Entwicklung einer thermischen Zustandsgleichung für Zellmembranen aus lipidartigen Molekülen (DMPC*)

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*1,2-Dimyristoyl-sn-glycero-3-phosphatidylcholine

Zusammenfassung

Viele biologische Membranen können in einfachster Nährung als Doppelschichten von Lipid - Molekülen, z.B. Phosphatidylcholin oder ähnlichen Triphosphatcholinen aufgefasst werden. Diese Moleküle besitzen elektrisch polare „Köpfe“ und unpolare „Schwänze“, die aus CH2-Gruppen gebildet werden.

In einer Membran sind die Köpfe der Moleküle nach außen, ihre Schwänze nach innen orientiert. Das Volumen einer solchen Membran in wässriger Lösung zeigt in Abhängigkeit von Druck und Temperatur einen Phasenübergang, bei welchem die Schwänze aus einem ungeordneten,quasi fluiden Zustand in einen durch parallele Anordnung der Schwänze gekennzeichneten, gelartigen Zustand übergehen. Da sich die Transport- und Speichereigenschaften der Membran, z.B. ihre Permeabilität für Wasser, in beiden Zuständen stark voneinander unterscheiden können, ist die Kenntnis der Phasenübergangsdaten (p, v, T) von grundsätzlichem biotechnischem Interesse.

Am Institut für Physikalische Chemie I der U Dortmund sind p, v, T-Daten von speziellen Lipidmembranen (DMPC*) gemessen worden.

Für diese Daten ist am Institut und Fluid- und Thermodynamik der U Siegen, ausgehend von der Vorstellung der wechselseitigen Adsorption der Lipidschwänze aufeinander beim Phasenübergang Fluid-Gel, eine thermische Zustandsgleichung entwickelt worden. Diese erlaubt es grundsätzlich, das Zustandsverhalten der Membran für beliebige Temperaturen und Drücke zu berechnen, d.h. auch ein Phasendiagramm zu erstellen.

Im vorliegenden Beitrag wird diese Zustandsgleichung explizit angegeben und ihre Eigenschaften diskutiert.

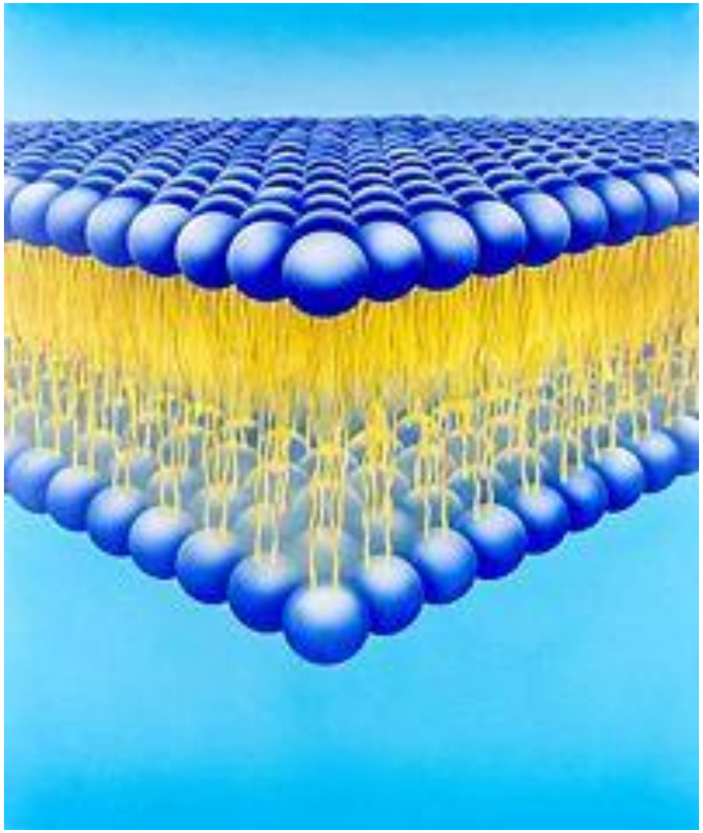
* 1,2-Dimyristoyl-s,n-glycero-3-phosphatidylcholin

Abstract

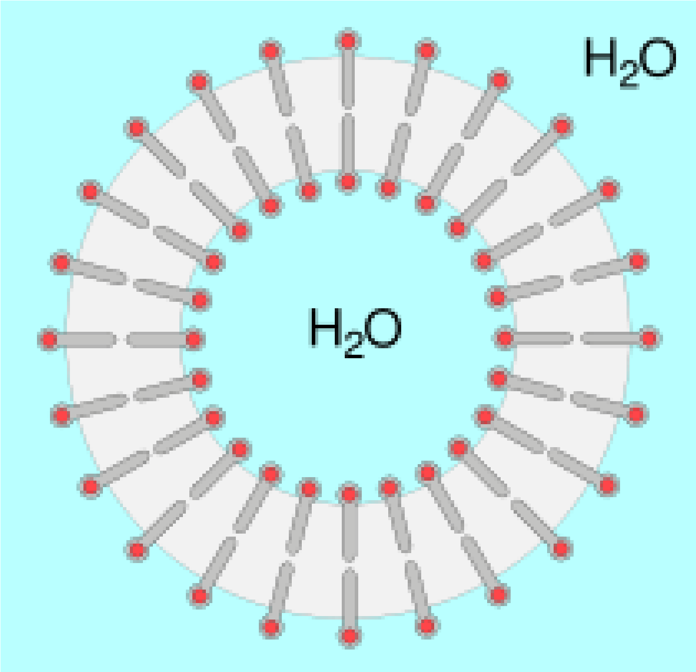
Biological membranes in a first approximation may be considered as double-layers of lipid molecules as for example phosphatidylcholine or triphospatidylcholine. These molecules have (electrically) polar “heads” and non-polar aliphatic “tails” often consisting of ethyl groups (-CH2-). A simple model for a biological membrane is a double layer of lipid molecules whereabout the “heads” form the external surfaces of the membrane and the “tails” are oriented to the interior of the membrane. The volume of such a membrane in aqueous solution depends – at constant PH - value on the pressure (p) and the temperature (T) of the solution.
For a special DMPC*-membrane the specific volume has been measured at various pressures and different temperatures at the Institute of Physical Chemistry I of the University of Dortmund.
Data show a phase transition whereby the “tails” in the interior of the membrane change their arrangement and motion from a chaotic, quasi-fluid state to a frozen, gel-like state with nearly parallel arrangement or self-adsorption of the CH2-elements on their neighbouring groups.
As the transport properties and the storage capacity of the membrane for water in both states differ considerably, knowledge of the phase transition data (p, v, T) is of importance for biotechnical and other applications.For the DMPC* membrane several sets of (p, v, T)-data have been measured at the University of Dortmund, namely isothermal (p, v) - data at 30 °C, and isobaric (T, v) - data at p = 1 atm and the phase transition curve fluid – gel (p = p (T)). From these data a thermal equation of state has been developed at the Institute of Fluid- and Thermodynamics of the University of Siegen. Basic for this equation is the concept of (reversible) self adsorption of the lipids’ tails on each other during the fluid-gel phase transition. This equation allows in principle to calculate the (specific) volume of the membrane at arbitrary temperatures (T) and pressures (p) and thus to get information on the fluid- or gel-state of the membrane.In the presentation the equation of state will be given explicitly and its properties will be discussed to a certain extend.

Cell Membranes: Thermal Equation of State

Double layer of lipid molecules
Polar „heads“ – Non-polar „tails“



Lipid bilayer forming a micelle



Lipids, Fatty Acids:Elements of Biological Membranes

Organic acids

$$\ldots\text{—}\underset{\substack{\parallel\\ \mathrm{O}}}{\mathrm{C}}\text{—}\mathrm{OH}$$

Acetic acid

$$\mathrm{CH_3}\text{—}\underset{\substack{\parallel\\ \mathrm{O}}}{\mathrm{C}}\text{—}\mathrm{OH}$$

Fatty Acids

$$\mathrm{CH_3}\text{—}\mathrm{(CH_2)_{n-2}}\text{—}\underset{\substack{\parallel\\ \mathrm{O}}}{\mathrm{C}}\ \mathrm{OH}$$

aliphatic tail | polar head

not soluble in water!

Examples: n=18

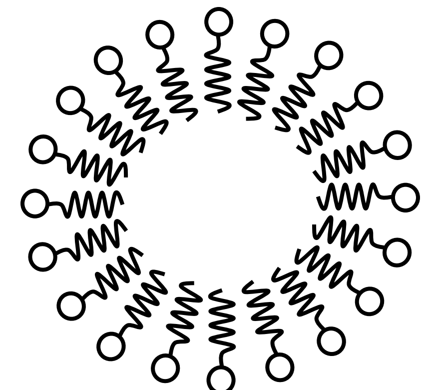
a) $\mathrm{CH_3}\text{—}\mathrm{(CH_2)_{16}}\text{—}\underset{\substack{\parallel\\ \mathrm{O}}}{\mathrm{C}}\ \mathrm{OH}$

Stearic acid, $T_m \cong 70°C$

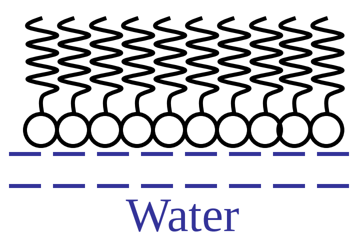
b) $\mathrm{CH_3}\text{—}\mathrm{(CH_2)_7}\text{—}\mathrm{C}=\mathrm{C}\text{—}\mathrm{(CH_2)_7}\text{—}\underset{\substack{\parallel\\ \mathrm{O}}}{\mathrm{C}}\ \mathrm{OH}$

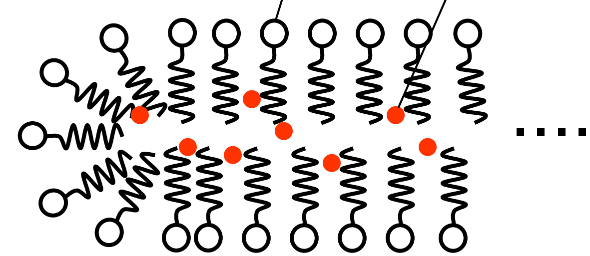
Oleic acid, $T_m \cong 13{,}4°C$

Micelles



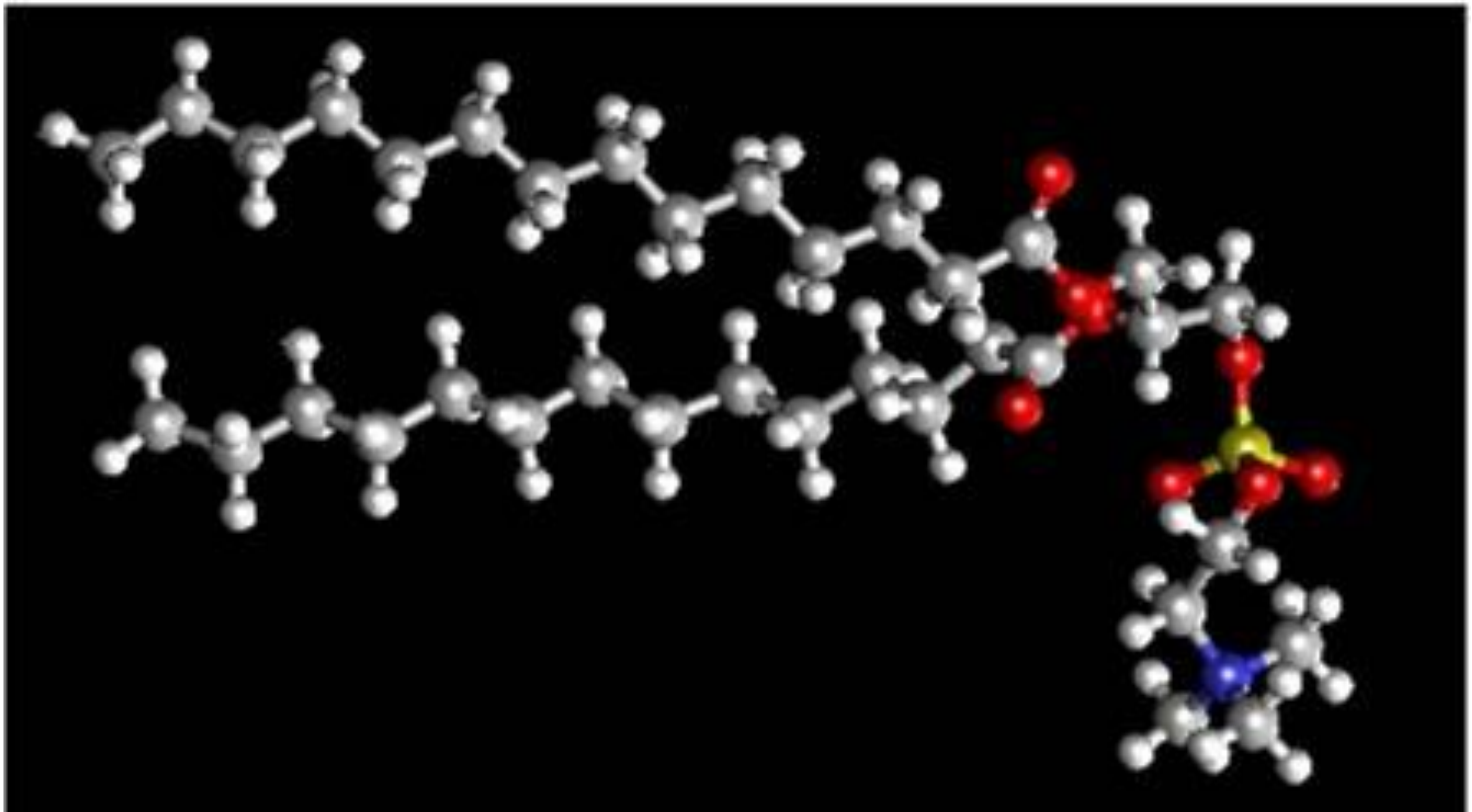
polar heads





Membranes

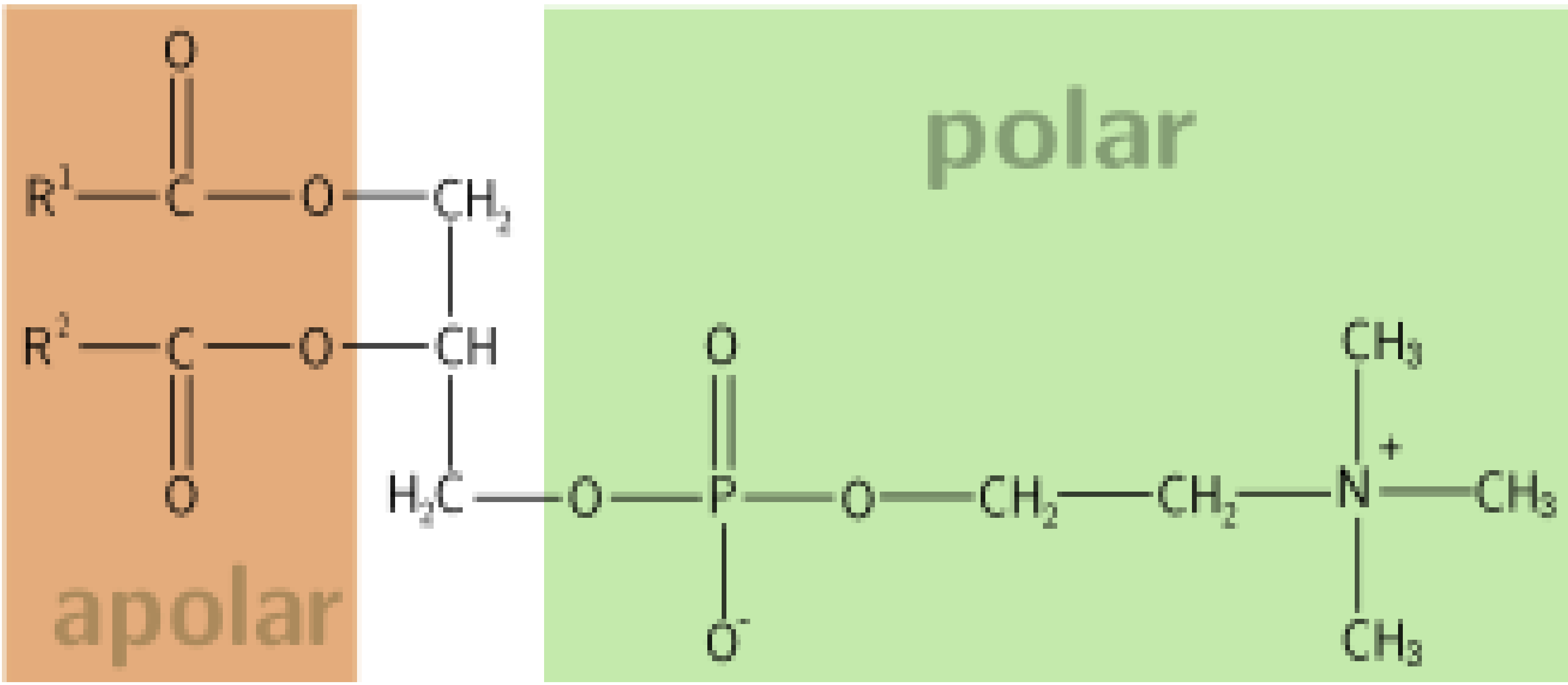
1,2-Dimyristoyl-sn-glycero-3-phosphatidylcholine



Ref.: R. Winter et al., JNE 32(2007),p.41…

Phosphatidylcholine / Lecithine

Fatty acids



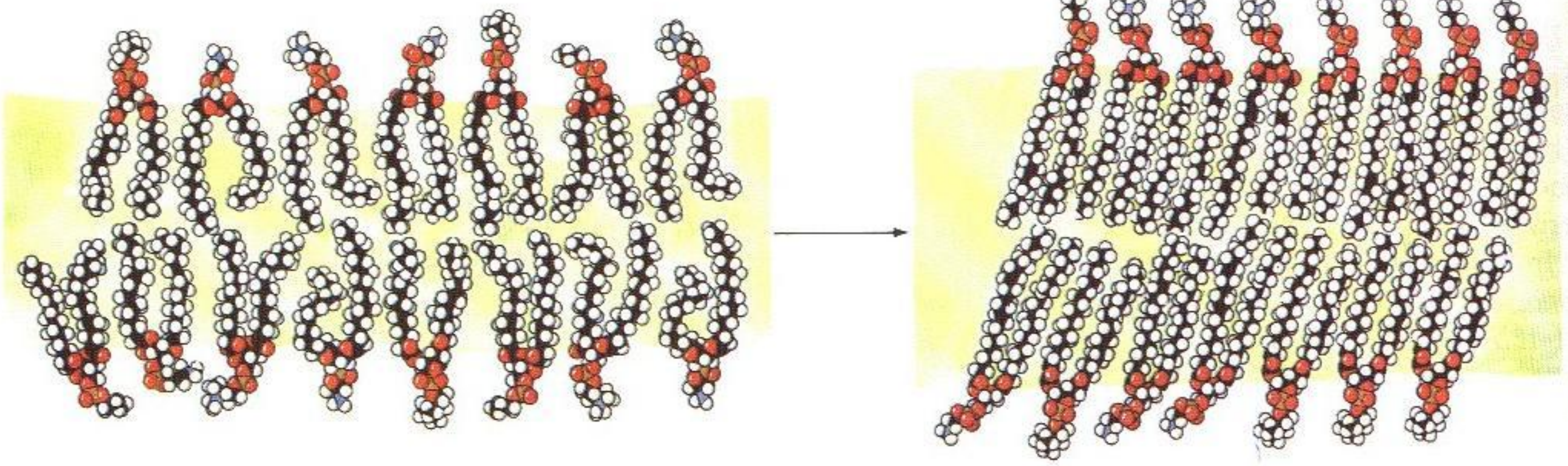
Glycerine   CH2 – CH – CH2
/ / /
O**H** O**H** O**H**

Choline

DMPC: R1 = R2 = C14

Lipid Membranes, Phase Transition Fluid - Gel

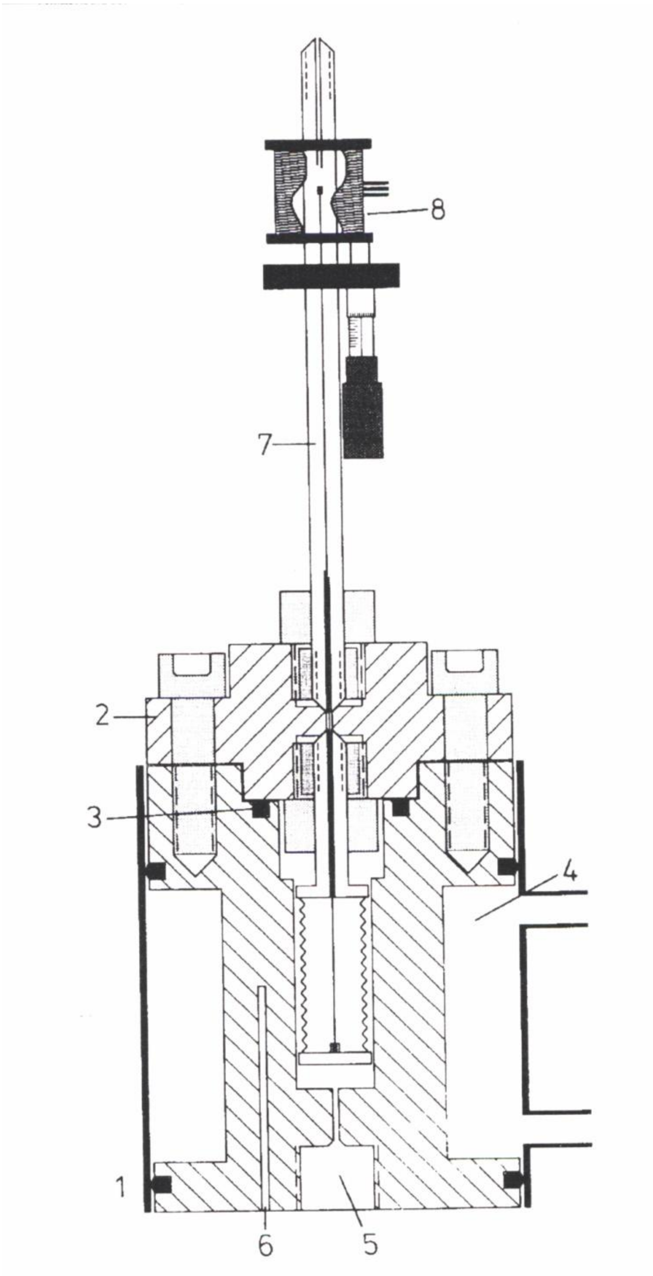
$T > T_t(p, ...)$ $T < T_t(p, ...)$



Fluid-Phase Gel-Phase

Lipid bylayer formed by phosphatidylcholine molecules (Voet&Voet, p. 288)

DMPC Solutions, pvT-Measurements Volumetric Cell T = (0 – 100) C P < 250 MPa



1 Pressure cell

2 Top flange

3 Viton O-ring

4 Thermostate

5 High pressure nut

6 Thermocouple inlet

7 High pressure pipe

8 Inductive coil

Ref. Böttner M. et al., High Pressure Volumetric Measurements on Phospholipid Bilayers, Z. Physik.Chemie 184(1994),p.205

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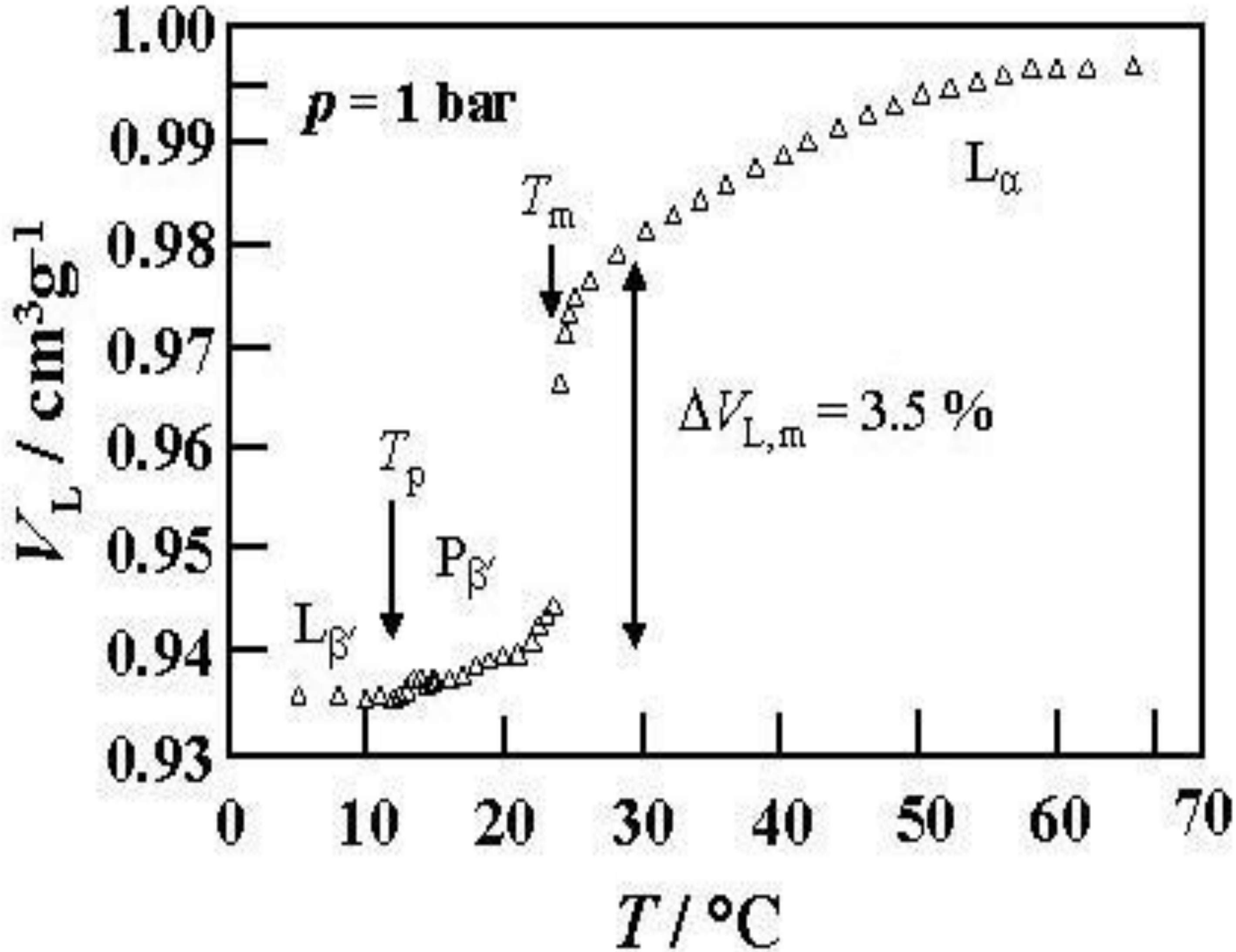
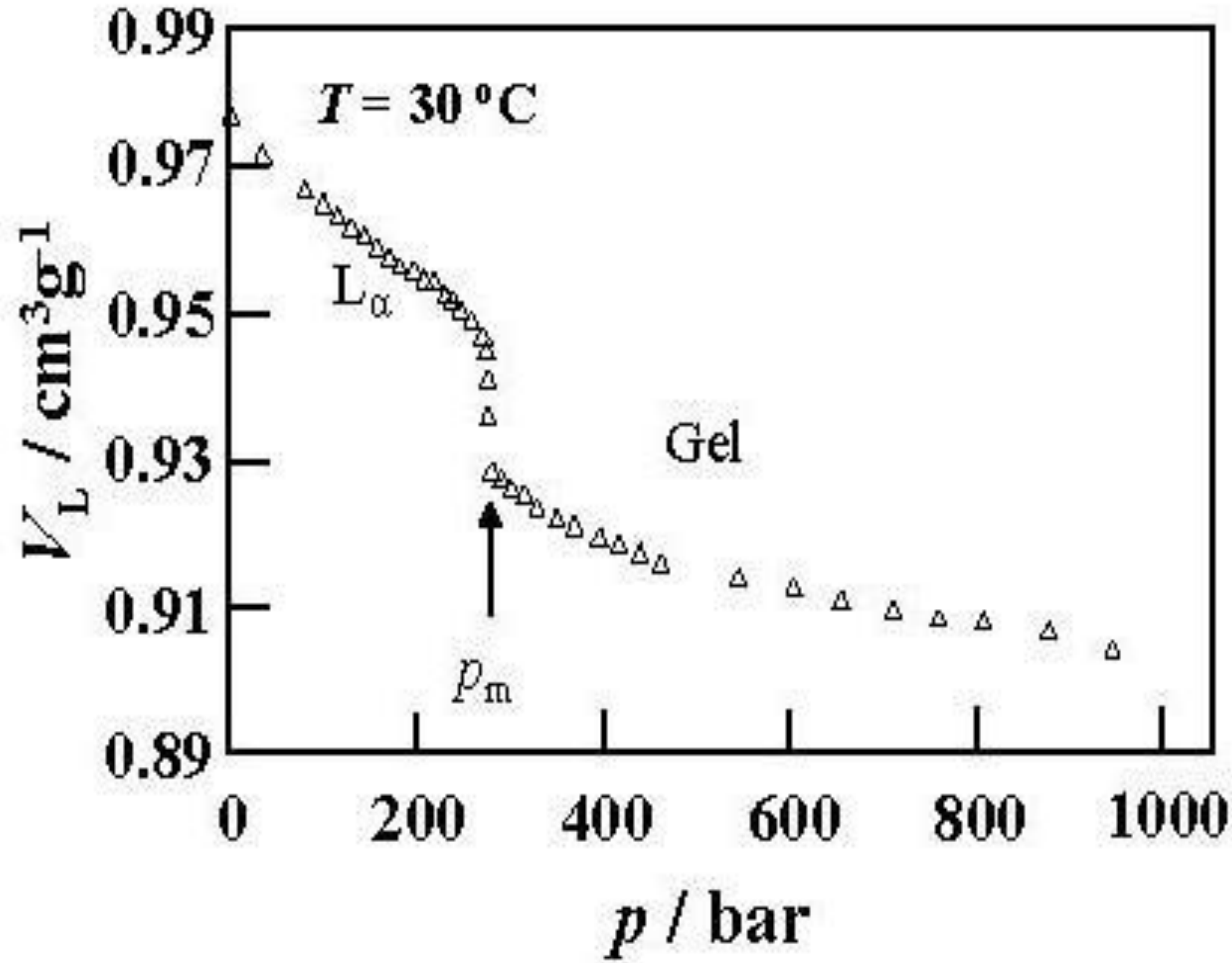


Temperature and pressure dependence of the specific volume of DMPC*) in water. (R. Winter, JNE 32(2007),p.41 *)1,2-dimyristoyl-s,n-glycero-3-phosphatidylcholine



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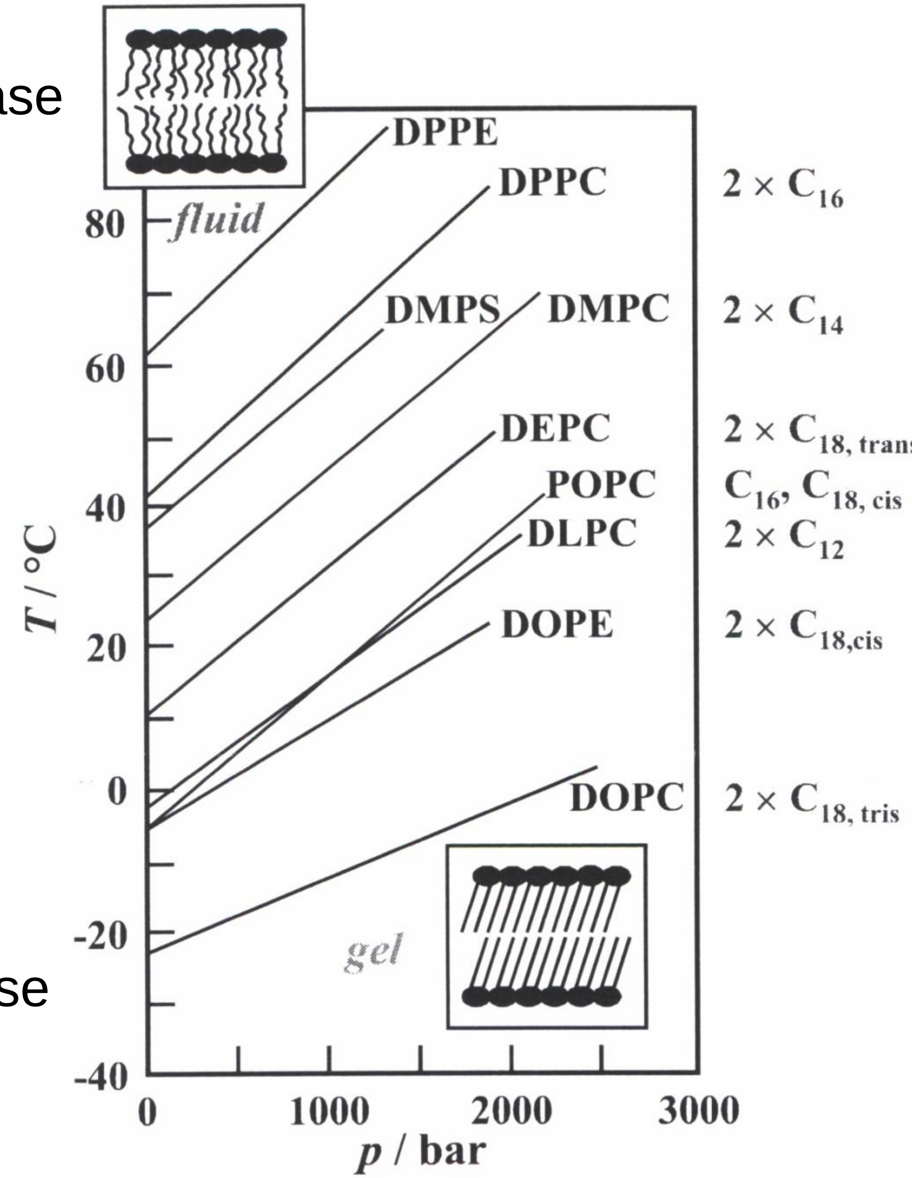
T,p-Phase Diagram of Various Phospholipid Bilayer Systems

(R. Winter, JNE 6-22, 2007)

Fluid Phase



Gel-Phase

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 (→ $v_{.0}$)   Gel state (→ $b_{.0}$)

Free volume

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

Fractality (→ γ)

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**

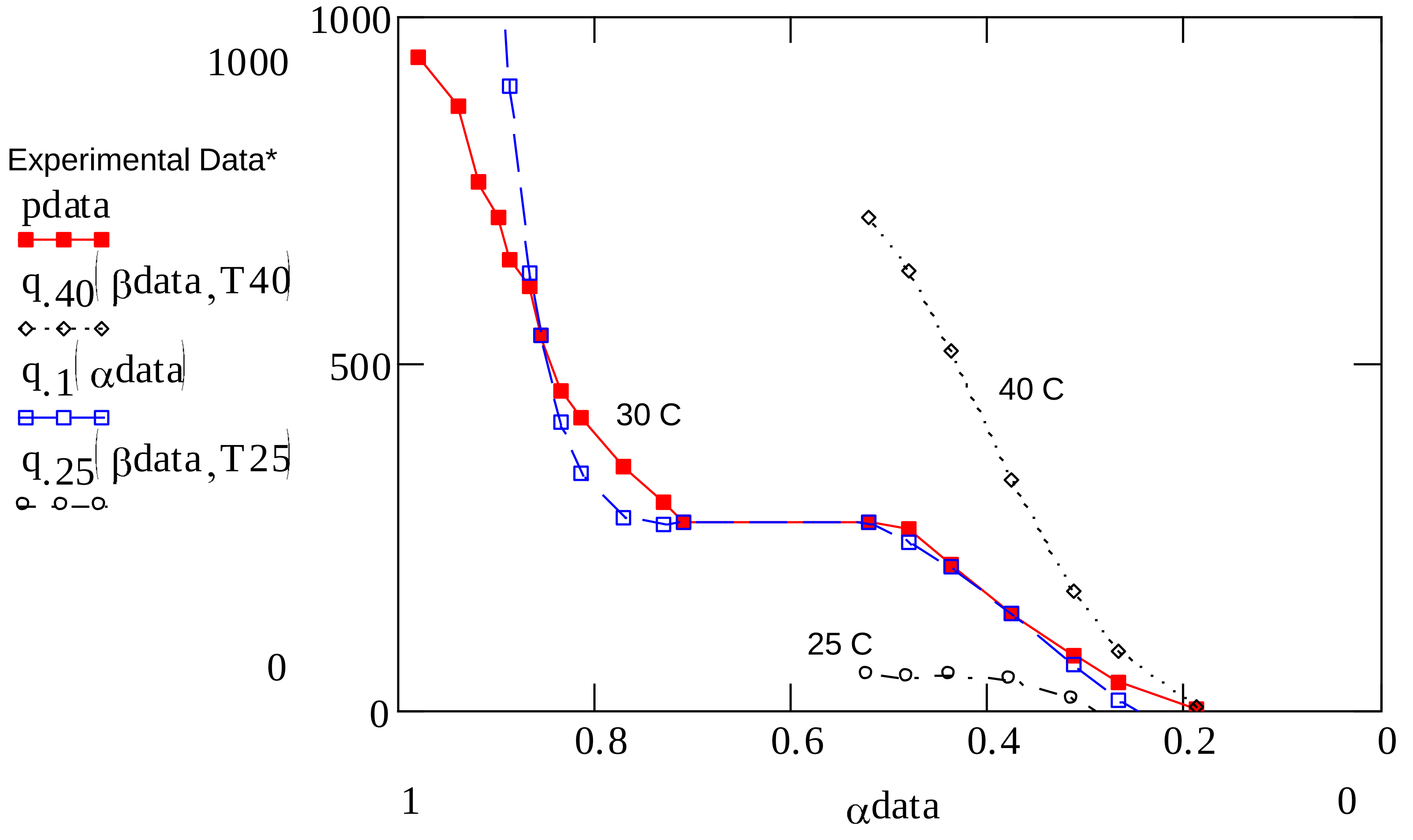
$$A(T) := A_{.0}\cdot\left[1 + a\cdot\left(T - T_{.0}\right)\right]$$

....

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

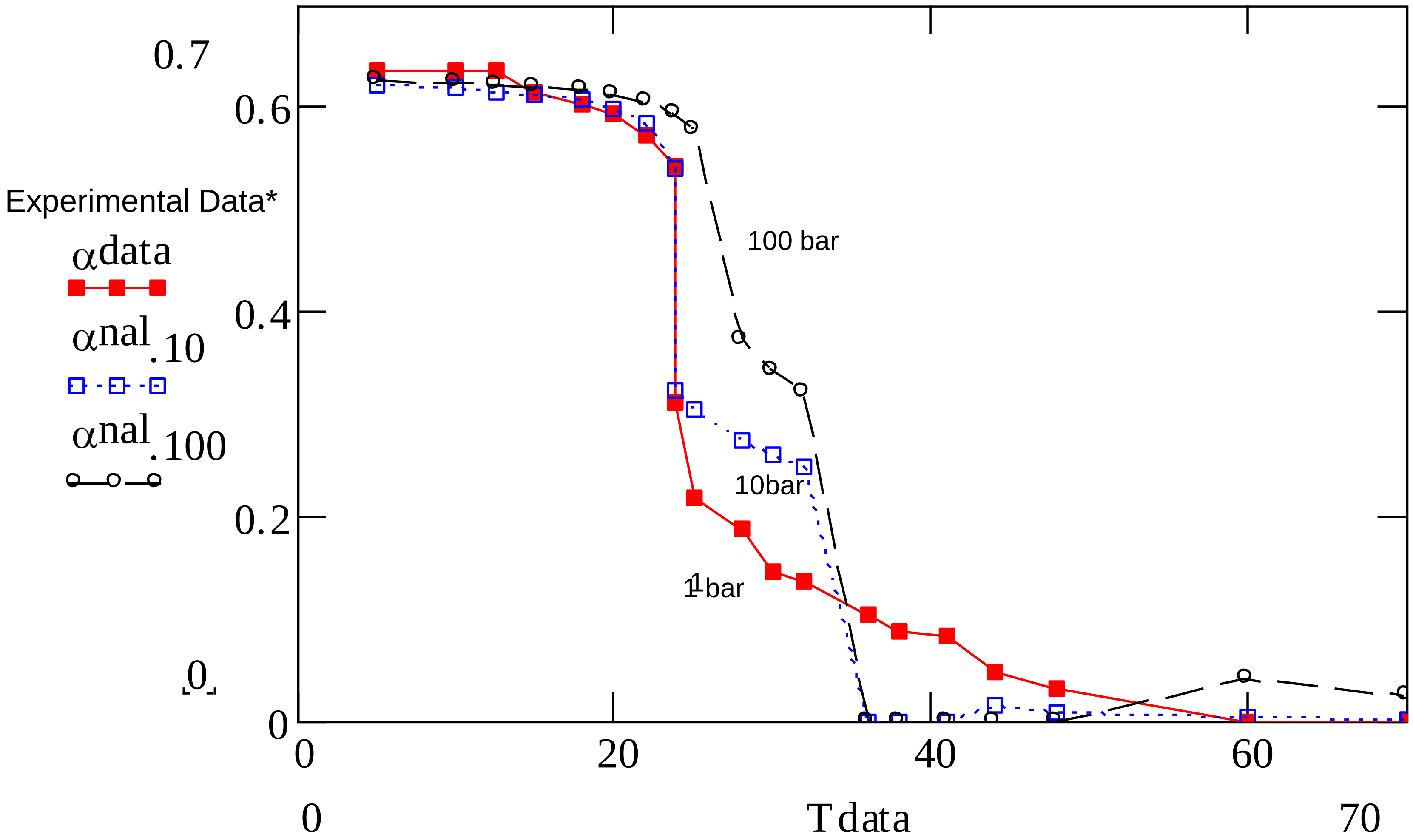
A= -1873 bar	a=-0.54
B=7942	b=-0.051
D=-8997	d=-0.429
C=333.34	c=-2.534

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



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

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



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