

Max-Planck-Institut
für Mathematik
in den Naturwissenschaften
Leipzig

On conformational behavior of solvophobic
polymer at high pressures

by

*Nikolaj Georgi, Yuriy Budkov, Gennady Chuev, Ivan Vyalov,
Michael Kiselev, and Andrey Kolesnikov*

Preprint no.: 49

2014



On conformational behavior of solvophobic polymer at high pressures

Yu. A. Budkov* and M. G. Kiselev

Institute of Solution Chemistry of the Russian Academy of Sciences, Ivanovo, Russia

I. I. Vyalov† and N. Georgi

Max Planck Institute for Mathematics in the Sciences, Leipzig, Germany

A. L. Kolesnikov

Ivanovo State University, Ivanovo, Russia and

Institut für Nichtklassische Chemie e.V., Universität Leipzig, Leipzig, Germany

G. N. Chuev

Max Planck Institute for the Physics of Complex Systems, Dresden, Germany and

Institute of Theoretical and Experimental Biophysics,

Russian Academy of Science, Pushchino, Moscow Region, Russia

We investigate the conformational changes of the polymer induced by a change of the strength of polymer solvophobicity and the co-solvent pressure in the bulk solution. We describe the polymer in solution by the Edwards model, where the partition function of the polymer chain with a fixed radius of gyration is described in a field-theoretical manner within random phase approximation. The polymer-co-solvent and the co-solvent-co-solvent interactions are treated in the framework of the mean-field approximation. We obtain the total Helmholtz free energy of the solution as a function of radius of gyration and the average co-solvent concentration within gyration volume. We obtain a system of coupled equations with respect to the radius of gyration of the polymer chain and the co-solvent concentration within the gyration volume. Varying the polymer solvophobic strength at high co-solvent pressure in the bulk we show that the coil-globule transition occurs accompanied by local co-solvent evaporation within gyration volume. On the other hand, varying the co-solvent pressure in the bulk we show that globule-rod transition of polymer chain can take place accompanied by co-solvent wetting transition within gyration volume.

PACS numbers: 64.75.Yz, 82.60.-s, 61.25.-f, 61.25.he

I. INTRODUCTION

Hydrophobic (solvophobic) effects manifest itself in various ways depending on whether the solutes are small molecular units or large clusters, or a combination of both [1]. Hydrophobic effects give rise to self-assembly in different physico-chemical systems like micelle formation, proteins folding, macro- and microphase separations in polymer solutions to name a few. Besides the size of the solutes the composition of the solvent (e.g. the presence of a co-solvent) and the thermodynamic state of the solvent can lead to attraction or repulsion of the solutes and give rise to additional phenomena. Pressure induced protein denaturation [3, 4] is a subject of long standing interest [5, 7, 8] since the pressure induced conformation change seemingly contradicts the accepted mechanism of formation of a hydrophobic core which results from a volume decrease of the protein upon collapse into the native conformation [15]. Several possible mechanisms were proposed for the denaturation mechanism [5, 9, 13, 14]. The pressure induced change of hydrophobicity has also

been investigated for smaller hydrophobic solutes [10, 12] like methane [11] and short hydrophobic chain molecules [6, 8] were considered.

In 2002 ten Wolde and David Chandler proposed a very elegant idea [2] stating that if a hydrophobic polymer chain is immersed in an aqueous medium, then in a neighborhood of the polymer surface dewetting can take place and as consequence a coil-globule transition of the macromolecule occurs. The authors speculated, based on the results of their computer simulations, that this effect is reminiscent of a first-order phase transition. It should be noted that this statement amounts to proposing a fundamentally new mechanism of the polymer collapse, which is distinct from the standard mechanism adopted in statistical mechanics of macromolecules. As is well known from the polymer statistical mechanics, when the solvent becomes poorer, the polymer coil shrinks leading eventually to a collapse of the polymer coil [16]. However, the theoretical models predominantly describe the solvent only implicitly [17–23, 26, 28–30], i.e. its influence on the macromolecule is taken into account through effective monomer-monomer interaction. Such an approach simplifies the model, however the details of the solvent behaviour - in particular the liquid-gas transition - are not taken into account. Therefore an explicit account of the solvent quality depending on the pressure of the bulk

*urabudkov@rambler.ru

†vyalovivan@yandex.ru

solution is needed to investigate the proposed mechanism of the polymer collapse.

In the present work such a self-consistent field model is developed. The study presented here is based on the formalism which has been developed in our previous work [37]. In contrast to our previous investigation where the co-solvent was treated as an ideal gas in the bulk solvent - an approximation valid only at low co-solvent concentration in the bulk - in the present work we lift this restriction by describing the low-molecular weight co-solvent via a Van-der-Waals equation of state. This allows to consider co-solvent regimes at high pressure and study the the solvophobic polymer chain in a wide range of densities and temperatures. As the solvophobic strength of the polymer chain increases the well-known collapse to a globular state occurs. However, if the osmotic pressure of the low-molecular weight co-solvent (at fixed solvophobic strength) in the bulk solution exceeds a threshold value, the polymer globule expands to a rod-like configuration in a regime of a first-order phase transition.

The paper organized as follows. In Sec. II, we present our theoretical formalism and in Sec. III the limiting regimes analysis is given. In section IV numerical results and their discussion are present. In Sec. V we summarize our findings.

II. THEORY

The polymer chain molecule and the low-molecular weight co-solvent at a specified concentration are immersed in a solvent described by a continuous, structureless medium, which is considered being a good solvent for the polymer. As already mentioned in the introductory section, in contrast to our previous investigation [37] (co-solvent in the bulk is ideal gas) we consider the co-solvent to obey the Van-der-Waals equation of state.

The thermodynamic state of the co-solvent can therefore be varied in wide range of temperatures and number densities as opposed to the previous case that was only valid for low co-solvent concentrations in the bulk. Moreover, we will describe the interaction polymer-co-solvent as purely repulsive. In other words, we assume that the polymer chain is solvophobic with respect to the co-solvent. As in the previous investigation, our aim is to study the dependence of the polymer chain conformation as a function of the co-solvent concentration and the strength of interaction between co-solvent and the monomers. We will describe the polymer in the framework of the Edwards model [17, 18].

We start from the canonical partition function of the solution which can be written as follows

$$Z(R_g) = \int d\Gamma_p(R_g) \int d\Gamma_c \exp[-\beta H_p - \beta H_c - \beta H_{pc}], \quad (1)$$

where the symbol $\int d\Gamma(R_g)(..)$ denotes the integration over microstates of polymer chain performed at a fixed radius of gyration R_g ; the symbol $\int d\Gamma_c(..) =$

$\frac{1}{N_c!} \int d\mathbf{r}_1.. \int d\mathbf{r}_{N_c}(..)$ denotes the integration over co-solvent molecules coordinates; N_c is a total number of co-solvent molecules;

$$\beta H_p = \frac{w_p}{2} \int_0^N ds_1 \int_0^N ds_2 \delta(\mathbf{r}(s_1) - \mathbf{r}(s_2)) = \frac{w_p}{2} \int d\mathbf{x} \hat{\rho}_p^2(\mathbf{x}) \quad (2)$$

is the Hamiltonian of the monomer-monomer interaction; w_p is a second virial coefficient for the monomer-monomer interaction and $\hat{\rho}_p(\mathbf{x}) = \int_0^N ds \delta(\mathbf{x} - \mathbf{r}(s))$ is the monomer microscopic density; N is degree of polymerization of the polymer chain;

$$\beta H_{pc} = w_{pc} \int_0^N ds \sum_{j=1}^{N_c} \delta(\mathbf{r}(s) - \mathbf{r}_j) = w_{pc} \int d\mathbf{x} \hat{\rho}_p(\mathbf{x}) \hat{\rho}_c(\mathbf{x}) \quad (3)$$

is the Hamiltonian of the polymer-co-solvent interaction; w_{pc} is the second virial coefficient for the polymer-co-solvent interaction and $\hat{\rho}_c(\mathbf{x}) = \sum_{i=1}^{N_c} \delta(\mathbf{x} - \mathbf{r}_i)$ is the microscopic density of co-solvent molecules;

$$H_c = \frac{1}{2} \sum_{j \neq i} V(\mathbf{r}_i - \mathbf{r}_j) = \frac{1}{2} \sum_{j \neq i} (V_{hc}(\mathbf{r}_i - \mathbf{r}_j) + V_{att}(\mathbf{r}_i - \mathbf{r}_j)) \quad (4)$$

is the Hamiltonian of co-solvent-co-solvent interaction;

$$V_{hc}(\mathbf{r}) = \begin{cases} \infty, & |\mathbf{r}| \leq d_c \\ 0, & |\mathbf{r}| > d_c \end{cases} \quad (5)$$

is the hard-core potential (d_c is a co-solvent molecule diameter); $V_{att}(\mathbf{r})$ is the attractive part of the total potential of the co-solvent-co-solvent interaction.

Now let us calculate the conditional partition function of the polymer solution at fixed radius of gyration R_g of the polymer chain. Applying the mean-field approximation (see, Appendix A) we obtain the following expression for the partition function of the solution

$$Z(R_g) = \mathcal{Z}_c(R_g, N_1) Z_p(R_g). \quad (6)$$

where partition function of co-solvent $\mathcal{Z}_c(R_g, N_1)$ has a form

$$\mathcal{Z}_c(R_g, N_1) = \frac{(V_g - N_1 v_c)^{N_1} (V - V_g - (N_c - N_1) v_c)^{N_c - N_1}}{(N_c - N_1)! N_1!} \times \exp \left[-\frac{w_{pc} N N_1}{V_g} + \beta a_c \left(\frac{N_1^2}{V_g} + \frac{(N_c - N_1)^2}{V - V_g} \right) \right], \quad (7)$$

where $V_g = \frac{4\pi R_g^3}{3}$ is a value of gyration volume, a_c is a Van-der-Waals attraction parameter for the co-solvent; v_c is a Van-der-Waals volume of co-solvent molecules.

The number of co-solvent molecules in gyration volume N_1 satisfies the extremum condition

$$\frac{\partial}{\partial N_1} \ln Z_c(R_g, N_1) = 0. \quad (8)$$

Now initial problem reduced to the following. The volume of the considered system consists of two parts: the gyration volume containing predominantly monomers of the polymer chain and a bulk solution. Thus, we have to consider the co-solvent concentration at equilibrium in the two subvolumes varying the solvophobic strength \tilde{w}_{pc} . In order to find the solution of the posed problem the minimum of the total Helmholtz free energy of the system $\beta F(R_g, N_1) = -\ln Z(R_g, N_1)$ as function of the radius of gyration R_g and the number of co-solvent molecules N_1 within the gyration volume is sought.

In order to perform the total free energy minimization we have to evaluate the polymer partition function $Z_p(R_g)$. Applying the field theoretical approach at the level of random phase approximation (RPA) [33] (see, Appendix B) we obtain the following expression for the polymer free energy

$$\beta F_p(R_g) = -\ln Z_p(R_g) = \beta F_{id}(R_g) + \frac{N^2 w_p}{2V_g} - \frac{V_g \kappa^3}{12\pi}, \quad (9)$$

where $\kappa^2 = \frac{2w_p N}{V_g R_g^2}$, $\beta F_{id}(R_g) = -\ln Z_{id}(R_g)$ is the Helmholtz free energy of the ideal polymer chain; $\beta = \frac{1}{k_B T}$ is an inverse temperature, k_B is a Boltzmann constant. Based on the results of Fixman [31] we construct an interpolation formula for the free energy of the ideal polymer chain:

$$\beta F_{id}(R_g) = \frac{9}{4} \left(\alpha^2 + \frac{1}{\alpha^2} \right) - \frac{3}{2} \ln \alpha^2, \quad (10)$$

where $\alpha = \frac{R_g}{R_{0g}}$ denotes the expansion factor, $R_{0g}^2 = \frac{N b^2}{6}$ is a mean-square radius of gyration of the ideal polymer chain and b is the Kuhn length of the segment. Rewriting the polymer free energy in terms of the expansion factor α we obtain

$$\beta F_p(\alpha) = \frac{9}{4} \left(\alpha^2 + \frac{1}{\alpha^2} \right) - \frac{3}{2} \ln \alpha^2 + \frac{9\sqrt{6} w_p \sqrt{N}}{4\pi b^3 \alpha^3} - \left(\frac{3}{\pi} \right)^{3/2} \frac{6^{1/4}}{N^{3/4}} \left(\frac{w_p}{\alpha^3 b^3} \right)^{3/2}. \quad (11)$$

The expression for the co-solvent Helmholtz free energy takes the form

$$\begin{aligned} \beta F_c(R_g, N_1) &= \frac{w_{pc} N N_1}{V_g} - N_1 \ln(V_g - N_1 v_c) \\ &\quad - (N_c - N_1) \ln(V - V_g - (N_c - N_1) v_c) \\ &\quad + N_1 (\ln N_1 - 1) + (N_c - N_1) (\ln(N_c - N_1) - 1) \\ &\quad - \beta a_c \left(\frac{N_1^2}{V_g} + \frac{(N_c - N_1)^2}{V - V_g} \right). \end{aligned} \quad (12)$$

Minimizing $\beta F_c(R_g, N_1)$ with respect to N_1 , i.e. equating to zero the derivative $\frac{\partial(\beta F_c(R_g, N_1))}{\partial N_1}$ and expressing N_1 we obtain (to the first order in $\frac{V_g}{V}$ and $\frac{N_1}{N_c}$)

$$\begin{aligned} \frac{N_1}{V_g - N_1 v_c} &\simeq \frac{N_c (V_g - N_1 v_c)}{V - N_c v_c} \exp \left[-\frac{N_1 v_c}{V_g - N_1 v_c} \right. \\ &\quad \left. + \frac{N_c v_c}{V - N_c v_c} - \frac{w_{pc} N}{V_g} + 2\beta a_c \left(\frac{N_1}{V_g} - \frac{N_c}{V} \right) \right]. \end{aligned} \quad (13)$$

Introducing the notations $\rho_1 = \frac{N_1}{V_g}$ and $\rho = \frac{N_c}{V}$ we finally obtain the equation for the density of the co-solvent ρ_1 within the gyration volume

$$\begin{aligned} \frac{\rho_1}{1 - \rho_1 v_c} &= \frac{\rho}{1 - \rho v_c} \exp \left[-\frac{w_{pc} N}{V_g} \right. \\ &\quad \left. - \frac{\rho_1 v_c}{1 - \rho_1 v_c} + \frac{\rho v_c}{1 - \rho v_c} - 2\beta a_c (\rho - \rho_1) \right], \end{aligned} \quad (14)$$

which valid for $V \gg V_g$ and $N_c \gg N_1$.

It should be noted that the value of the expansion factor, which corresponds to a minimum of the total Helmholtz free energy. Thus, using the equations (11-14), and calculating a derivative of the total free energy with respect to α and equating it to zero, we obtain

$$\begin{aligned} \alpha^5 - \frac{2}{3} \alpha^3 - \alpha &= \frac{3\sqrt{6}}{2\pi} \tilde{w}_p \sqrt{N} - 6^{1/4} \left(\frac{3}{\pi} \right)^{3/2} \frac{\tilde{w}_p^{3/2}}{N^{3/4} \alpha^{3/2}} \\ &\quad - \frac{2\pi\sqrt{6}}{81} N^{3/2} \alpha^6 \frac{\tilde{P}(\tilde{\rho}, \tilde{T}) - \tilde{P}(\tilde{\rho}_1, \tilde{T})}{\tilde{T}} + \frac{2}{3} N \tilde{w}_{pc} \tilde{\rho}_1 \alpha^3, \end{aligned} \quad (15)$$

where $\tilde{w}_p = w_p b^{-3}$, $\tilde{w}_{pc} = w_{pc} b^{-3}$, $\tilde{\rho} = \rho b^3$, $\tilde{v}_c = \frac{v_c}{b^3}$; $\tilde{\rho}_1 = \rho_1 b^3$ satisfies the equation

$$\begin{aligned} \frac{\tilde{\rho}_1}{1 - \tilde{\rho}_1 \tilde{v}_c} &= \frac{\tilde{\rho}}{1 - \tilde{\rho} \tilde{v}_c} \exp \left[-\frac{9\sqrt{6} \tilde{w}_{pc}}{2\pi \sqrt{N} \alpha^3} - \frac{\tilde{\rho}_1 \tilde{v}_c}{1 - \tilde{\rho}_1 \tilde{v}_c} \right. \\ &\quad \left. + \frac{\tilde{\rho} \tilde{v}_c}{1 - \tilde{\rho} \tilde{v}_c} - \frac{2(\tilde{\rho} - \tilde{\rho}_1)}{\tilde{T}} \right]. \end{aligned} \quad (16)$$

In addition, in (15-16) we enter the dimensionless temperature $\tilde{T} = \frac{k_B T b^3}{a_c}$, and co-solvent pressure $\tilde{P} = \frac{P b^6}{a_c}$ which within our model satisfies well-known Van-der-Waals equation of state

$$\tilde{P}(\tilde{\rho}, \tilde{T}) = \frac{\tilde{\rho} \tilde{T}}{1 - \tilde{\rho} \tilde{v}_c} - \tilde{\rho}^2. \quad (17)$$

The first term in a right hand side of equation (15) relates to the monomer-monomer volume interaction. The second term is a fluctuation correction to the mean-field approximation. This term gives very small correction to the mean-field approximation for long polymer chains. The third term relates to a pressure difference between the co-solvent molecules within gyration volume and in the bulk solution. The last term is related to the polymer-co-solvent interaction.

III. ANALYSIS OF LIMITING REGIMES

In this section we present an analysis of limiting regimes for the radius of gyration which follow from equations (15–16).

At $\tilde{\rho} \rightarrow 0$ a swelling regime occurs $\alpha \sim \tilde{w}_p^{1/5} N^{1/10}$ ($\frac{R_g}{b} \sim \tilde{w}_p^{1/5} N^{0.6}$) that is described by the classical Flory mean-field theory [35].

As a next step, we consider the regime when $\frac{\tilde{w}_{pc}}{2\pi\sqrt{N}\alpha^3} \gg 1$, i.e. when interaction co-solvent-polymer is strongly repulsive (strong solvophobic regime). In this case $\tilde{\rho}_1 \ll \tilde{\rho}$ and the equation (15) simplifies to

$$\alpha^5 - \frac{2}{3}\alpha^3 - \alpha = \frac{3\sqrt{6}}{2\pi}\tilde{w}_p\sqrt{N}$$

$$- \left(\frac{3}{\pi}\right)^{3/2} 6^{1/4} \frac{\tilde{w}_p^{3/2}}{N^{3/4}\alpha^{3/2}} - \frac{2\pi\sqrt{6}}{81} N^{3/2} \frac{\tilde{P}(\tilde{\rho}, \tilde{T})}{\tilde{T}} \alpha^6. \quad (18)$$

If the third term on the right hand side of equation (18) dominates then neglecting all except the first and third terms we obtain the simple limiting laws for the expansion factor and radius of gyration

$$\alpha \simeq \left(\frac{243}{4\pi^2}\right)^{1/6} \left(\frac{\tilde{w}_p\tilde{T}}{\tilde{P}}\right)^{1/6} N^{-\frac{1}{6}},$$

$$\frac{R_g}{b} \simeq \frac{\sqrt{6}}{6} \left(\frac{243}{4\pi^2}\right)^{1/6} \left(\frac{\tilde{w}_p\tilde{T}}{\tilde{P}}\right)^{1/6} N^{1/3}, \quad (19)$$

which corresponds to a globular conformation. In this case, the size of the globule is determined by a competition between the co-solvent osmotic pressure which tends to shrink the polymer chain and the monomer excluded volume effect which tends to expand it. We would like to stress that at $\tilde{T} \gg 1$ and $\tilde{\rho} \ll 1$ (regime of the ideal gas) expressions (19) reduce to previously obtained results [37]:

$$\alpha \simeq \left(\frac{243}{4\pi^2}\right)^{1/6} \left(\frac{\tilde{w}_p}{\tilde{\rho}}\right)^{1/6} N^{-\frac{1}{6}},$$

$$\frac{R_g}{b} \simeq \frac{\sqrt{6}}{6} \left(\frac{243}{4\pi^2}\right)^{1/6} \left(\frac{\tilde{w}_p}{\tilde{\rho}}\right)^{1/6} N^{1/3}. \quad (20)$$

In the regime of a very dense fluid, when $\tilde{\rho} \sim \frac{1}{v_c}$ the effect of a bulk pressure is dominating over the solvophobic effect leading to an expansion of the polymer chain. In this case $\tilde{\rho}_1 \sim \tilde{\rho}$ and equation (15) simplifies to

$$\alpha^5 \simeq \frac{2}{3} N \tilde{w}_{pc} \tilde{\rho} \alpha^3. \quad (21)$$

Thus we obtain the following limiting laws for the expansion factor and radius of gyration which corresponds to the rod-like polymer chain conformation

$$\alpha \simeq \left(\frac{2}{3}\tilde{w}_{pc}\tilde{\rho}\right)^{1/2} N^{0.5}, \quad \frac{R_g}{b} \simeq \frac{1}{3} (\tilde{w}_{pc}\tilde{\rho})^{1/2} N. \quad (22)$$

In this regime the size of the macromolecule is determined by the competition between conformational entropy which tends to coil the polymer chain and the polymer-co-solvent interaction which tends to stretch it.

IV. NUMERICAL RESULTS AND DISCUSSION

Turning to the numerical analysis of the system of equations (15-16) we will fix the Van-der-Waals volume of the co-solvent molecule $\tilde{v}_c = 1$, the monomer-monomer volume interaction parameter $\tilde{w}_p = 1$, and the degree of polymerization $N = 10^3$.

We first discuss the case when the temperature \tilde{T} of the solution is below the critical temperature $\tilde{T}_c = \frac{8}{27}$ of the co-solvent ($\tilde{T} < \tilde{T}_c$) for different solvophobic strength \tilde{w}_{pc} . Hence, we will proceed along the isotherm $\tilde{P} = \tilde{P}(\tilde{\rho}, \tilde{T})$ varying $\tilde{\rho}$ and crossing the binodal. Fig. 1 (a) shows the co-solvent concentration in the gyration volume as a function of the co-solvent pressure in the bulk for two values of solvophobic strength \tilde{w}_{pc} . The co-solvent concentration varies sufficiently nonmonotonic with the co-solvent pressure. At moderate solvophobic strengths ($\tilde{w}_{pc} \sim 1$) increasing the co-solvent pressure \tilde{P} the co-solvent concentration in the gyration volume increases up to a point of co-solvent condensation in the bulk (pronounced peak). The polymer chain collapse in this case occurs as second-order phase transition. Increasing the pressure \tilde{P} further the co-solvent concentration in gyration volume decreases monotonically and at some threshold value jumps to a value which is very close to the bulk co-solvent concentration. The expansion factor in this range (Fig.1 (b)) abruptly changes to the globular regime (19) and then jumps to the regime of the rod-like polymer chain (22). The jumps of $\tilde{\rho}_1$ and α arise due to the penetration of the co-solvent into the gyration volume and, as consequence, due to equalization of pressures in gyration volume and the bulk solution. This amounts to a wetting transition of the co-solvent in the gyration volume. In the strong solvophobic regime ($\tilde{w}_{pc} \gg 1$) a different behavior occurs at small pressures. The co-solvent concentration in gyration volume, shown in Fig. 1 (a) exhibits a pronounced maximum at smaller pressures. Such behaviour of the co-solvent concentration in the gyration volume has been discussed in our previous investigation [37]. In the present case the globular state of the polymer chain prevails (Fig. 1 (b)) over a wider range of bulk pressures. The different behaviors of the expansion factor can be explained by the fact that polymer chain adopts the globular state at pressures at which co-solvent in the bulk is still in a gas phase, so that co-solvent condensation in the bulk does not affect the polymer conformation. However, at sufficiently high pressures in this regime a wetting-induced globule expansion occurs as well (Fig. 1 (b)).

Now we turn to the discussion of the region where $\tilde{T} > \tilde{T}_c$. As in the previous case we investigate the regimes of moderate and strong solvophobicity. As shown

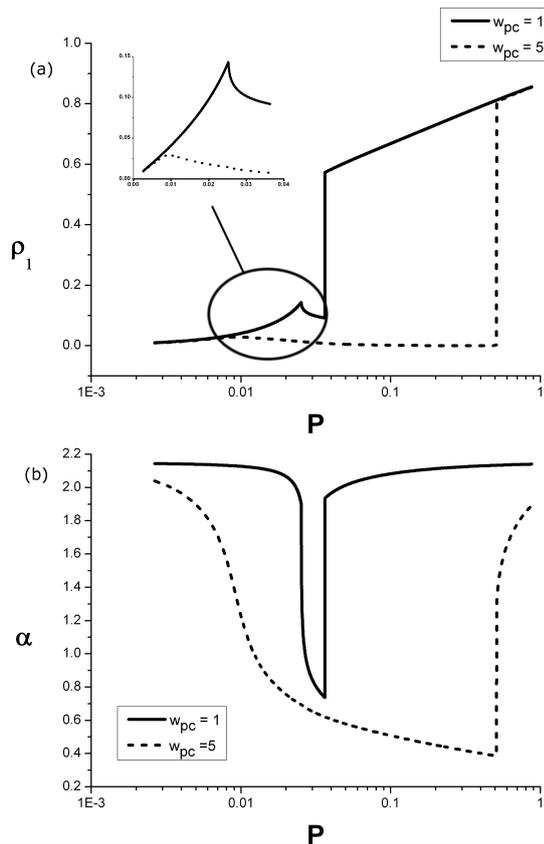


Figure 1: The region below the critical isotherm of co-solvent ($\tilde{T} < \tilde{T}_c$). (a) The average co-solvent concentration in the gyration volume $\tilde{\rho}_1$ as a function of the co-solvent pressure in the bulk \tilde{P} shown for two different solvophobic strength $\tilde{w}_{pc} = 1; 5$. (b) The expansion factor α as a function of the co-solvent pressure in the bulk solution \tilde{P} shown for the same solvophobic strengths $\tilde{w}_{pc} = 1; 5$. The bulk co-solvent pressure at which the globule chain expansion occurs coincides with the jump in the co-solvent concentration within the gyration volume (dewetting-induced globule-rod transition). Values are shown for $\tilde{v}_c = 1$, $\tilde{w}_p = 1$, $N = 10^3$, $\tilde{T} = 0.27$.

in Fig. 2 (a,b), the co-solvent concentration in the gyration volume and the expansion factor in the moderately solvophobic regime differ qualitatively from the case when $\tilde{T} < \tilde{T}_c$. The co-solvent concentration in the gyration volume monotonically increases at increasing the bulk co-solvent pressure. The expansion factor in this regime is almost independent of the bulk co-solvent pressure. However, in the strong solvophobic regime quite similar behaviour occurs as in the case $\tilde{T} < \tilde{T}_c$. The presence of jumps in the co-solvent concentration $\tilde{\rho}_1$ and in the expansion factor α are also related to the effect of the co-solvent molecules intruding into the gyration volume which in turn leads to an equality between the pressure in the gyration volume and the bulk.

It is instructive to regard the dependence of the ex-

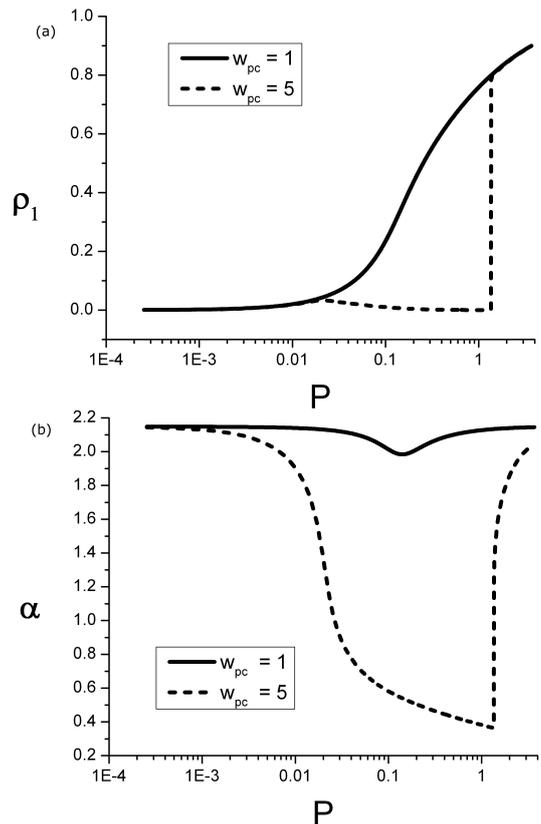


Figure 2: The region above the critical isotherm of the co-solvent ($\tilde{T} > \tilde{T}_c$). (a) The average co-solvent concentration in the gyration volume $\tilde{\rho}_1$ as a function of the co-solvent pressure in the bulk \tilde{P} shown for the solvophobic strength $\tilde{w}_{pc} = 1; 5$. (b) The expansion factor α as a function of the co-solvent pressure in the bulk solution \tilde{P} shown for the same solvophobic strength $\tilde{w}_{pc} = 1; 5$. At the moderate solvophobic strength ($\tilde{w}_{pc} = 1$) the average co-solvent concentration in the gyration volume monotonically increases at the increasing the bulk co-solvent pressure. The expansion factor exhibits a weakly pronounced minimum. In the strong solvophobic regime ($\tilde{w}_{pc} = 5$) the behavior of the expansion factor and the average co-solvent concentration within the gyration volume is quite similar to the behavior in region below critical isotherm ($\tilde{T} < \tilde{T}_c$). Values are shown for $\tilde{v}_c = 1$, $\tilde{w}_p = 1$, $N = 10^3$, $\tilde{T} = 2$.

pansion factor on the solvophobic strength in the regions below ($\tilde{T} > \tilde{T}_c$) and above ($\tilde{T} < \tilde{T}_c$) the critical isotherm of the co-solvent. The Fig.3 (a) shows such dependence at fixed bulk co-solvent concentration. In both cases at a certain value of the solvophobic strength the polymer chain collapse occurs. It should be noted, that the polymer chain collapse in region $\tilde{T} > \tilde{T}_c$ occurs at higher solvophobic strength than in the region $\tilde{T} < \tilde{T}_c$. We would also like to stress that the polymer chain collapse occurs as a first-order phase transition, confirming the hypothesis of ten Wolde and Chandler [2]. Indeed, as shown in Fig. 3 (b) the co-solvent concentration in the

gyration volume jumps to very small values when the polymer chain collapse takes place. In the region below the co-solvent critical isotherm this jump corresponds to a dewetting transition which results in a formation of a polymer globule surface surrounded by a layer of co-solvent gas. In the region above the critical isotherm a similar mechanism is responsible for the transition. However, in this case the collapse is caused by a layer of rarefied fluid.

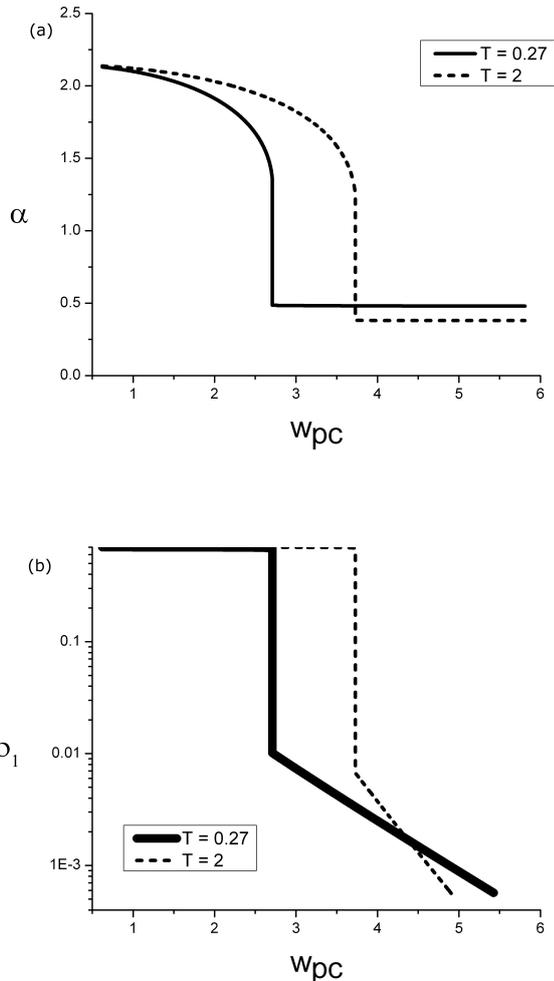


Figure 3: (a) The expansion factor α as a function of solvophobic strength \tilde{w}_{pc} at fixed co-solvent concentration in the bulk solution ($\tilde{\rho} = 0.7$) below and above the critical isotherm of the co-solvent. (b) The average co-solvent concentration within the gyration volume $\tilde{\rho}_1$ as a function of solvophobic strength \tilde{w}_{pc} at fixed co-solvent concentration in the bulk solution ($\tilde{\rho} = 0.7$) below and above the critical isotherm of the co-solvent. In both cases at some threshold value of solvophobic strength the polymer chain collapse occurs. For a polymer chain collapse above the critical isotherm a sufficiently higher solvophobic strength is required than that in region below critical isotherm. Polymer chain collapse occurs as a first-order phase transition Shown for $\tilde{v}_c = 1$, $\tilde{w}_p = 1$, $N = 10^3$.

V. SUMMARY

We have developed a simple statistical theory of conformational changes of a solvophobic polymer chain depending on the co-solvent pressure in the bulk solution and the polymer solvophobic strength. We have found that explicit account of the co-solvent leads to the new effects: dewetting-induced polymer collapse due to the solvophobic interaction and wetting-induced globule expansion at high co-solvent pressures in the bulk solution. The latter happens as a globule-rod first-order phase transition, which has not been reported previously for neutral polymer solutions. The similar rod-globule transition for highly charged polyelectrolytes due to many-body electrostatic effects was predicted in works [38, 39]. Moreover, the present theory gives a quantitative explanation at the level of the mean-field approximation of the dewetting-induced polymer chain collapse predicted by ten Wolde and Chandler [2].

Taking into account the effect of the co-solvent concentration fluctuations would lead to the appearance of an additional correction term in the expression of the total free energy and, as consequence, to an additional term in co-solvent pressure which is related to the so-called short-ranged solvent-mediated interactions discovered by Fisher and de Gennes [45]. In works [40–42] the coarse-grained models of solvation and hydrophobic effect where taken into account the influence of water density fluctuations on the solvation at small and large scales were developed. As shown in work [43], short-ranged solvent-mediated interaction may cause a colloidal self-assembly in a vicinity of the solvent critical point. Moreover, it can be reason of an effective attraction of planar walls confining a nematic fluid in the vicinity of spontaneous ordering point [44]. We believe, that this correction will not change qualitatively our final mean-field results, although it will become significant in the vicinity of the binodal. This problem can be a subject for forthcoming publications.

In conclusion we would like to hypothesise about possible applications of the presented theory. Firstly, in our opinion, the theory could describe a possible mechanism of protein unfolding at high pressures which is observed in experiments [46, 47]. Secondly, we believe that our theoretical model can help to interpret experimental data on the solubility of solvophobic polymers in supercritical solvents at high pressures [48–50]. However, these speculations require the further investigations.

Acknowledgments

The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under grant agreement N//247500 with //project acronym "Biosol".

VI. APPENDIX A

To address a derivation of expression (6) for the partition function we make the following identity transformation in (1)

$$\begin{aligned} Z(R_g) &= \int d\Gamma_p(R_g) e^{-\beta H_p} \int d\Gamma_c e^{-\beta H_c - \beta H_{pc}} \\ &= Z_p(R_g) \int d\Gamma_c e^{-\beta H_c} \langle e^{-\beta H_{pc}} \rangle_p, \end{aligned} \quad (23)$$

where

$$Z_p(R_g) = \int d\Gamma(R_g) e^{-\frac{w_p}{2} \int_0^N \int_0^N ds_1 ds_2 \delta(\mathbf{r}(s_1) - \mathbf{r}(s_2))} \quad (24)$$

is the polymer partition function; the symbol $\langle (\dots) \rangle_p = \frac{1}{Z_p(R_g)} \int d\Gamma(R_g) (\dots)$ denotes averaging over polymer microstates with a fixed radius of gyration. Using the cumulant expansion [36] at first order we obtain

$$\langle e^{-\beta H_{pc}} \rangle_p \approx e^{-\beta \langle H_{pc} \rangle_p}. \quad (25)$$

Therefore one can obtain

$$\beta \langle H_{pc} \rangle_p = w_{pc} \int d\mathbf{x} \hat{\rho}_c(\mathbf{x}) \langle \rho_p(\mathbf{x}) \rangle_p \simeq \frac{N w_{pc}}{V_g} \int d\mathbf{x} \hat{\rho}_c(\mathbf{x}), \quad (26)$$

where the approximation

$$\langle \hat{\rho}(\mathbf{x}) \rangle_p \simeq \begin{cases} \frac{N}{V_g}, & |\mathbf{x}| \leq R_g \\ 0, & |\mathbf{x}| > R_g \end{cases} \quad (27)$$

has been introduced; $V_g = \frac{4\pi R_g^3}{3}$ is a value of the gyration volume. Thus we obtain the following expression for the partition function of the solution

$$Z(R_g) = Z_p(R_g) Z_c(R_g), \quad (28)$$

where $Z_c(R_g)$ has a form

$$\begin{aligned} Z_c(R_g) &= \int d\Gamma_c e^{-\beta H_c - \frac{w_{pc} N}{V_g} \int d\mathbf{x} \hat{\rho}_c(\mathbf{x})} \\ &= \frac{1}{N_c!} \int d\mathbf{r}_1 \dots \int d\mathbf{r}_{N_c} e^{-\beta H_c - \frac{w_{pc} N}{V_g} \int d\mathbf{x} \hat{\rho}_c(\mathbf{x})}. \end{aligned} \quad (29)$$

Rewriting the last expression in the form

$$Z_c(R_g) = \sum_{n=0}^{N_c} \mathcal{Z}_c(R_g, n), \quad (30)$$

where

$$\begin{aligned} \mathcal{Z}_c(R_g, n) &= \frac{e^{-\frac{w_{pc} N n}{V_g}}}{(N_c - n)! n!} \int_{V_g} d\mathbf{x}_1 \dots \int_{V_g} d\mathbf{x}_n \\ &\times \int_{V - V_g} d\mathbf{y}_1 \dots \int_{V - V_g} d\mathbf{y}_{N_c - n} e^{-\beta H_c} \end{aligned} \quad (31)$$

is the co-solvent partition function with fixed number n of co-solvent molecules in the gyration volume and applying the mean-field approximation we finally arrive at

$$\begin{aligned} Z_c(R_g) &= \sum_{n=0}^{N_c} \frac{(V_g - n v_c)^n (V - V_g - (N_c - n) v_c)^{N_c - n}}{(N_c - n)! n!} \\ &\times \exp \left[-\frac{w_{pc} N n}{V_g} + \beta a_c \left(\frac{n^2}{V_g} + \frac{(N_c - n)^2}{V - V_g} \right) \right], \end{aligned} \quad (32)$$

where a_c is a Van-der-Waals attraction parameter for the co-solvent; v_c is a Van-der-Waals volume of co-solvent molecules. We would like to stress that the above equation is based on the same mean-field approximation as the Van-der-Waals theory. In the thermodynamic limit ($N_c \rightarrow \infty$) in the sum (32) only the highest order term giving the main contribution is relevant. This term corresponds to the number $n = N_1$ which can be obtained from the extremum condition

$$\begin{aligned} \frac{\partial}{\partial n} \ln \left(\frac{(V_g - n v_c)^n (V - V_g - (N_c - n) v_c)^{N_c - n}}{(N_c - n)! n!} e^{-\frac{w_{pc} N n}{V_g}} \right. \\ \left. \times \exp \left[\beta a_c \left(\frac{n^2}{V_g} + \frac{(N_c - n)^2}{V - V_g} \right) \right] \right) = 0. \end{aligned} \quad (33)$$

Therefore we arrive at the expression which already has been used in the main text:

$$\begin{aligned} Z_c(R_g) &\simeq \mathcal{Z}_c(R_g, N_1) = e^{-\frac{w_{pc} N N_1}{V_g} + \beta a_c \left(\frac{N_1^2}{V_g} + \frac{(N_c - N_1)^2}{V - V_g} \right)} \\ &\times \frac{(V_g - N_1 v_c)^{N_1} (V - V_g - (N_c - N_1) v_c)^{N_c - N_1}}{(N_c - N_1)! N_1!}. \end{aligned} \quad (34)$$

VII. APPENDIX B

The conditional partition function for polymer chain with fixed radius of gyration R_g has a form

$$Z_p(R_g) = \int d\Gamma(R_g) e^{-\frac{w_p}{2} \int_0^N \int_0^N ds_1 ds_2 \delta(\mathbf{r}(s_1) - \mathbf{r}(s_2))}. \quad (35)$$

We will use the field theoretical approach at level of random phase approximation. Using the standard Hubbard-Stratonovich transformation

$$\begin{aligned} \exp \left[-\frac{w_p}{2} \int_0^N \int_0^N ds_1 ds_2 \delta(\mathbf{r}(s_1) - \mathbf{r}(s_2)) \right] \\ = \int \frac{\mathcal{D}\varphi}{C} \exp \left[-\frac{1}{2w_p} \int d\mathbf{x} \varphi^2(\mathbf{x}) + i \int_0^N ds \varphi(\mathbf{r}(s)) \right], \end{aligned} \quad (36)$$

we rewrite $Z_p(R_g)$ as follows

$$\begin{aligned} Z_p(R_g) &= \int \frac{\mathcal{D}\varphi}{C} e^{-\frac{1}{2w_p} \int d\mathbf{x} \varphi^2(\mathbf{x})} \int d\Gamma(R_g) e^{i(\hat{\rho}\varphi)} \\ &= Z_{id}(R_g) \int \frac{\mathcal{D}\varphi}{C} e^{-\frac{1}{2w_p} \int d\mathbf{x} \varphi^2(\mathbf{x})} \langle e^{i(\hat{\rho}\varphi)} \rangle_{R_g}, \end{aligned} \quad (37)$$

where $Z_{id}(R_g)$ is the partition function of the ideal gaussian polymer chain at a fixed radius of gyration R_g ; $C = \int \mathcal{D}\varphi e^{-\frac{1}{2w_p} \int d\mathbf{x} \varphi^2(\mathbf{x})}$ is a normalization constant; the symbol $\langle (\dots) \rangle_{R_g} = \frac{1}{Z_{id}(R_g)} \int d\Gamma(R_g) (\dots)$ means the averaging over microstates of the ideal polymer chain at a fixed radius of gyration; $\hat{\rho}(\mathbf{x}) = \int_0^N ds \delta(\mathbf{x} - \mathbf{r}(s))$ is the microscopic density of monomers. Furthermore, we introduce a following short-hand notation $(\hat{\rho}\varphi) = \int d\mathbf{x} \hat{\rho}(\mathbf{x}) \varphi(\mathbf{x})$. Evaluating the functional integral (37) in the case when $N \gg 1$ the following relations hold

$$\hat{\rho}(\mathbf{x}) = \langle \hat{\rho}(\mathbf{x}) \rangle_{R_g} + \delta\hat{\rho}(\mathbf{x}), \quad (38)$$

$$\langle \hat{\rho}(\mathbf{x}) \rangle_{R_g} \simeq \begin{cases} \frac{N}{V_g}, & |\mathbf{x}| \leq R_g \\ 0, & |\mathbf{x}| > R_g; \end{cases} \quad (39)$$

$$\varphi(\mathbf{x}) = \phi(\mathbf{x}) + \psi(\mathbf{x}), \quad (40)$$

$$\phi(\mathbf{x}) = \begin{cases} \phi_0, & |\mathbf{x}| \leq R_g \\ 0, & |\mathbf{x}| > R_g. \end{cases} \quad (41)$$

Note, that the coordinates are taken with the origin at the center of mass of the polymer. The random field $\psi(\mathbf{x})$ satisfies a following condition

$$\int_{V_g} d\mathbf{x} \psi(\mathbf{x}) = 0. \quad (42)$$

Using equalities (38-42), one can express for the partition function of the polymer in the following form

$$Z_p(R_g) = Z_{MF}(R_g) Z_{fl}(R_g), \quad (43)$$

where

$$\begin{aligned} Z_{MF}(R_g) &= Z_{id}(R_g) \int_{-\infty}^{\infty} \frac{d\phi_0}{C_0} e^{-\frac{V_g \phi_0^2}{2w_p} + iN\phi_0} \\ &= Z_{id}(R_g) e^{-\frac{N^2 w_p}{2V_g}} \end{aligned} \quad (44)$$

is the partition function in the framework of the mean-field approximation with $C_0 = \int_{-\infty}^{+\infty} d\phi_0 e^{-\frac{V_g \phi_0^2}{2w_p}} = \sqrt{\frac{2\pi w_p}{V_g}}$ as a normalization constant;

$$Z_{fl}(R_g) = \int \frac{\mathcal{D}\psi}{C_1} e^{-\frac{1}{2w_p} \int d\mathbf{x} \psi^2(\mathbf{x})} \langle e^{i(\delta\hat{\rho}\psi)} \rangle_{R_g} \quad (45)$$

is the partition function describing the fluctuation corrections to mean-field approximation; $C_1 = \int \mathcal{D}\psi e^{-\frac{1}{2w_p} \int d\mathbf{x} \psi^2(\mathbf{x})}$ is a normalization constant in a

gaussian measure for the functional integral (45). In the framework of RPA the fluctuation partition function can be written as

$$\begin{aligned} Z_{fl}(R_g) &= \int \frac{\mathcal{D}\psi}{C_1} e^{-\frac{1}{2w_p} \int d\mathbf{x} \psi^2(\mathbf{x})} \\ &\times e^{-\frac{1}{2} \int d\mathbf{x} \int d\mathbf{y} \langle \delta\hat{\rho}(\mathbf{x}) \delta\hat{\rho}(\mathbf{y}) \rangle_{R_g} \psi(\mathbf{x}) \psi(\mathbf{y})} \end{aligned} \quad (46)$$

For $N \gg 1$ the correlation function of local density fluctuations becomes translationally invariant, i.e.

$$\langle \delta\hat{\rho}(\mathbf{x}) \delta\hat{\rho}(\mathbf{y}) \rangle_{R_g} \simeq \frac{N}{V_g} S(\mathbf{x} - \mathbf{y}). \quad (47)$$

The structure factor $S(\mathbf{x} - \mathbf{y})$ is nonzero when ends of radius vectors \mathbf{x}, \mathbf{y} lie within the gyration volume, so that

$$\begin{aligned} Z_{fl}(R_g) &\simeq \int \frac{\mathcal{D}\psi}{C_1} \exp \left[-\frac{1}{2w_p} \int d\mathbf{x} \psi^2(\mathbf{x}) \right] \\ &\times \exp \left[-\frac{1}{2} \int_{V_g} d\mathbf{x} \int_{V_g} d\mathbf{y} \langle \delta\hat{\rho}(\mathbf{x}) \delta\hat{\rho}(\mathbf{y}) \rangle_{R_g} \psi(\mathbf{x}) \psi(\mathbf{y}) \right] \\ &\simeq \exp \left[-\frac{V_g}{2} \int \frac{d\mathbf{k}}{(2\pi)^3} \ln \left(1 + w_p \frac{N}{V_g} S(\mathbf{k}) \right) \right]. \end{aligned} \quad (48)$$

In the last expression in the exponent it is necessary to exclude due to convergence reasons a term related to the self-interaction energy of the polymer chain $\frac{Nw_p}{2} \int \frac{d\mathbf{k}}{(2\pi)^3} S(\mathbf{k})$ [34, 37]. Using the well known interpolation formula for the structure factor $S(\mathbf{k})$ [32]

$$S(\mathbf{k}) = \frac{1}{1 + \frac{k^2 R_g^2}{2}} \simeq \frac{2}{k^2 R_g^2}, \quad (49)$$

excluding the self-interaction energy we arrive at an expression for the fluctuation partition function within the RPA

$$Z_{fl}(R_g) = e^{\frac{V_g \kappa^3}{12\pi}}, \quad (50)$$

where $\kappa^2 = \frac{2w_p N}{V_g R_g^2}$. Therefore, we have a following expression for the polymer free energy in the framework of RPA

$$\begin{aligned} \beta F_p(R_g) &= -\ln Z_p(R_g) \\ &= \beta F_{id}(R_g) + \frac{N^2 w_p}{2V_g} - \frac{V_g \kappa^3}{12\pi}, \end{aligned} \quad (51)$$

which already has been used in the main text.

- [1] *Chandler D.* Interfaces and the driving force of hydrophobic assembly // *Nature*. - 2005. - V. 437. - no. 29. - P. 640.
- [2] *ten Wolde P.R., Chandler D.* Drying-induced hydrophobic polymer collapse // *PNAS*. - 2002. - Vol. 99. - no. 10. - P. 6539-6543.
- [3] *Royer C. A.* Revisiting volume changes in pressure-induced protein unfolding // *Biochimica et Biophysica Acta* - 2002. - V. 1595 - P. 201.
- [4] *Meersman F., Daniel I., Bartlett D.H., Winter R., Hazael R. McMillan P.F.* High-pressure biochemistry and biophysics // *Reviews in Mineralogy and Geochemistry* - 2013. - V. 75 - no. 1 - P. 607-648
- [5] *G. Hummer, S. Garde, A. E. Garcia, M. E. Paulaitis, and L. R. Pratt* The pressure dependence of hydrophobic interactions is consistent with the observed pressure denaturation of proteins // *PNAS* - 95 - 4 - 1998 - 1552-1555
- [6] *M. V. Athawale, G. Goel, T. Ghosh, T. M. Truskett and S. Garde* Effects of lengthscales and attractions on the collapse of hydrophobic polymers in water // *PNAS* - 104 - 3 - 2007 - 733-738
- [7] *T. Ghosh, A. E. Garcia and S. Garde* Molecular Dynamics Simulations of Pressure Effects on Hydrophobic Interactions // *J. Am. Chem. Soc.* - 123 - 2001 - 10997-11003
- [8] *D. Paschek, S. Gnanakaran, and A. E. Garcia* Simulations of the pressure and temperature unfolding of an alpha-helical peptide // *PNAS* - 102 - 19 - 2005 - 6765-6770
- [9] *J. Rochea, J. A. Carob, D. R. Norbertoa, P. Barthea, C. Roumestanda, J. L. Schlessmand, A. E. Garciae, Bertrand Garcia-Moreno E, and C. A. Royera* Cavities determine the pressure unfolding of proteins // *PNAS* - 109 - 18 - 2012 - P. 6945.
- [10] *V. A. Payne, N. Matubayasi, L. R. Murphy and R. M. Levy* Monte Carlo Study of the Effect of Pressure on Hydrophobic Association // *J. Phys. Chem. B* - 101 - 11 - 1997 - 2054-2060
- [11] *A. Wallqvist* Pressure dependence of methane solvation in aqueous mixtures and the relation to the structure of liquid water // *J. Chem. Phys.* - 1992. - 96.
- [12] *R. Sarma and S. Paul* The effect of pressure on the hydration structure around hydrophobic solute: A molecular dynamics simulation study // *J. Chem. Phys.* - 2012 - 136. - 114510.; doi: 10.1063/1.3694834
- [13] *J. R. Grigeraemail, A. N. McCarthy* The Behavior of the Hydrophobic Effect under Pressure and Protein Denaturation // *Biophysical Journal* - 98 - 8 - 2010 - 1626-1631
- [14] *Harano Y., Yoshidome T., Kinoshita M.* Molecular mechanism of pressure denaturation of proteins // *J. Chem. Phys.* - 2008. - V. 129. - P. 145103.
- [15] *W. Kauzmann* // *Nature* - 1987. - V. 325. - P. 763-764.
- [16] *A. Yu. Grosberg, A. R. Khokhlov* Statistical Physics of Macromolecules // *AIP*, New York, 1994.
- [17] *Edwards S.F.* The statistical mechanics of polymers with excluded volume. // *Proc. Phys. Soc.* - 1965. - Vol. 85 - p. 613.
- [18] *Edwards S.F.* The theory of polymer solutions at intermediate concentration. // *Proc. Phys. Soc.* - 1966. - Vol. 88 - p. 265.
- [19] *Birshtein T.M., Pryamitsyn V.A.* Coil-Globule Type Transitions in Polymers. 2. Theory of Coil-Globule Transition in Linear Macromolecules // *Macromolecules*. - V. 24. - 1991. - P. 1554.
- [20] *Moore M.A.* Theory of the polymer coil-globule transition // *J. Phys. A: Math. Gen.* - V. 10 (2) - 1977. - P. 305.
- [21] *de Gennes P.G.* Collapse of a polymer chain in poor solvents // *Le Journal De Physique - Letters*. - V. 36 (2) - 1975. - P. L-55.
- [22] *Lifshitz I.M., Grosberg A. Yu* State diagram of a polymer globule and the problem of self-organization of its spatial structure // *Soviet physics JETP*. - V. 38 (6). - 1974. - P. 1198.
- [23] *Lifshitz I.M.* Some problems of the statistical theory of biopolymers // *Soviet physics JETP*. - V. 28 (6) - 1975. - P. L-55.
- [24] *Muthukumar M.* Collapse transition of a stiff chain // *J. Chem. Phys.* - V. 81. - 1984. - P. 6272.
- [25] *Sanchez I.C.* Phase Transition Behavior of the Isolated Polymer Chain // *Macromolecules*. - V. 12 (5). - 1979. - P. 980.
- [26] *Birshtein T.M., Pryamitsyn V.A.* Theory of the coil-globule transition // *Polymer Science U.S.S.R.* - V. 29 (9). - 1987. - P. 2039.
- [27] *Grosberg A. Yu., Kuznetsov D.V.* Quantitative Theory of the Globule-to-Coil Transition. 1. Link Density Distribution in a Globule and Its Radius of Gyration // *Macromolecules*. - V. 25. - 1992. - P. 1970.
- [28] *Khohlov A.R.* Theory of the polymer chain collapse for the d-dimensional case // *Physica*. - V. 105 A. - 1981. - P. 357.
- [29] *van den Oever J.P.M., Leermakers F.A.M., Fleer G.J., et.al.* Coil-globule transition for regular, random, and specially designed copolymers: Monte Carlo simulation and self-consistent field theory // *Phys. Rev. E*. - V. 65. - P. 041708.
- [30] *Kholodenko A.L., Freed K.F.* Globule-to-Coil Transition of a Single Homopolymer Chain in Solution // *J. Phys. A: Math. Gen.* - V. 17. - 1984 - P. 2703.
- [31] *Fixman M.* Radius of Gyration of Polymer Chains // *J. Chem. Phys.* - V. 36 (2) - 1962. - P. 306.
- [32] *Doi, M., Edwards, S. F.* The Theory of Polymer Dynamics // Clarendon Press: Oxford, 1986.
- [33] *Fredrickson G. H.* The equilibrium theory of inhomogeneous polymers. Oxford: Clarendon Press, 2006. 437 p.
- [34] *Borue V. Yu., Erukhimovich I. Ya.* A Statistical Theory of Weakly Charged Polyelectrolytes: Fluctuations, Equation of State, and Microphase Separation // *Macromolecules*. - Vol. 21. - 11. - 1988. - p. 3240-3249.
- [35] *Flory P.* Statistical Mechanics of Chain Molecules // New York: Wiley-Interscience. - 1969.
- [36] *Kubo R.* Generalized cumulant Expansion Method // *J. Phys. Soc. Jap.* - V.17 - 1962 - P. 1100.
- [37] *Budkov Yu. A., Kolesnikov A.L., Georgi N., Kiselev M.G.* A Statistical Theory of co-solvent-induced coil-globule transitions in dilute polymer solution // Preprint 36, Max Planck Institute of mathematics in the Science, 2014 (submitted to *J. Chem. Phys.*).
- [38] *Brilliantov N.V., Kuznetsov D.V., Klein R.* Chain Col-

- lapse and Counterion Condensation in Dilute Polyelectrolyte Solutions. // *Phys. Rev. Lett.* - 1998. - Vol. 81 (7). - P. 1433.
- [39] *Schiessel H., Pincus P.* Counterion-Condensation-Induced Collapse of Highly Charged Polyelectrolytes // *Macromolecules.* - 1998. - V. 31. - P. 7953.
- [40] *ten Wolde P.R., Sun S.X., Chandler D.* Model of a fluid at small and large length scales and the hydrophobic effect // *Phys. Rev. E.* - 2001 - V. 65. - P. 011201.
- [41] *Willard A.P., Chandler D.* The Role of Solvent Fluctuations in Hydrophobic Assembly *J. Phys. Chem. B.* - 2008. - V. 112. - P. 6187.
- [42] *Varilly P., Patel A.J., Chandler D.* An improved coarse-grained model of solvation and the hydrophobic effect // *J. Chem. Phys.* - 2011. - V. 134. - P. 074109.
- [43] *Edison J.R., Tasios N., Evans R., et.al.* Can Near-Critical Solvents Drive Colloidal Self-Assembly? // *arXiv:1403.4872*
- [44] *Haddadan F.K.P., Naji A., Seifi A.K., Podgornik R.* Pseudo-Casimir interactions across nematic films with disordered anchoring axis // *J. Phys.: Condens. Matter.* - 2014. - V. 26. - P. 075103.
- [45] *Fisher, M. E., de Gennes, P. G.* Wall Phenomena in a critical binary mixture // *C. R. Acad. Sci. Paris B.* - 1978. - V. 287.- P. 207.
- [46] *Woenckhaus J., Koehling R., Thiyagarajan P., Littrell K.C., Seifert S., et.al.* Pressure-Jump Small-Angle X-Ray Scattering Detected Kinetics of Staphylococcal Nuclease Folding // *Biophysical Journal.* - V. 80. - 2001. - P. 1518.
- [47] *Herberhold H., Winter R.* Temperature- and Pressure-Induced Unfolding and Refolding of Ubiquitin: A Static and Kinetic Fourier Transform Infrared Spectroscopy Study // *Biochemistry.* - V. 41. - 2002. - P. 2396.
- [48] *Dardin A., Cain J.B., DeSimone J.M. et. al.* High-Pressure NMR of Polymers Dissolved in Supercritical Carbon Dioxide // *Macromolecules.* - V.30. - P. 3593.
- [49] *Andre P., Lacroix-Desmazes P., Taylor D.K., Boutevin B.* Solubility of fluorinated homopolymer and block copolymer in compressed CO_2 // *J. of Supercritical Fluids.* - V. 37. - 2006. - P. 263.
- [50] *Kiran E.* Polymer miscibility, phase separation, morphological modifications and polymorphic transformations in dense fluids // *J. of Supercritical Fluids.* - V. 47. - 2009. - P. 466.