An Outlook to Biothermodynamics

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Biothermodynamics
Overview, Historical Remarks

1. Photosynthesis

2. Lipid Membranes :
Phase Transition
DMPC-EOS (E2)

3. Proteins : Thermal Denaturation

4. Metabolism of Bacteria
Kleiber‘s Law(s)

Bacteria Escherichia Coli
Th. Escherich, 1919

Biothermodynamics (BTH):

Application of Thermodynamics, i.e.Thermostatics (TST) and Thermodynamics of Irreversible Processes (TIP) to Biological and Bioengineering Systems.

Biotechnology (BT):

Technology using living systems like cells, bacteria, fungi etc. as chemical reactors.

White BT	Industrial sized biocatalytic processes (fermentation) Breweries, Production vitamine B12, steroid hormones etc.;
Green BT	Plants and transgene variations for production of biofuels etc. in biorefineries;
Red BT	Medical applications of substances and processes related to living organisms, as for example interferones etc. (cancer,viruses)
Yellow BT	Pharmaceutical molecules, recombinant proteins, penicilline and other fungi;
Blue BT	Seawater based microorganisms as reactors; extremophiles... Extraction noble metals from seawater, production of new molecules

Fields of Research in Biothermodynamics

3rd Int. Symposium on Biothermodynamics
DECHEMA, Bologna, September 2010

Biomolecules

- **Protein adsorption on surfaces**
- **Protein folding, interactions and stability**

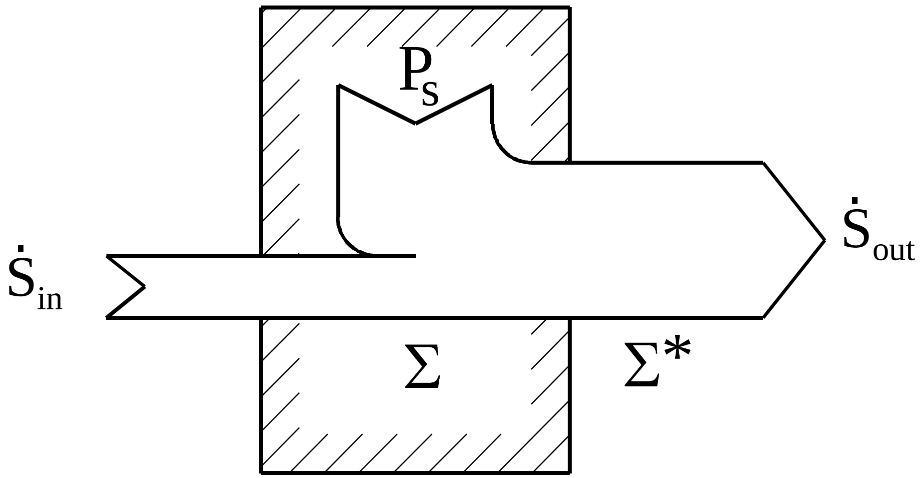
Bacteria

- **Active masstransport in biological membranes**
- **Thermodynamics of metabolic pathways**
- **Intracellular Thermodynamics**

Bioreactors

- **Biocalorimetry**
- **Thermodynamics of downstream processing**
- **Thermodynamics in biological energy conversion processes**
- **Thermodynamic aspects of Systems Biology and Synthetic Biology**

1. Thermodynamics of Photosynthesis



Evaporation of Additional Water:

$$\dot S_{in} = \dot S_{out} + 0.24\,\frac{kJ}{mol\,K}\cdot \dot n_{GL}$$

$$2.2\,\Big|\ \dot S\ H_2O\ _L = \dot S\ H_2O\ _V - 0.11\,\frac{kJ}{mol\,K}\cdot \dot n_W$$

$$\dot n_W = 2.2\cdot \dot n_{GL}$$

E. Schrödinger (~1940)

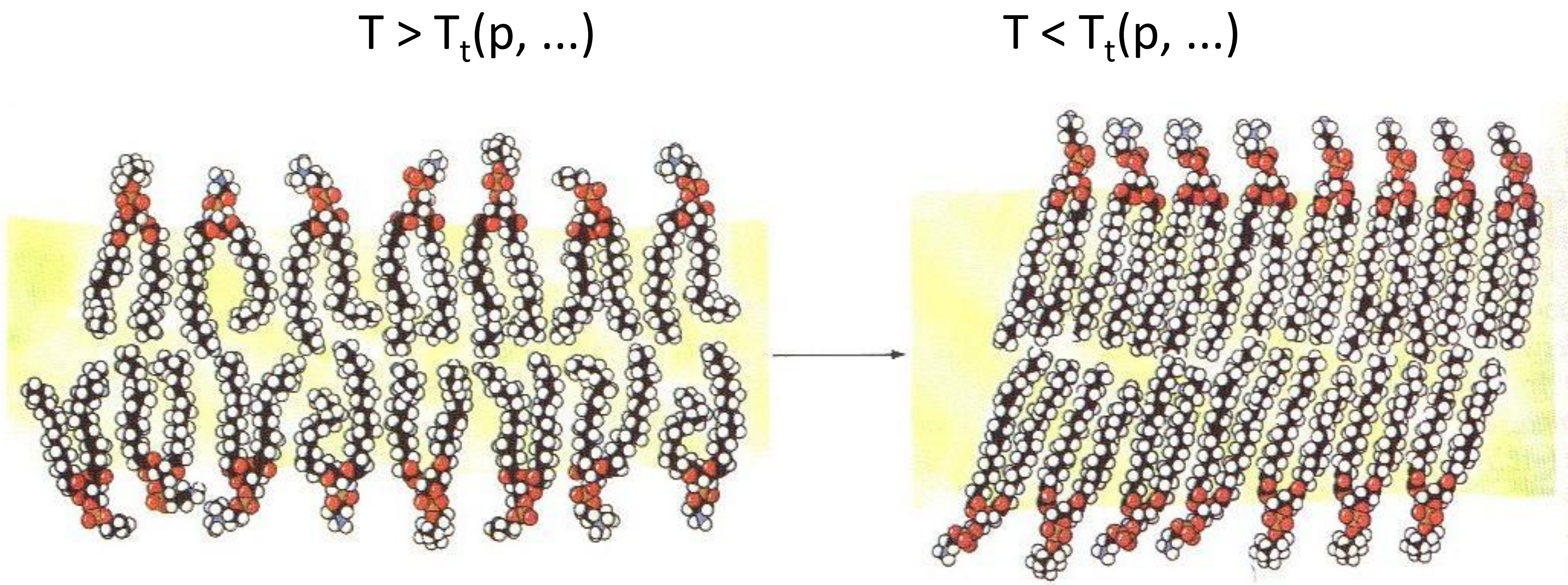
$$\underbrace{\underline{6\,CO_2 + 6\,H_2O}}\underline{\rightarrow}\underbrace{\underline{C_6H_{12}O_6 + 6\,O_2}}$$

$$\dot S_{in} \quad = \quad \dot S_{out} + 0.24\,\frac{kJ}{mol\,K}\cdot \dot n_{GL}$$

$$\left\| \begin{array}{l} 6\,CO_2 + 6\,H_2O \rightarrow C_6H_{12}O_6 + 6\,O_2 \\ +\,2.2\ H_2O\ _L \rightarrow 2.2\ H_2O\ _V \end{array} \right\|$$

2nd Law: $\dot S_{in} \quad \leq \quad \dot S_{out} \qquad ?$

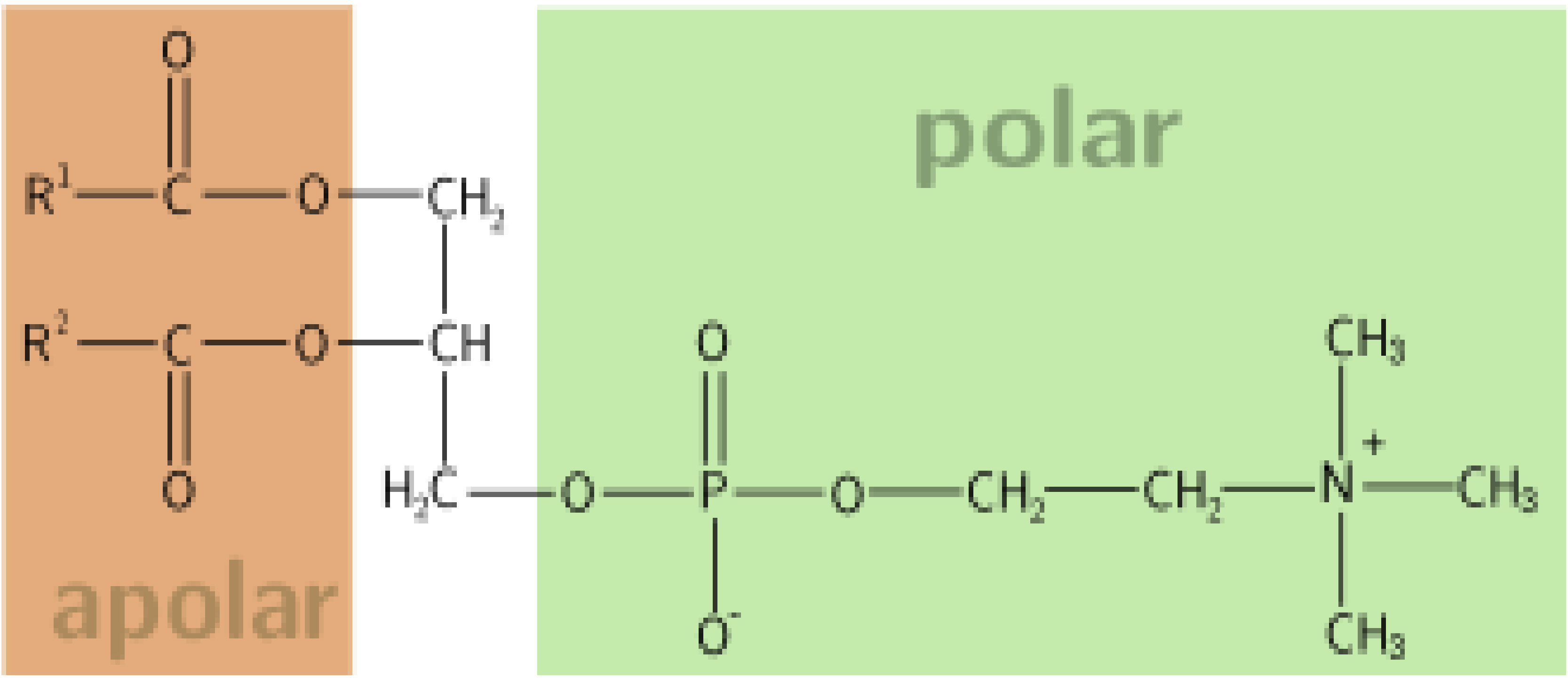
2. Lipid Membranes, Phase Transition Fluid - Gel



Lipid bi-layer formed of phosphatidylcholine (Voet & Voet, p. 288)

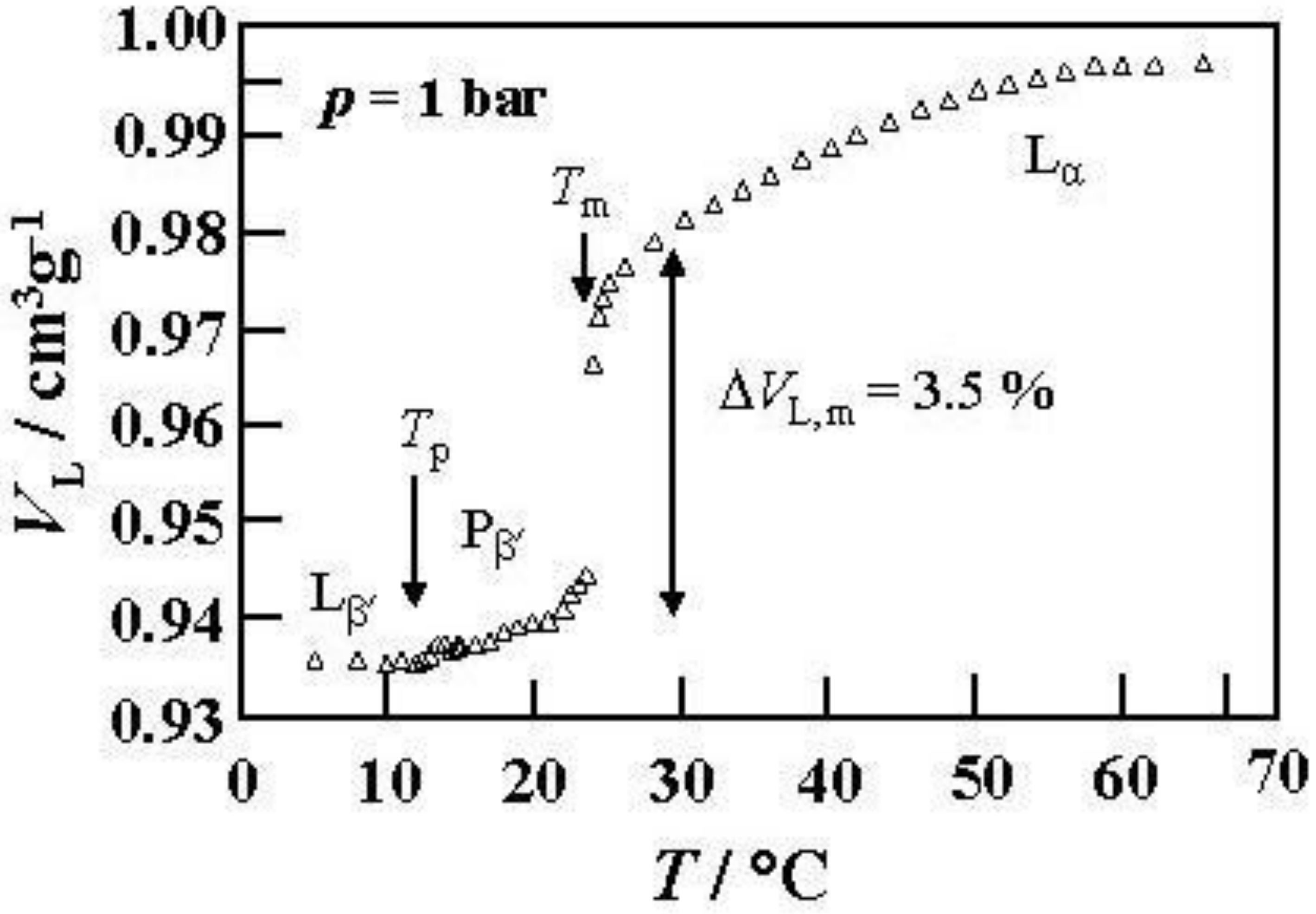
DMPC – Strukture: Phosphatidylcholine / Lecithine

Fatty acids



Glycerine   CH2 – CH – CH2
/ / /
OH OH OH

Choline



Temperature and pressure dependence of the specific volume of DMPC*) in water.
(R. Winter, JNE 6-22, 2007) *)1,2-dimyristoyl-s,n-glycero-3-phosphatidylcholine

DMPC Thermal Equation of State (EOS)

Aliphatic tails of DMPC-molecules may aggregate/adsorb on each other.

Degree of aggregation:

$$\alpha(v) := \frac{v_{.0} - v}{v_{.0} - b_{.0}} \qquad 0 < \alpha(v) < 1$$

Fluid state Gel state

Free volume

$$\beta(v) := \frac{v - b_{.0}}{v_{.0} - b_{.0}}$$

Fractality

EOS:

$$p(\alpha, T) := A(T)\cdot\alpha + B(T)\cdot\alpha^{2} + D(T)\cdot\alpha^{3} + C(T)\cdot\frac{\alpha^{\gamma}}{1-\alpha^{\gamma}} \qquad \gamma := 1$$

Virial expansion ... **Adsorption term**

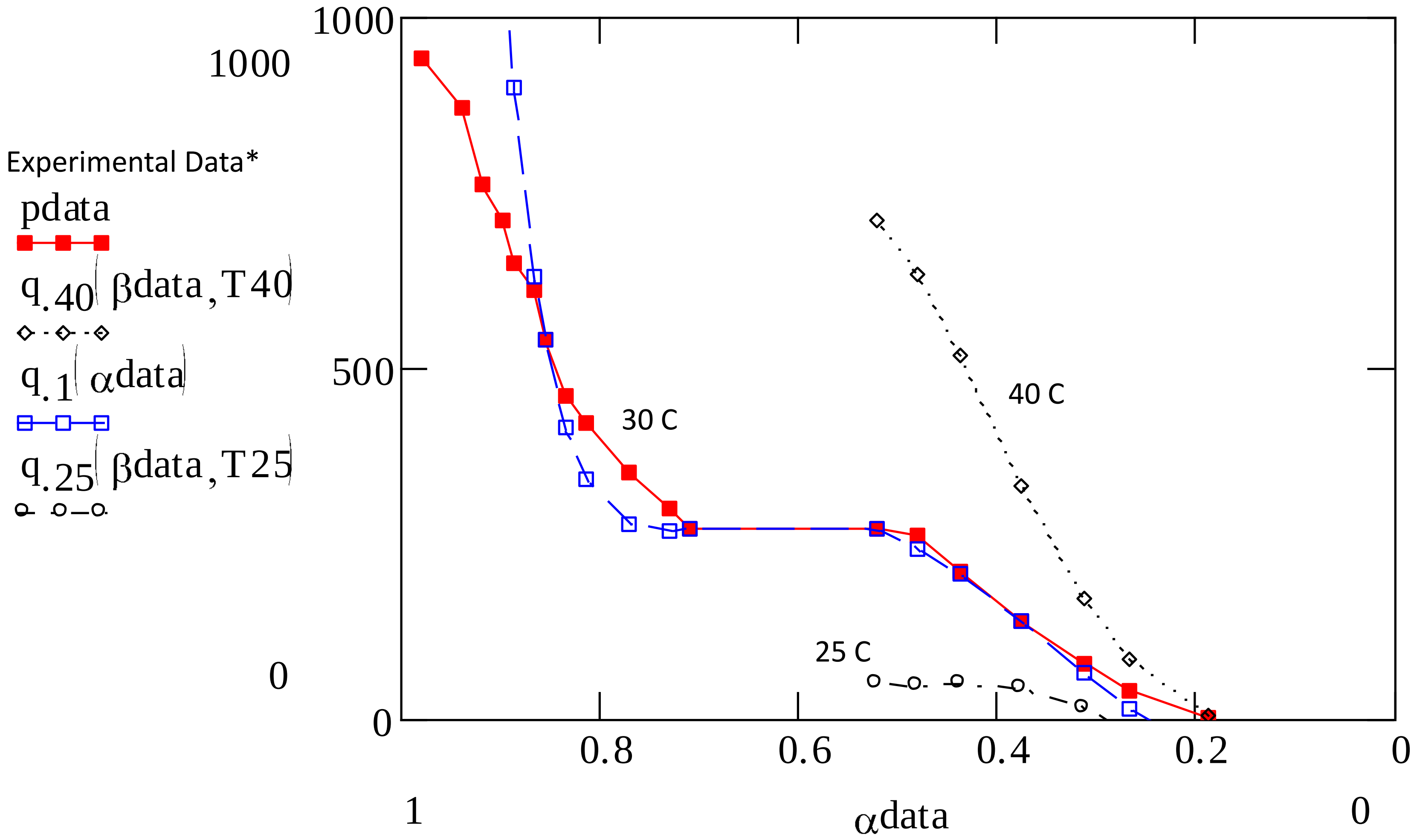
$$A(T) := A_{.0}\cdot\left[1 + a\cdot(T - T_{.0})\right]$$

....

$$D(T) := D_{.0}\cdot\left[1 + d\cdot(T - T_{.0})\right]$$

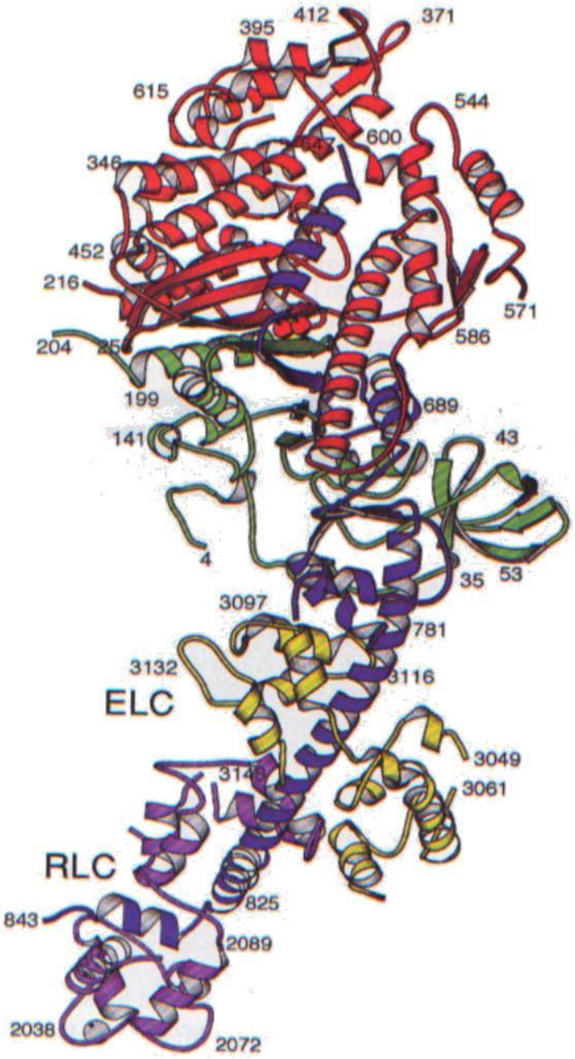
A= -1873 bar	a=-0.54
B=7942	b=-0.051
D=-8997	d=-0.429
C=333.34	c=-2.534

DMPC Thermal Equation of State (EOS)
Correlation of Isothermal Data



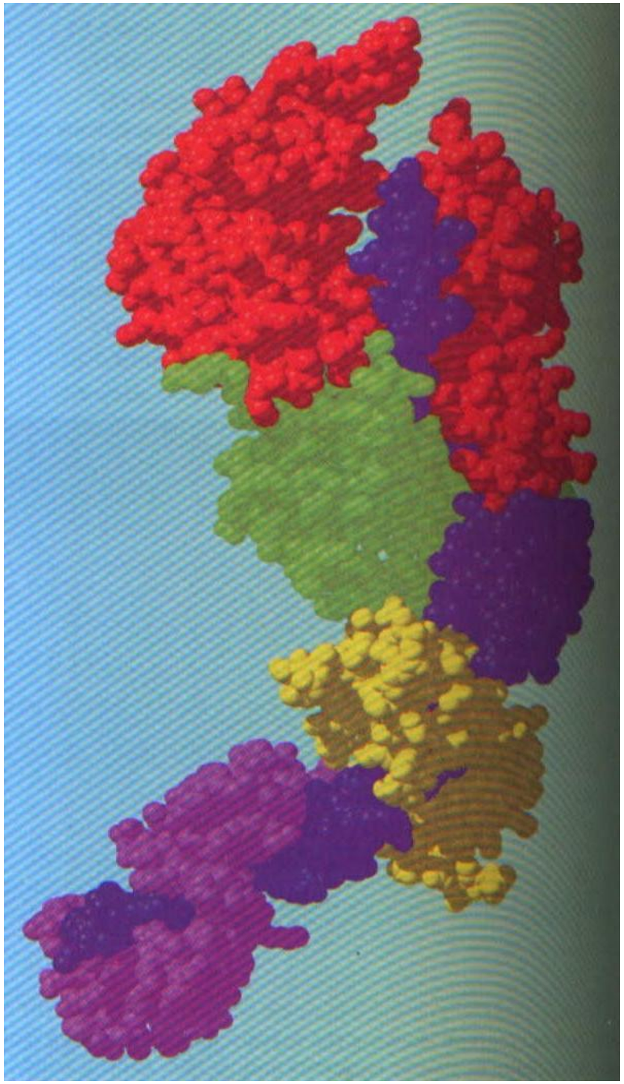
* R. Winter et al.,JNE 32(2007),p.41

3. Proteins (Example): Myosin from Chicken Muscle



Secondary Structure

Voet&Voet
Biochemistry
Wiley,N.Y.
1995

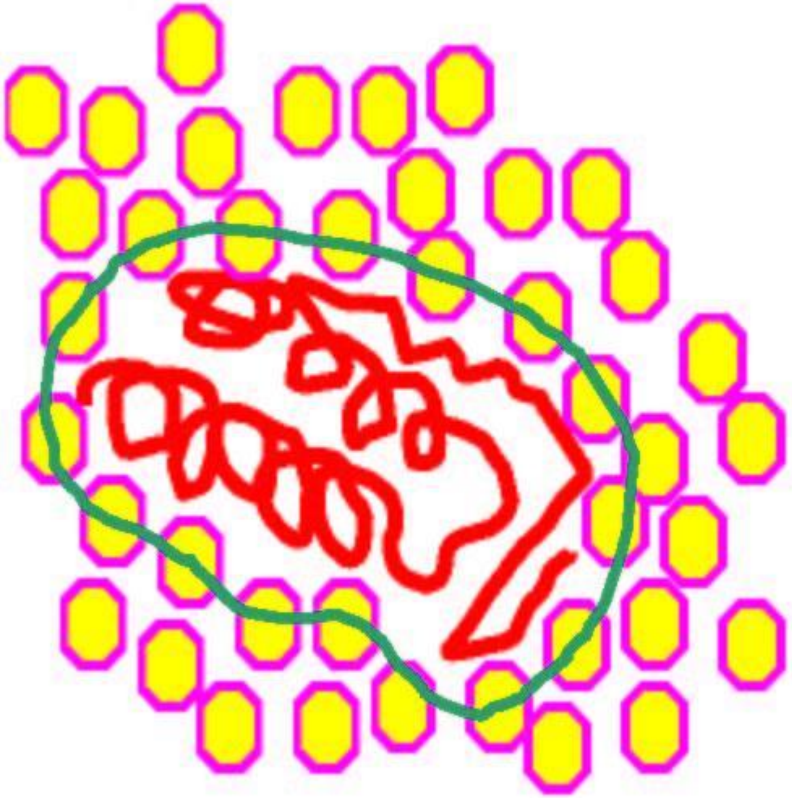


Tertiary Structure (X-Ray)

Protein(P) - Water(W) Interactions (E4)

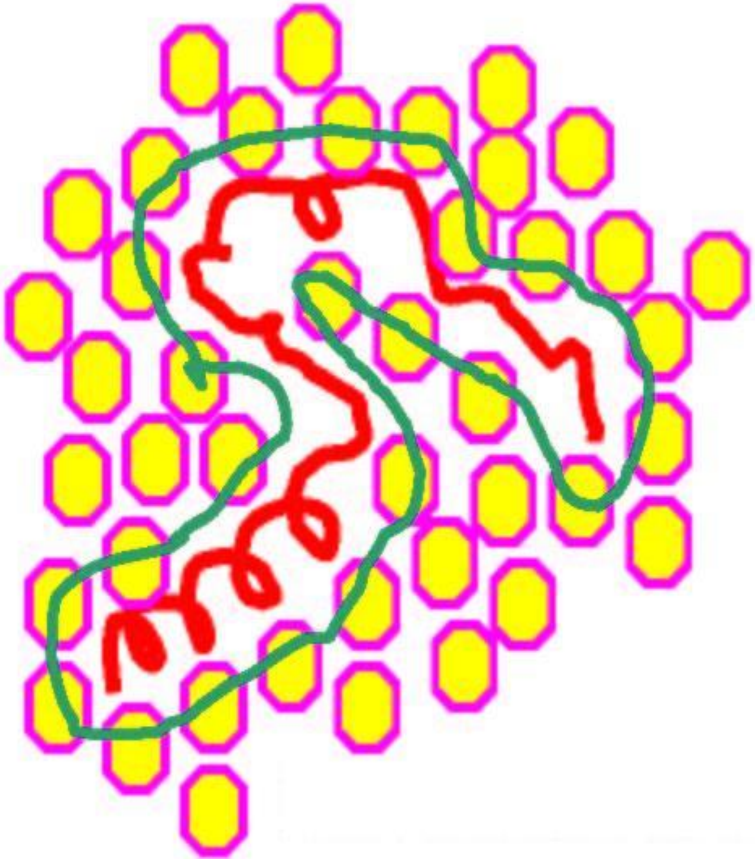
P: Conformational Changes, Unfolding

W: Adsorption, Intrusion, Coating of (P) > Stabilization



Ref.: T. Randolph, U of Colorado, USA

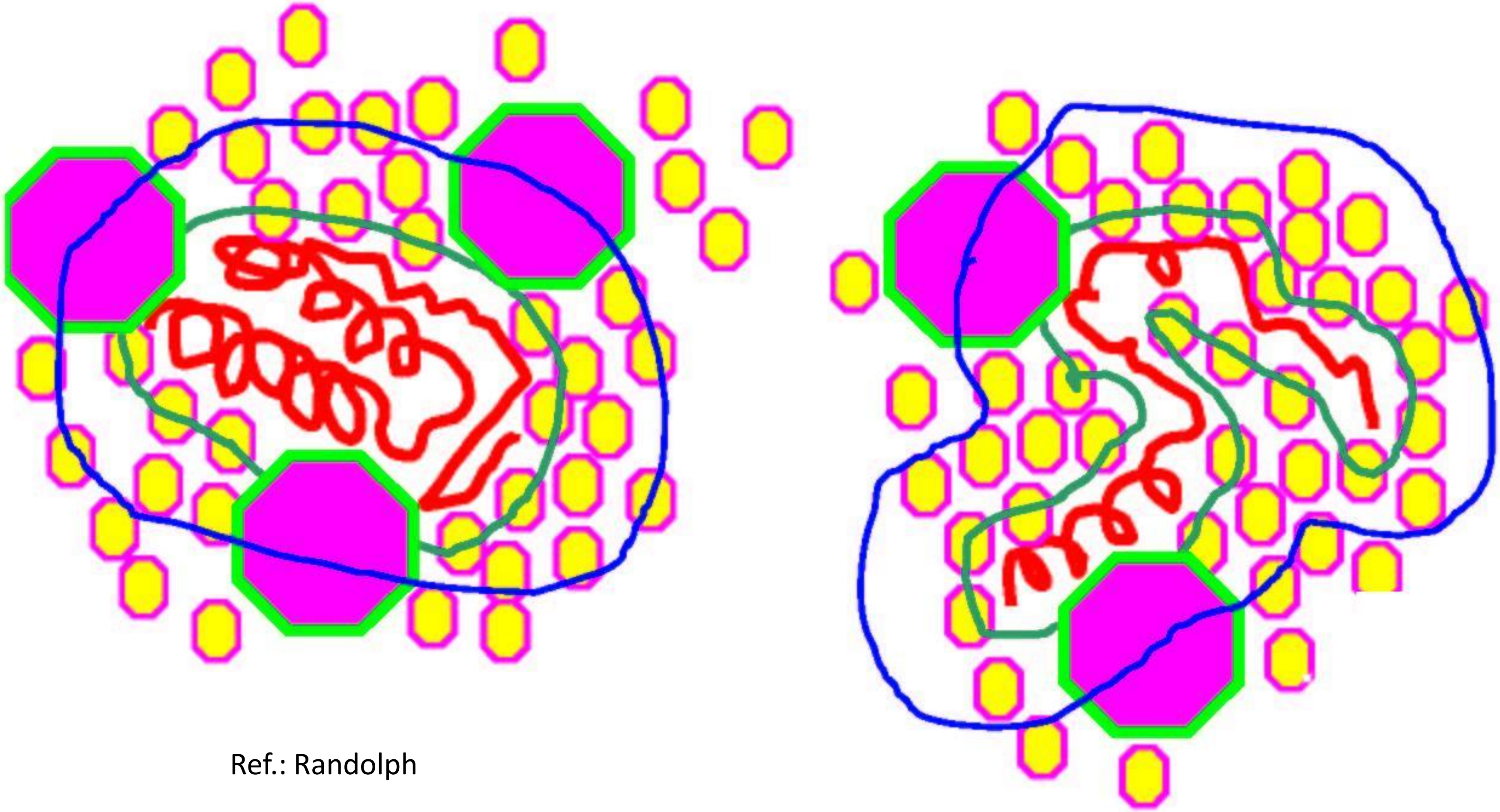
Native State (N):
compact, surface area small



Unfolded State (D):
expanded, surface area high

Protein(P) - Water(W) – Sugar(S) Interactions

S: Adsorption, Desorption upon unfolding of protein.



Ref.: Randolph

S-W: Coadsorption on surface may stabilize (P).

Thermal Denaturation of Myoglobine

153 Amino acids

Seize: (44x44x25)Å^3

Molecular Weight $\approx$ 18kD

N ... Native (folded) State

D ... Denaturated (unfolded) State

Equilibrium at T=const, p=const

$$\Delta G_{DN}(p,T) = -RT\ln\left(\frac{\gamma_D x_D}{\gamma_N x_N}\right)$$

$$\Delta G_{DN} = \mu_{D0} - \mu_{N0}$$

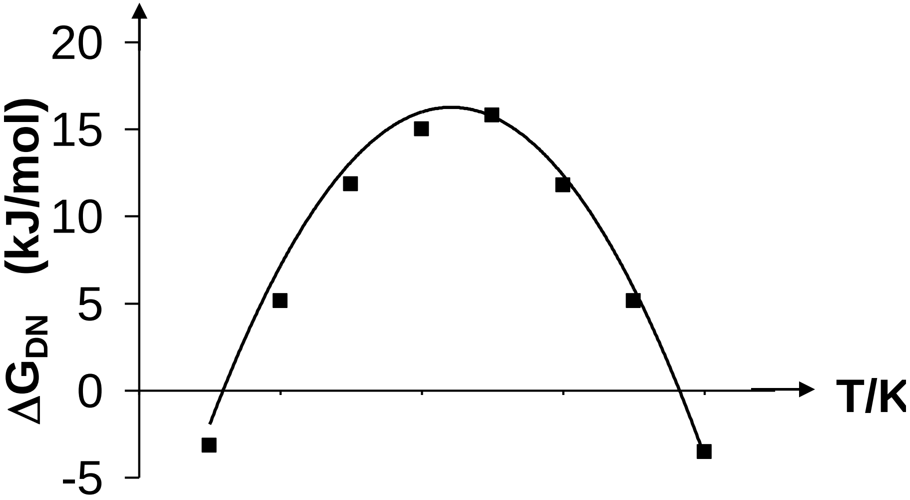
Approx.: $\gamma_D = \gamma_N = 1$

$\Delta G_{DN} > 0 \rightarrow x_D \ll x_N$...N...stable

$\Delta G_{DN} < 0 \rightarrow x_D \gg x_N$...N...unstable

Experimental Data

T/K	270	280	290	300	310	320	330	340
ΔG_{DN} (kJ/mol)	-3.16	5.13	11.8	15	15.8	11.8	5.13	-3.53
ΔH_{DN} (kJ/mol)	-289.	-204	-115	-23	72.2	170	272	376
ΔS_{DN} (kJ/mol K)	-1.06	-0.75	-0.44	-0.13	0.18	0.49	0.81	1.12



(U. von Stockar, EPFL,et al., MV Seminar,2000)

4. Kleiber's Law of Metabolism in Aerobic Living Systems

Allometry

Metabolic Rate

$$\Gamma = a \;\; T, T_0 \quad M^{\gamma}$$

$$a \cong (1-2)\mathrm{mW/g}$$

$$\frac{2}{3} < \gamma \le 1$$

$$\gamma \cong \frac{3}{4}$$

B. Ahlborn, Zoological Physics

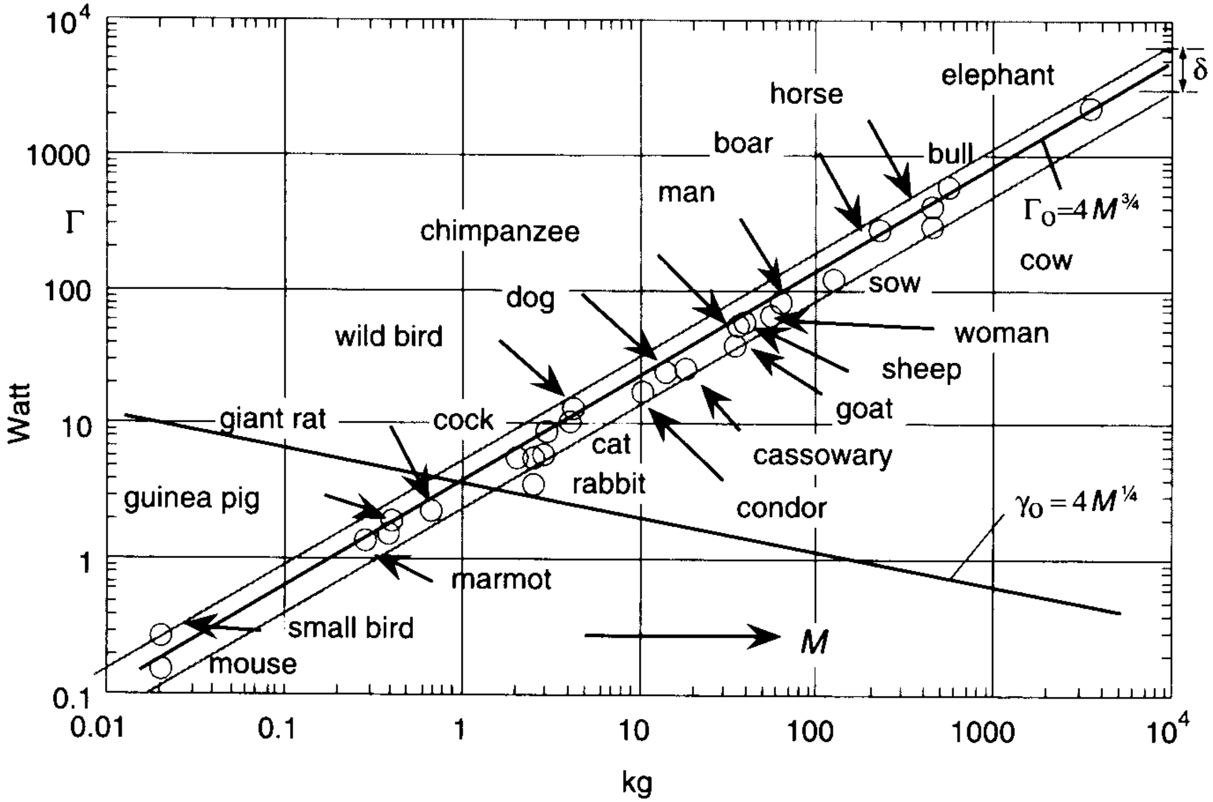
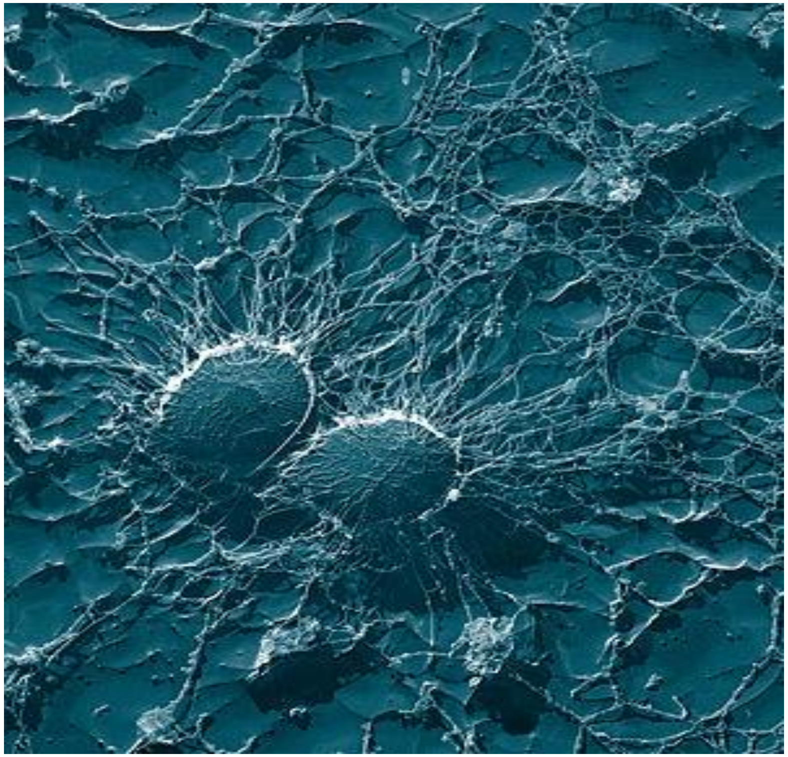


Figure A3
Metabolic rate of oxygen consumption based living systems. Mouse-Elephant-curve, B. Ahlborn, 2004. This curve also holds for bacteria (M $\cong 10^{-4}$ g).

Bacteria: Colony Forming Units (CFU)

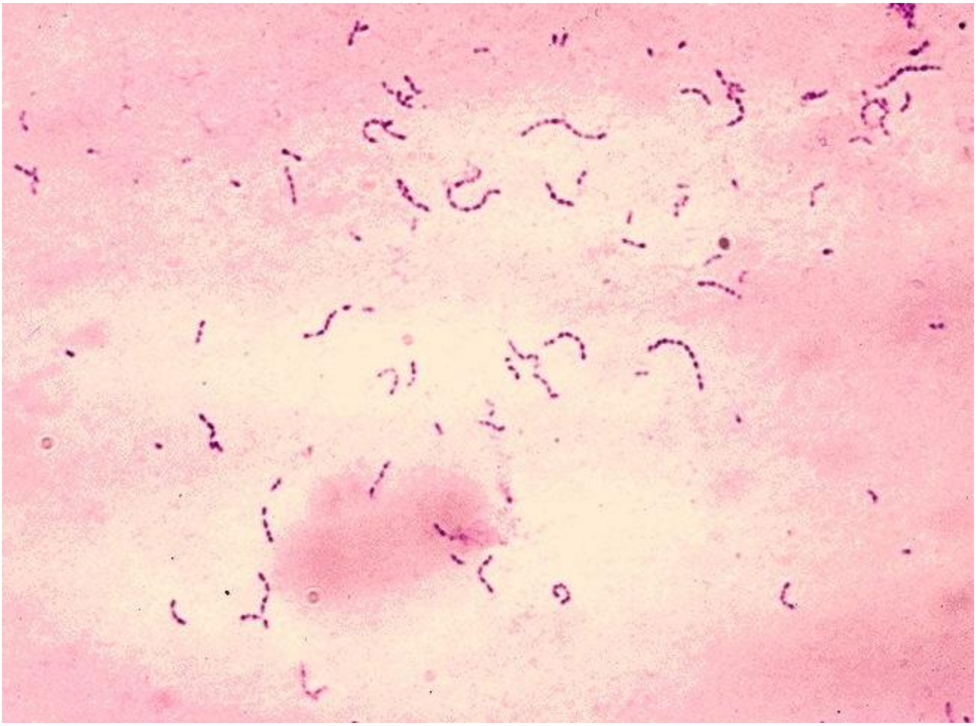


Staphylococcus aureus

$$Size: \quad 50.000:1$$

$$Diameter: \quad (0{,}8-1{,}2)\mu m$$

$$Density: \simeq 0{,}8 \ g/cm^3$$



Bacteria Streptococcus Mutans (Caries), Clarke (1924)

Basic Metabolic Rate of Living Systems

Creature	Mass/kg	Metabolic Rate J0 / W	Food Substrate	Heating Value MJ/kg	Consump-tion kg/day
Bacteria Staphylococcus aureus	$0{,}5 \bullet 10^{-15}$	120 nW	glucose	15,6	0,665. 10*(-9)
Men	80 kg	94 W	various	20	0,40
Lion	120 kg	127 W	meat	30	0,37
Elephant	3000 kg	1,418 W	grass	10	12,3

Activation factor : $J_0 \rightarrow (2\text{-}5) J_0$

Kleiber‘s Constant : Temperature Dependence

Bacteria growth processes, sterilisation.

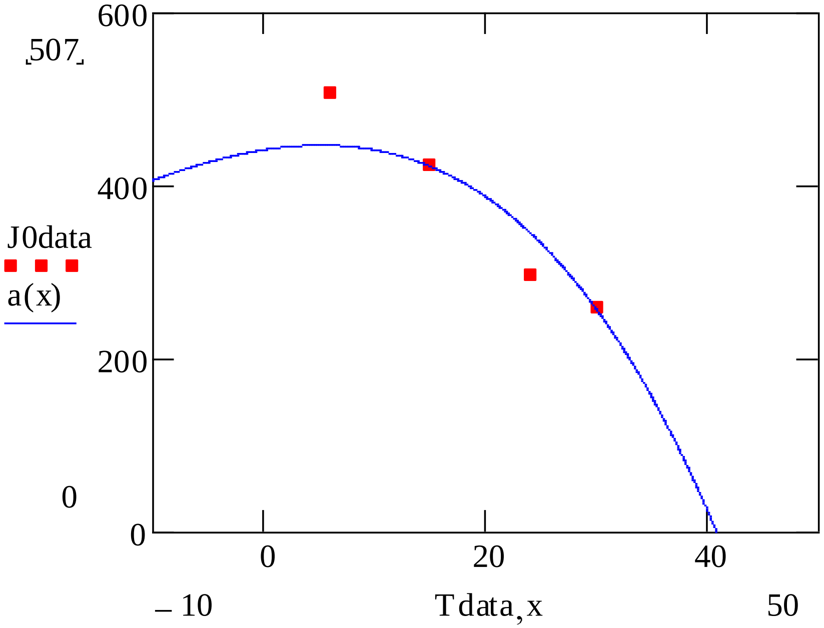
$$a = a(T_B, T^*) = A.(T_B - T^*).e^{-q^*/RT^*}$$

Example : Dogs,
hair cut,TB=41 C
Data : Jeroch et.al.(1999)

T_B.... Characteristic temperature
of living system

T^*....Environmental temperature

q^*....Energy (metabolism, heat transfer)



Enviromental temperature
for maximum metabolism

$$T^*_{\text{max}} = \frac{q^*}{2R} \quad -1 + \quad 1 + 4RT_B / q^* \quad {}^{1/2}$$

Autometabolism of Bacteria and CFUs

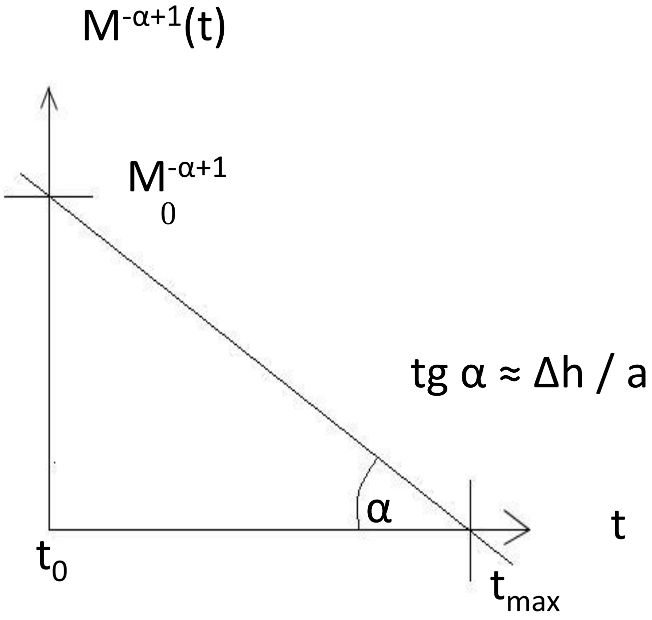
Lack of substrate: Living period ? Heat production ?

$$J_0 = -\Delta h \bullet \dot{M}$$

$$J_0 = aM^{\alpha}$$

$$\dot{M} + \frac{a}{\Delta h} M^{\alpha} = 0$$

$$M(t)^{-\alpha+1} = M_0^{-\alpha+1} - \frac{a}{\Delta h} \; t - t_0$$



Living period: $M \geq 0$

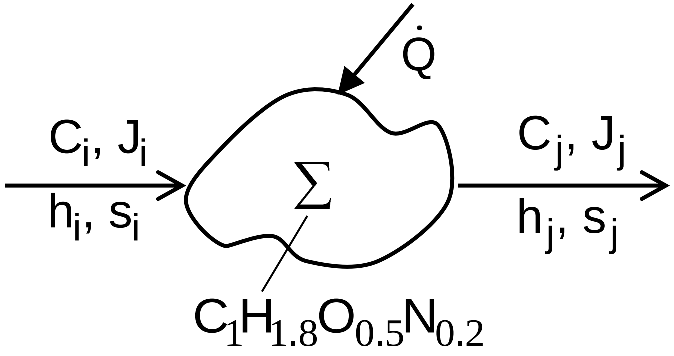
$$t_{\max} - t_0 = \frac{\Delta h}{a} M_0^{-\alpha+1} \geq 0$$

Example : Staph. Aureus

M_0=0,5 pg; Δh=18 MJ/kg;

$t_{max} \simeq 4$h

4c. Bacterial Metabolism for Stationary States



Net metabolic reaction:

$$\sum_{k}^{N} \nu_k \cdot C_k = 0 \tag{1}$$

Energy balance

$$\dot{H} = \sum_{i}^{N} h_i \cdot n_i + \dot{Q} = 0 \tag{2}$$

Entropy balance

$$\dot{S} = \sum_{i}^{N} s_i \cdot n_i + \frac{\dot{Q}}{T} + P_S = 0 \tag{3}$$

Metabolic rate $\dot{\xi}$

$$dn_i = \nu_i \cdot d\xi \tag{4}$$

Entropy production

$$(1 - 4) \quad P_S = \left(\sum_{i}^{N} \nu_i \cdot \mu_i \right) \dot{\xi} \; > 0$$

TIP

$$\dot{\xi} = L \left(\sum_{i}^{N} \nu_i \cdot \mu_i \right) \tag{5}$$

Kleiber‘s Law

$$\dot{\xi} = a_m \cdot M^{\alpha} \tag{6}$$

2 Organisms with same metabolism:

$$(5, 6): \quad \frac{L_1}{L_2} = \left(\frac{M_1}{M_2} \right)^{\alpha}$$

4d. Bacterial Metabolism – External Stability Limits

Σ: Thermodynamic system:
Stability of Accompanying
equilibrium state

$$T = \text{const}, p = \text{const}$$

$$\sum_i^N d\mu_i \cdot dn_i \geq 0 \qquad (7)$$

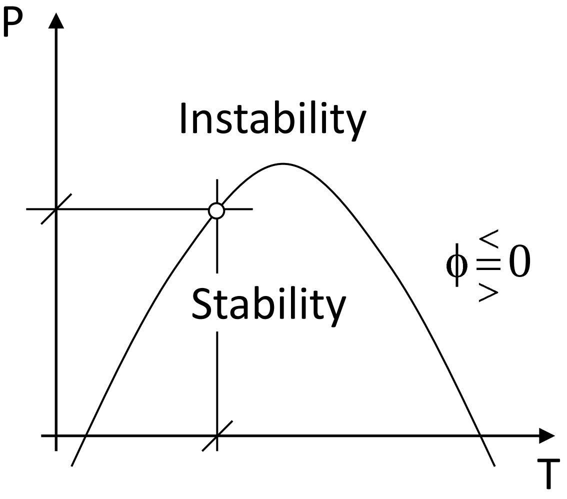
$$\mu_i = \mu_i \;\; T, p, x_1 \ldots x_N$$

$$x_i = n_i \Big/ \sum_k^N n_k$$

$$dn_i = \nu_i \cdot d\zeta \qquad (4)$$

$$(7) \quad \sum_{i,k} \left(\frac{\partial \mu_i}{\partial n_k} \right)_{T,p} \nu_i \cdot \nu_k \geq 0 \quad (8)$$

$(8 =)$



$$(4,7) \quad \sum_{ik} \left(\frac{\partial \mu_i}{\partial n_k} \right)_{T,p} \nu_i \cdot \nu_k \doteq 0 \quad (8)$$

$$(8 =) \quad \phi(T, p, x_1 \ldots x_N) = 0$$

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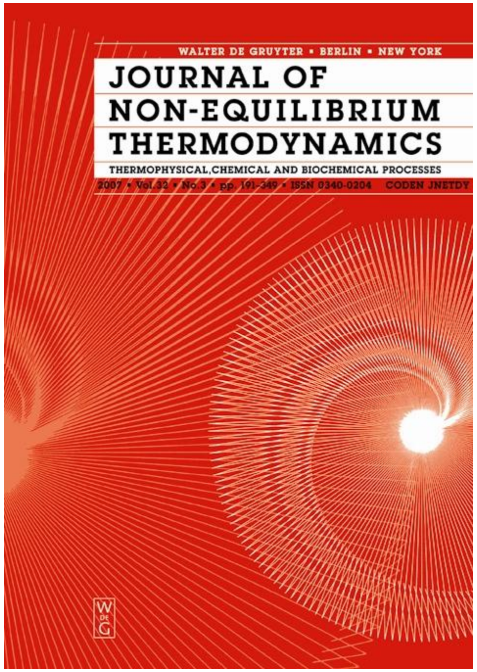

KISS

Keep it smart and simple.

MORENE

More research needed.

Ötztaler Alpen, 5-9-2007
Similaunhütte, 3012m, (T= -10C / -30C)