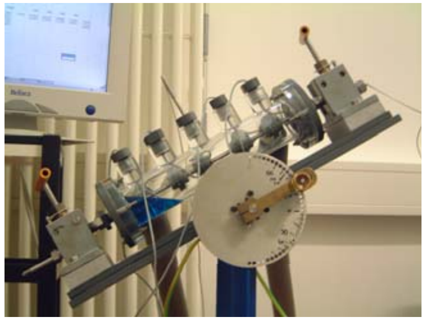

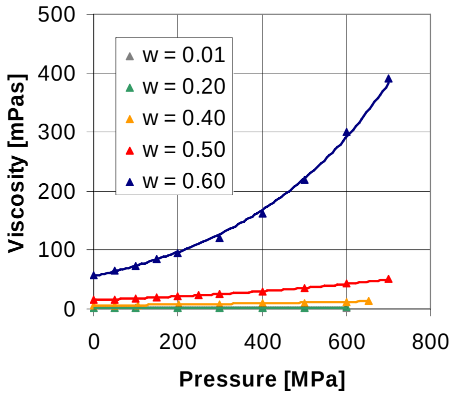

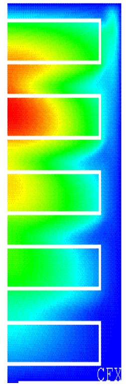

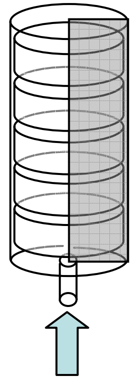

High Pressure Rheology of Liquid Biomaterials

Albert J. Baars
Institute of Fluidmechanics (LSTM)
Friedrich-Alexander-University Erlangen-Nuremberg

PAN – Warsaw 20.12.2006

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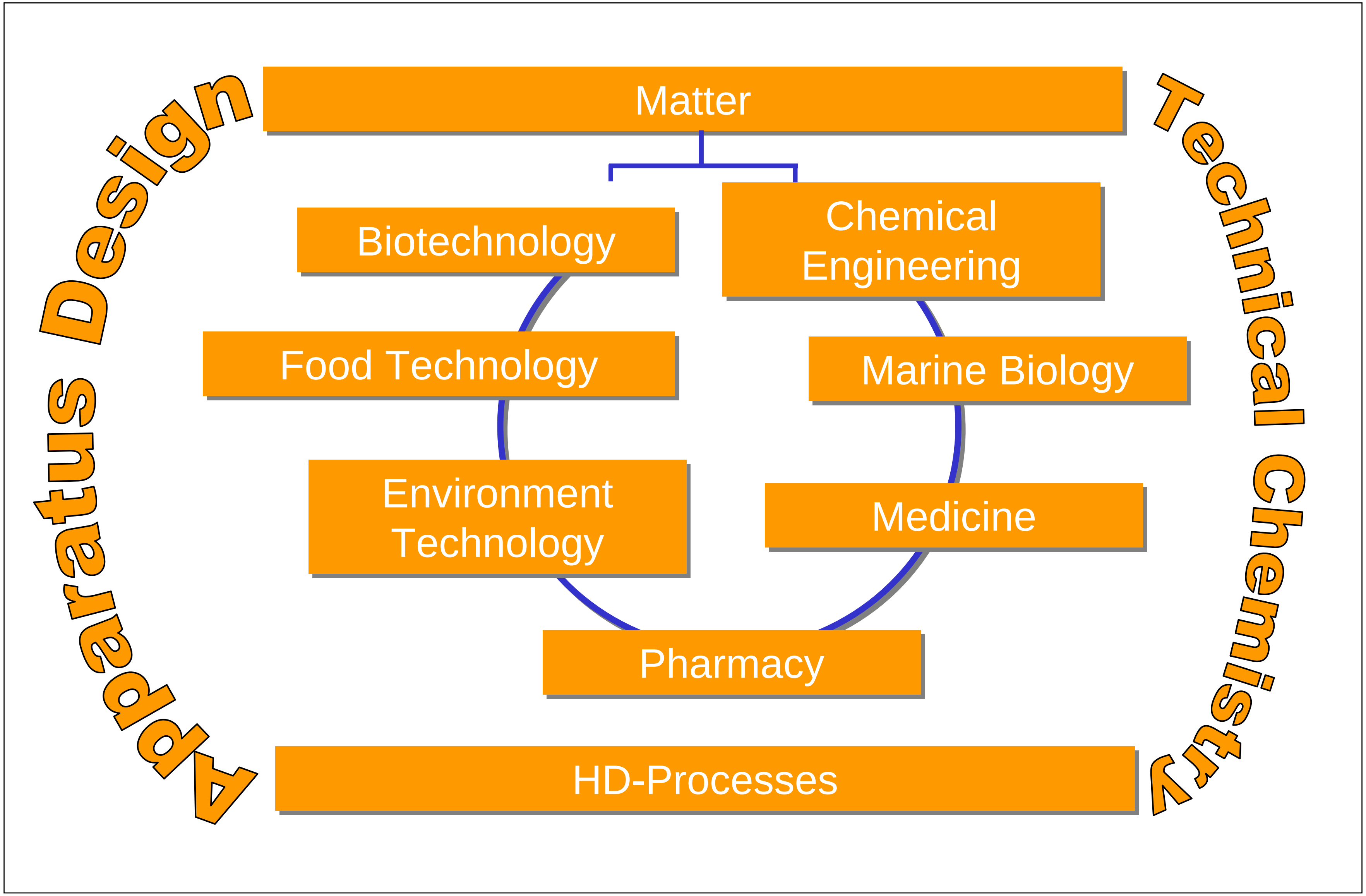
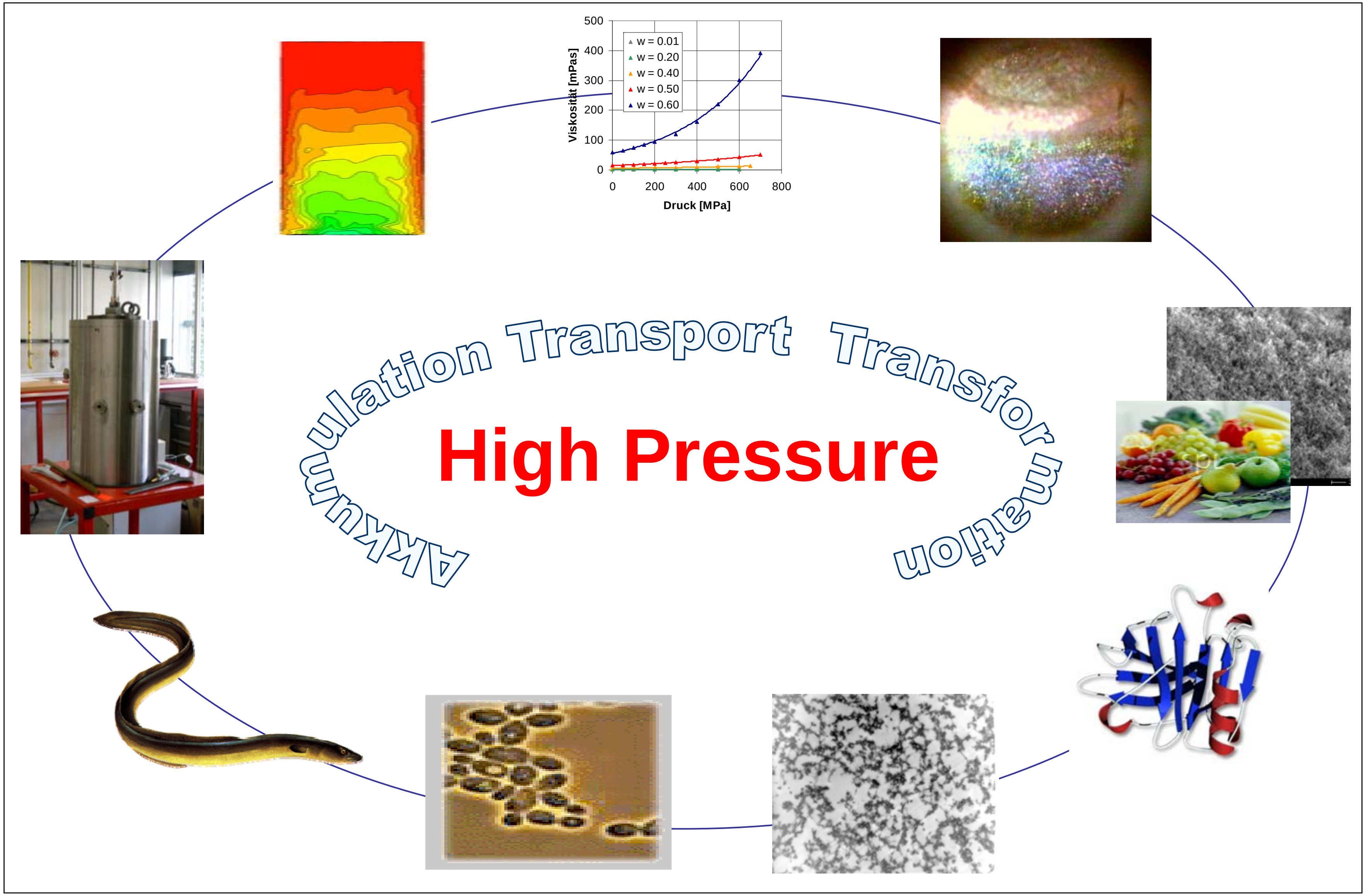

Apparatus Design
Technical Chemistry
Matter
Biotechnology
Chemical Engineering
Food Technology
Marine Biology
Environment Technology
Medicine
Pharmacy
HD-Processes



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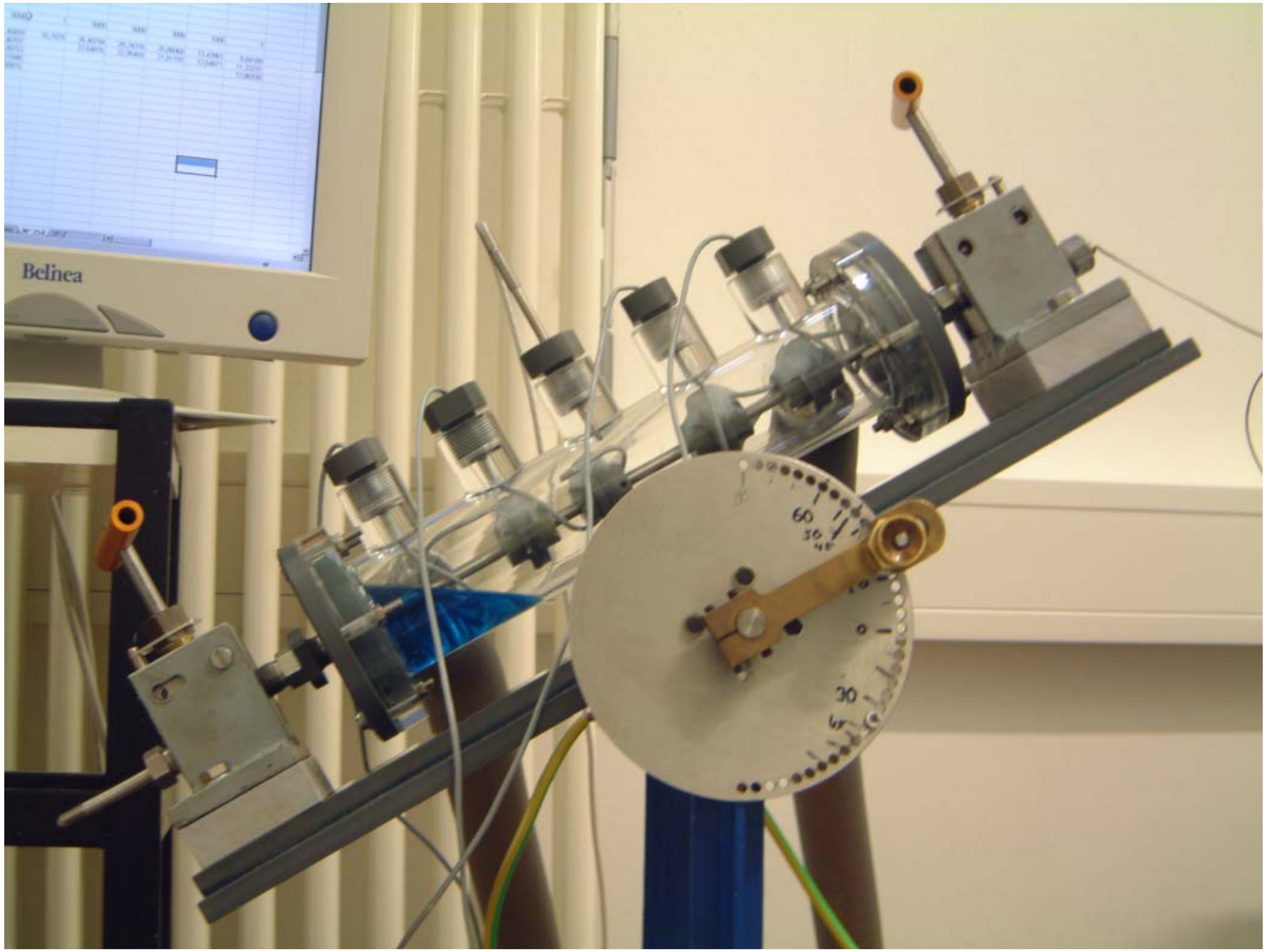
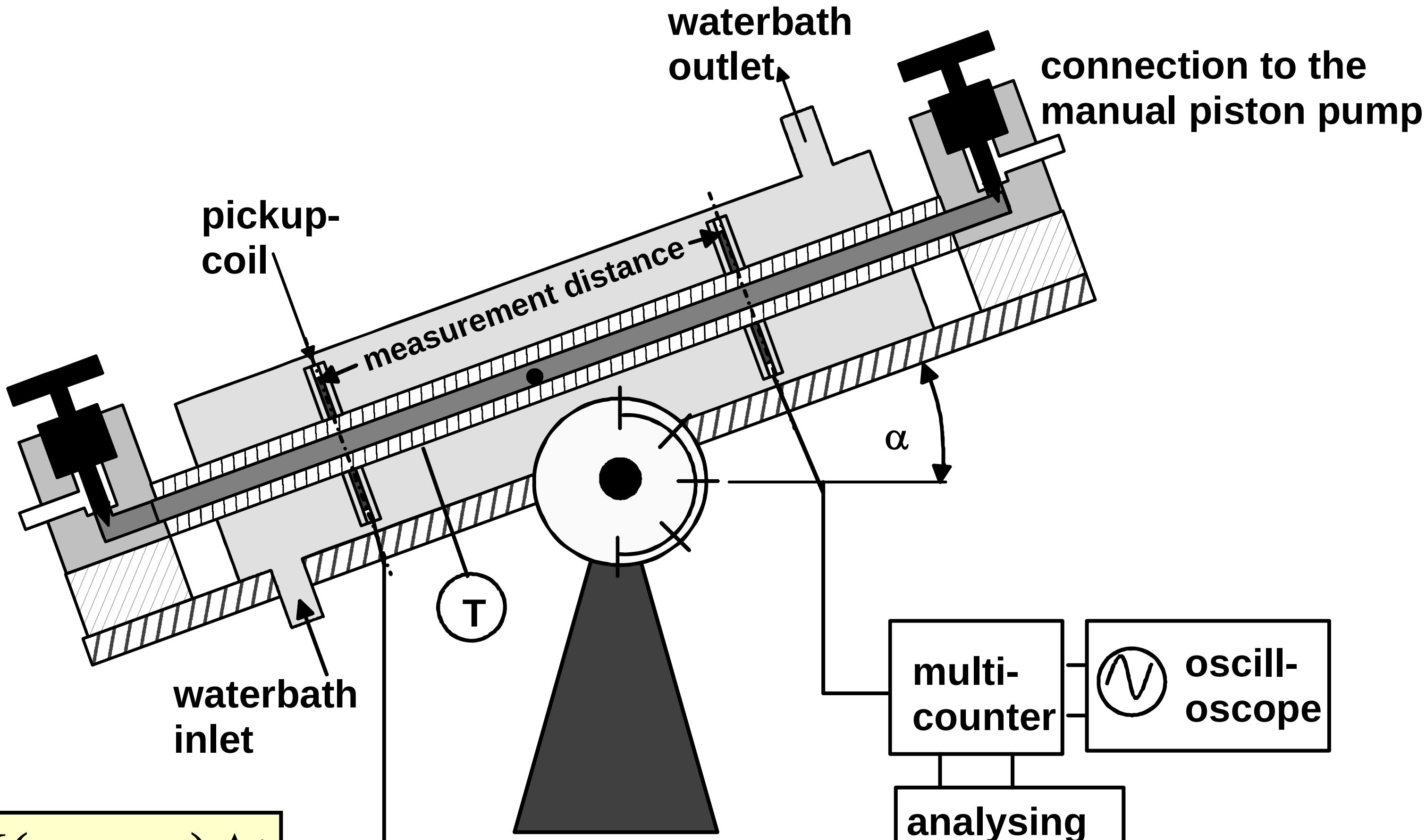
Höppler Viscosimeter



Höppler Viscosimeter



$$\eta = K(\rho_K - \rho)\,\Delta t$$

Först et al. (2000)

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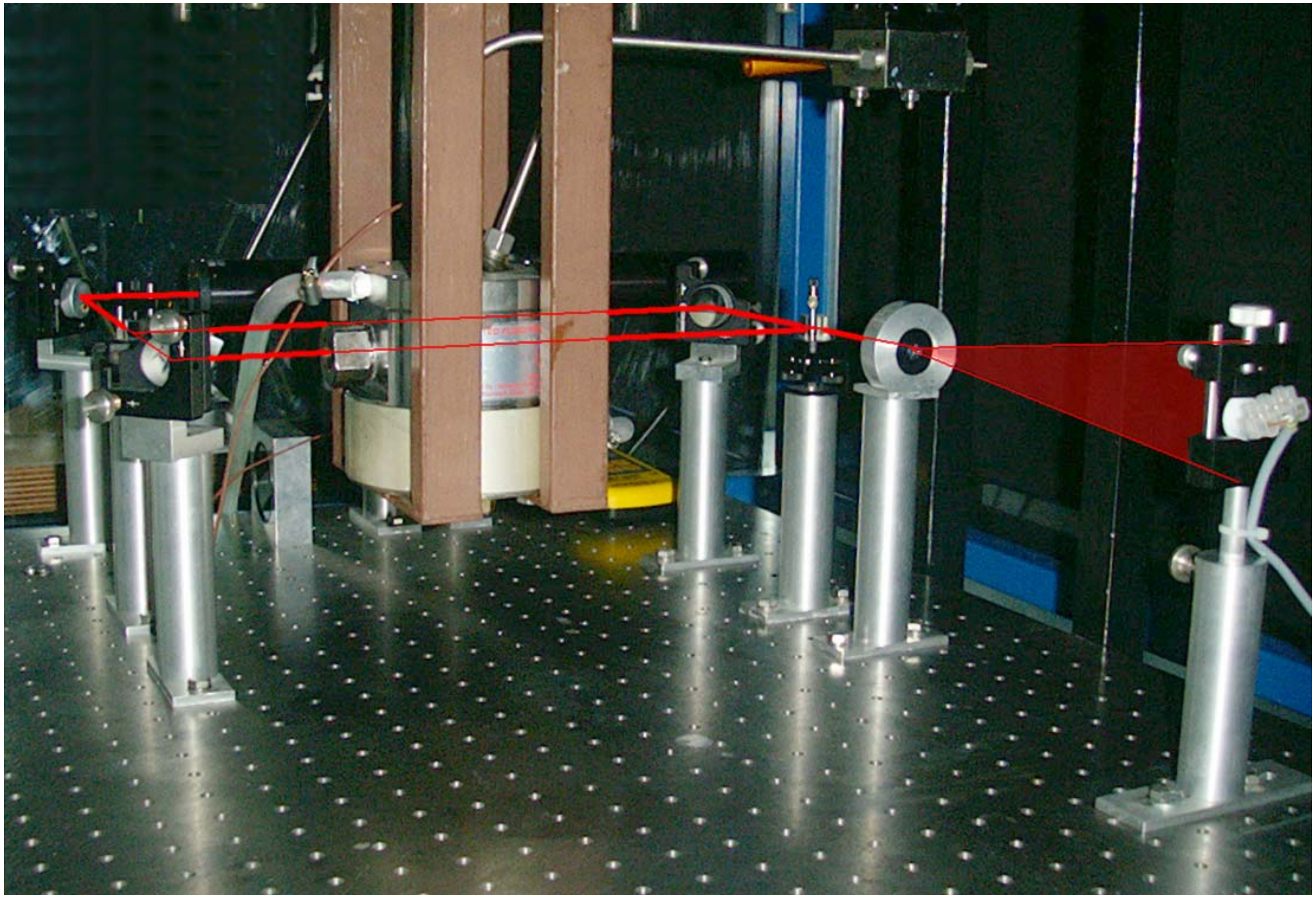
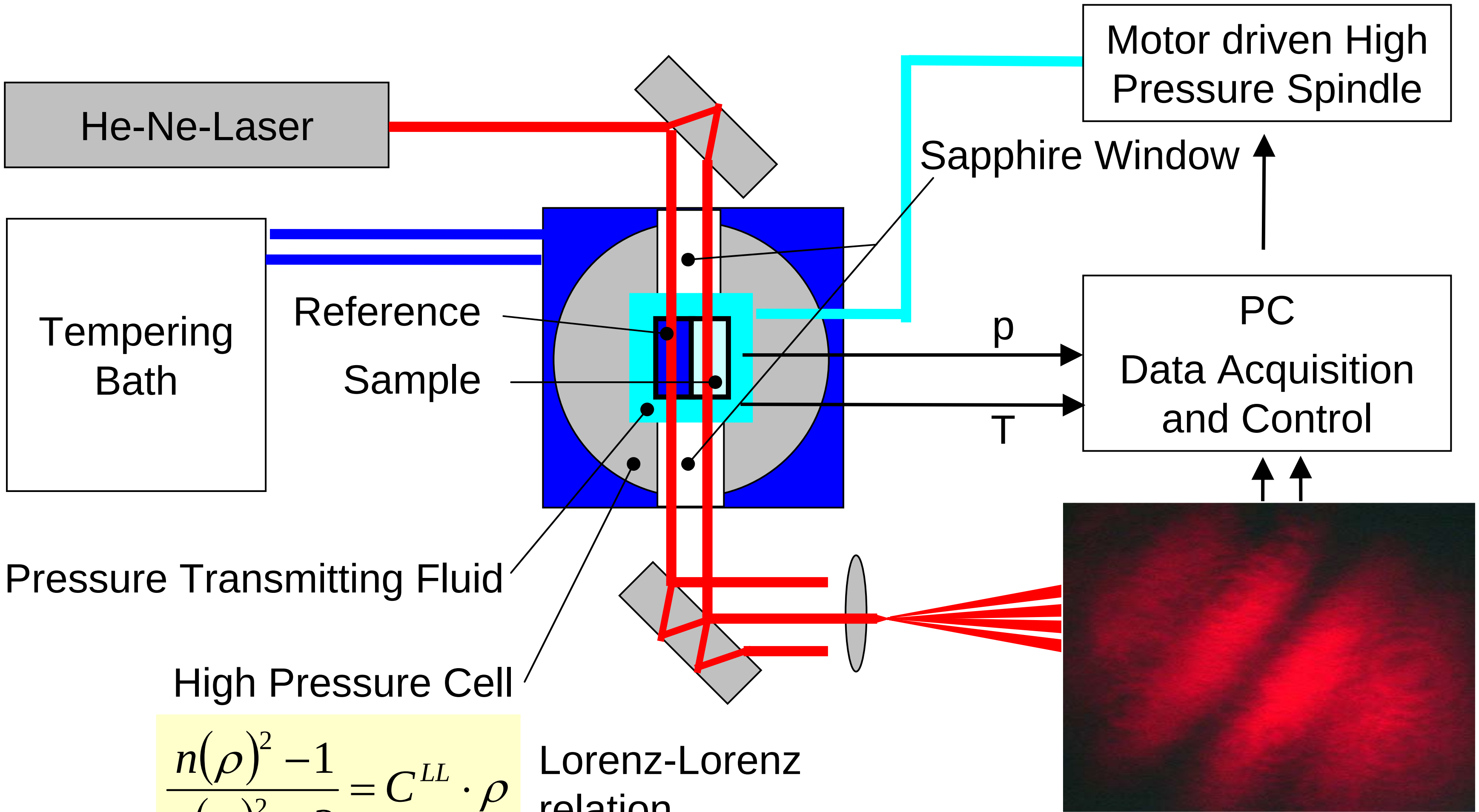
Jamin Interferometer



Eder et al. (2004)

Jamin Interferometer



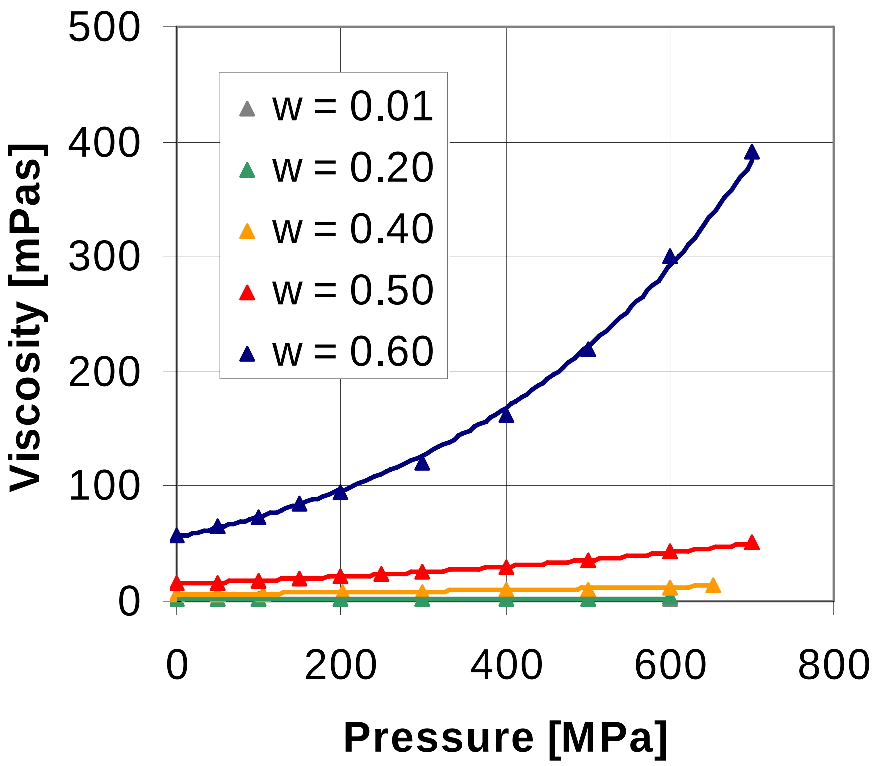
$$\frac{n(\rho)^2 - 1}{n(\rho)^2 + 2} = C^{LL} \cdot \rho$$

Lorenz-Lorenz relation

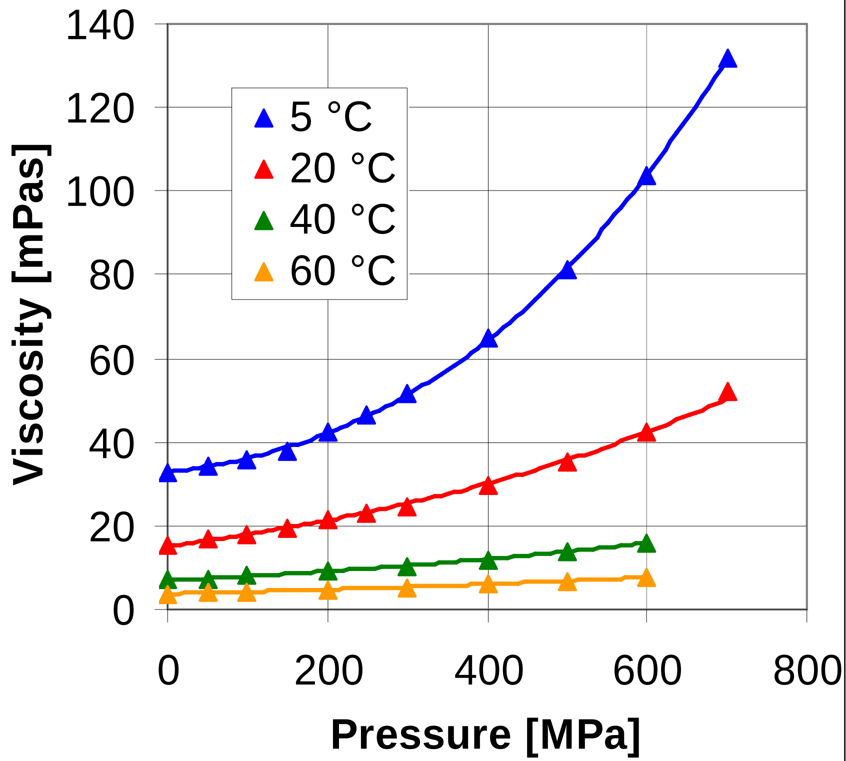
Eder et al. (2004)

Viscosity of Aqueous Sucrose Solution

T = 20 °C



w = 0.5



Förster et al.

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Viscosity of Aqueous Sucrose Solution

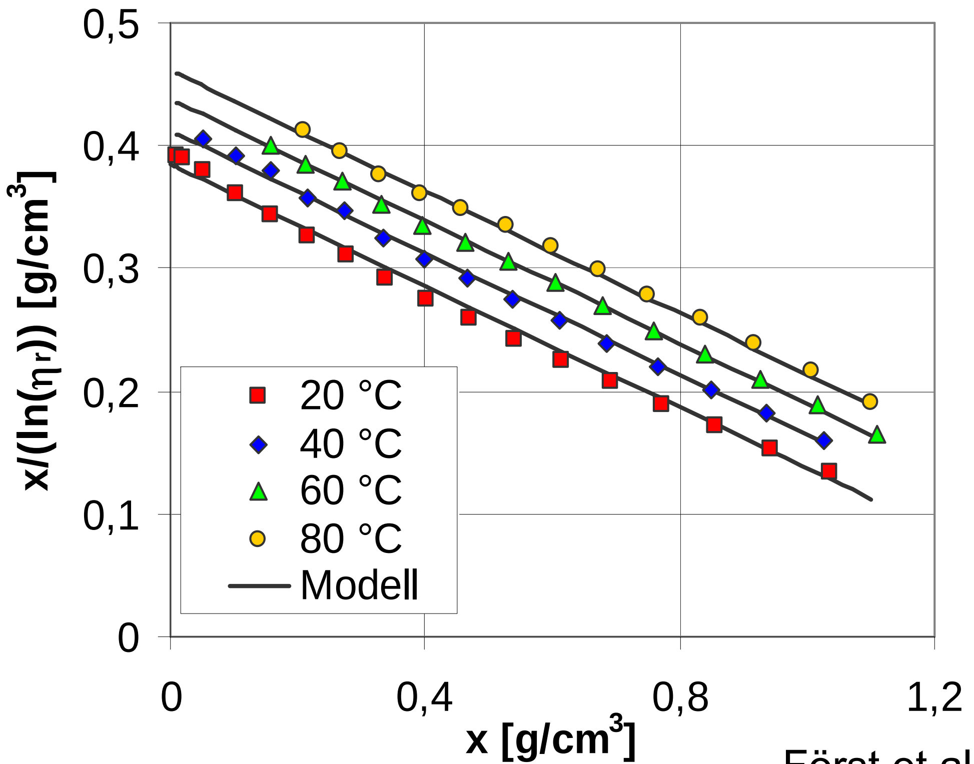
Sucrose Solution – Microscopic Suspension of Rigid Particles (Vand, 1947)

$$\frac{x}{\ln(\eta_r)} = q_0 + q_1 x + ...$$

$$\eta_r = \frac{\eta(T, p_0)}{\eta_L(T, p_0)}$$

$$x = \rho \cdot w \quad ; \quad q_0 = \frac{\rho_S}{h_0 k_1}$$

$$q_1 = \frac{3(h_0 - 1)}{h_0 k_1 (h_0 + 2)} - \frac{r_2 (k_2 - k_1)}{k_1^2} - \frac{Q}{k_1}$$



Förster et al.

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Viscosity of Aqueous Sucrose Solution

Extension of Vands Model

$$\frac{x}{\ln(\eta_r)} = q_0 + q_1 x + ...$$

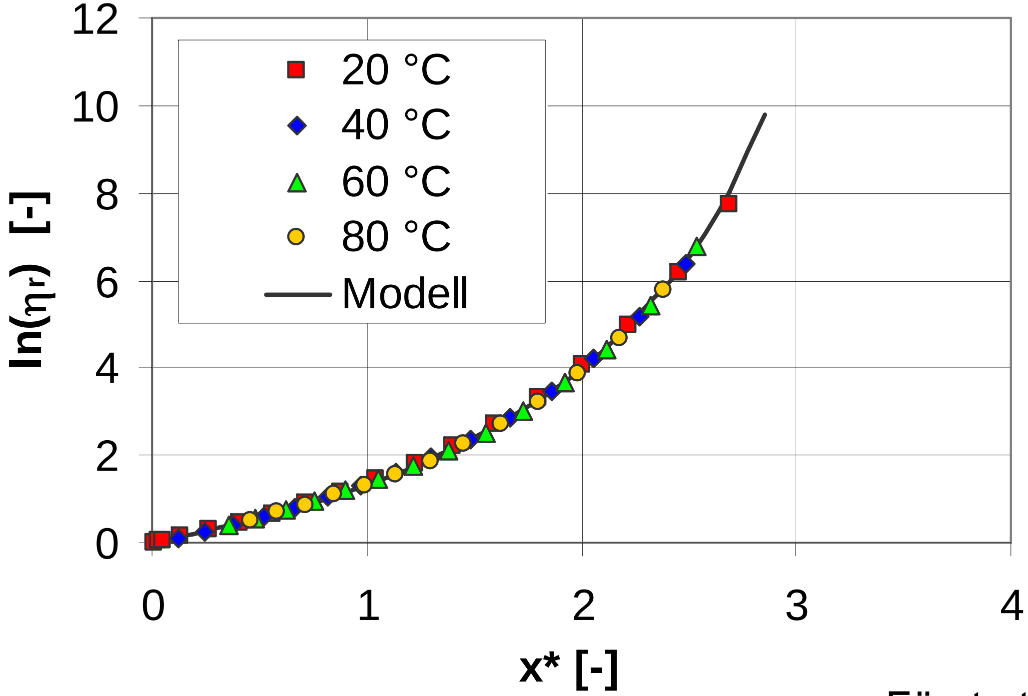
Relation of Arrhenius

$$q_0 = q_\infty e^{-\frac{E}{RT}}$$

Coordinate Transformation

$$x^* = \frac{x}{q_\infty e^{-\frac{E}{RT}}}$$

$$\ln \eta_r = \frac{x^*}{1 + q_1 x^*}$$



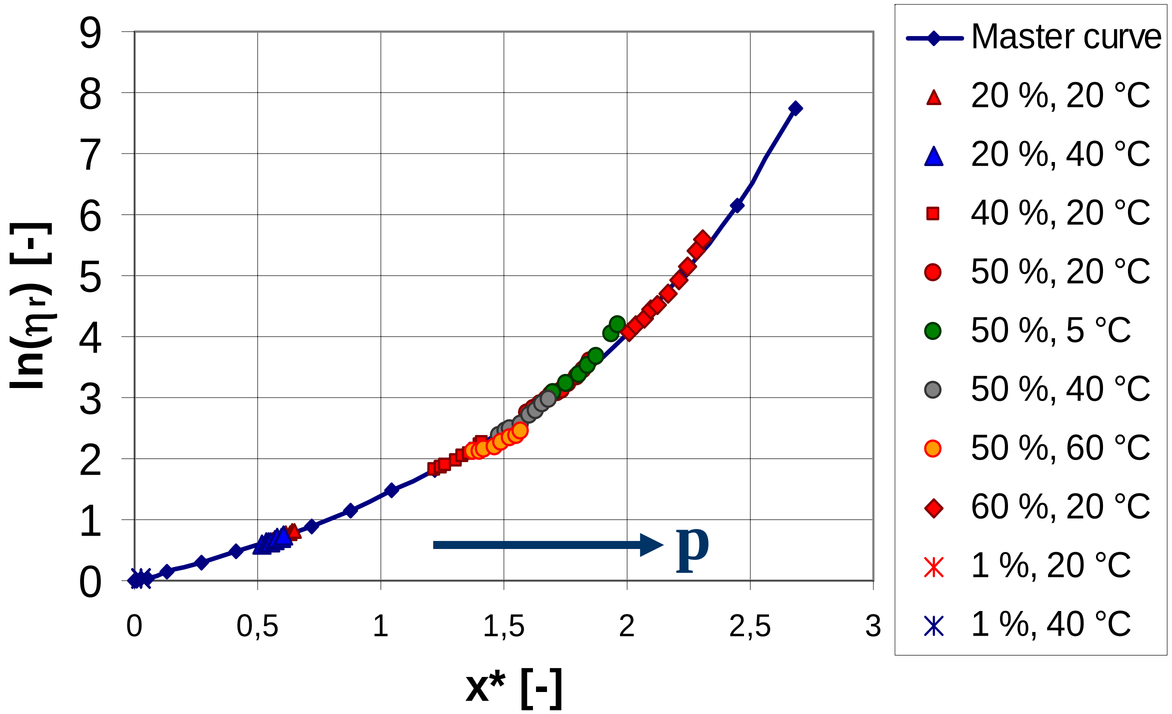
Först et al.

Viscosity of Aqueous Sucrose Solution

Extension of Vands Model

$$\ln \eta_r = \frac{x^*}{1 + q_1 x^*}$$

$$\eta_r = \frac{\eta(T,p)}{\eta_L(T,p)}$$



Först et al.

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Viscosity of Aqueous ß-Lg Solution

Production of the solution

β-LG (Sigma-Aldrich, purity 80 %)

solvent: water

mass fraction w = 0.01…0.06

↓

agitation at 40 °C for 30 min

↓

storing at 4 °C for 12 h

Experimental procedure

filling

↓

pressure/temperature setting
(0.1; 50; 100; 140; 180; 220; 260; 300; 400; 500; 600; 0.1 MPa, 20 °C)

↓

measurement ca. every 2 min

↓

Change of pressure after equilibrium and measurement of n > 10 values

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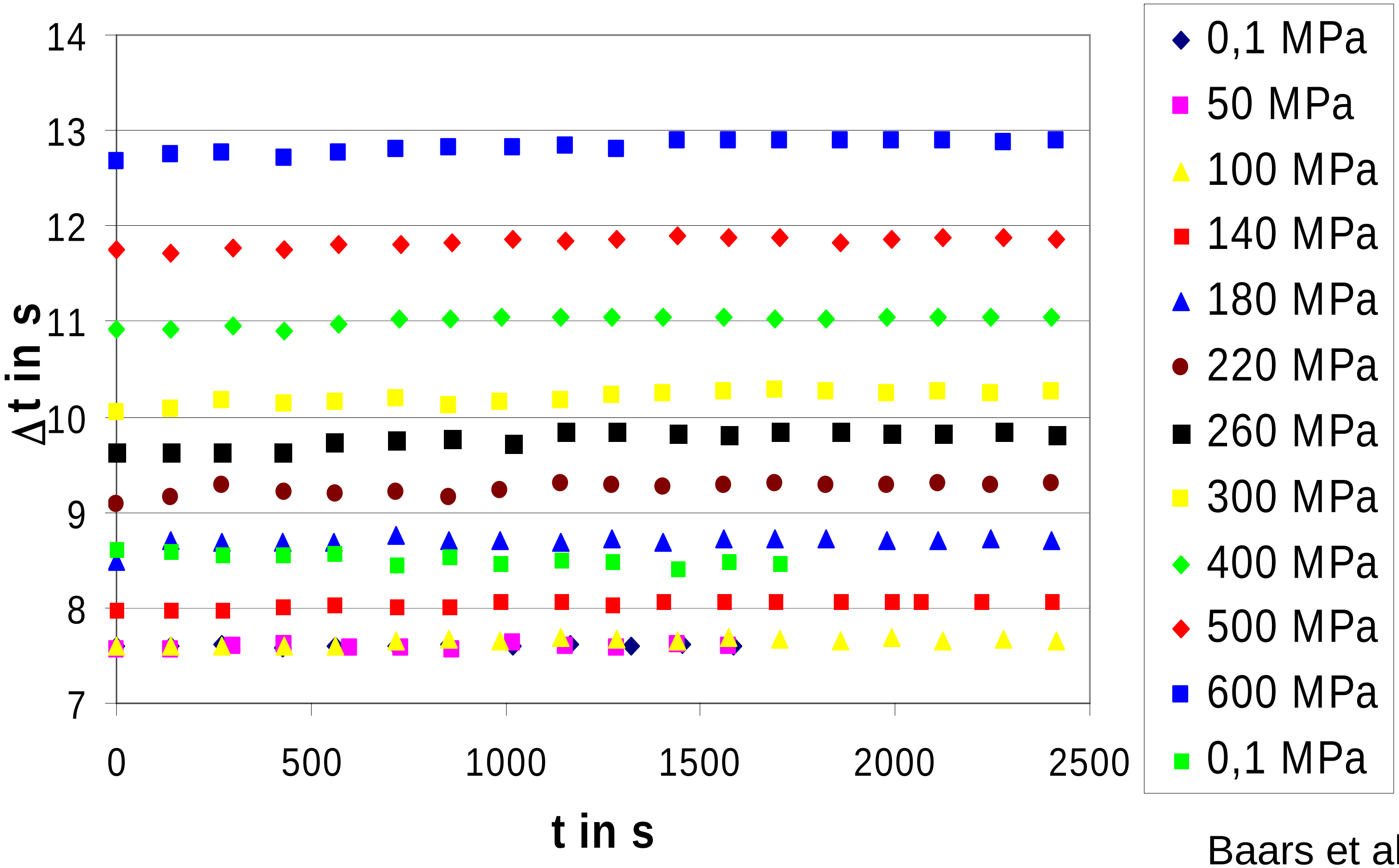
Viscosity of Aqueous ß-Lg Solution

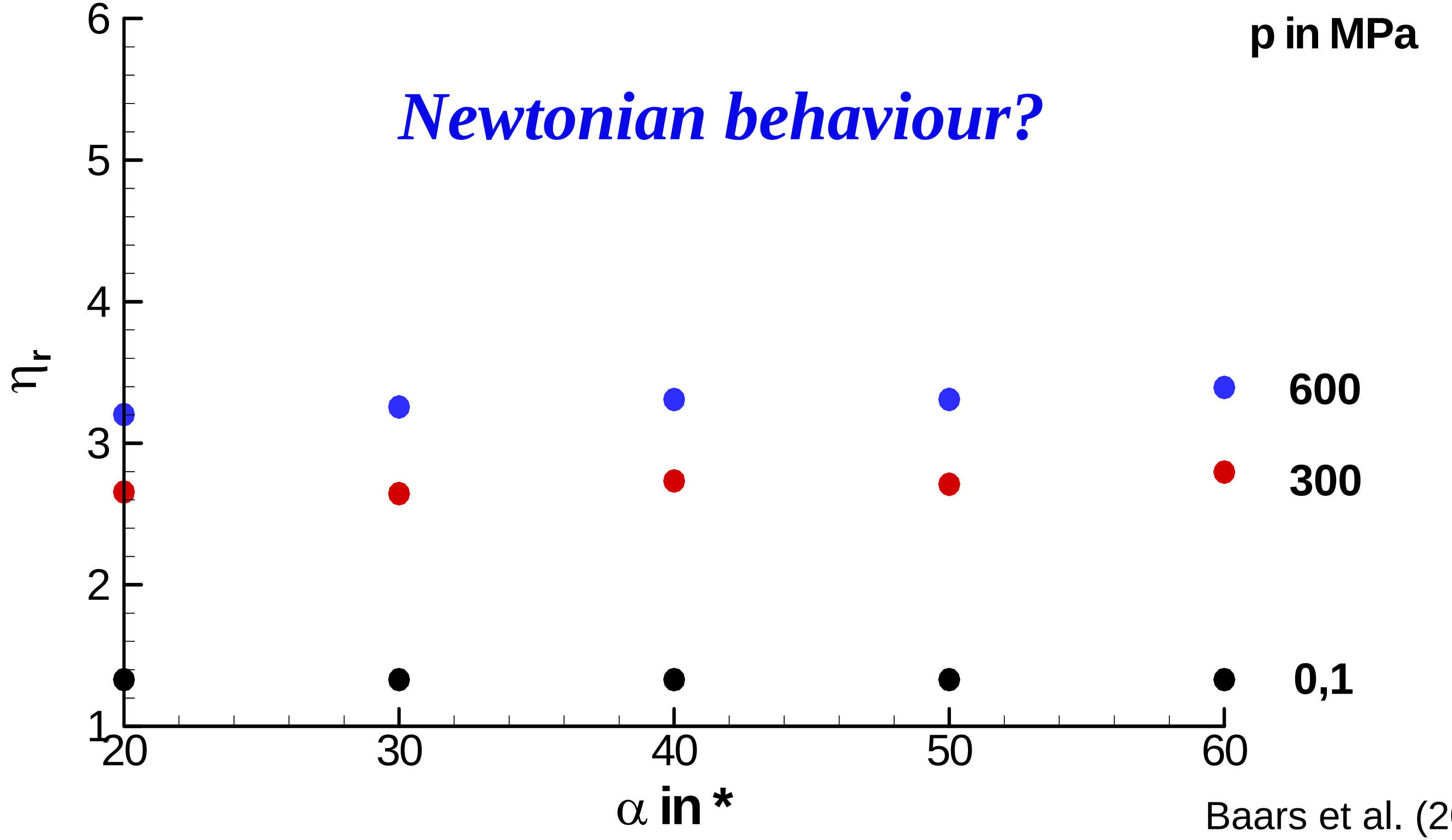
Measured time differences Δt (w = 0.04)



Baars et al. (2006)

Viscosity of Aqueous ß-Lg Solution

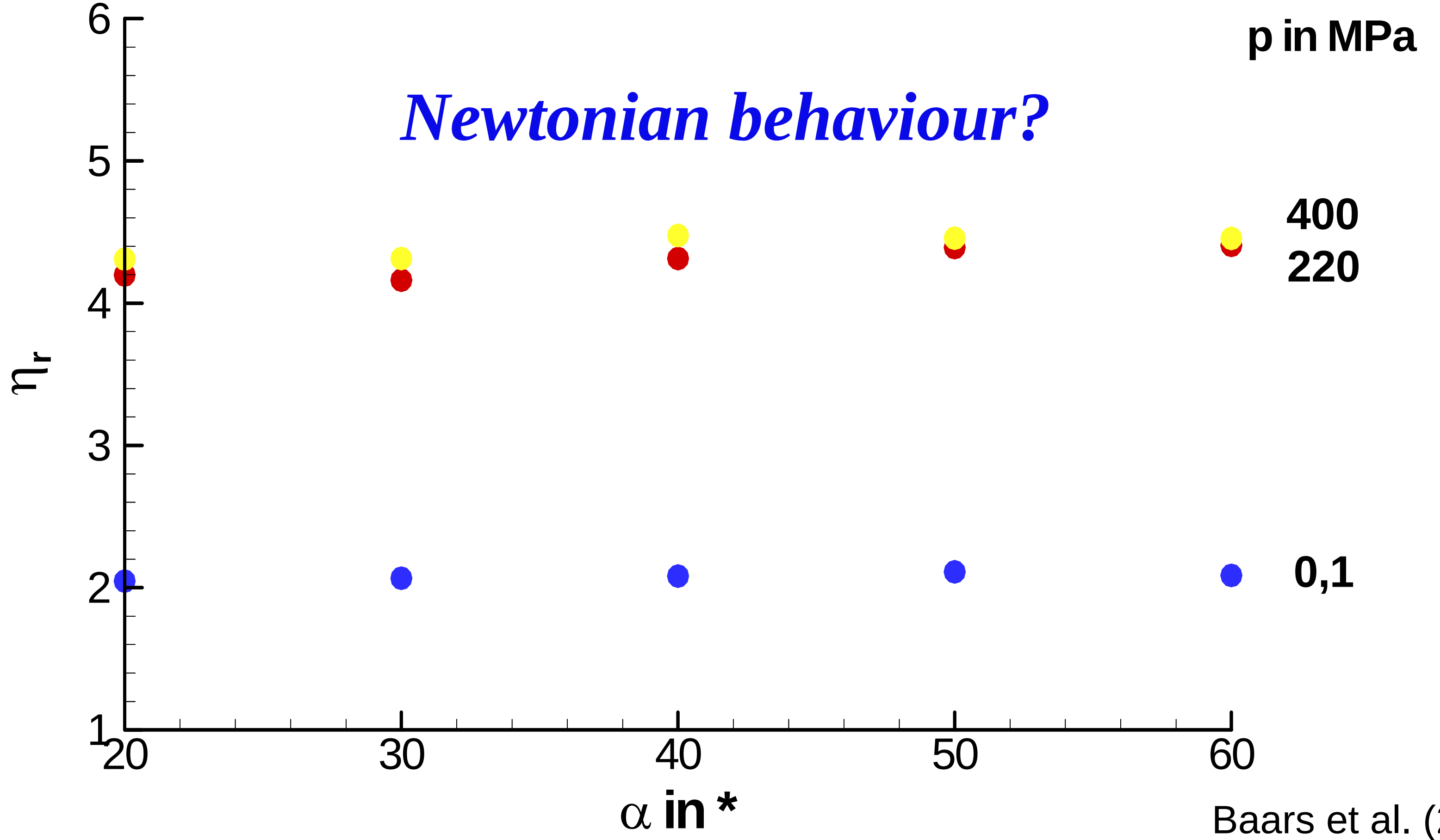
β-LG solution *w* = 0.06 (without pre-treatment)



Baars et al. (2006)

Viscosity of Aqueous ß-Lg Solution

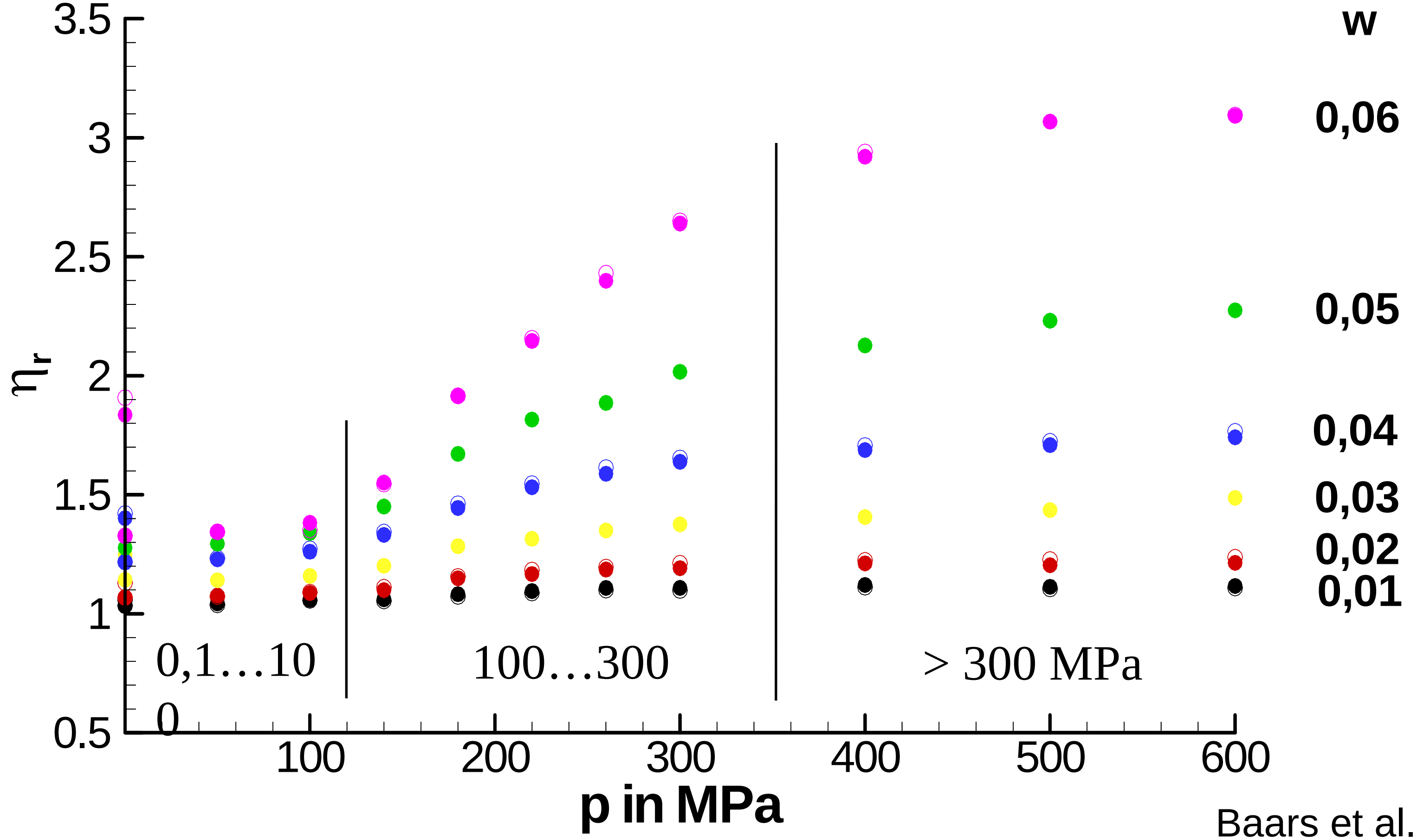
β-LG solution *w* = 0,06 (with pre-treatment at 600 MPa)



Baars et al. (2006)

Viscosity of Aqueous ß-Lg Solution

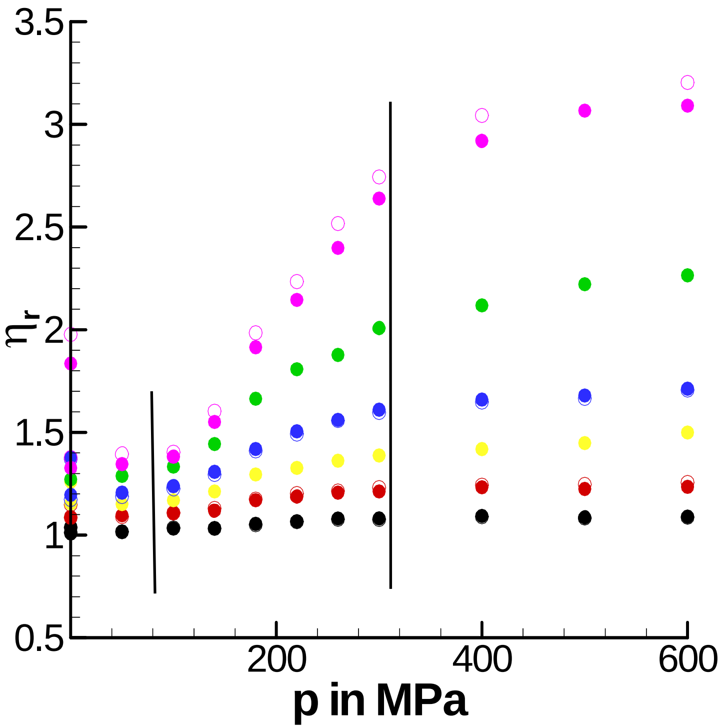
Relative viscosity η_r



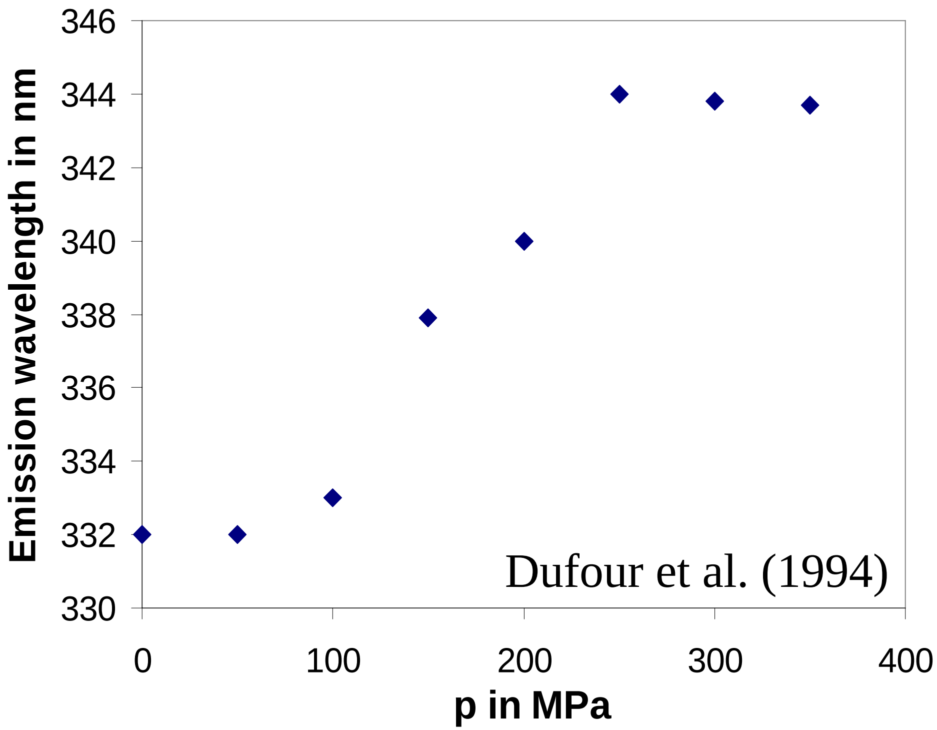
Baars et al. (2006)

Viscosity of Aqueous ß-Lg Solution

Relative viscosity η_r



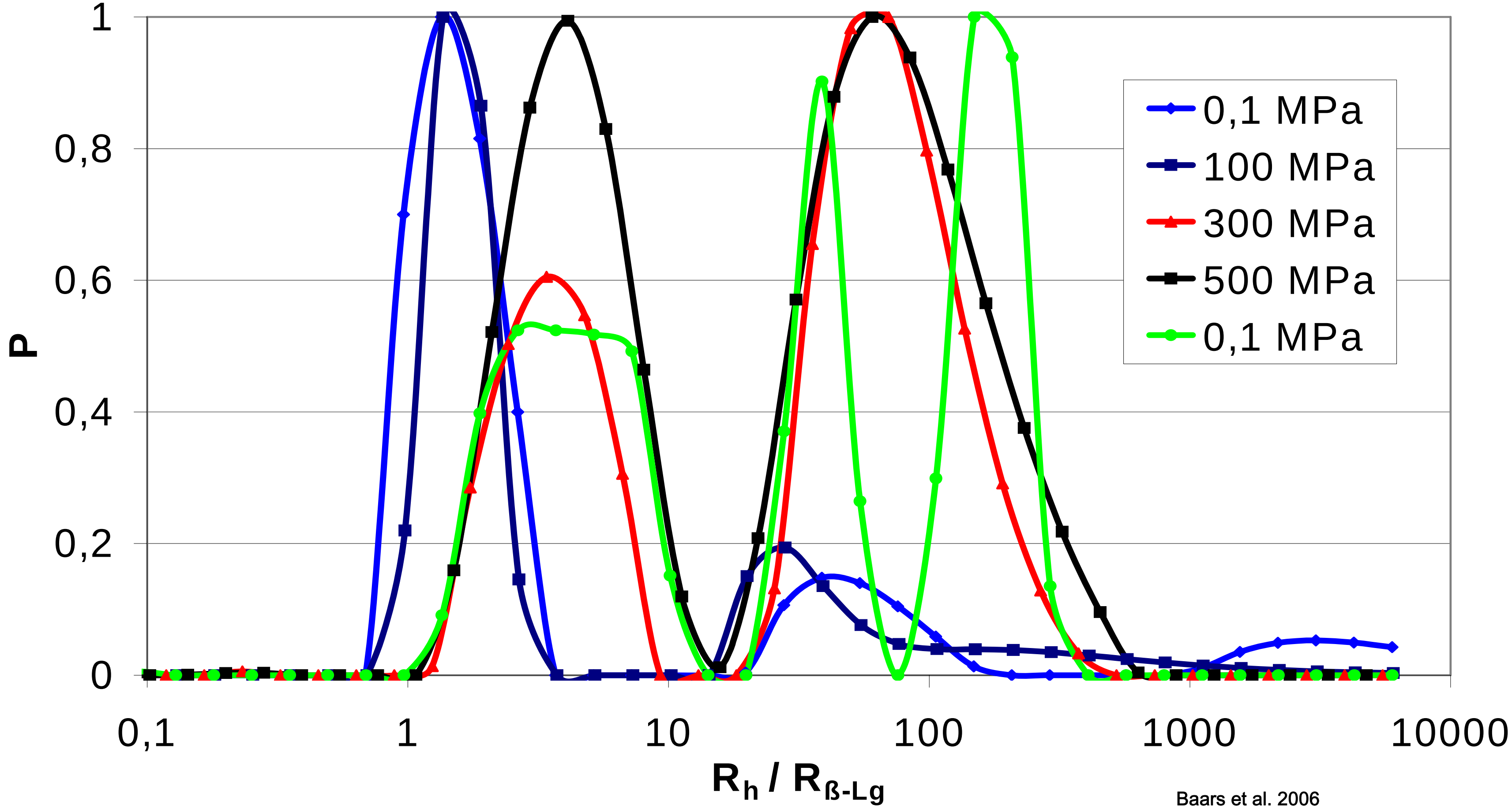
Fluorescence spectroscopy



Baars et al. (2006)

Dynamic / Static Light Scattering

Unweighted distribution of hydrodynamic radius (w = 0.02; 20 °C)



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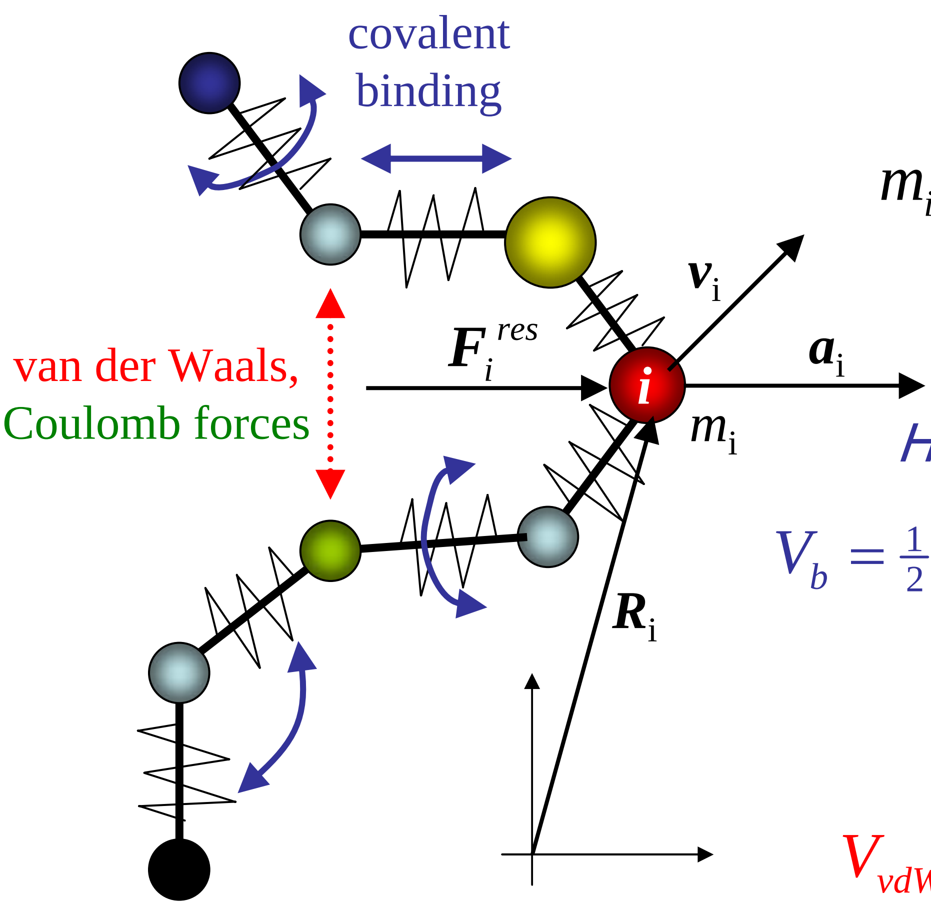
Molecular dynamic simulation - CHARMM



Newton's second law

$$m_i \frac{d^2 \boldsymbol{R}_i}{d t^2} = \boldsymbol{F}_i^{res} = -\frac{d}{d \boldsymbol{R}_i} \sum_k V_i^k$$

Potentials

Hooke

$$V_b = \tfrac{1}{2} k_b (b - b_0)^2$$

Coulomb

$$V_{el} = \sum_{i,j} \frac{q_i q_j}{4\pi\varepsilon_0 \varepsilon_{eff} r_{ij}}$$

Lennard-Jones

$$V_{vdW} = \sum_{i,j} 4\varepsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right]$$

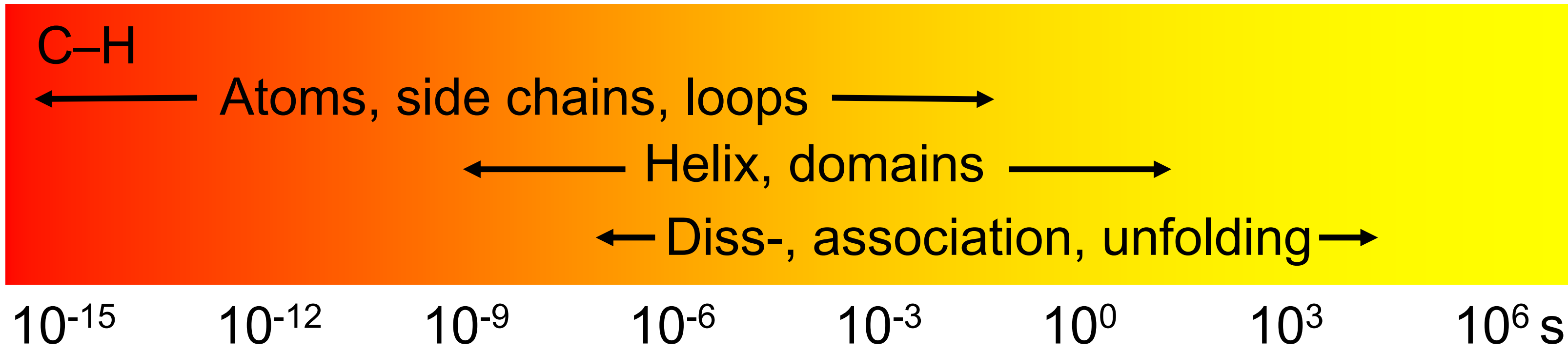
Molecular dynamic simulation

Numerical procedure

- Leap Frog - Algorithm

$$\boldsymbol{a}_i(t) = \frac{\boldsymbol{F}_i^{res}}{m_i} \quad \rightarrow \quad \begin{aligned} \boldsymbol{v}_i(t+0.5\Delta t) &= \boldsymbol{v}_i(t-0.5\Delta t) + \boldsymbol{a}_i(t)\Delta t \\ \boldsymbol{r}_i(t+\Delta t) &= \boldsymbol{r}_i(t) + \boldsymbol{v}_i(t+0.5\Delta t)\Delta t \end{aligned}$$

- Time step (Δt)



$$\Delta t = \Delta t_{\min}/10 \quad \rightarrow \quad \Delta t_{C-H} = 1\,\text{fs}$$

SHAKE-BONH-Algorithm $\rightarrow \quad \Delta t_{C-H} = 2\,\text{fs}$

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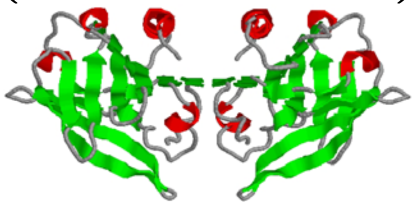
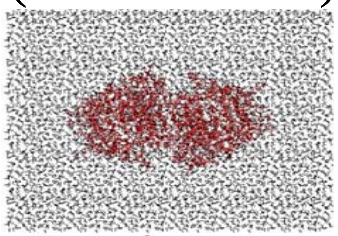
Procedure

Dimer ß-Lactoglobulin B
(RCSB Data Bank)



Solution in water box
(120x90x90 Å)



P = 0.1 MPa, T = 298 K, pH 7
Equilibration (1 ns)
Energy minimization

Start

P = 0.1 MPa, T = 298 K

P = P + 50 MPa (2 ps)

Equilibration (40 ps)
Energy minimization

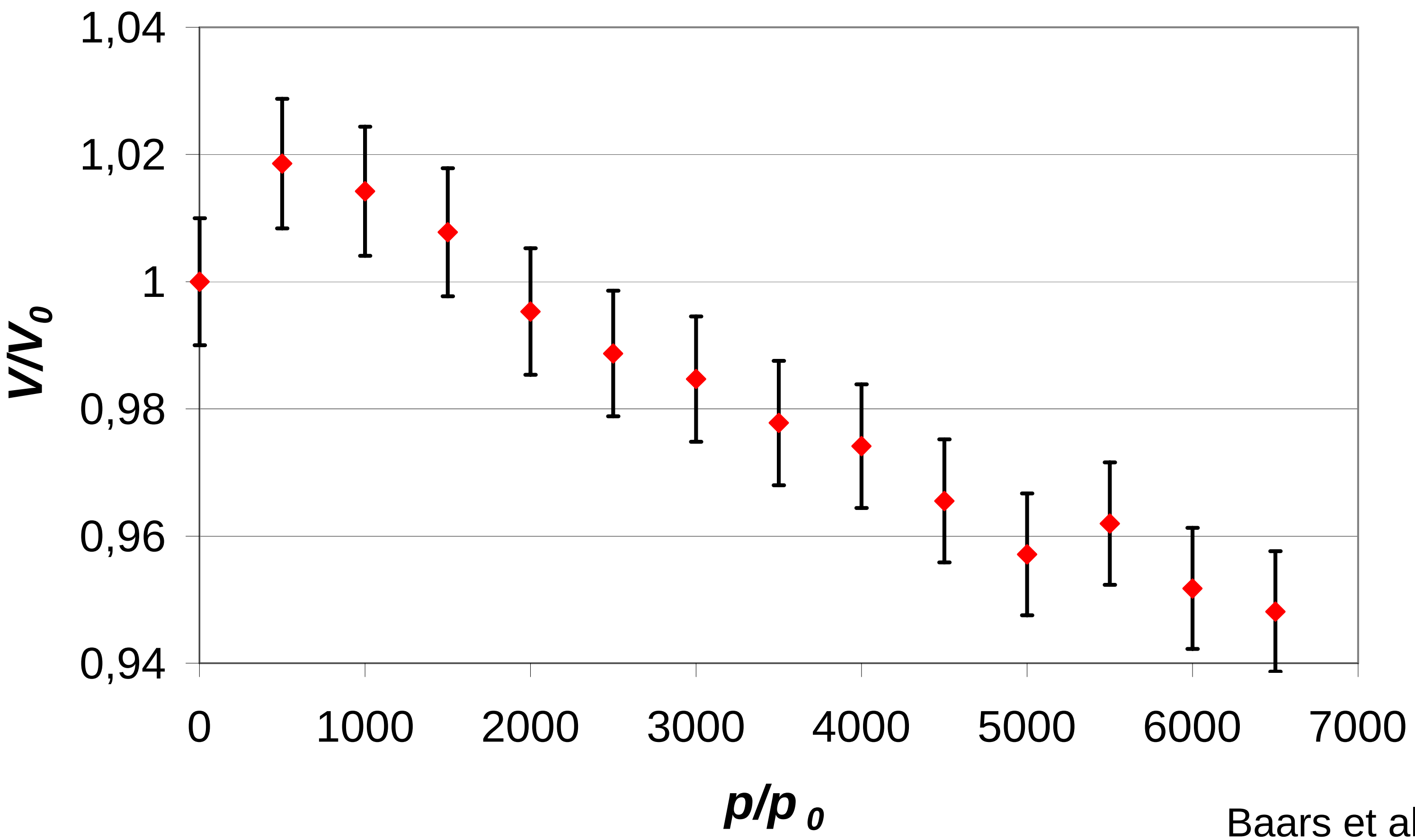
Storage of structure

P > 650 MPa

End

Results

Intrinsic volume (Voronoi)



Baars et al. (2006)

Results

Isothermal Compressibility (in GPa^{-1})

	Own results		*Literature*
Total protein	0.110	+/- 0.040	0.14[a,b]
α-helices	0.087	+/- 0.019	
ß-Strands	0.115	+/- 0.019	
Loops	0.118	+/- 0.019	
Cavities	0.500	+/- 0.140	0.35-0.69[b]
Core (-400 MPa)	0.126	+/- 0.030	
Core (450-650 MPa)	0.017	+/- 0.060	

[a] Kharakoz et al. 1993

[b] Mori et al. 2006

Baars et al. (2006)

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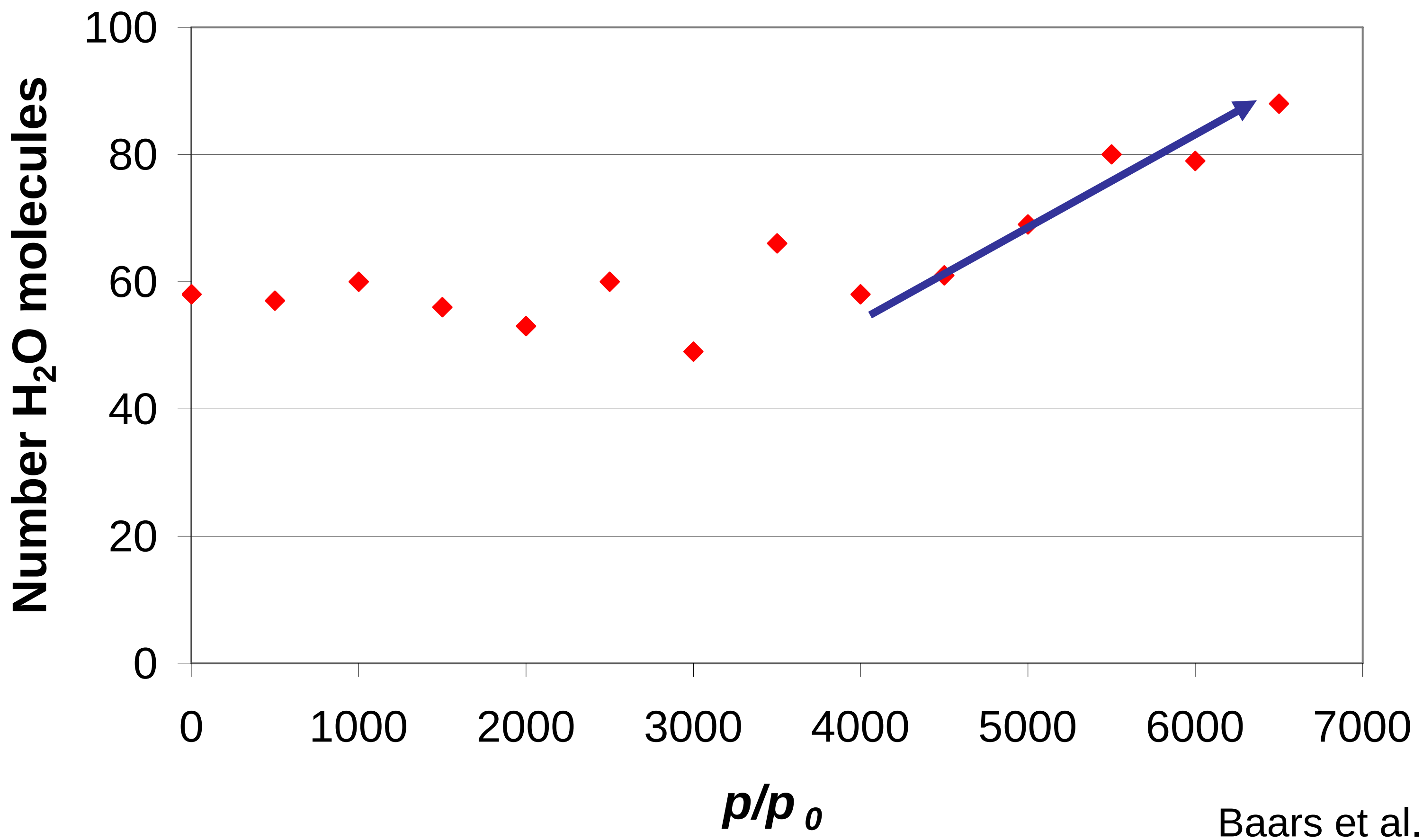
Results

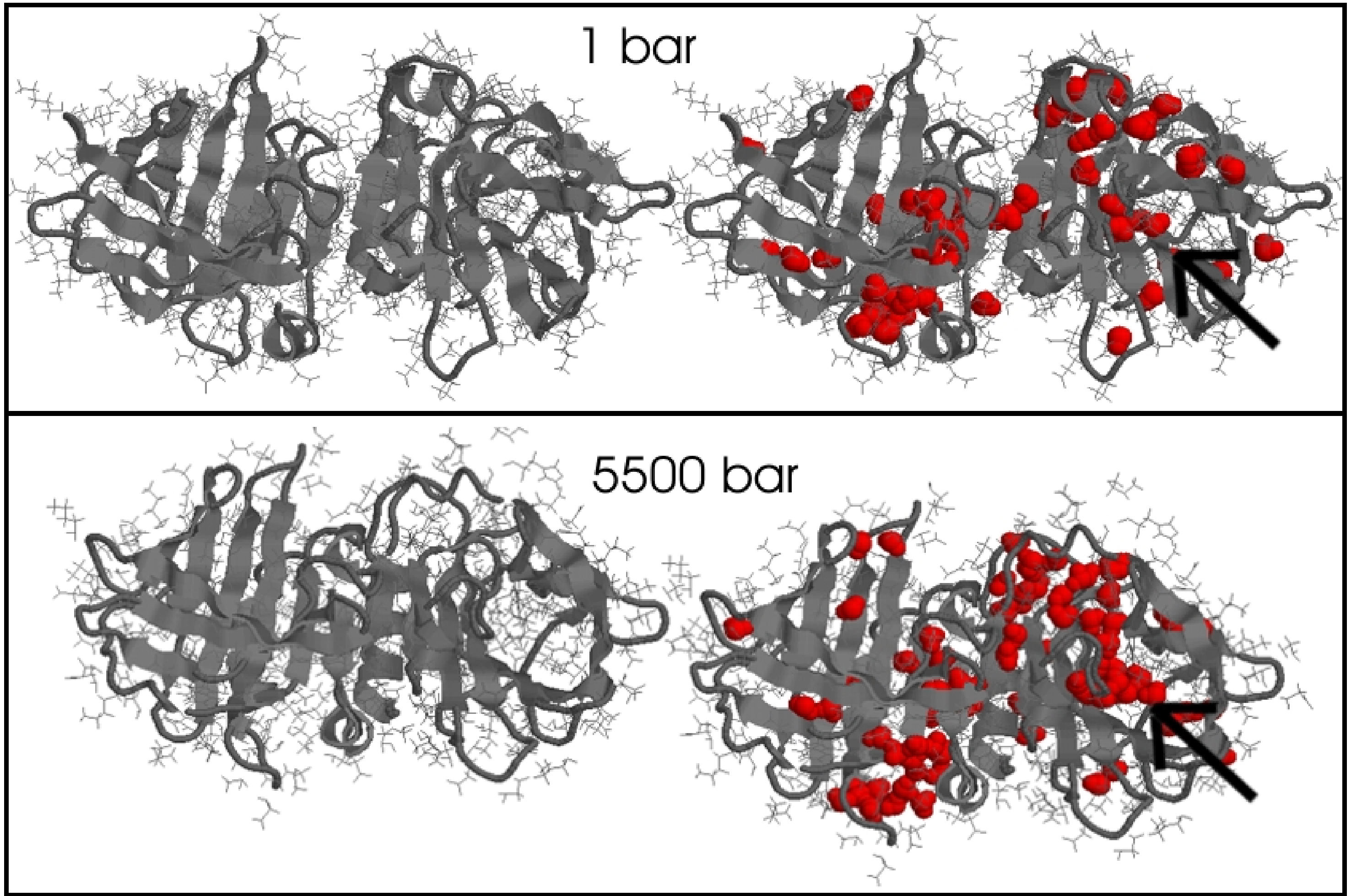
Number of H_2O molecules in the protein



Baars et al. (2006)

Results

Number of H_2O molecules in the protein



Baars et al. (2006)

Results

Change of conformation / relative movement of monomers (650 MPa)

Baars et al. (2006)

Thank You for Attention!

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