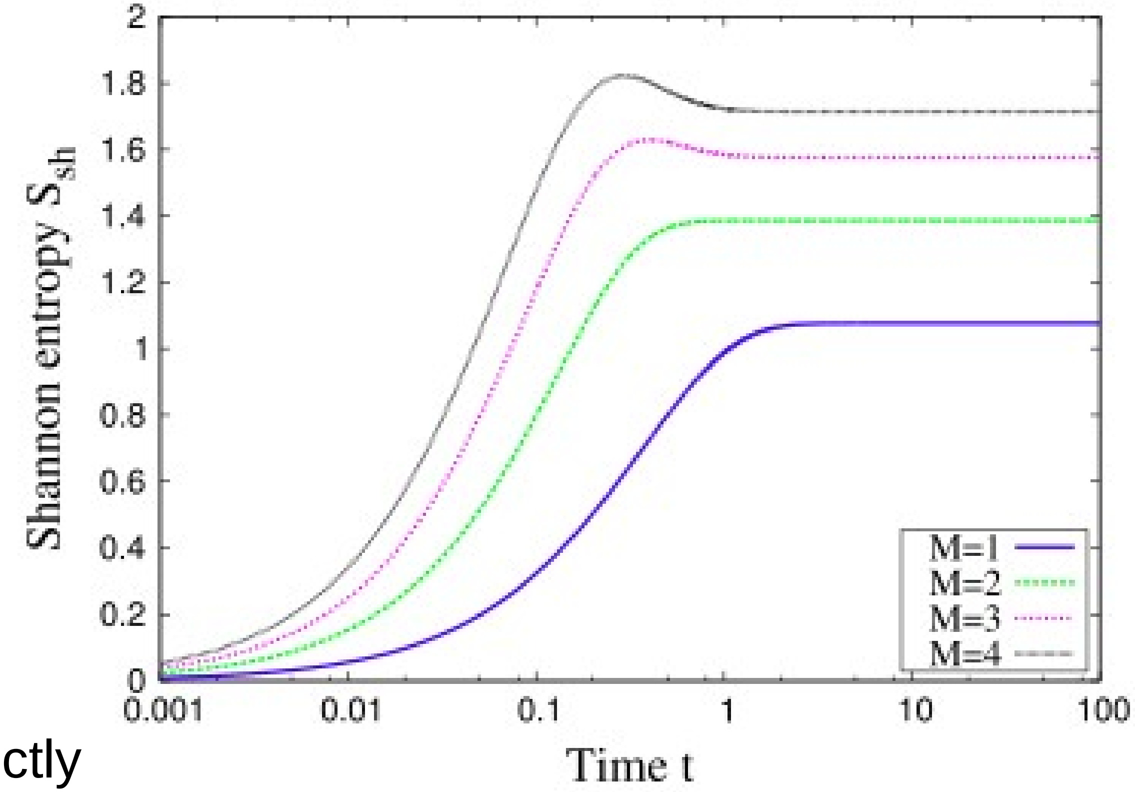
It appears that metabolism is organised as an interplay of 'entropic' and 'energetic' enzymes

- Why?
- Are there principles behind this organisation?
- How is this connected to resource allocation?

Theoretical advances

Lahiri et al (2015), *New J Phys*

In simulations: a temporary ***decrease*** of entropy when molecule number is not conserved!



Solution:
Entropy production rate is not correctly captured by increase in Shannon entropy

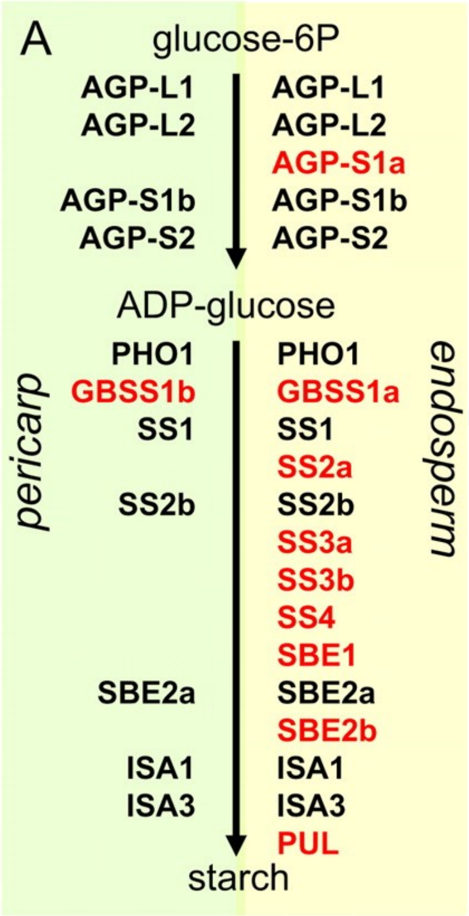
$$T\Sigma = -\frac{\mathrm{d}}{\mathrm{d}t}\left[\mathcal{H} - TS - RTC \ln\frac{C}{C^{\mathrm{eq}}} - RT\left(C^{\mathrm{eq}} - C\right)\right] \geqslant 0.$$

Can we use in vitro polymer biochemistry systems to verify novel results from theoretical physics??

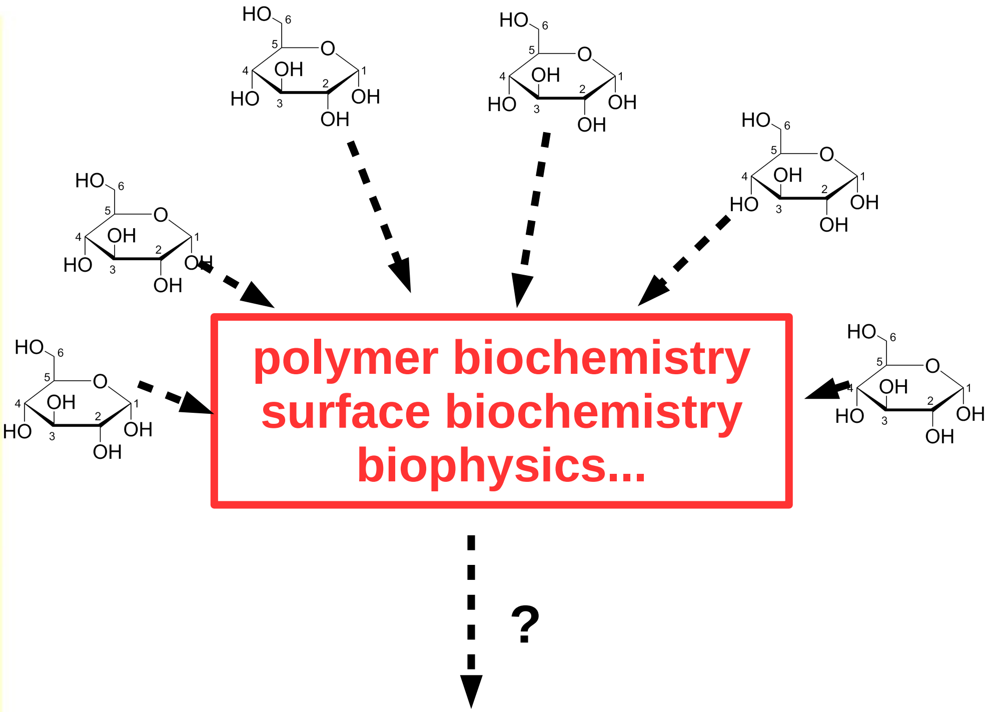
Outlook: Towards synthetic starch

Many different processes play together!

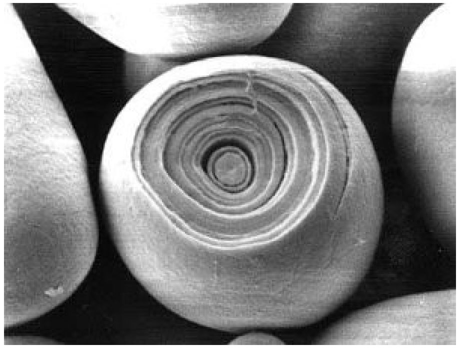
- starch synthases
- branching enzymes
- phosphorylases
- isoamylases



(Radchuk et al, 2009)



polymer biochemistry
surface biochemistry
biophysics...




www.nobelprize.org

Richard Feynman:

“What I cannot create, I do not understand!”

www.nobelprize.org

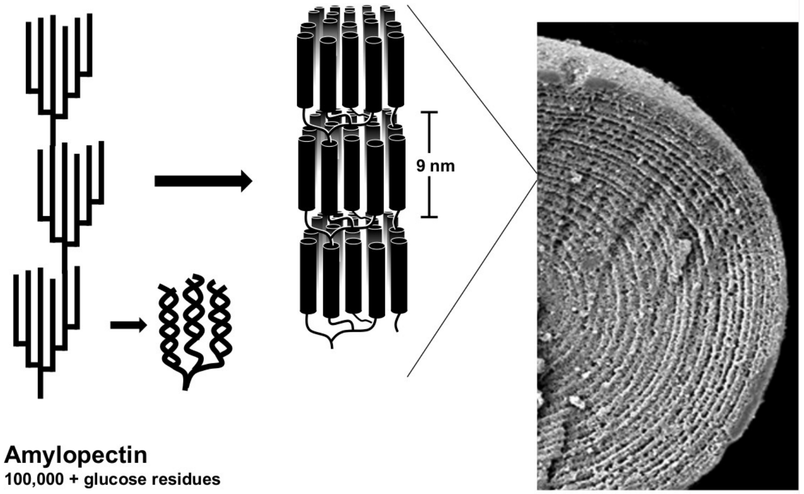
Richard Feynman:

“What I cannot create, I do not understand!”

⇒ Let's build starch!

Preliminary work:
expressing starch-like polymers in yeast

The branching pattern matters!



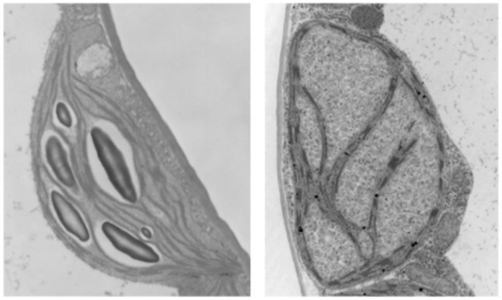
Sam Zeeman, ETH Zurich

ADPglucose → Chain elongation → Branching → Debranching !

5 iso-enzymes 2+ iso-enzymes 3 iso-enzymes

Plants

SS1	Synthesis of short chains
SS2	Elongation of intermediate chains
SS3	Synthesis of long cluster-spanning chains
SS4	Granule initiation and shape
GBSS	Amylose synthesis within the granule



Normal -1 debranching enzyme

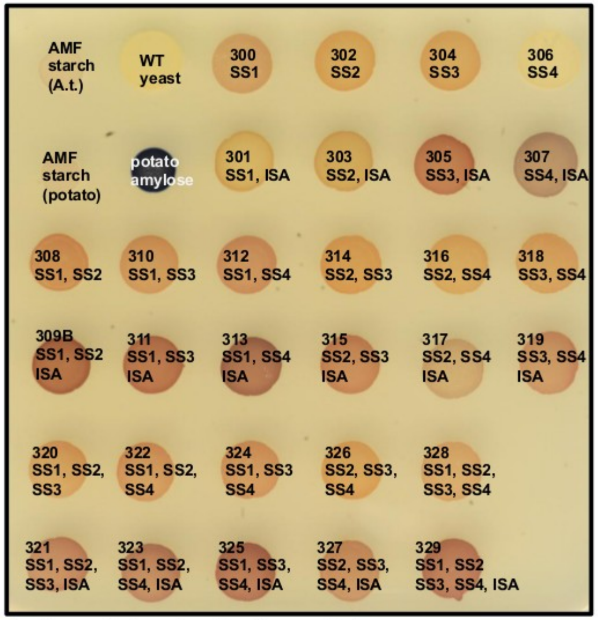
Debranching enzymes are critical for making branched glucans!

Preliminary work:
expressing starch-like polymers in yeast

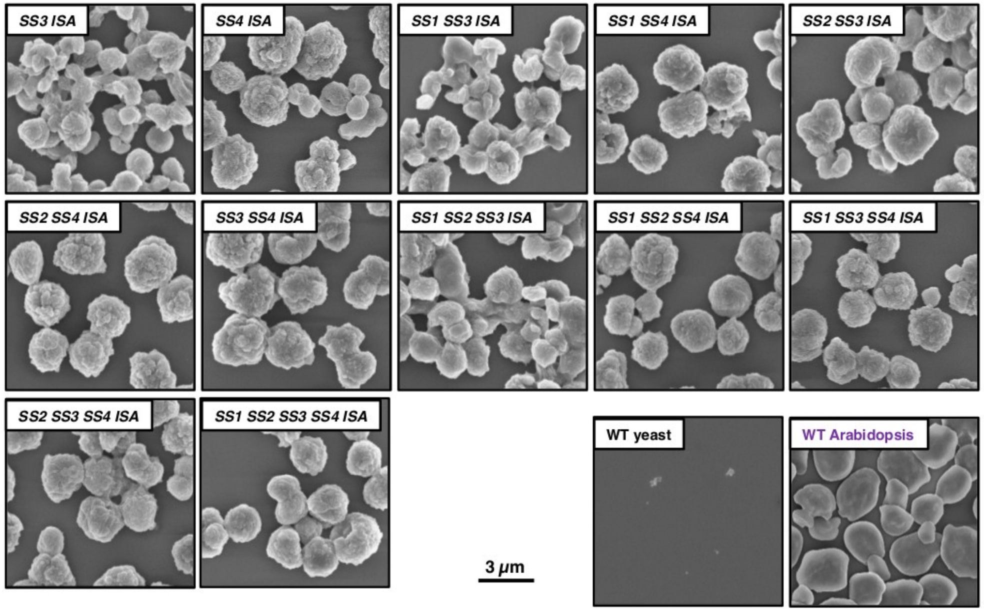
STARCH IN YEAST?

Barbara Pfister,
ETH Zurich

- Delete all 7 glycogen biosynthesis genes
- Progressively add Arabidopsis genes
- All lines express AGPase and both BE isoforms
- Variable combinations of starch synthases with the presence/absence of ISA



Iodine-stained galactose plate

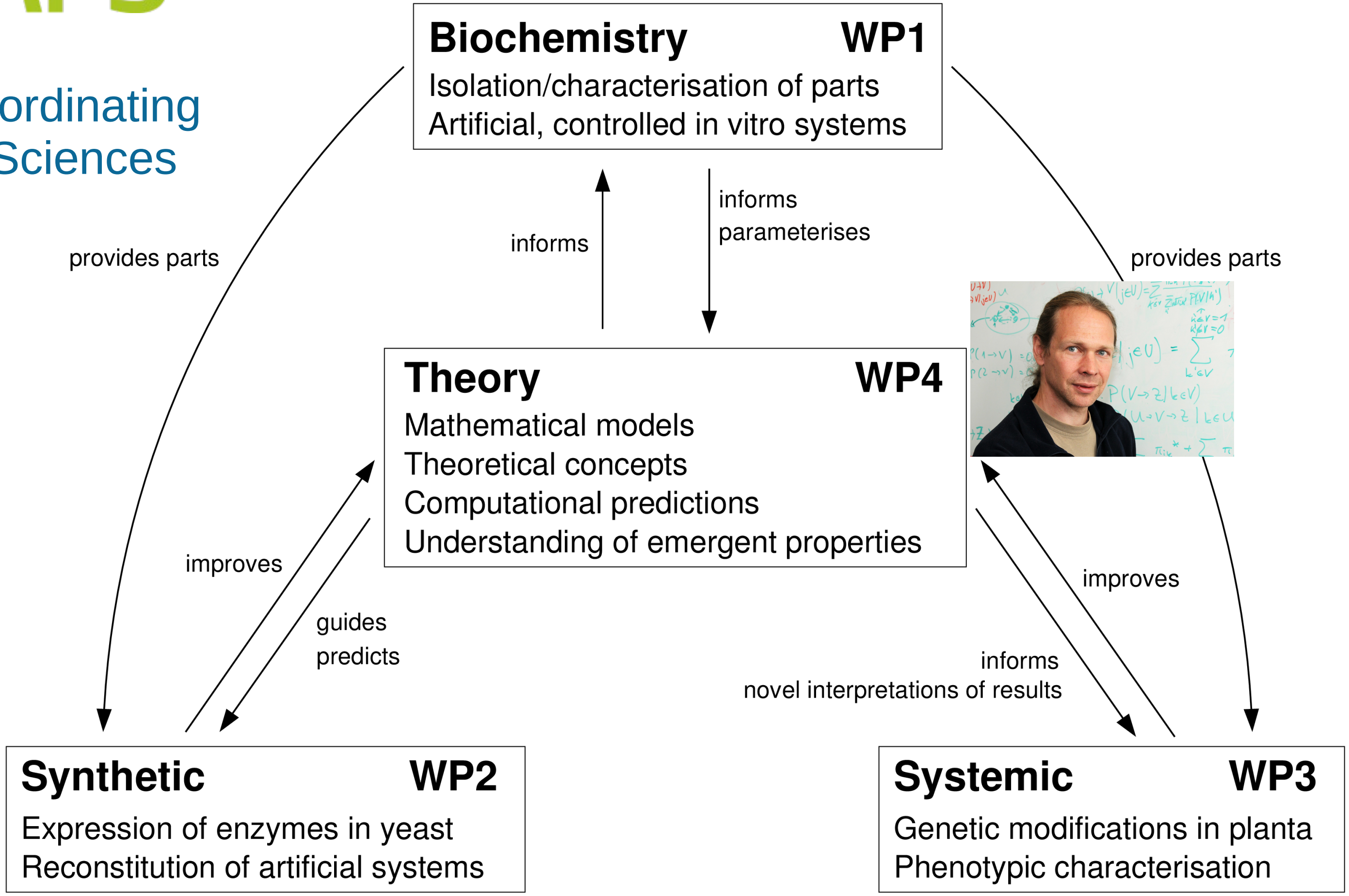


DesignStarch

ERA-CAPS

ERA-NET for Coordinating Action in Plant Sciences

Rob Field, JIC Norwich



Biochemistry **WP1**
Isolation/characterisation of parts
Artificial, controlled in vitro systems

Theory **WP4**
Mathematical models
Theoretical concepts
Computational predictions
Understanding of emergent properties

Synthetic **WP2**
Expression of enzymes in yeast
Reconstitution of artificial systems

Systemic **WP3**
Genetic modifications in planta
Phenotypic characterisation

Sam Zeeman, ETH Zurich

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Zurich:	Önder Kartal Sam Zeeman Barbara Pfister
Luxemburg:	Alexander Skupin

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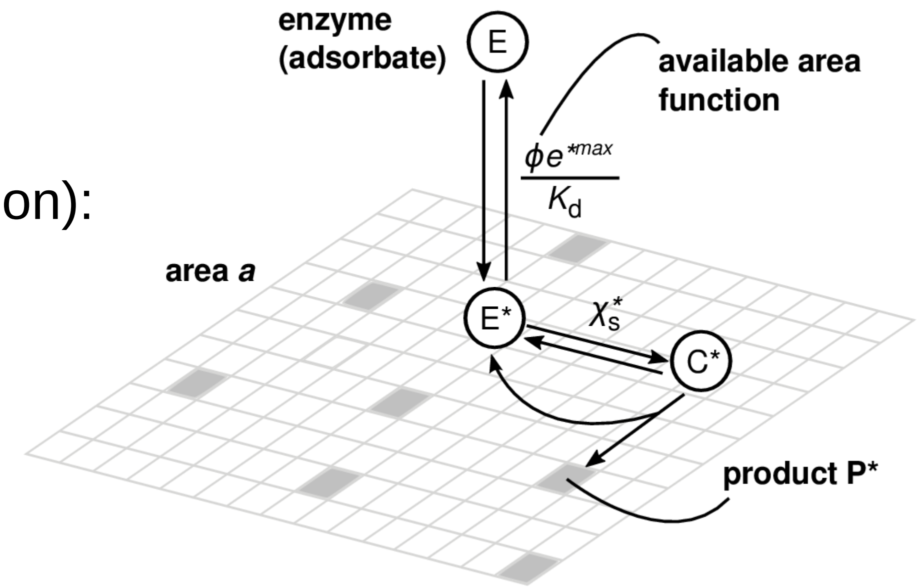
The adsorption equilibrium



The Langmuir isotherm
(a concept from surface physics)

Adsorption coverage (surface concentration):

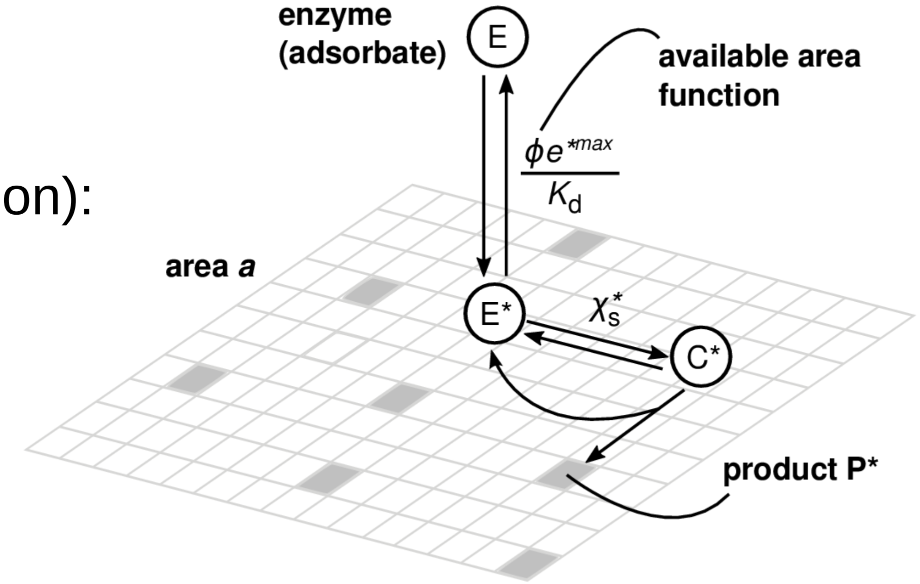
$$\theta_E = \frac{n(E)}{n(E)_{\max}} = \frac{n(E)}{E_{\max} \cdot S}$$

Adsorption rate: $r_a \propto c(E) \cdot (1 - \theta_E)$

Desorption rate: $r_d \propto \theta_E$

The adsorption equilibrium

The Langmuir isotherm
(a concept from surface physics)



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Available area function

Desorption rate: $r_d \propto \theta_E$

Polydisperse mixtures as statistical ensembles

x_i : molar fraction of glucans with length *i*
corresponds to occupation number of state *i*

The distribution $\{x_i\}$ fully characterises the polydisperse reactant mixture

The entropy of the statistical ensemble is $S = -\sum x_k \ln x_k$

Equilibrium is determined by maximal entropy:

$$S = -\sum x_k \ln x_k \rightarrow \max!$$

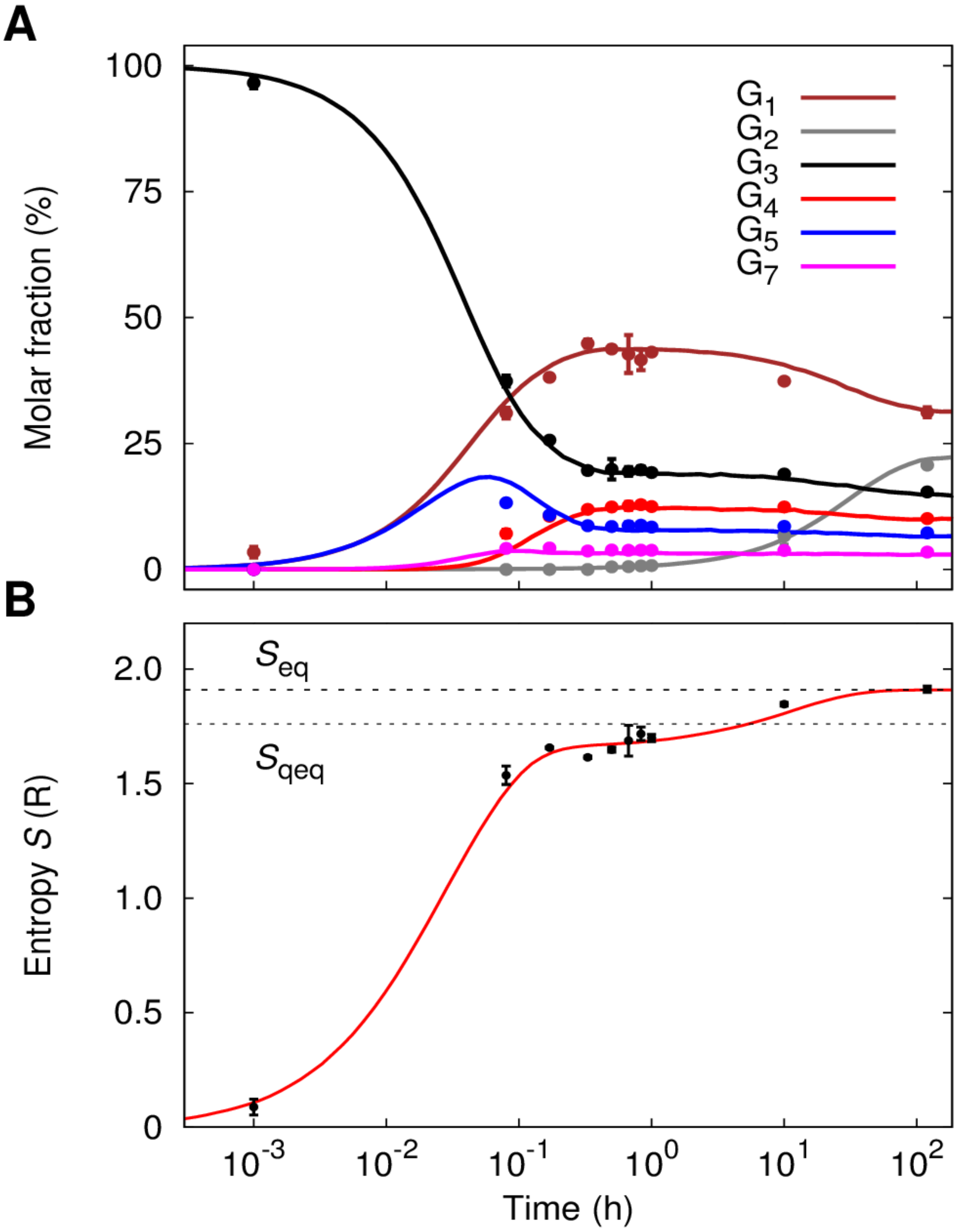
Maximum entropy principle under constraint that #bonds and #molecules is conserved!

conservation of #molecules: $\sum x_k = 1$

conservation of #bonds: $\sum k \cdot x_k = b$ ←

determined by initially applied mixture of maltodextrins

This system allows to follow the entropy *experimentally*!



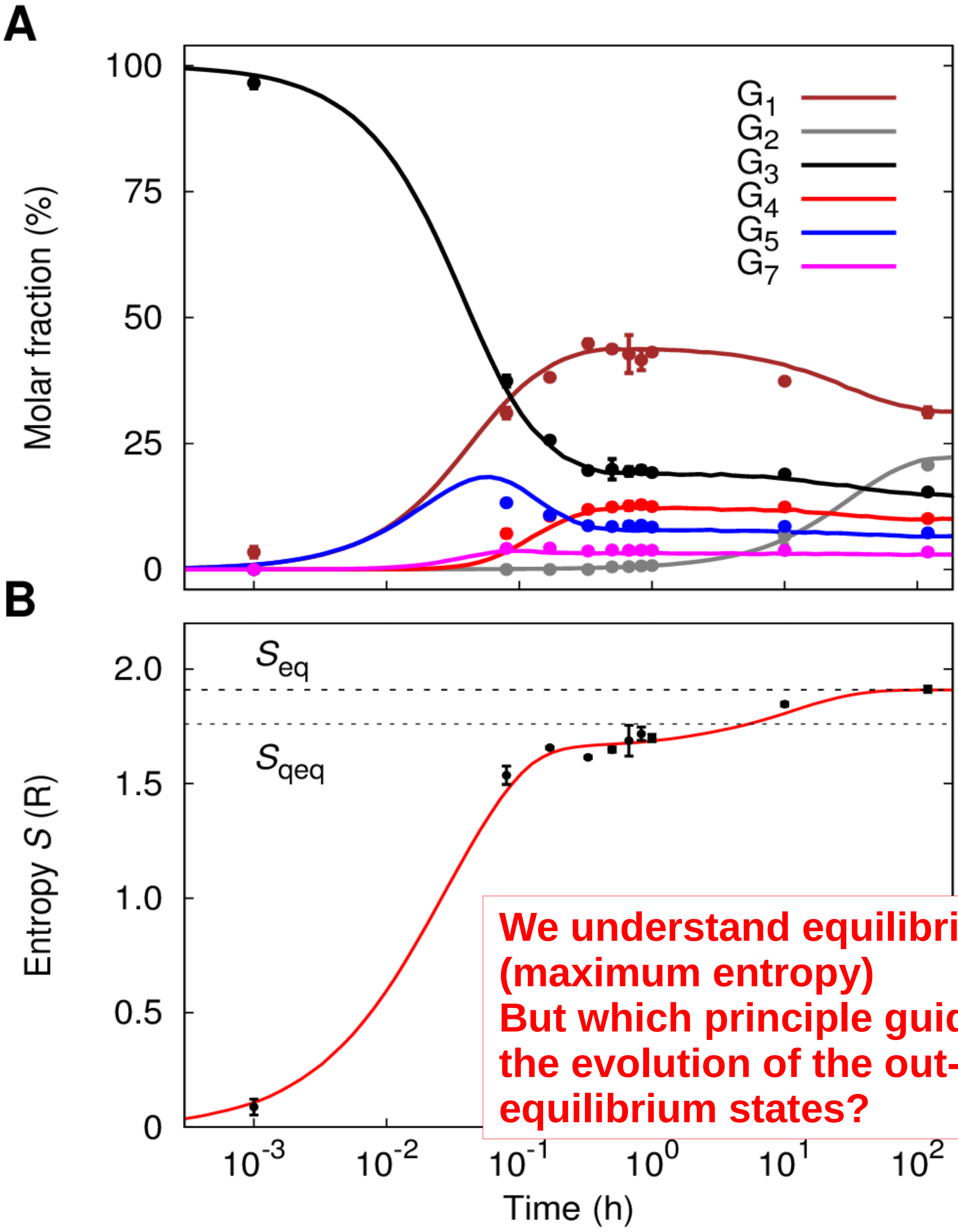
“true” equilibrium

(calculated as previously)

“quasi” equilibrium

(calculated with the same approach but omitting maltose from the statistical ensemble)

This system allows to follow the entropy *experimentally*!



“true” equilibrium

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We understand equilibrium (maximum entropy)
But which principle guides the evolution of the out-of-equilibrium states?

Maltose turnover