CEPLAS
Cluster of Excellence on Plant Sciences

HEINRICH HEINE
UNIVERSITÄT DÜSSELDORF

Energy Metabolism and Thermodynamics

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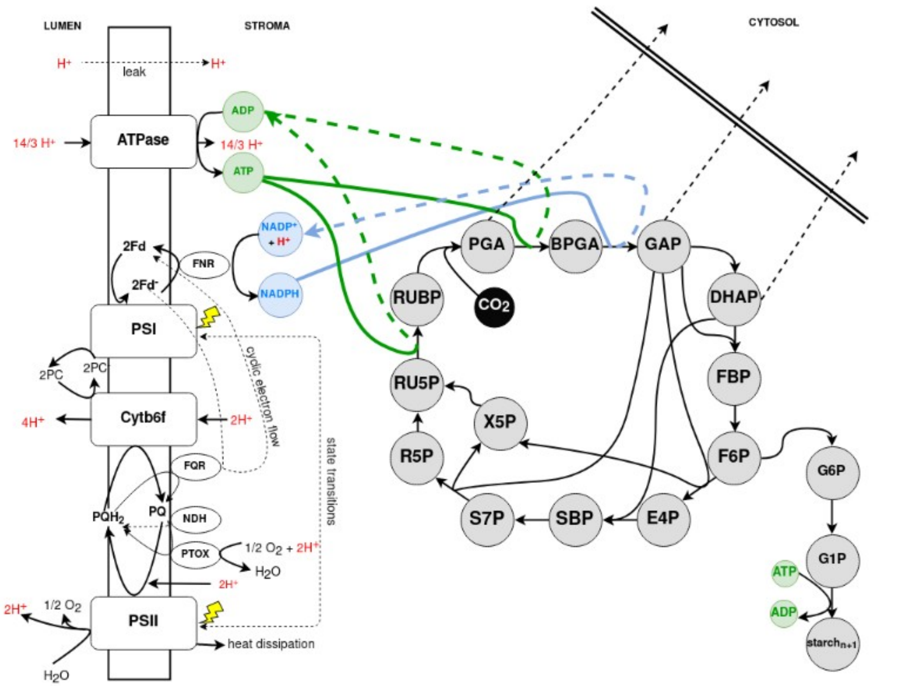
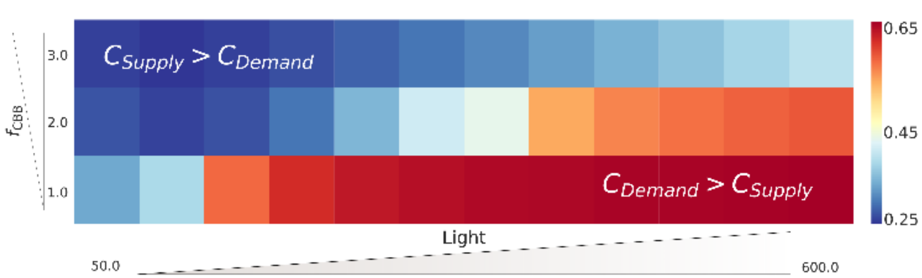
Institut für
Quantitative & Theoretische
Biologie

Ringvorlesung Masterstudium Biologie, 20.12.2018

Institut für Quantitative & Theoretische Biologie

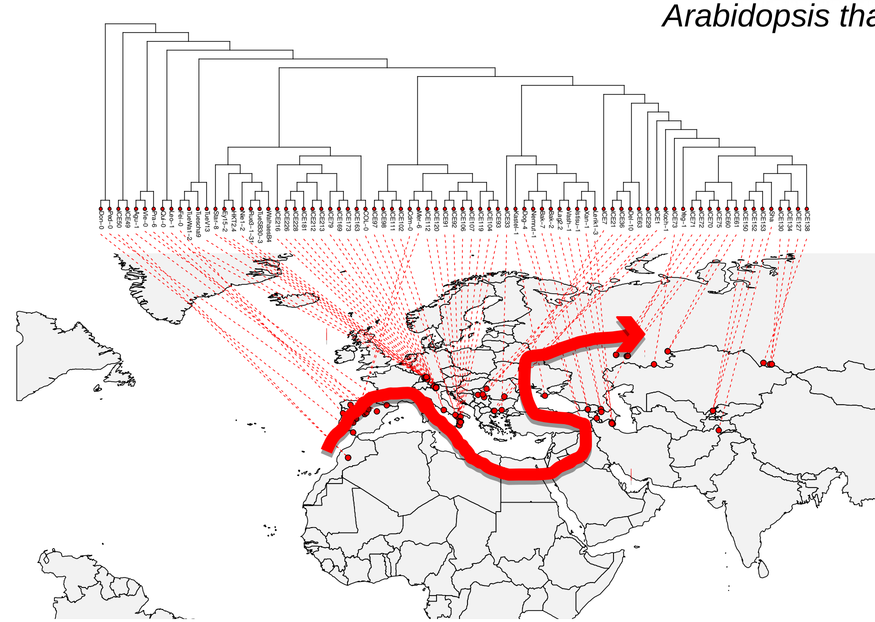
Mathematical modelling

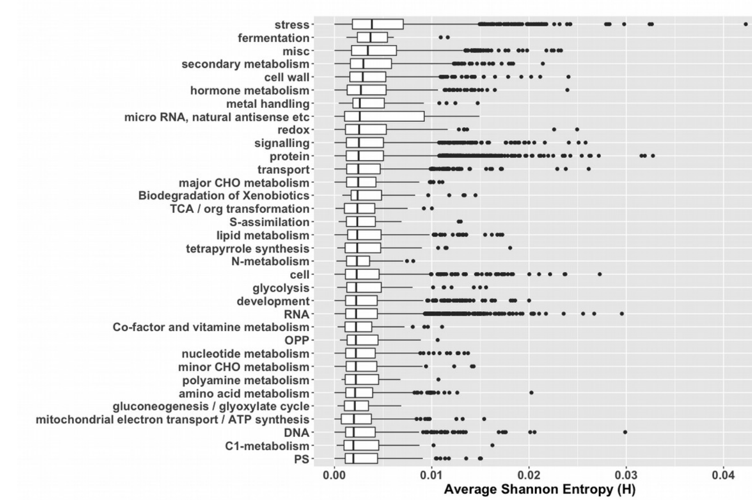




Bioinformatics

Arabidopsis thaliana





Thermodynamics

Science concerned with heat and its relation to energy and work

Developed out of a desire to increase the efficiency of steam engines

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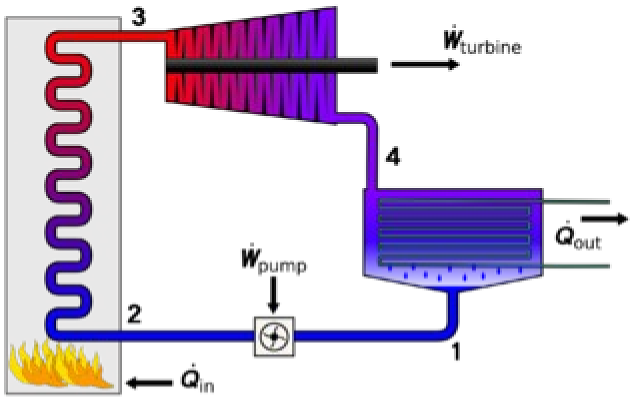

wikipedia.org

Efficiency: $$\frac{\text{energy output of mechanical work that the engine produces}}{\text{energy input to the engine by the burning fuel}}$$

Thermodynamics in Biology?

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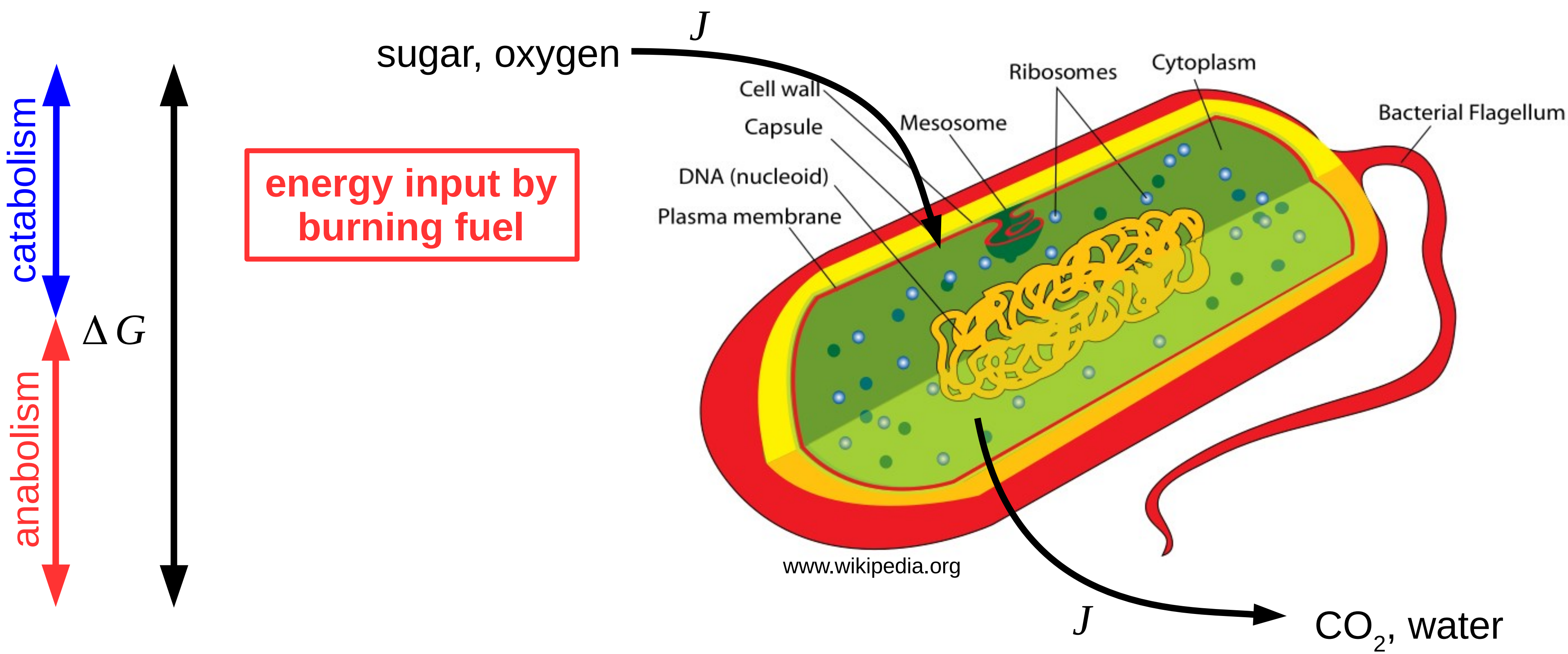
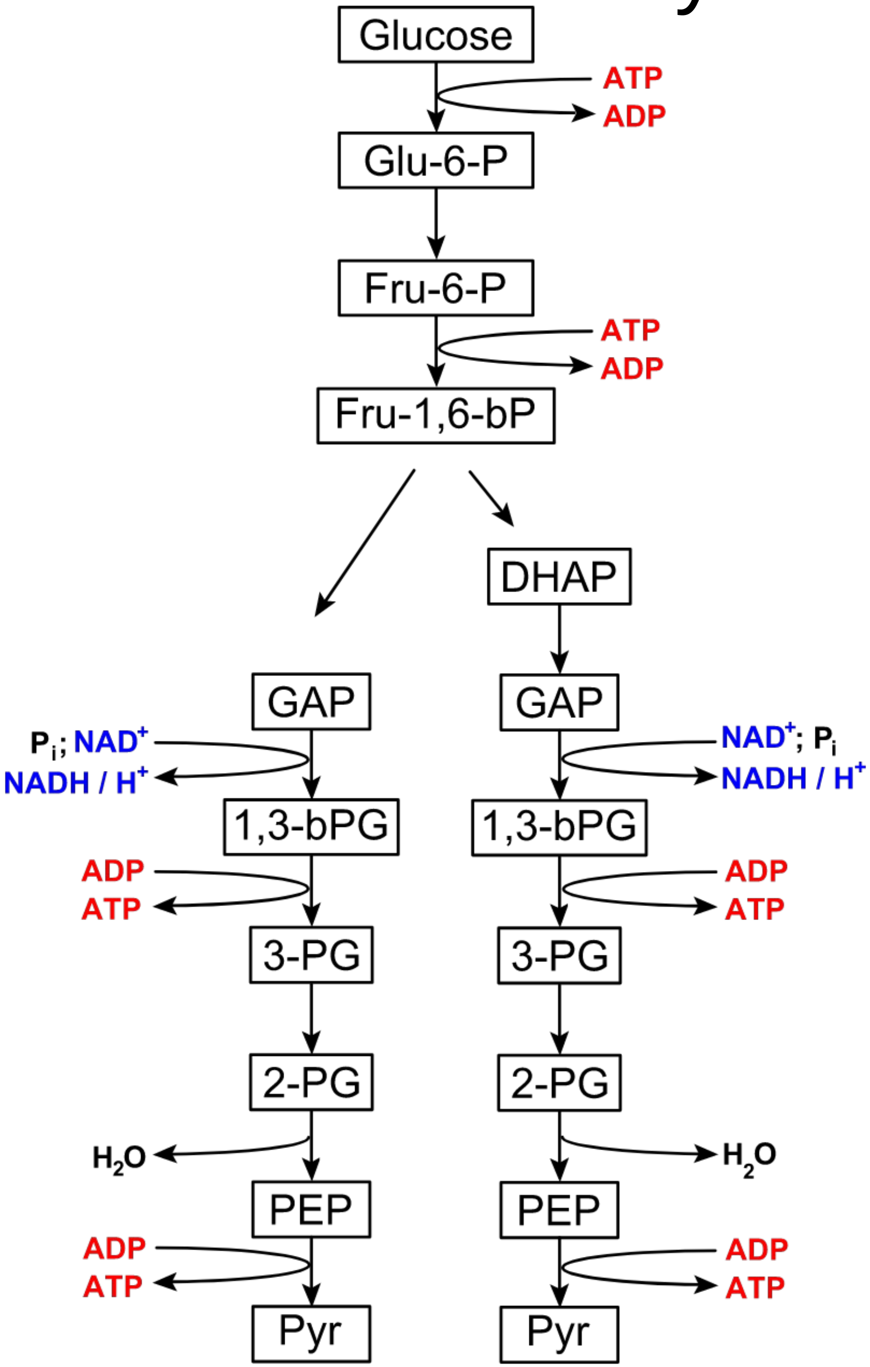


What is the output?

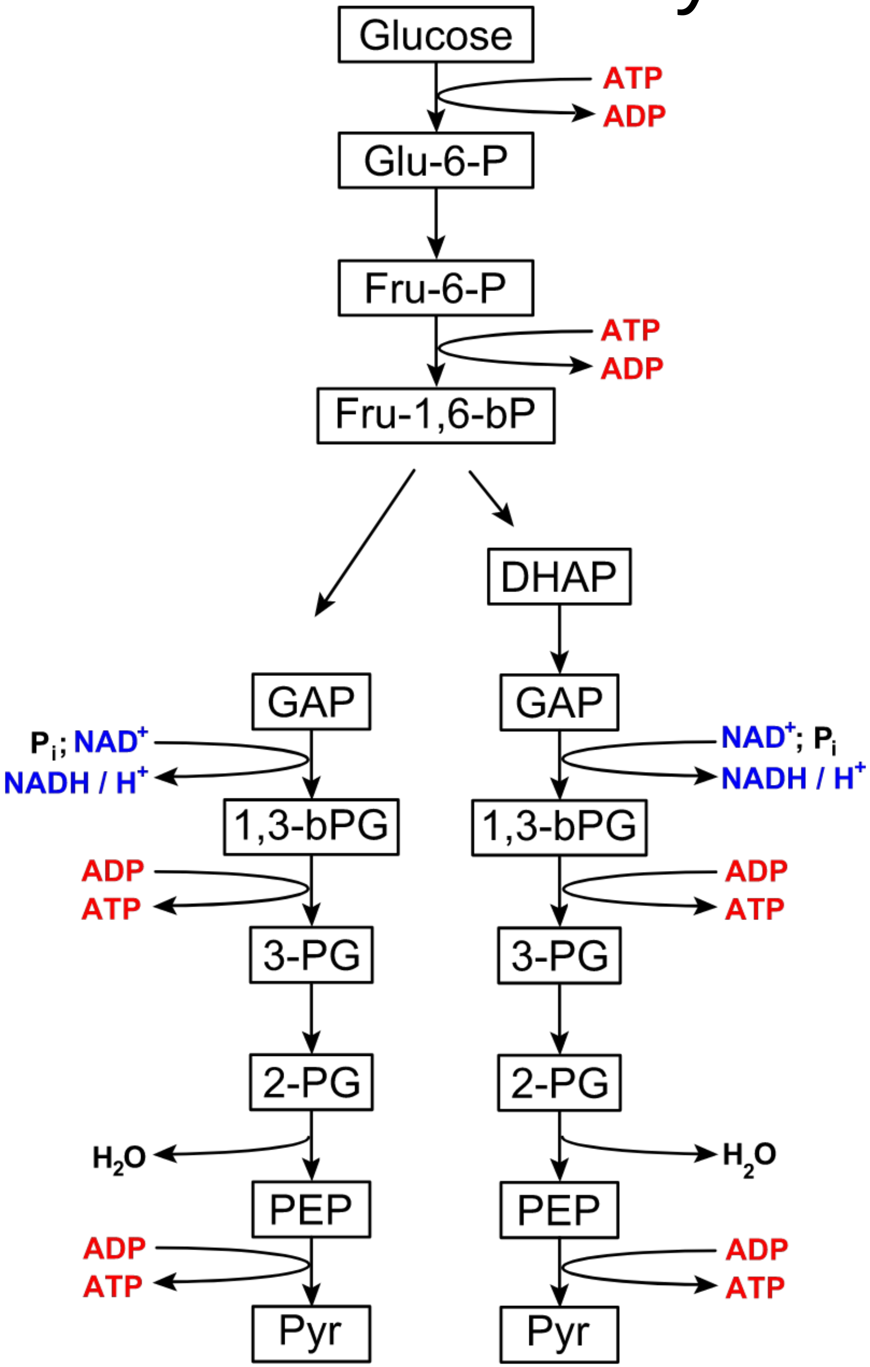
For unicellular organisms (E. coli): growth

Thermodynamics in Metabolism



www.libretexts.org

Thermodynamics in Metabolism



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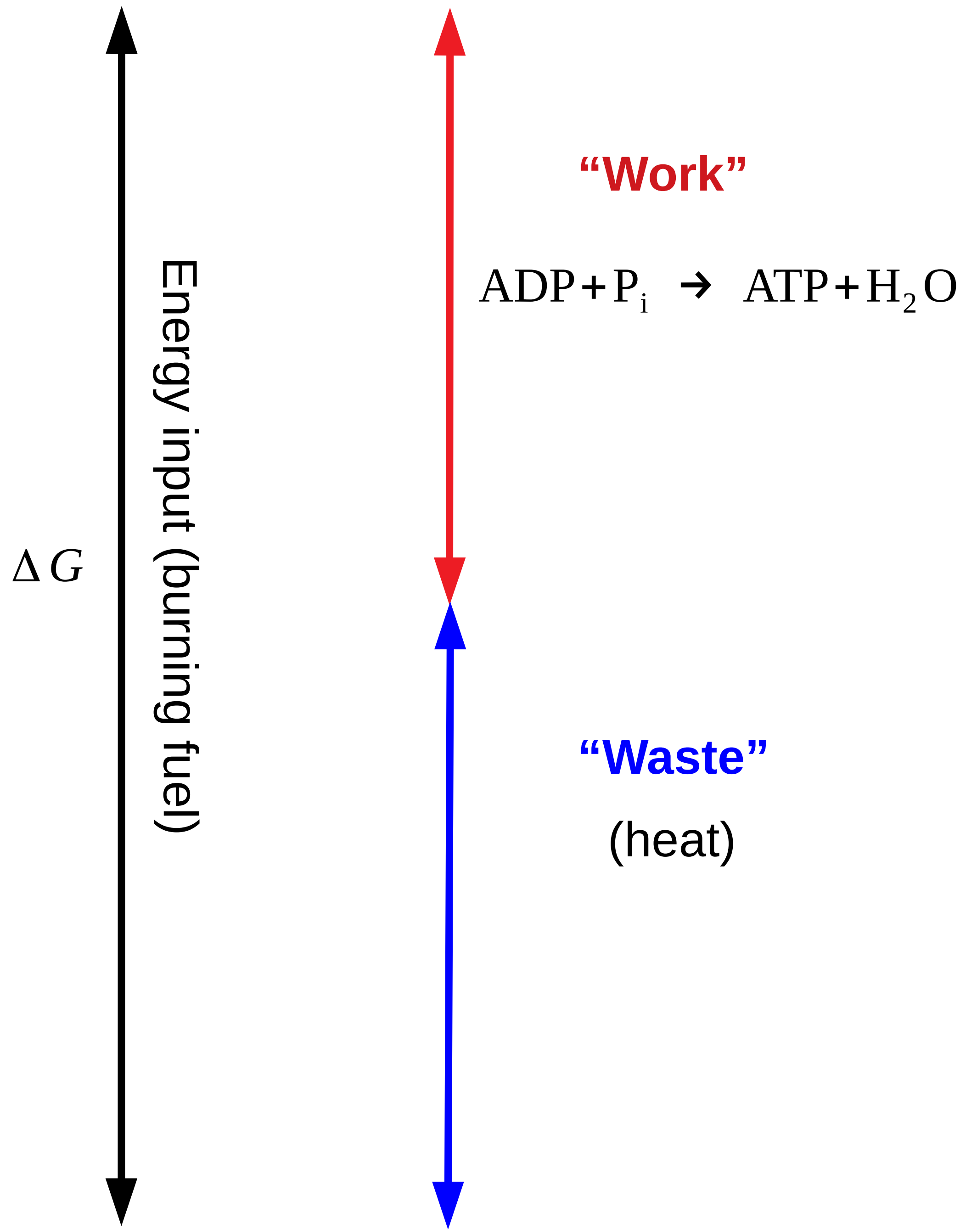

Laws of Thermodynamics

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0: If systems A and B are in thermal equilibrium, and B and C are in thermal equilibrium, then also A and C are in thermal equilibrium

$\Rightarrow$ **Temperature**

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⇨ **Temperature**

1: The increase in internal energy of a closed system is equal to the difference of the heat supplied to it and the work done by it

⇨ **Internal energy** (as opposed to kinetic, potential energy etc.)

$$\Delta U = \Delta Q - \Delta W$$

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⇨ **Entropy**

3: As a system approaches absolute zero the entropy of the system approaches a minimum value

Important for small absolute T, not relevant for biology

Energy

Internal energy is the total energy contained in a thermodynamic system.

It is the energy needed to create the system

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Usually, we are concerned with changes in energy: $\Delta U = \Delta Q - \Delta W$

energy change (ΔU), heat added (ΔQ), work done (ΔW)

The same as energy conservation!

Work: $\Delta W = p \cdot \Delta V$

Heat: $\Delta Q = T \cdot \Delta S$

p: pressure

V: volume

T: temperature

S: entropy

Entropy

2^{nd} law: The entropy of the universe is always increasing!

⇓

The arrow of time!

Entropy

2^{nd} law: The entropy of the universe is always increasing!

⇩

The arrow of time!

[medium.com]

[streetsmash.com]

WHY?

Low entropy

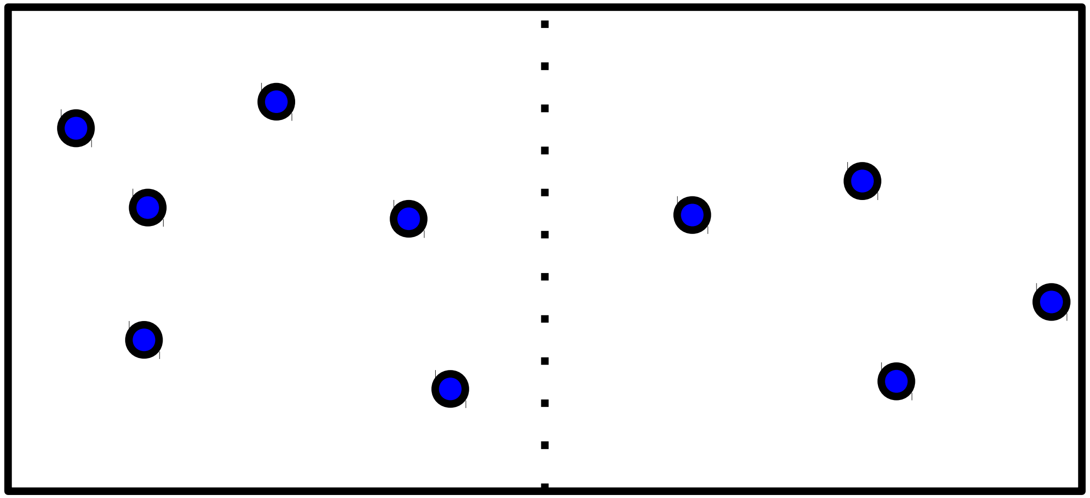
High entropy

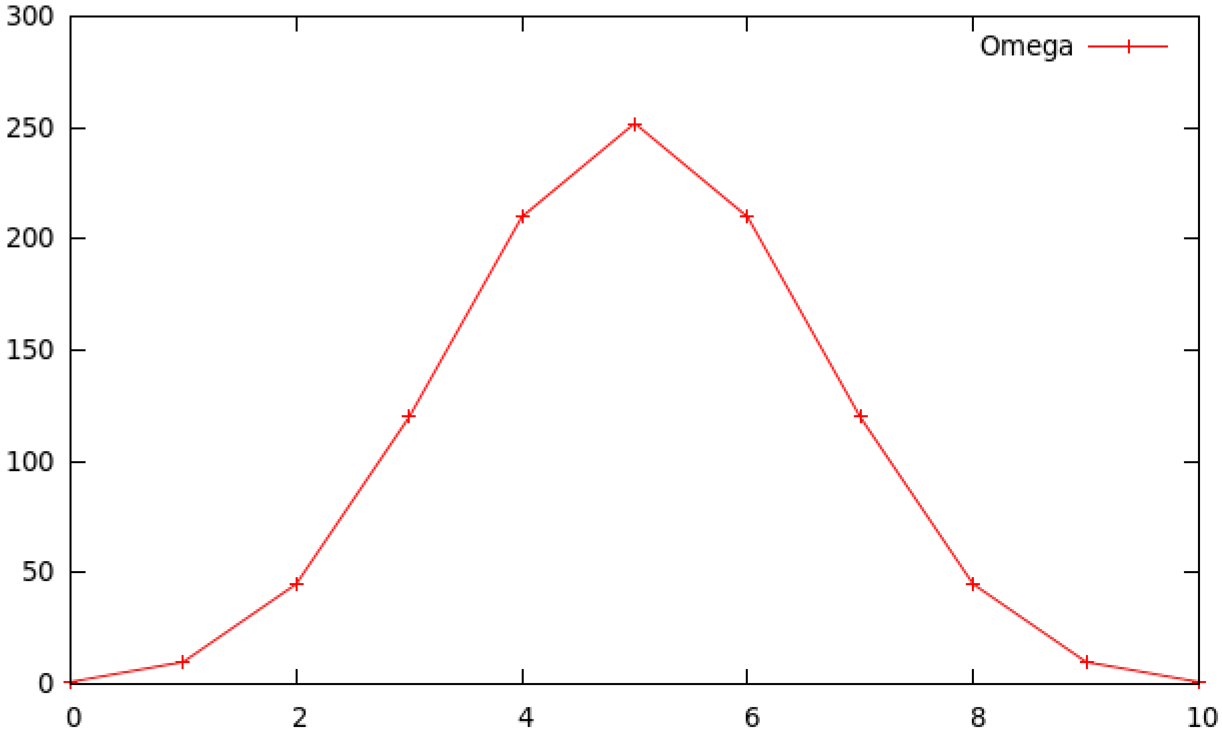
Entropy

Gas: *N* particles, can be either left or right

N=10

left	right	Ω
0	10	1
1	9	10
2	8	45
3	7	120
4	6	210
5	5	252
6	4	210
7	3	120
8	2	45
9	1	10
10	0	1





Entropy

Ω: # microstates for macrostate

The famous Boltzmann formula:

$$S = k_B \ln(\Omega)$$

For large numbers this becomes:

$$S = -k_B \sum_i p_i \ln(p_i)$$

left	right	Ω
0	10	1
1	9	10
2	8	45
3	7	120
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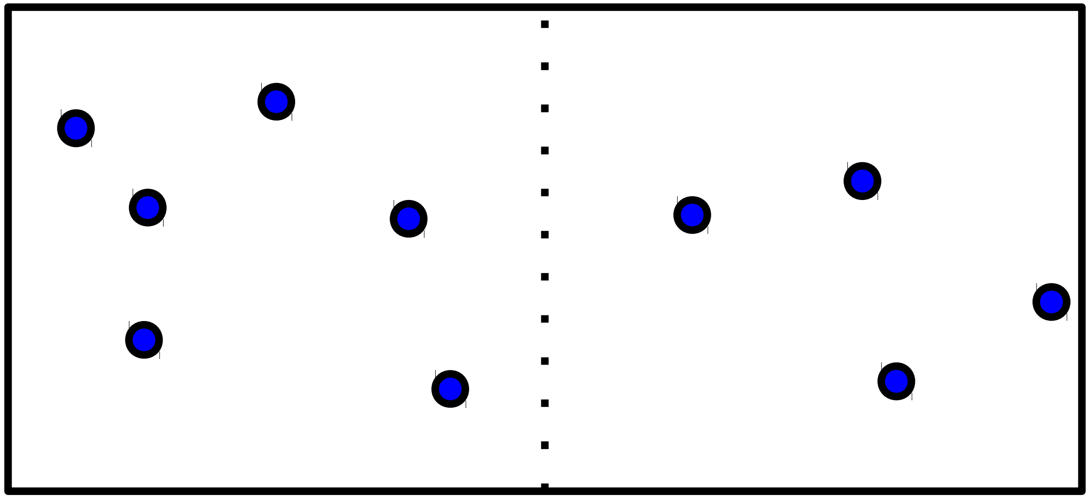
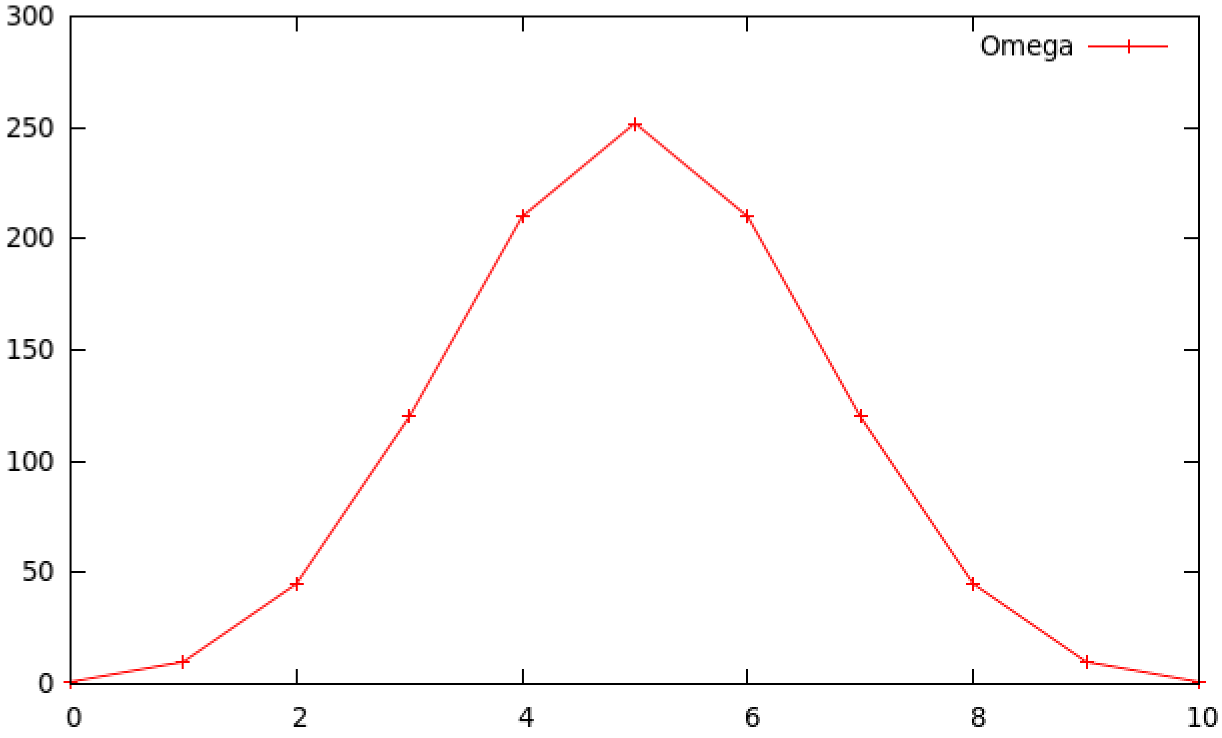




Entropy

2nd law: The entropy of the universe is always increasing!

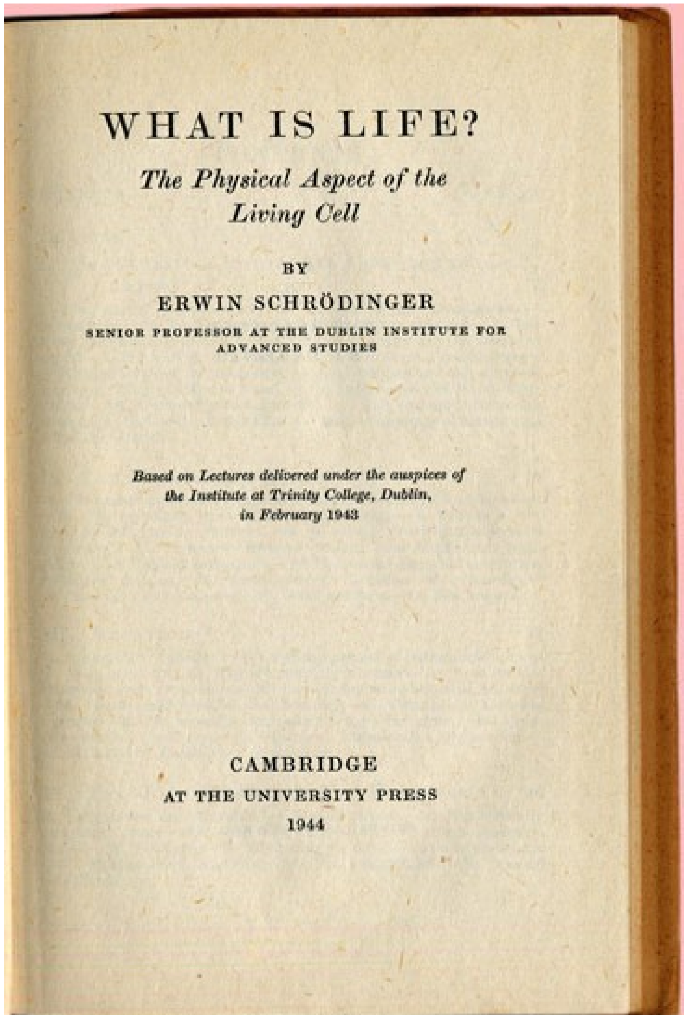
⇩

The universe will reach equilibrium (‘heat death’)

How can something like life, with all its patterns and structure, exist if entropy always increases?

Consume food?
(one atom is as good as any other;
one calorie is as good as any other)

Export entropy!!


WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

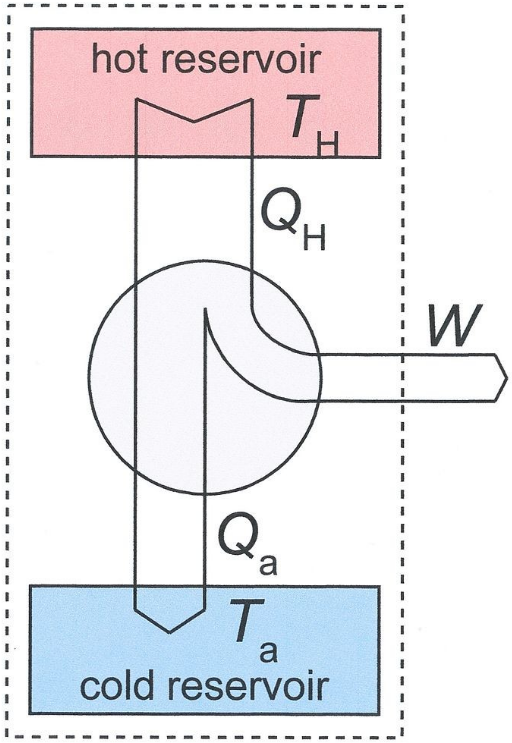
SENIOR PROFESSOR AT THE DUBLIN INSTITUTE FOR ADVANCED STUDIES

Based on Lectures delivered under the auspices of the Institute at Trinity College, Dublin, in February 1943

CAMBRIDGE
AT THE UNIVERSITY PRESS
1944

Entropy (classical)

Entropy is defined as $\Delta S = \frac{\Delta Q}{T}$ Amount of heat added to a system divided by its temperature



"heat engine"

1st law (energy conservation): $W = Q_H - Q_a$

Entropy change: $S_i = -\frac{Q_H}{T_H} + \frac{Q_a}{T_a} \geq 0$ (2nd law)

Work done: $W = \left(1 - \frac{T_a}{T_H}\right) Q_H - T_a S_i$

$= W_{max} - T_a S_i$

Energy lost due to entropy production!

isolated (no exchange of matter)

adiabatic (no exchange of heat)

not closed! (exchange of work!)

The entropy balance of a living cell

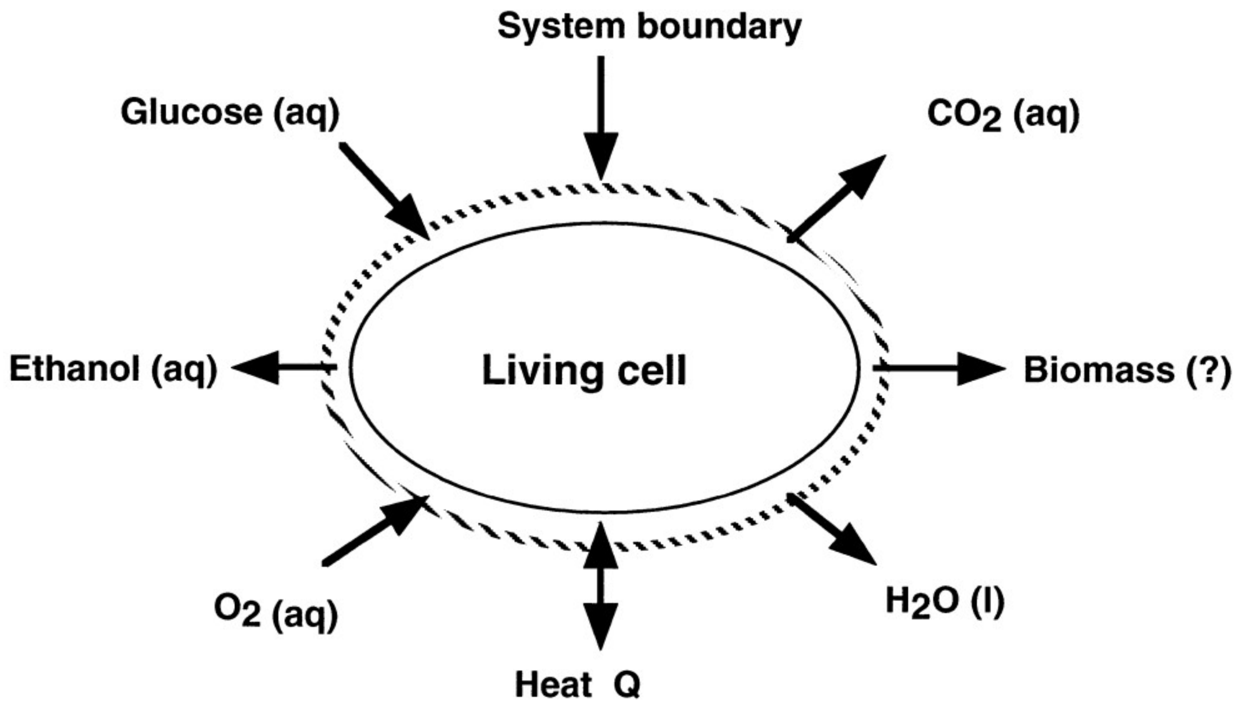


Fig. 1. Living cells as open systems.

$$\frac{dS}{dt} = \frac{d_{\mathrm{int}}S}{dt} + \frac{d_{\mathrm{e}}S}{dt} = \underline{\dot{S}_{\mathrm{Prod}}} + \underline{\frac{\dot{Q}}{T}} + \underline{\sum_i s_{e,i}\dot{n}_{e,i}} \leq 0$$

Internally produced entropy (>0) heat exchange metabolite exchange

- Entropy is always produced (metabolism, maintenance, …)
- This needs to be balanced by exporting entropy (e.g. as heat or as low entropy molecular products)

von Stockar and Liu (1999), “Does microbial life always feed on negative entropy?”, BBA 1412:191-211

Thermodynamic potentials

Internal energy: $\Delta U = T\Delta S - p\Delta V$

S and *V* constant: *U* decreases and reaches a minimum at equilibrium

capacity to do work plus the capacity to release heat

(Helmholtz) Free energy: $F = U - TS \;\Rightarrow\; \Delta F = -S\Delta T - p\Delta V$

T and *V* constant: *F* decreases and reaches a minimum at equilibrium

capacity to do mechanical work

Enthalpy: $H = U + pV \;\Rightarrow\; \Delta H = T\Delta S + V\Delta p$

S and *p* constant: *H* decreases and reaches a minimum at equilibrium

capacity to do non-mechanical work plus the capacity to release heat

Gibbs free energy: $G = U + pV - TS \;\Rightarrow\; \Delta H = -S\Delta T + V\Delta p$

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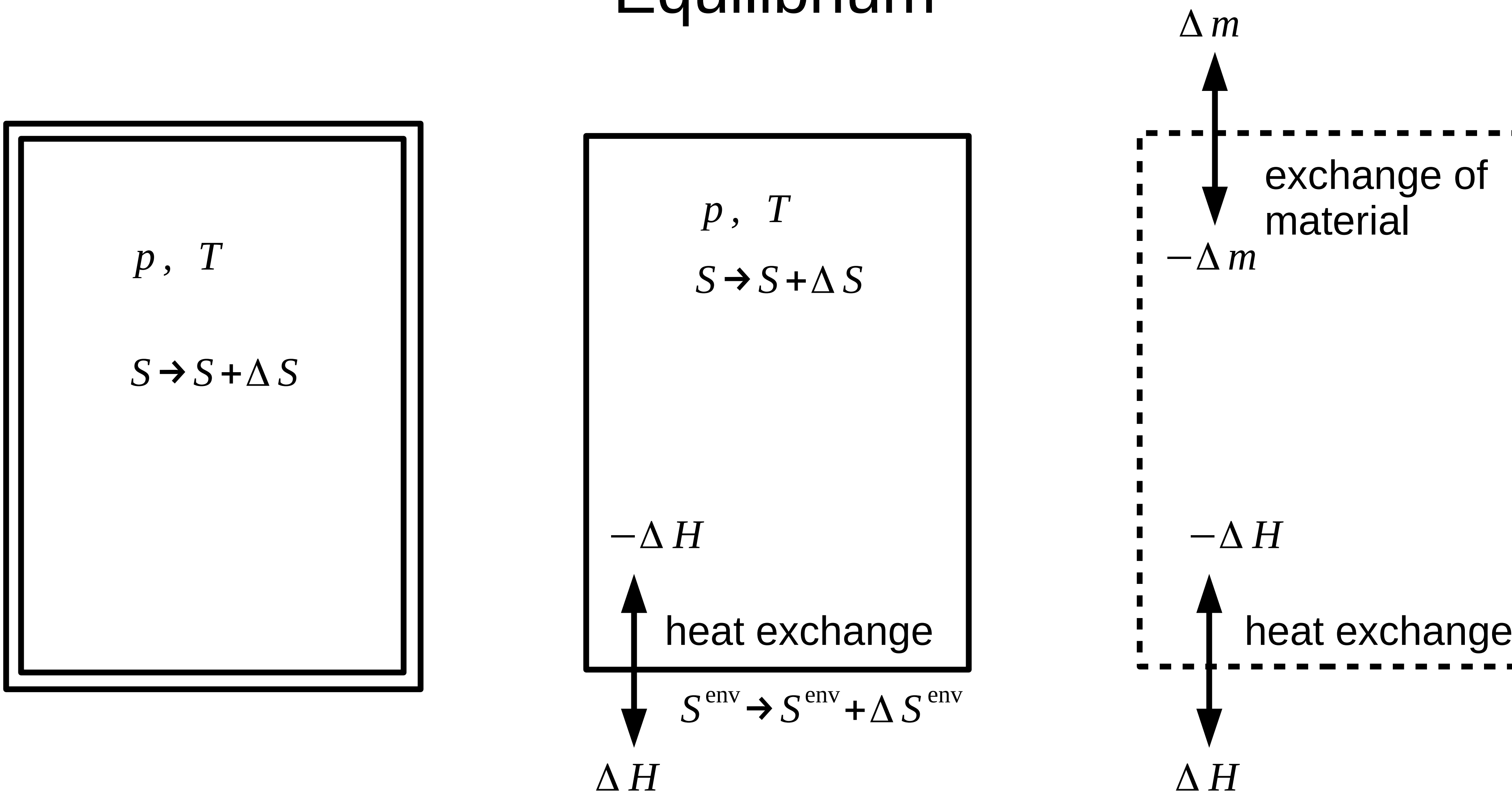
Constant *T* and *p* are relevant for biochemical processes!!

Equilibrium



isolated system

$S \rightarrow \max, \quad \Delta S = 0$

closed system

$S^{\mathrm{tot}} = S^{\mathrm{env}} + S \rightarrow \max$

$\Leftrightarrow \quad G = H - TS \rightarrow \min, \quad \Delta G = 0$

open system

does not reach equilibrium

Chemical reactions

$$A \rightleftharpoons B$$

We can measure concentrations: $[A]_{obs}, [B]_{obs}$

and in equilibrium: $[A]_{eq}, [B]_{eq}$

Equilibrium constant: $K_{eq} = \frac{[B]_{eq}}{[A]_{eq}}$ Mass-action ratio: $\Gamma = \frac{[B]_{obs}}{[A]_{obs}}$

In equilibrium: $\Gamma = K_{eq}$

$$\Delta G = -RT \ln\left(K_{eq}/\Gamma\right)$$

If $\Gamma > K_{eq}$: $\Delta G > 0$ reaction proceeds from B to A

If $\Gamma < K_{eq}$: $\Delta G < 0$ reaction proceeds from A to B

Standard Gibbs free energy of a reaction

$$A \rightleftharpoons B$$

What is ΔG^0 ?

Change in Gibbs free energy if all reactants are present in standard concentrations (1M)

$$\Rightarrow \; \Gamma = 1\mathrm{M}/1\mathrm{M} = 1$$

$$\Rightarrow \; \Delta G^0 = -RT \ln\left(K_{\mathrm{eq}}/\Gamma\right) = -RT \ln K_{\mathrm{eq}}$$

A simple example: triose phosphate isomerase

Dihydroxyacetone phosphate ⇌ glyceraldehyde-3-phosphate

DHAP ⇌ GAP

Experimental: $\Delta G^0 = +1.82\,\mathrm{kcal/mol} = +7.61\,\mathrm{kJ/mol}$ (Bassham & Krause, 1969)

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$$\left.\begin{array}{l} R = 8.314\,\mathrm{J/(mol \cdot K)} \\ T = 298\,\mathrm{K} \end{array}\right\} \quad RT = 2.478\,\mathrm{kJ/mol}$$

$$\Rightarrow K_{eq} = e^{-7.61/2.478} = e^{-3.1} = 0.045 = 1/22$$

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If TPI is in equilibrium, the concentration of DHAP is 22 times higher than of GAP

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Now standard conditions imply $\Gamma = \frac{[\text{B}]_{\text{obs}} \cdot [\text{C}]_{\text{obs}}}{[\text{A}]_{\text{obs}}} = 1\text{M} \cdot 1\text{M}/1\text{M} = 1\text{M}$

and $K_{eq} = \frac{[\text{B}]_{\text{eq}} \cdot [\text{C}]_{\text{eq}}}{[\text{A}]_{\text{eq}}}$ has the dimension of 1M !

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The numerical values of Γ and K_{eq} depend on the measurement system!

Example

Aldolase: FBP ⇌ GAP + DHAP $K_{eq} = \frac{[\text{GAP}]_{eq} \cdot [\text{DHAP}]_{eq}}{[\text{FBP}]_{eq}}$

Here: $\Delta G^0 = 23.8\,\text{kJ/mol}$

Thus: $K_{eq}/1\text{M} = \exp\left(-\Delta G^0/RT\right) = 6.7 \cdot 10^{-5}$

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But who cares what happens at 1M?

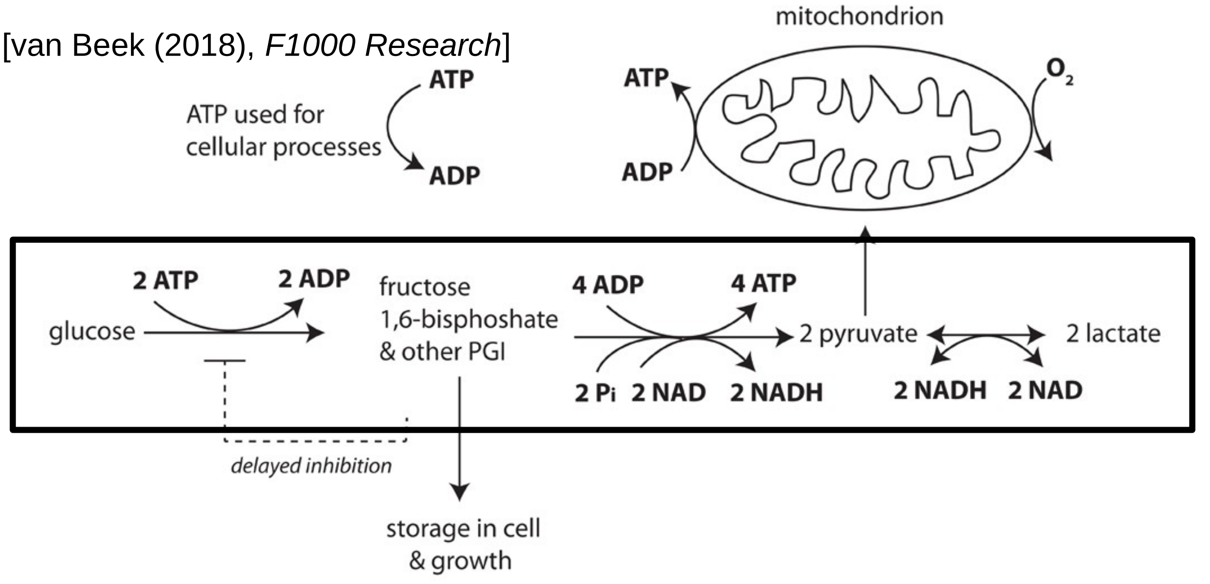
If $[\mathrm{GAP}]_{eq} = 50\,\mu\mathrm{M}$ and $[\mathrm{DHAP}]_{eq} = 50\,\mu\mathrm{M}$ then

$$[\mathrm{FBP}]_{eq} = \frac{[\mathrm{GAP}]_{eq} \cdot [\mathrm{DHAP}]_{eq}}{K_{eq}} = \frac{5 \cdot 10^{-5}\mathrm{M} \cdot 5 \cdot 10^{-5}\mathrm{M}}{6.7 \cdot 10^{-5}\mathrm{M}} = 3.8 \cdot 10^{-5}\mathrm{M} = 38\,\mu\mathrm{M}$$

(see Cornish-Bowden, 1981, “Thermodynamic aspects of glycolysis”)

An engineering view of glycolysis

[van Beek (2018), *F1000 Research*]



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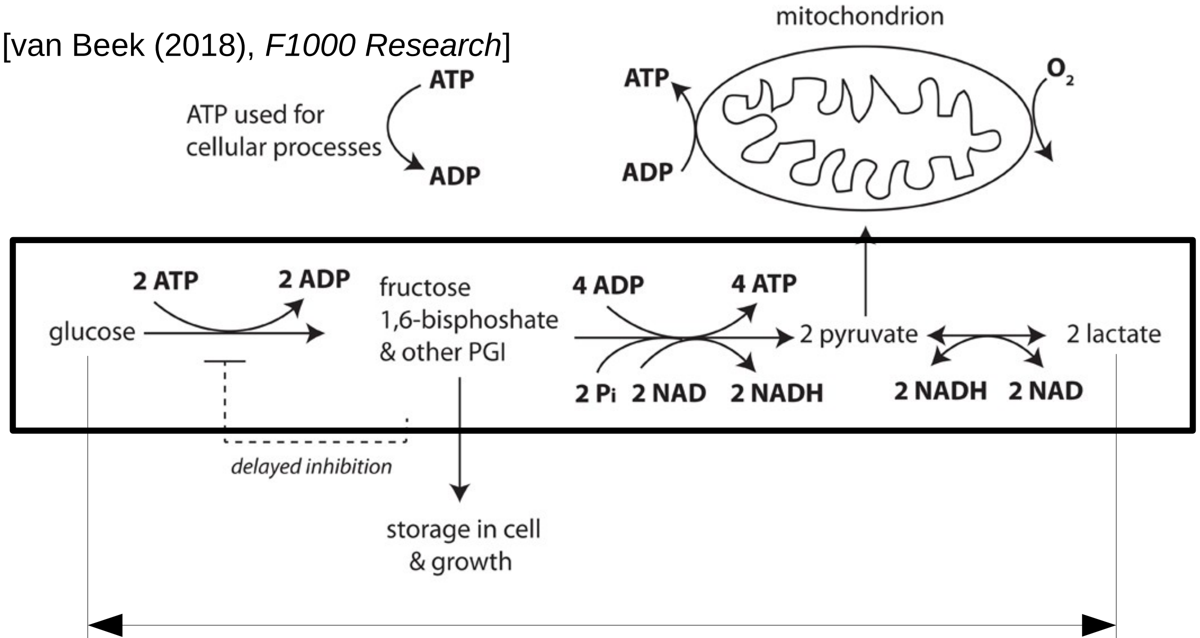

thermodynamic driving force: ΔG_{driv}

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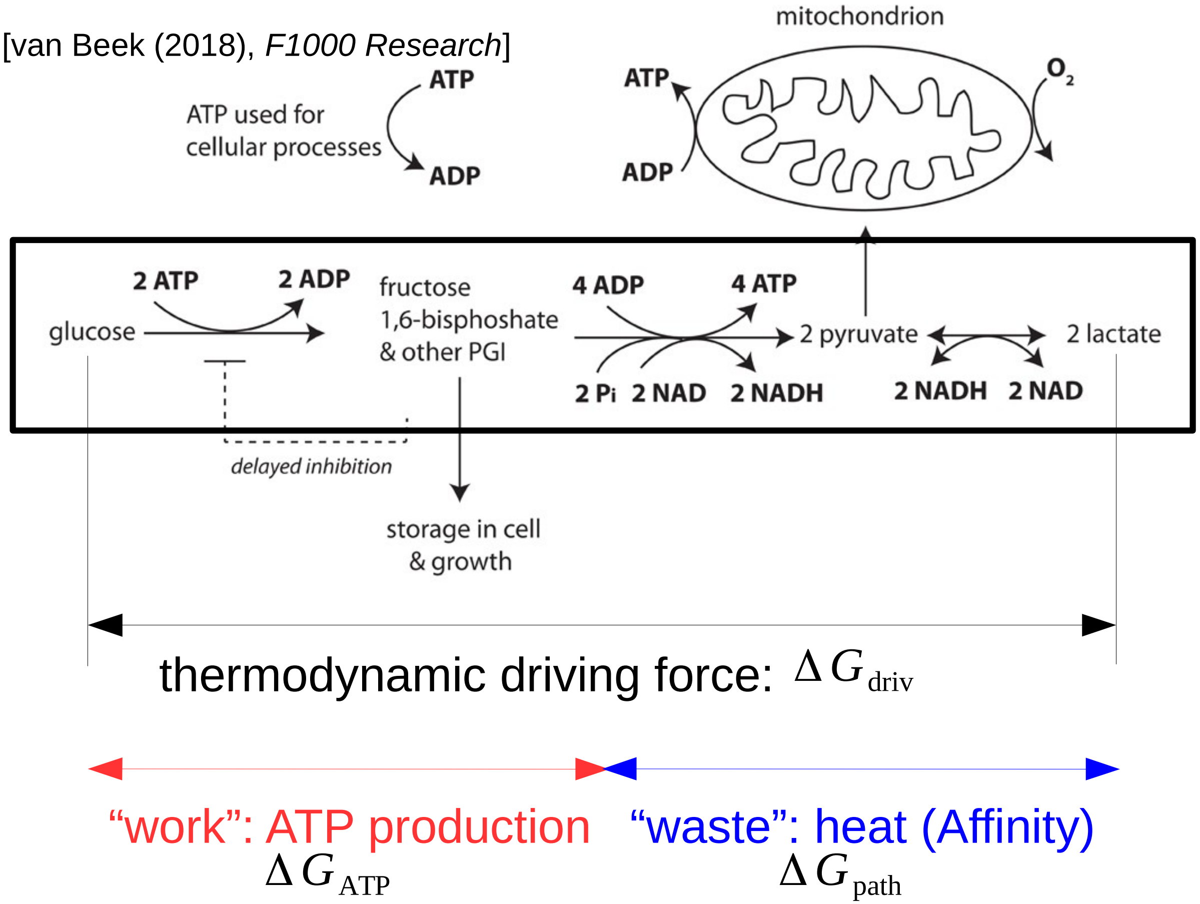

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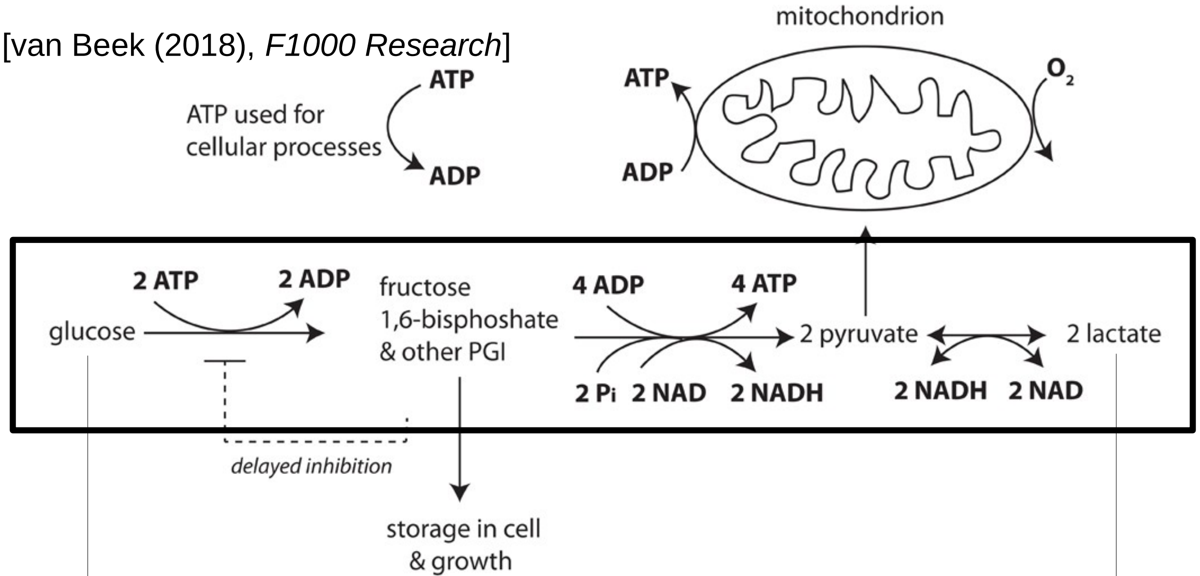


thermodynamic driving force: ΔG_{driv}

"work": ATP production ΔG_{ATP}

"waste": heat (Affinity) ΔG_{path}

<u>Experimental data</u>

under physiological conditions in muscle cells (anaerobic)

Driving force: Glucose ⇌ 2 Lactate$^-$ + 2 H$^+$ $\quad \Delta G_{\text{driv}} = -205\,\text{kJ/mol}$

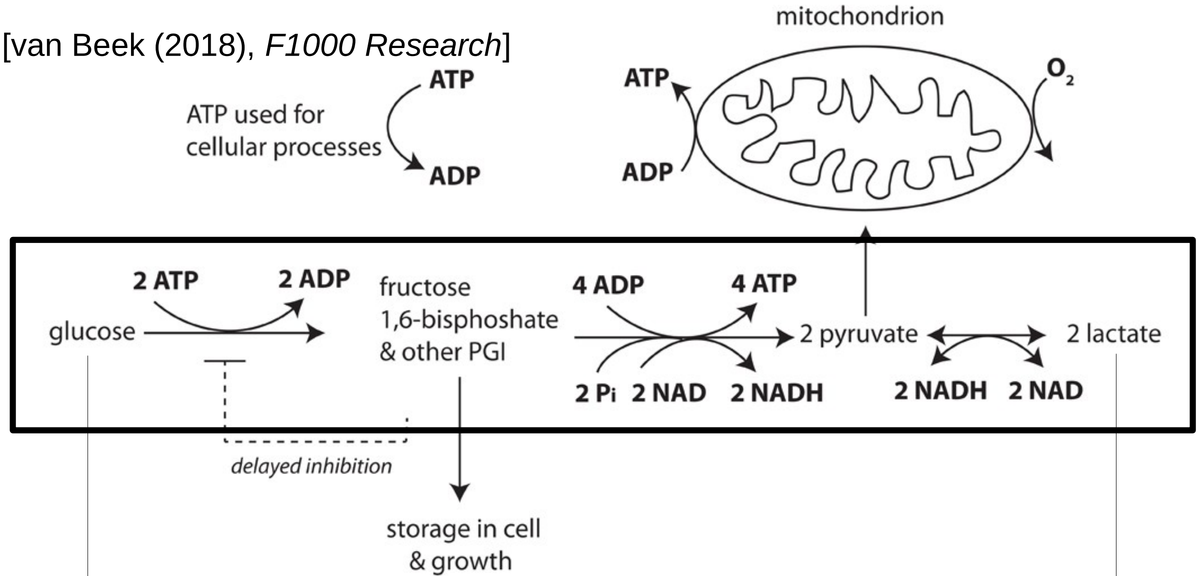
Work stoichiometry: ADP + P$_i$ ⇌ ATP $\quad \Delta G_{\text{ATP}} = +52\,\text{kJ/mol}$

Overall stoichiometry: Glucose + 2 ADP + 2 P$_i$ ⇌ 2 Lactate$^-$ + 2 H$^+$ + 2 ATP

$$\Delta G_{\text{path}} = \Delta G_{\text{driv}} + 2\Delta G_{\text{ATP}} = -101\,\text{kJ/mol}$$

An engineering view of glycolysis

[van Beek (2018), *F1000 Research*]



thermodynamic driving force: ΔG_{driv}

"work": ATP production ΔG_{ATP}

"waste": heat (Affinity) ΔG_{path}

About half of the energy is "wasted"! Is this optimal?

<u>Experimental data</u>

under physiological conditions in muscle cells (anaerobic)

Driving force: Glucose ⇌ 2 Lactate$^-$ + 2 H$^+$ $\quad \Delta G_{\text{driv}} = -205\,\text{kJ/mol}$

Work stoichiometry: ADP + P$_i$ ⇌ ATP $\quad \Delta G_{\text{ATP}} = +52\,\text{kJ/mol}$

Overall stoichiometry: Glucose + 2 ADP + 2 P$_i$ ⇌ 2 Lactate$^-$ + 2 H$^+$ + 2 ATP

$$\Delta G_{\text{path}} = \Delta G_{\text{driv}} + 2\Delta G_{\text{ATP}} = -101\,\text{kJ/mol}$$

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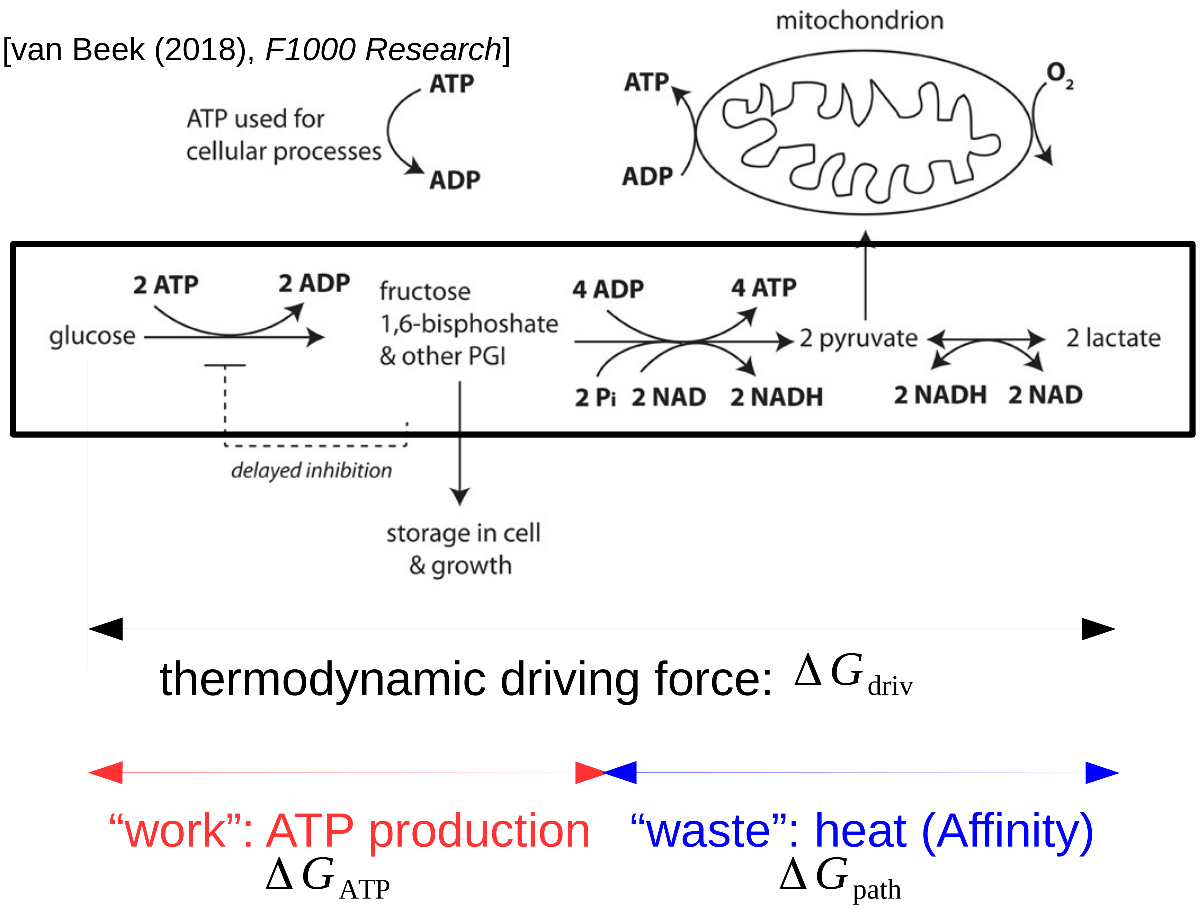

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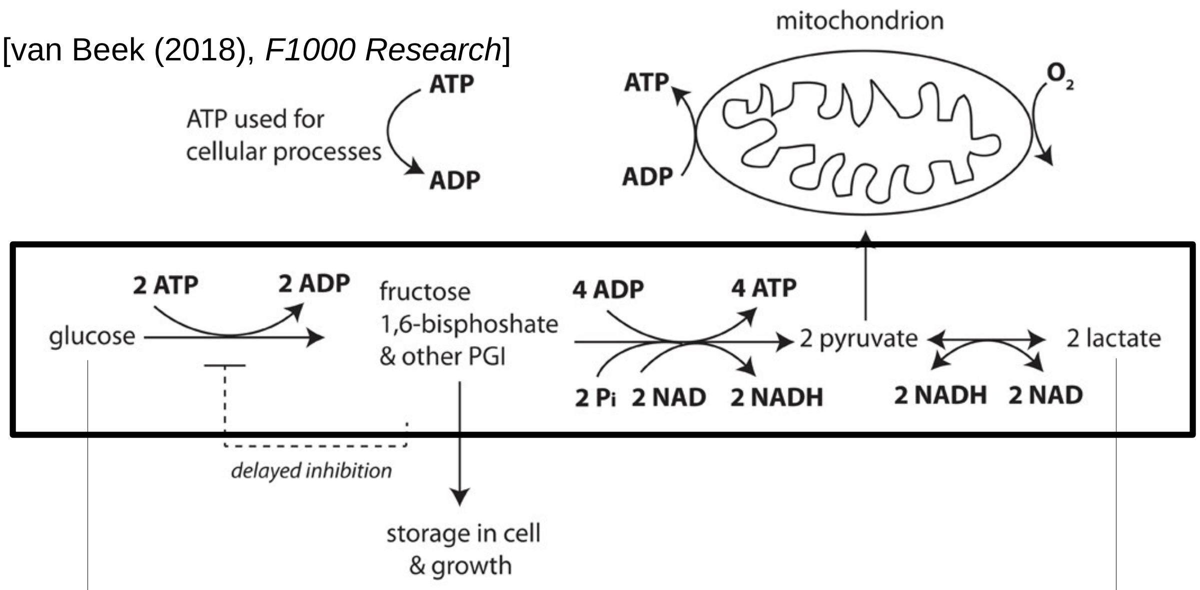

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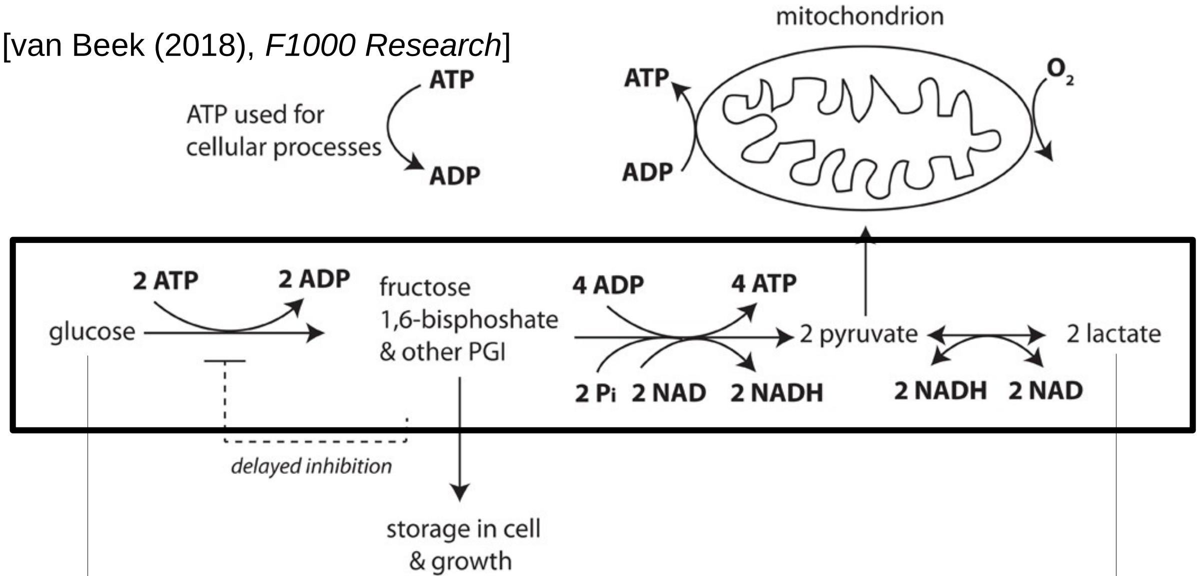

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Find the optimal x, $0 \leqslant x \leqslant 1$,

for maximal ATP production rate J_{ATP}

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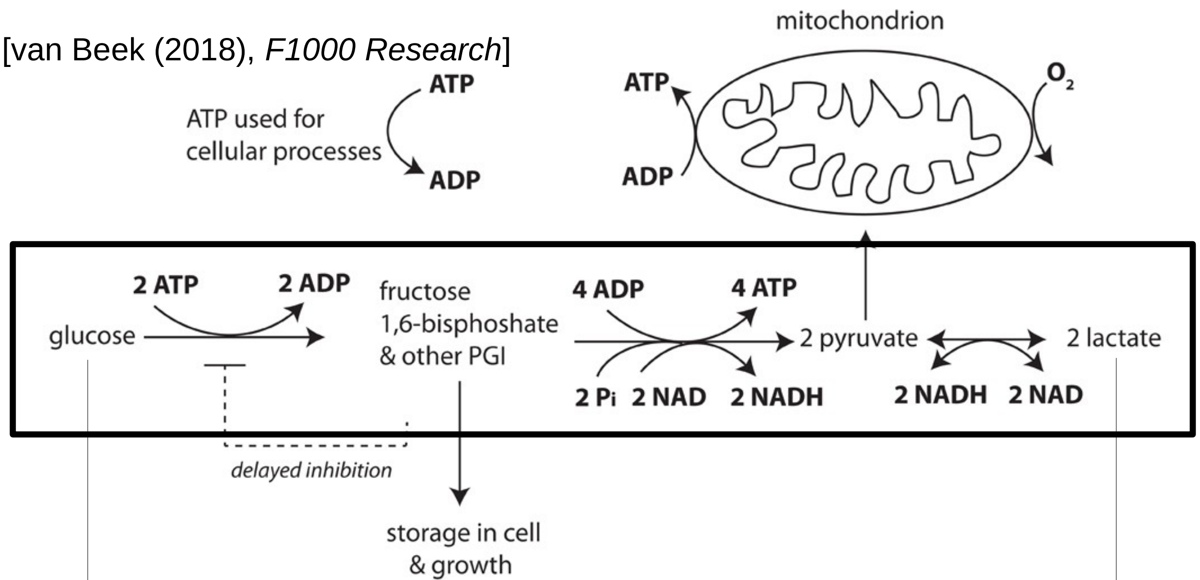

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1. Rate proportional to affinity (affinity drives flux)
2. Rate proportional to x (more work, more yield)

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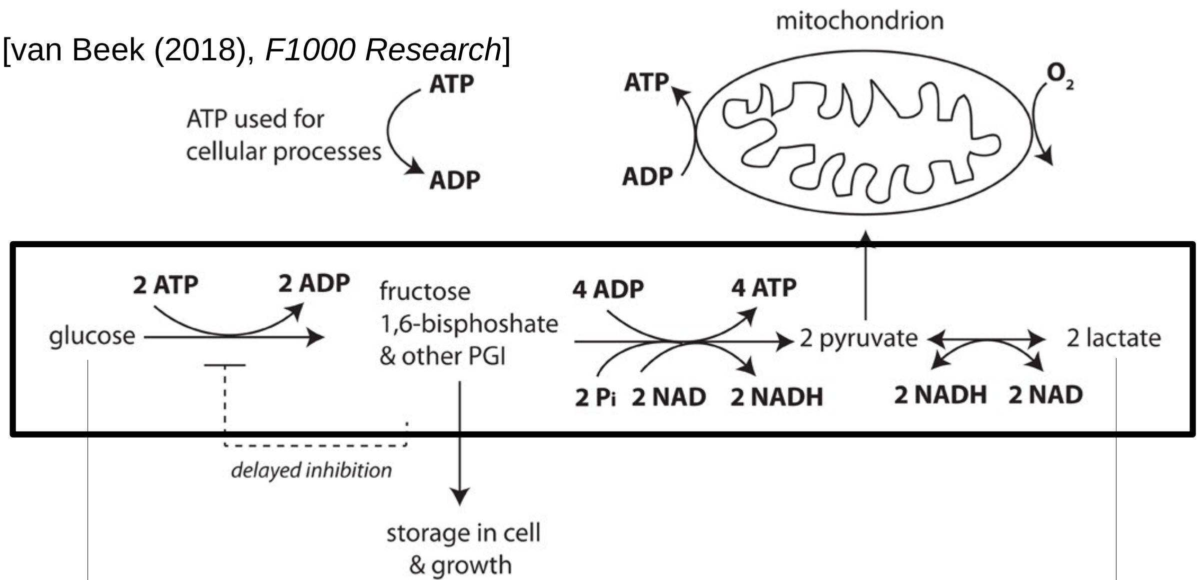

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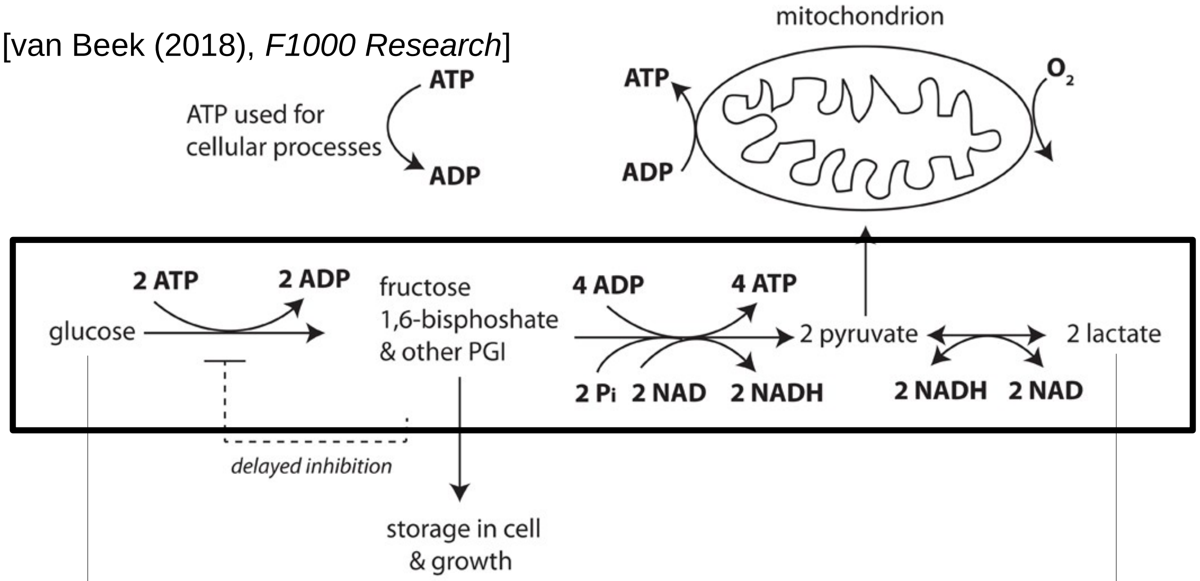

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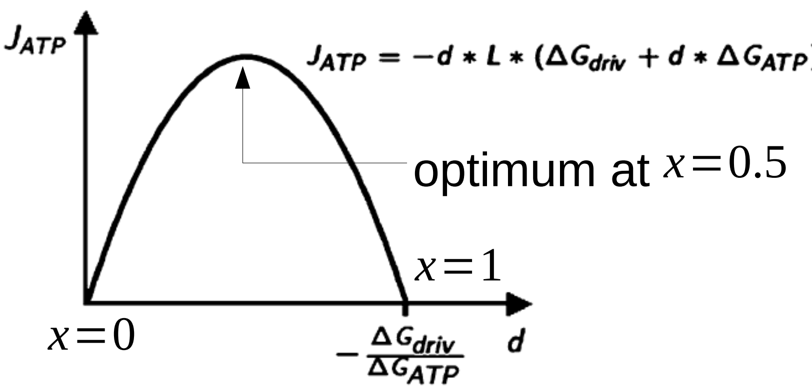

[Werner et al. (2010), *J Mol Evol*]

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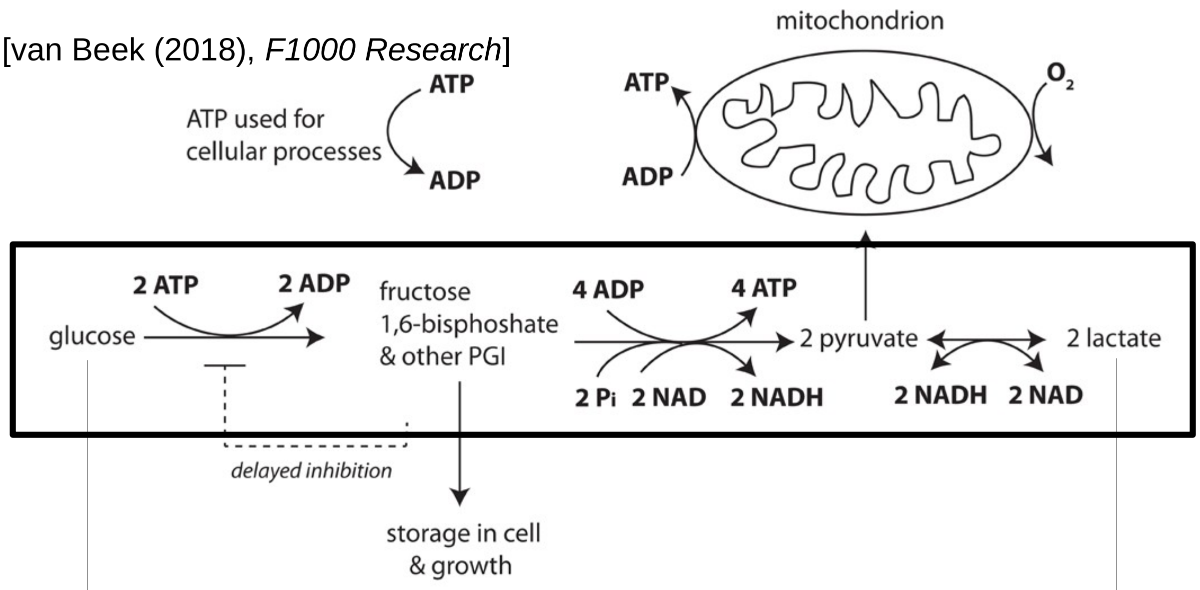

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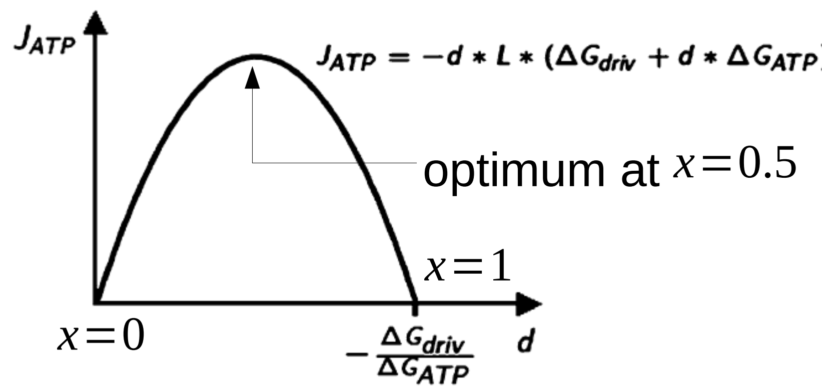
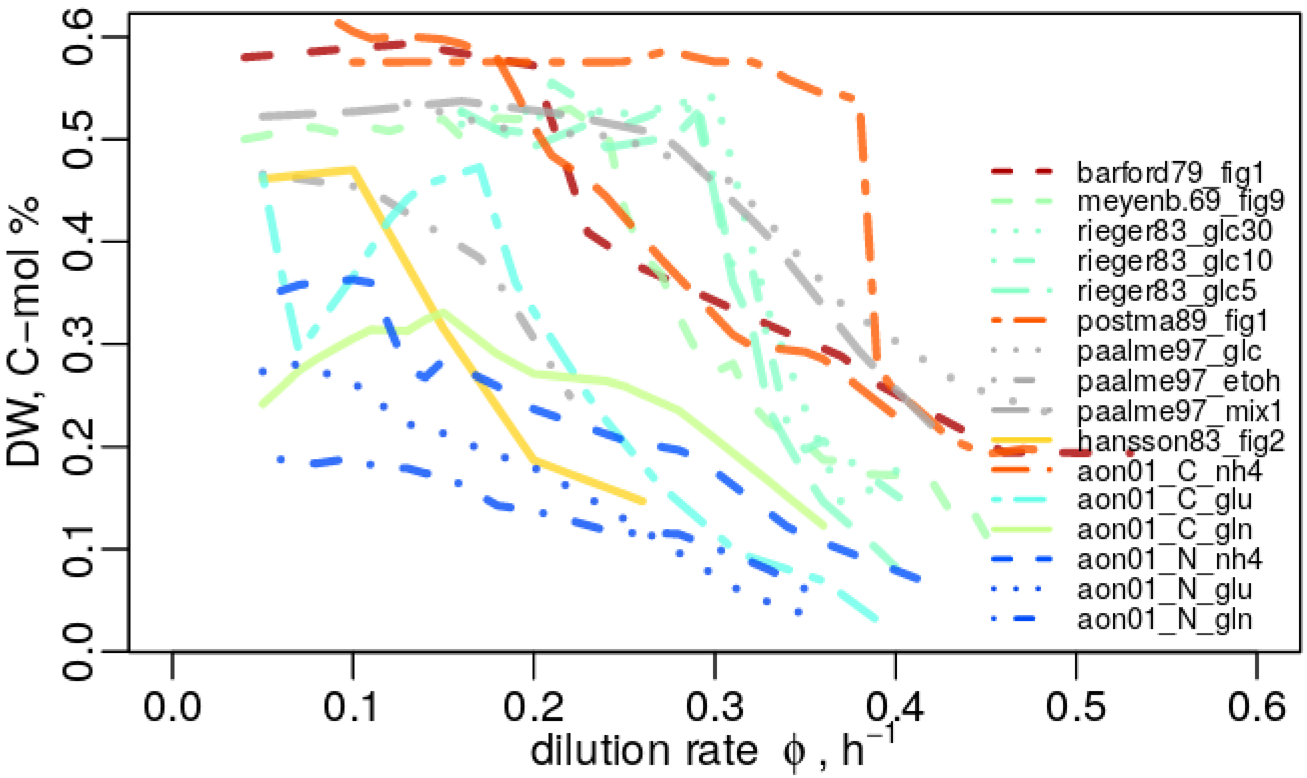


[Werner et al. (2010), *J Mol Evol*]

<u>Conclusion</u>:
Under physiological conditions in muscle cells, a ratio of 2 ATP per glucose is optimal!

Carbon balance in yeast

Data for yeast growing in fermentors, summary from many publications
(from Rainer Machné, PhD thesis 2017)



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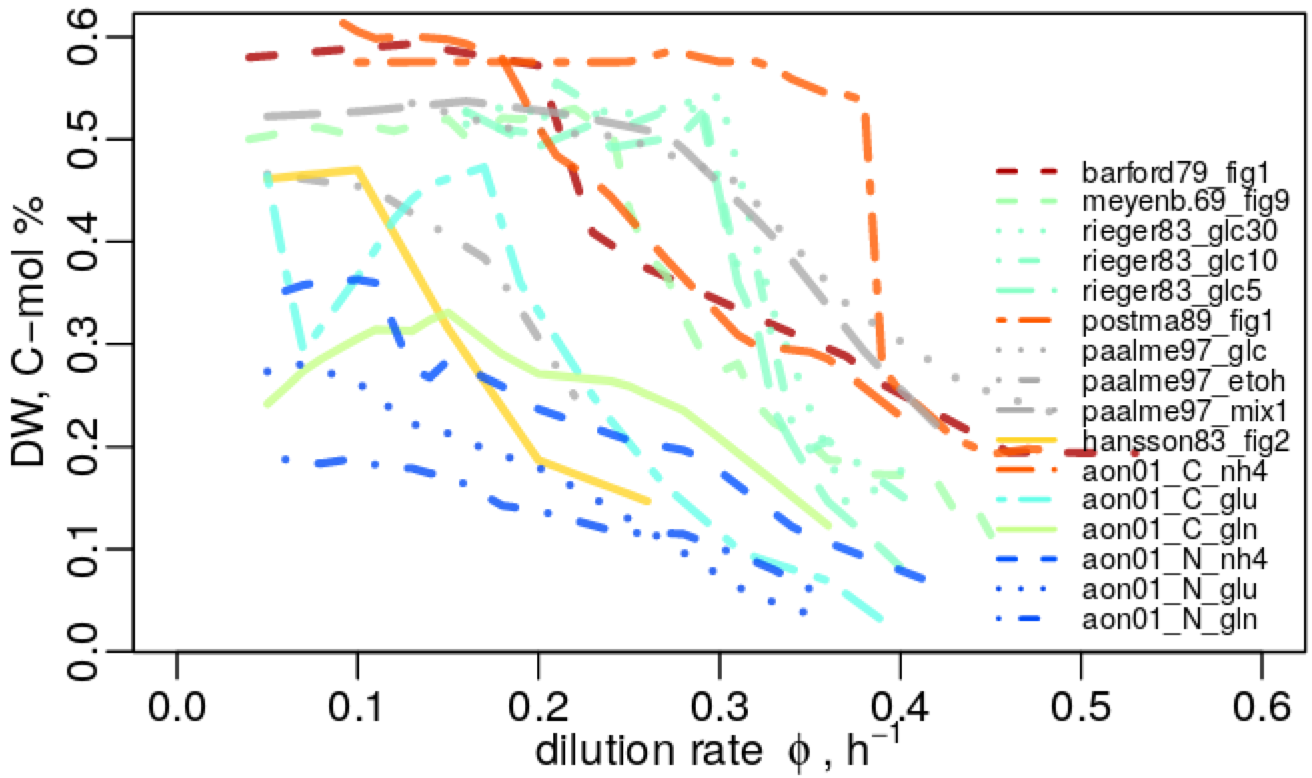

For non N-limiting conditions: 40-60% of C in medium goes to biomass!

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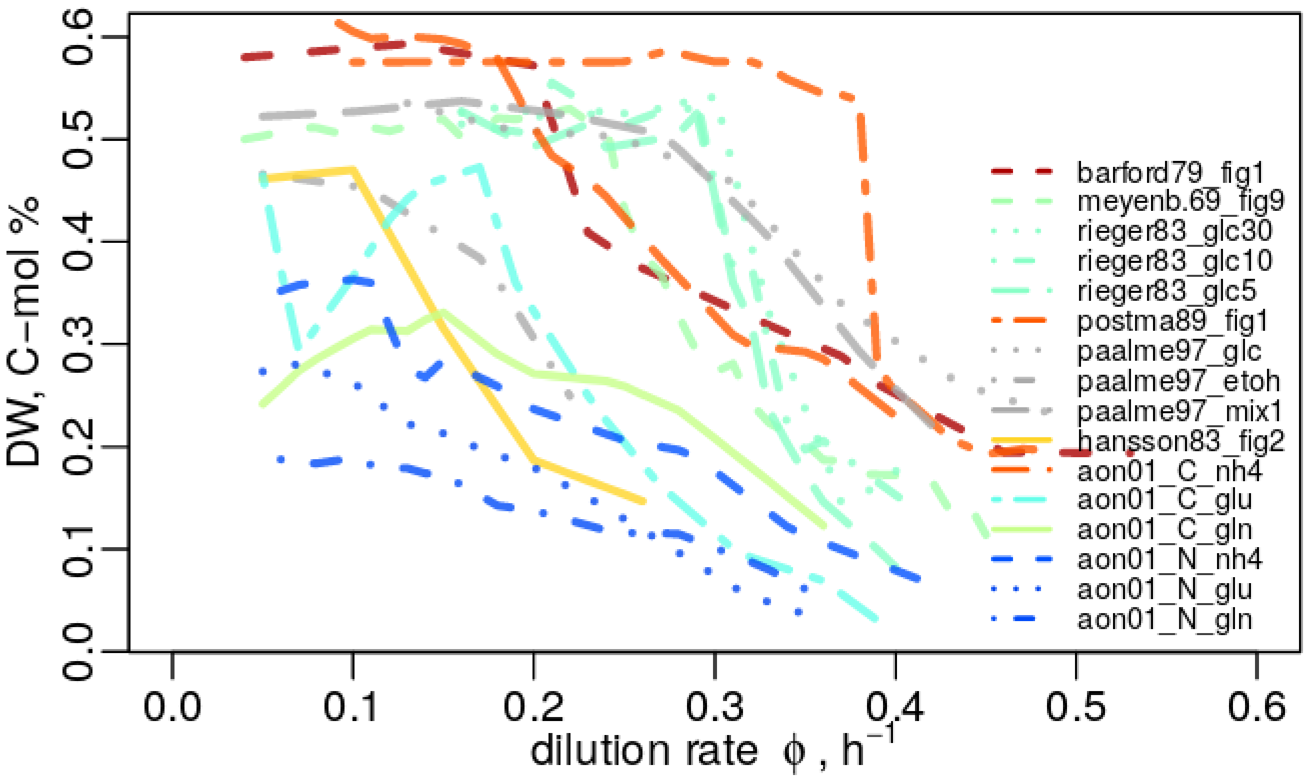

For non N-limiting conditions: 40-60% of C in medium goes to biomass!

Approximately half is used as “work” (biomass production) and half released as heat!

The entropy balance of a living cell

$$\frac{dS}{dt} = \frac{d_{\text{int}} S}{dt} + \frac{d_{\text{e}} S}{dt} = \underline{\dot{S}_{\text{Prod}}} + \underline{\frac{\dot{Q}}{T}} + \underline{\sum_i s_{e,i} \dot{n}_{e,i}} \leq 0$$

Internally produced entropy (>0) heat exchange metabolite exchange

How do cells really export entropy?

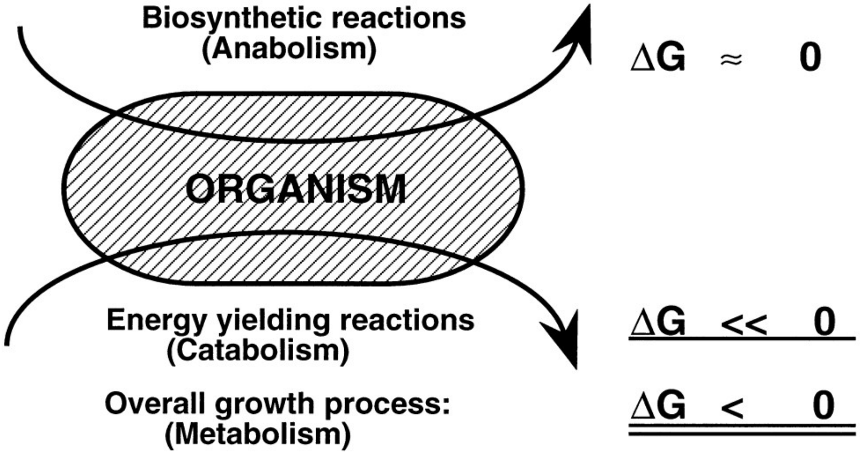

Fig. 2. Coupling of catabolism and anabolism during growth.

von Stockar and Liu (1999), “Does microbial life always feed on negative entropy?”, BBA 1412:191-211

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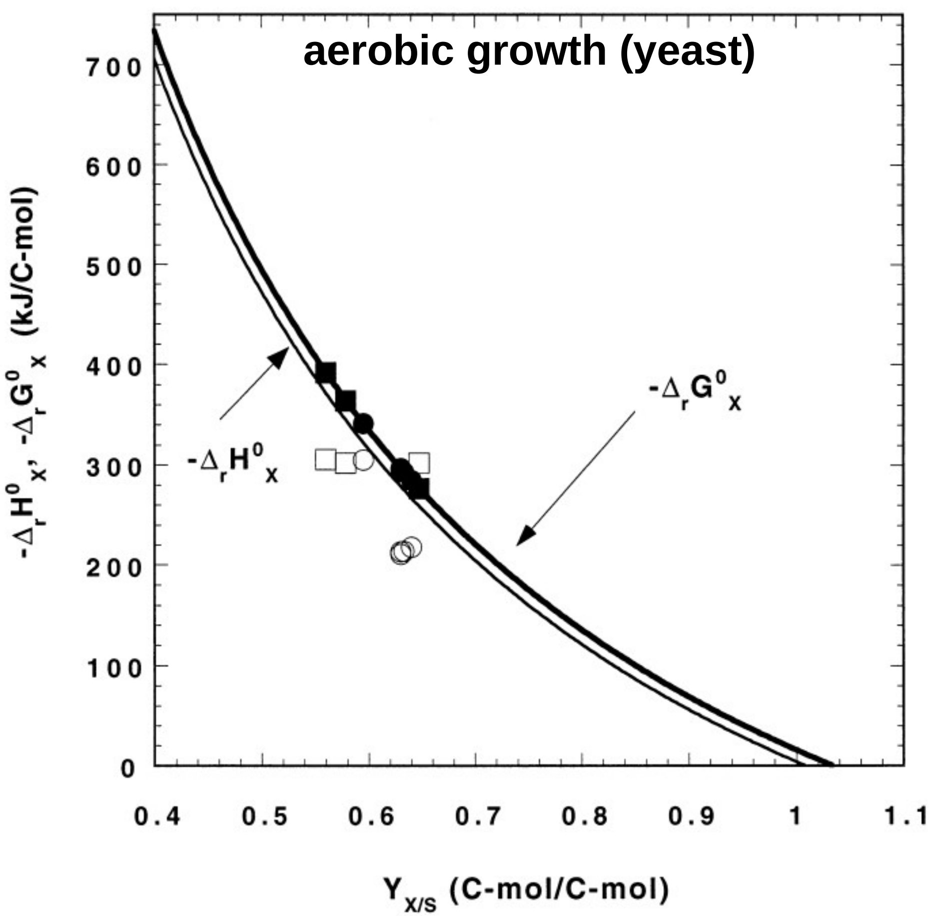

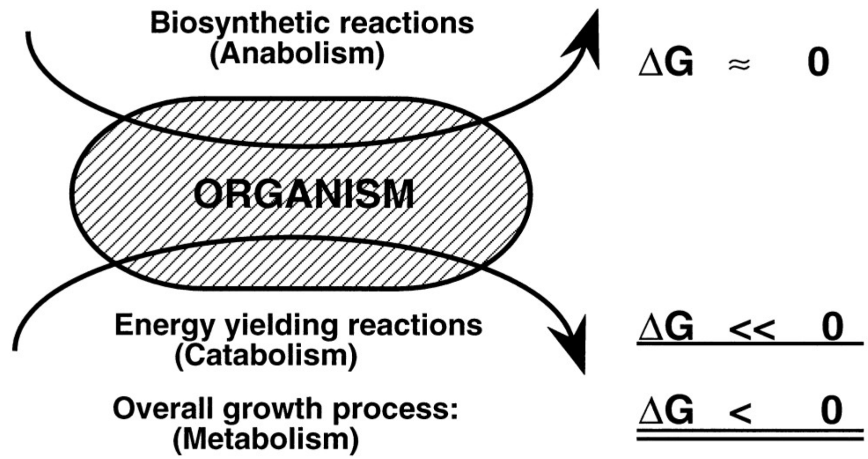

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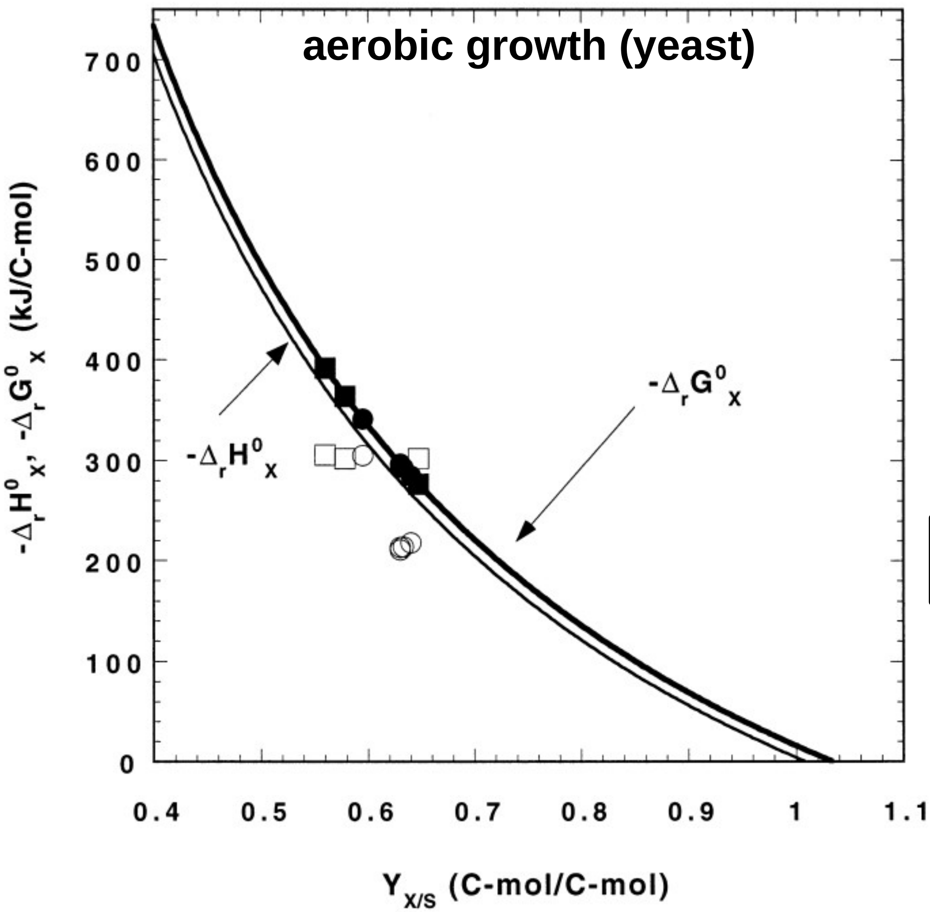

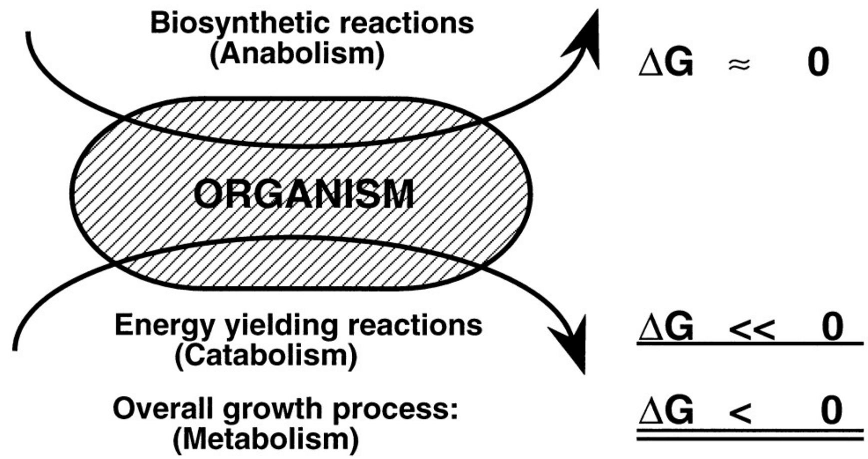

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Yeast (aerobic) exports energy as heat

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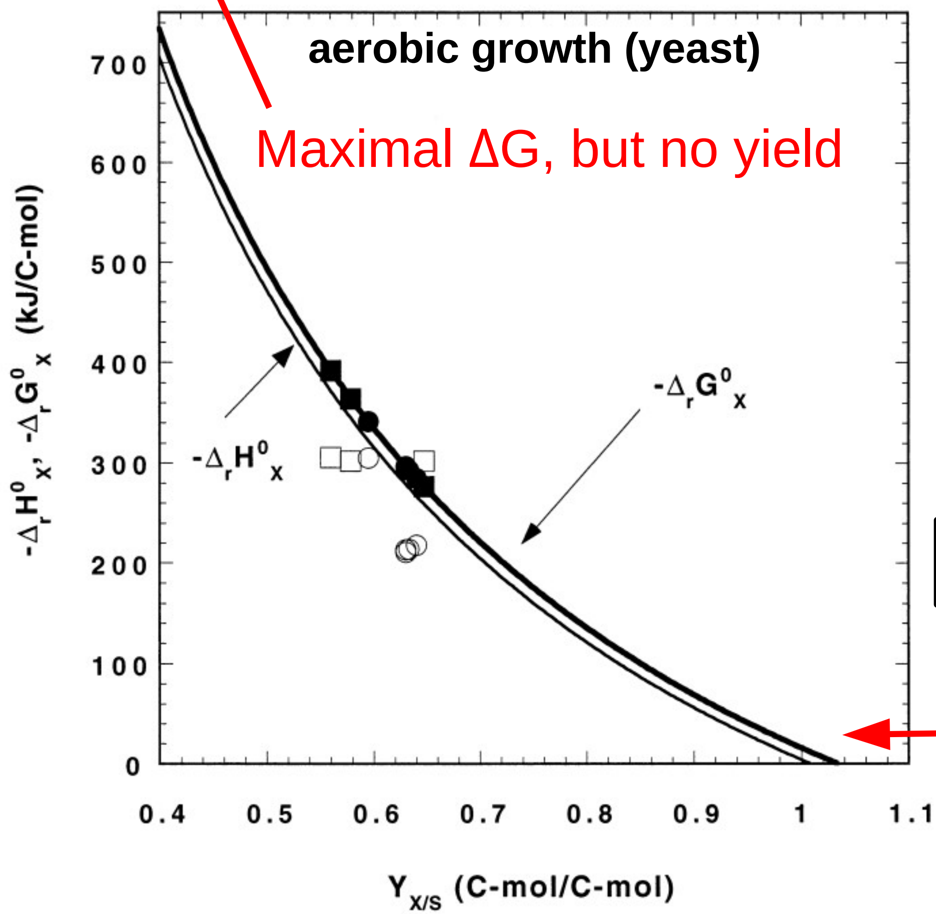
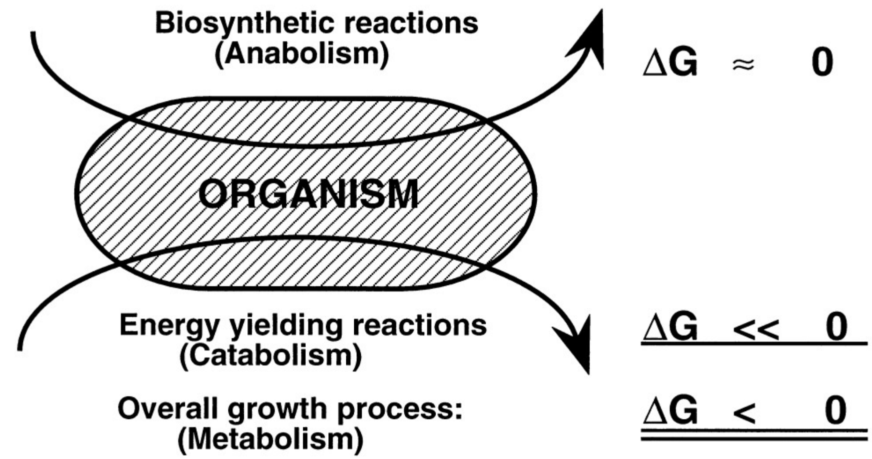


Maximal ΔG, but no yield

Maximal yield, but ΔG=0: no growth



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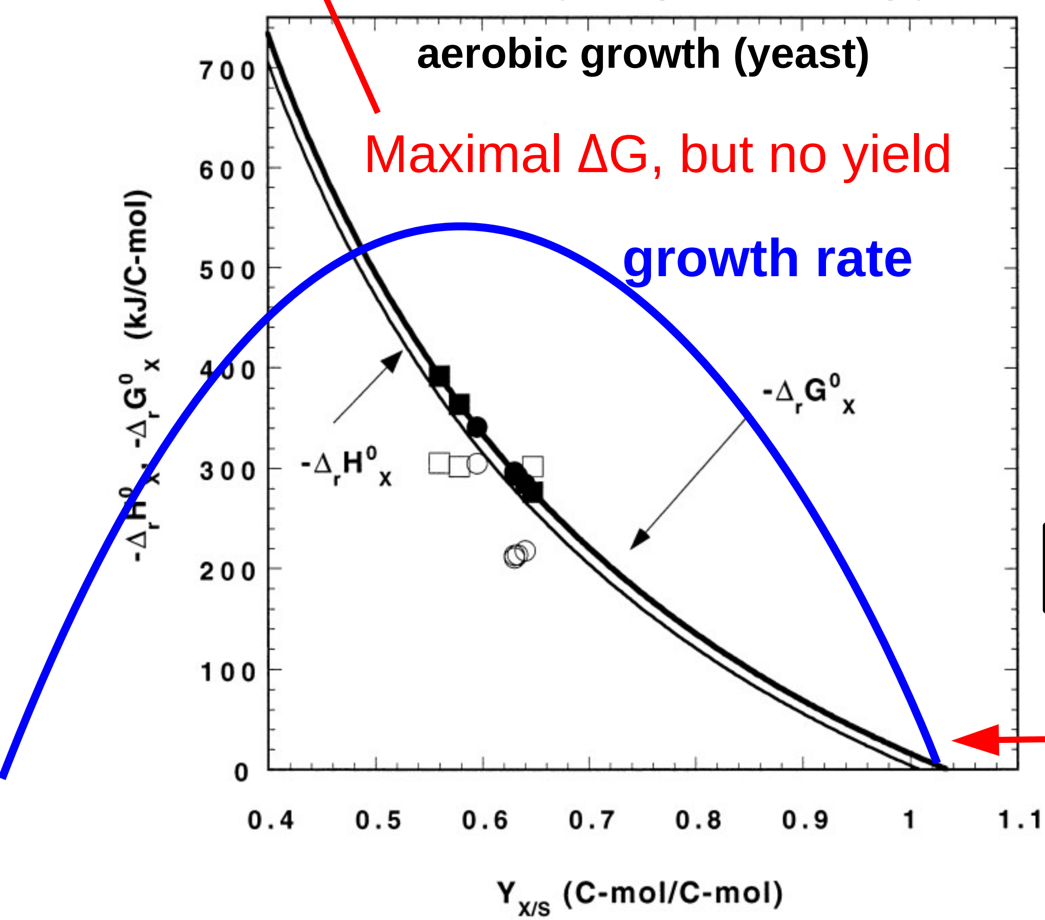

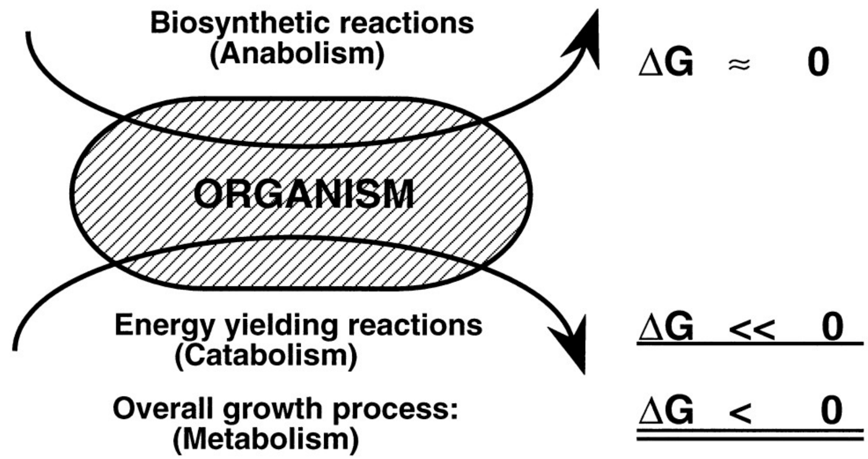

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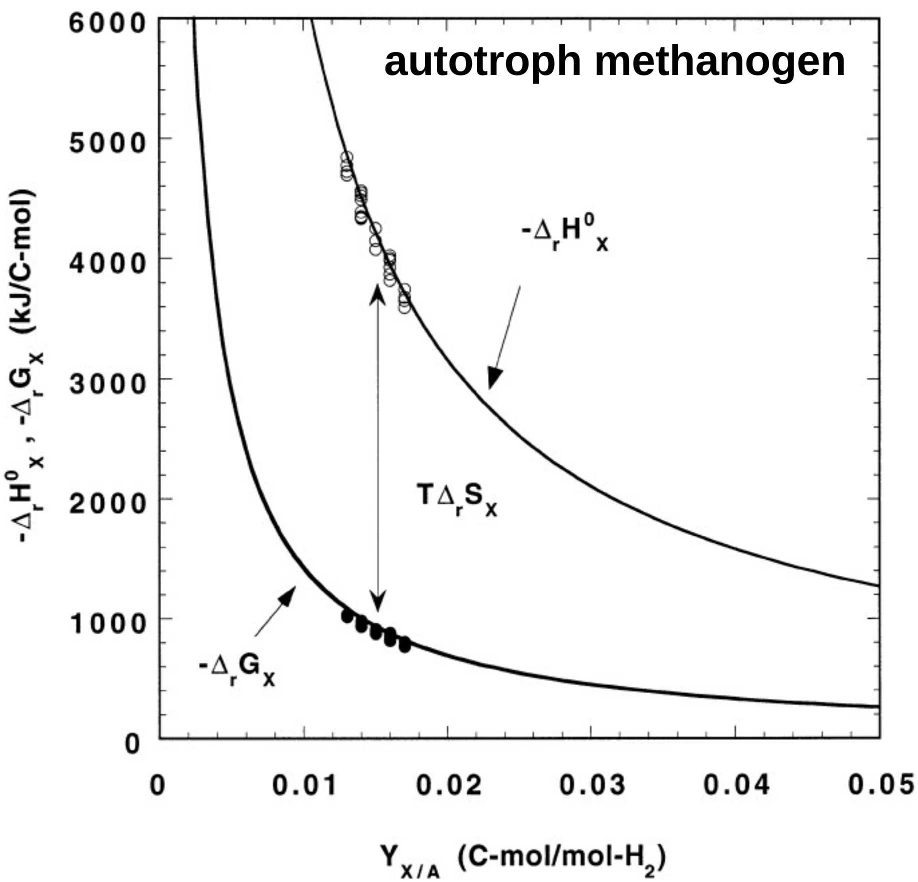

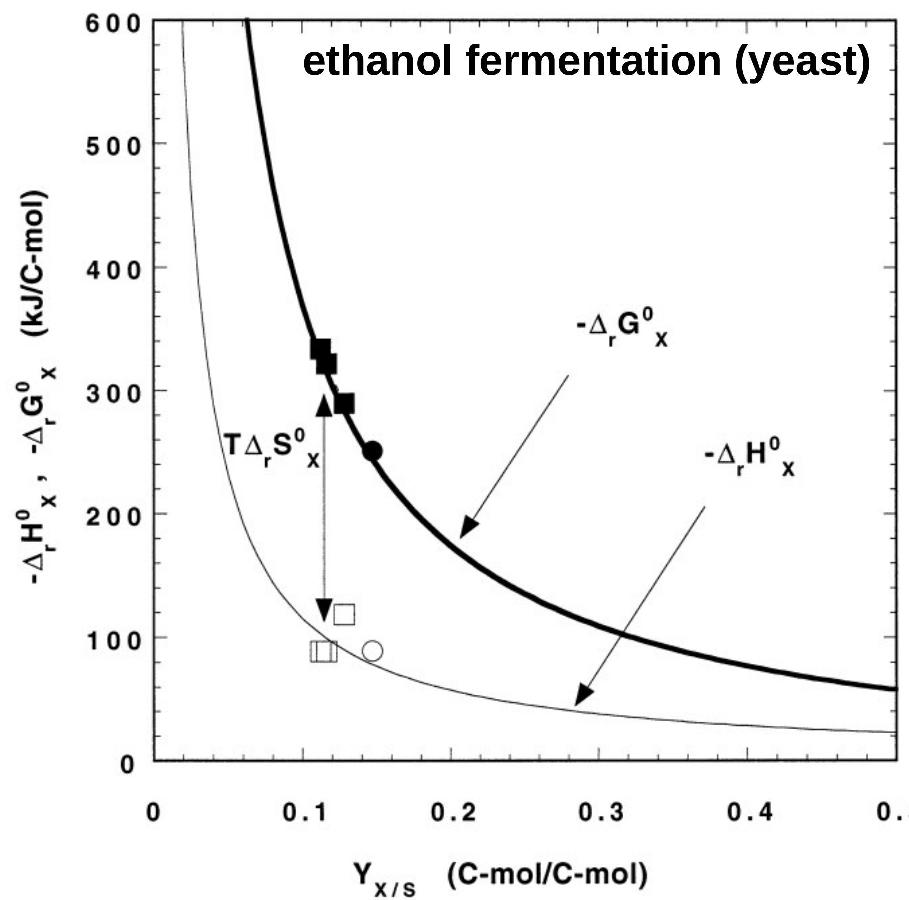

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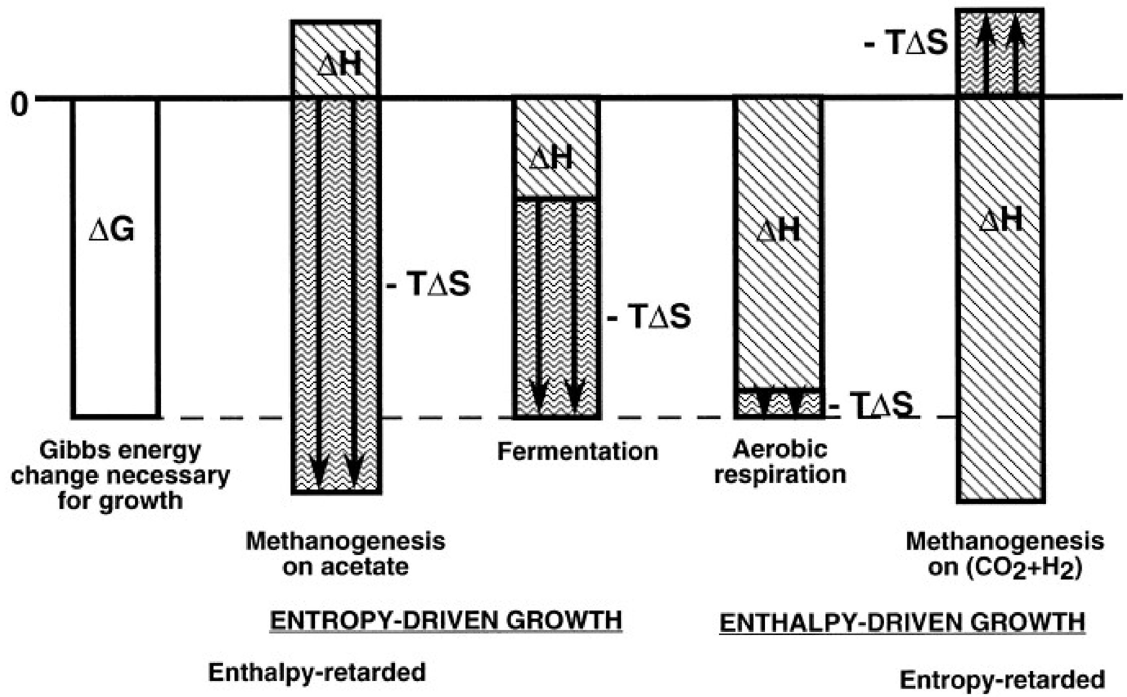

Fig. 11. Schematic of enthalpic and entropic contributions to the driving force of microbial growth.

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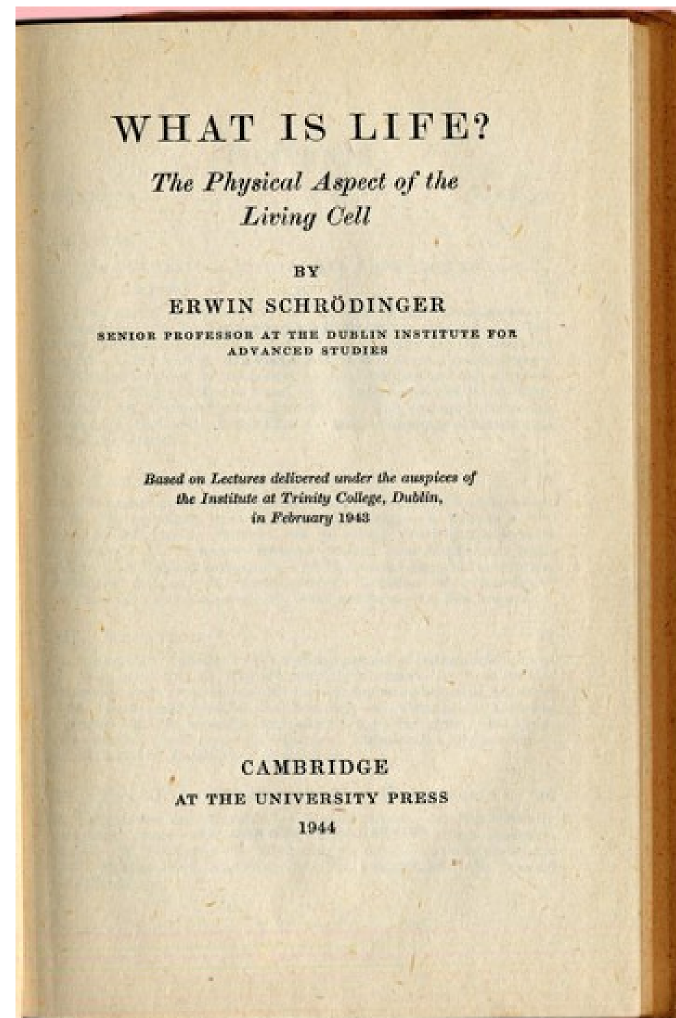
Summary

- Life is based on entropy export!
- Everything is entropy!
- Read Schrödinger's "What is Life?"

Merry Christmas!



WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

SENIOR PROFESSOR AT THE DUBLIN INSTITUTE FOR ADVANCED STUDIES

Based on Lectures delivered under the auspices of the Institute at Trinity College, Dublin, in February 1943

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