A non–equilibrium approach for polymer solutions

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Summary. — We extend the Gaussian self–consistent method, earlier developed for a single polymer chain, to arbitrary number of chains in a dilute or semidilute solution. It is also straightforward to consider in this framework copolymer solutions, and thus the method is quite general. Importantly, it permits a complete study of the equilibrium thermodynamic functions and kinetics of conformational changes within the same theoretical treatment. We find that within the two phase coexistence region there are additional metastable states of mesoglobules composed of a number of distinct chains. We argue that this can explain a recent experimental observation of small globular aggregates with a relatively monodisperse size in a dilute aqueous solution of PNIPAM. Turning to copolymer solutions we find that the mesoglobules may become thermodynamically stable in a narrow region of the phase diagram.

PACS 61.25.Hq – Macromolecular and polymer solutions.
PACS 01.30.Cc – Conference proceedings.

1. – Introduction

Polymer solutions are examples of interesting complex fluids in which a variety of complicated morphologies and nontrivial kinetic behaviour can be observed at phase separation. Considerable theoretical effort has been directed towards elucidation of the equilibrium behaviour of homopolymer and copolymer concentrated solutions, mixtures and blends [1-4]. From the classical Flory–Huggins theory to more advanced scaling theories, to the Lifshitz theory and the self–consistent treatments — these approaches have been developed based on the density variables formalism. The low density region, however, was more difficult for theoretical study. The experimental situation regarding the kinetics at the collapse transition of even the simple homopolymer [5] continued to be a matter of controversy due to a complicated interplay of the collapse and aggregation phenomena. From a somewhat different perspective, the conformational transitions of a single chain have been attracting a renewed interest of theorists in the past few years in

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an attempt to gain some insights into the mysteries of folding of complex biopolymers such as proteins and nucleic acids.

Recent experiments in our laboratory on dilute aqueous solutions of Poly-N-isopropylacylamide using the Dynamic Light Scattering and Electron Microscopy techniques [6] have led to an interesting observation. At sufficiently low concentrations within the two phase coexistence region small spherical aggregates composed of a few distinct chains with a rather monodisperse size distribution have been found to form and preserve during many hours.

Therefore, it seems important to develop a new theoretical approach that could describe heterogeneities in microstructure for both equilibrium and kinetics of heteropolymer solutions that would be valid in the limit of only one, or a few distinct chains and up to semi–dilute and concentrated solutions. Such a general approach, based on the extension of the Gaussian self–consistent (GSC) method [7, 8] that we earlier applied to the single chain problems, is presented below. The GSC method is a natural extension to the realm of kinetics of the equilibrium Gibbs–Bogoliubov variational principle with a generic quadratic trial Hamiltonian. At each moment in time the trial parameters of a linear stochastic ensemble are determined to approximate in the best possible way the mean squared distances between all pairs of monomers found from the exact kinetic equations. The current formalism generalises the equations obtained in our first attempt to describe multiple chain systems in Ref. [9], where we have suggested a plausible thermodynamic interpretation for the mesoglobules. We have also shown there that, as regards the two phase coexistence region, our equations can be reduced in the thermodynamic limit to those of the Flory–Huggins theory.

2. – Method

We denote by $\mathbf{X}_n^a$ the coordinates of n-th monomer in the a-th chain. N and M will be the number of monomers in a chain and the number of chains respectively. It is convenient to introduce multi–indices $A = (a, n)$ and so on. The coarse–grained time evolution of the system is well represented by the Langevin equation,

$$\zeta_b \frac{d}{dt}\mathbf{X}_A = -\frac{\partial H}{\partial \mathbf{X}_A} + \boldsymbol{\eta}_A(t), \tag{1}$$

where ζ_b is the friction constant per monomer and the Gaussian noise has the second momentum proportional to $2k_BT\zeta_b$. Treatment of the hydrodynamic effect and some technical details of the single chain formalism can be found in Ref. [10].

The effective free energy functional, H, is given by,

$$\begin{aligned} H = {} & \frac{k_BT}{2L^2}\sum_a \left(\mathbf{Y}^a - \mathbf{Y}\right)^2 + \frac{k_BT}{2l^2}\sum_{a,n}\left(\mathbf{X}_n^a - \mathbf{X}_{n-1}^a\right)^2 \\ & + \frac{k_BT\,\lambda}{2l^3}\sum_{a,n}\left(\mathbf{X}_{n+1}^a + \mathbf{X}_{n-1}^a - 2\mathbf{X}_n^a\right)^2 + \sum_{J\geq 2}\sum_{\{A\}} u_{\{A\}}^{(J)} \prod_{i=1}^{J-1}\delta(\mathbf{X}_{A_{i+1}} - \mathbf{X}_{A_1}), \end{aligned} \tag{2}$$

where $\mathbf{Y}^a$ and $\mathbf{Y}$ are the centres–of–mass of the a-th chain and the whole system; L, l and λ are the linear system size, the statistical length and the persistent length of a chain respectively. The virial coefficients $u_{\{A\}}^{(J)}$ are allowed to be arbitrary to describe the most general case of any mixture of heteropolymers with any composition. The main idea of

the GSC method is to replace nonlinear Eq. (1) by a linear stochastic ensemble,

$$\frac{d}{dt}\mathbf{X}_A = -\sum_{A'} V_{AA'}(t)\,\mathbf{X}_{A'} + \boldsymbol{\eta}_A(t), \tag{3}$$

with coefficients chosen at each moment in time according to the criterion,

$$\left\langle \mathbf{X}_A \frac{\partial H}{\partial \mathbf{X}_{A'}} \right\rangle_0 = \left\langle \mathbf{X}_A \frac{\partial H_0}{\partial \mathbf{X}_{A'}} \right\rangle_0, \qquad H_0 = \frac{1}{2}\sum_{A,A'} V_{A\,A'}\,\mathbf{X}_A\,\mathbf{X}_{A'}. \tag{4}$$

At equilibrium these equations become exactly the extrema conditions for the trial free energy in the Gibbs–Bogoliubov variational principle based on minimising the variational free energy, $\mathcal{A} = -k_BT \log \mathrm{Tr}\exp(-H_0/k_BT) + \langle H - H_0\rangle_0$, with respect to $V_{A\,A'}$.

It is possible to exclude the effective potentials $V_{AA'}$ from the consideration and obtain closed differential equations. These are most conveniently written in terms of the mean–squared distances between monomers, $D_{A\,A'}(t) \equiv (1/3)\left\langle (\mathbf{X}_A(t) - \mathbf{X}_{A'}(t))^2 \right\rangle$. After rather long derivations analogous to those of Ref. [10] we find that by introducing the instantaneous free energy, $\mathcal{A}(t) = \mathcal{E} - T\mathcal{S}$, we can express the equations as,

$$\frac{\zeta_b}{2}\frac{d}{dt}D_{AA'} = -\frac{2}{3}\sum_{A''}(D_{AA''} - D_{A'A''})\left(\frac{\partial \mathcal{A}}{\partial D_{AA''}} - \frac{\partial \mathcal{A}}{\partial D_{A'A''}}\right). \tag{5}$$

The entropic and energetic parts of $\mathcal{A}$ can be written as,

$$\mathcal{S} = \frac{3}{2}k_B \log \det{}' R, \qquad R_{AA'} = \frac{1}{N^2\,M^2}\sum_{BB'} D_{AB,A'B'}, \tag{6}$$

$$\begin{aligned}\mathcal{E} = {} & \frac{3k_BT\lambda}{2l^3}\sum_{n,a}(D^a_{n+1\,n} + D^a_{n-1\,n} + 2D^a_{n+1\,n,n-1\,n}) + \frac{3k_BT}{2l^2}\sum_{n,a} D^a_{n\,n-1} \\ & + \frac{3k_BT}{2L^2}M\left(\mathcal{R}^2 - \sum_a \frac{\mathcal{R}^2_a}{M}\right) + \sum_{J=2}^{\infty}\sum_{\{A\}} \frac{u^{(J)}_{\{A\}}}{(2\pi)^{3(J-1)/2}}(\det\Delta^{(J-1)})^{-3/2},\end{aligned} \tag{7}$$

where $D_{AA',BB'} = (1/2)(D_{AB'} + D_{A'B} - D_{AB} - D_{A'B'})$. We have used the notations $\Delta^{(J-1)}_{ij} \equiv D_{A_1A_{i+1},A_1A_{j+1}}$ and introduced the total, $\mathcal{R}^2 = (1/2N^2M^2)\sum_{AA'} D_{AA'}$, and the partial, $\mathcal{R}^2_a = (1/2N^2)\sum_{nn'} D^{aa}_{nn'}$, radii of gyration.

3. – Results and discussion

In Ref. [9] we have studied the GSC equations for the solution of ring homopolymers upon an additional assumption that the mean squared distances between any two monomers from different chains are all equal to each other. The phase diagram obtained in this way (Fig. 1 in Ref. [9]) has the two phase coexistence region in agreement with the standard Flory–Huggins theory. The curve of vanishing $\partial^2\mathcal{A}/\partial M^2$ there (curve II) corresponds to spinodal of two phase separation. Naturally, there are two pure states for negative $u^{(2)}$: the gas of single globules and the precipitate. The transition between the two is first order up to the semidilute regime (curve I) terminating in a critical point (A) of a liquid–gas type, then at higher concentrations the transition from the swollen coils to the precipitate becomes continuous (curve II). Note that, since we have first order transition, there are two "spinodals" (I' and I") corresponding to the transition curve (I), which

designate the boundaries of existence of the metastable precipitate and the metastable gas of single globules respectively. An important observation is that the free energy is concave with respect to M at both branches in the two phase coexistence region. Thus, we have used the Maxwell construction for both the stable and the metastable branches. While the former produces the conventional two phase coexistence picture of the high and low density phases, the latter has lead us to believe that in the region between the transition curve (I) and the lower "spinodal" (I") there appears a metastable coexistence of interacting gas of mesoglobules, obtained by collapse of a few distinct chains, with a gas of single chain globules.

Now, we are in position to prove this directly. The extended GSC method can describe formation of clusters since it is possible to distinguish the mean squared distances between various chains. In Fig. 1 we present the mean squared radius of clusters corresponding to various stationary points of Eqs. (5) for 4 chains in a box. The curves 1x4 and 4x1 correspond to the precipitate (macroglobule from 4 chains) and 4 single chain globules respectively, with I being the point of phase transition between them. Detailed analysis shows that there are also other stationary points (local minima of the free energy), such as curve 1+3 (1 single chain globule and 1 globule from three chains) and curve 2+2 (two globules from 2 chains), which are displayed as long as they exist. For a given $u^{(2)}$ these branches have a somewhat higher value of the free energy, and hence they are metastable states. The difference in the free energy values between these and thermodynamically dominant states, however, is rather small, but the barrier between them is quite high. Therefore, if the system is trapped in one of such states, it remains there for a long time. Also, it seems likely that metastable mesoglobules have a kinetic preference to be of equal size. In practice, this would lead to a rather monodisperse distribution of mesoglobule sizes, but only in a rather narrow region at low concentrations around the transition I.

In Fig. 2 we present the phase diagram at a fixed concentration for the solution of periodic (ab) copolymer with $u^{(2)}_{mm'} = \bar{u}^{(2)} + \Delta(\sigma_m + \sigma_{m'})/2$, where $\sigma_m = 1$ for even m and -1 for odd m. For small amphiphilicity parameter Δ we find a picture quite similar to the homopolymer. However, for higher values of Δ the 2+2 minimum of mesoglobules becomes the main free energy minimum in a narrow region designated as 'Mesoglobules' in Fig. 2, with the surrounding transitions to other phases being naturally first order. Such phase diagram turns out to be quite typical for other more complicated copolymer sequences. Thus, the mesoglobules that exist in the first place due to a delicate balance of the volume interactions and the entropy resisting further aggregation, are additionally stabilised by the micro–phase separation in copolymers. Their size is related to the mesoscale at which the micro–phase separation is more preferable.

Finally, we would like to comment that stabilisation of mesoglobules can occur due to many other monomer specific interactions. For example, if monomers become less sticky as the forming globule dries with the solvent being expelled from it, further coalescence of the mesoglobules becomes impeded and they would behave nearly as hard spheres. This hardening of the mesoglobules is in some sense analogous to formation of the prohibitive hydrophilic shell on the surface of copolymer globules. We believe that the entropic barriers dependent on the conformational state of the chain, i.e. the amount of water surrounding monomers, may explain the additional stabilisation of mesoglobules in PNIPAM solution.

4. – Conclusion

The formalism presented in the final form here is capable of describing mixtures of any number of heteropolymer species of arbitrary composition. Complicated microstructure is well described by the method since it distinguishes the mean squared distances between all pairs of monomers. As a practically important application of the method we have given a direct and conclusive evidence in favour of the mesoglobules and explained their size monodispersity. We have shown that the mesoglobules are long–lived metastable states for the homopolymer, but they may become thermodynamically stable for copolymers in a rather narrow region of the phase diagram at very low concentrations.

We hope that the GSC method can be useful for study of dilute and semi–dilute solutions of heteropolymers with complicated sequences. This is especially important for biotechnology for control and suppression of undesirable aggregation, what is a long standing problem. Another challenge is to understand why certain prion proteins in vivo can cause an avalanche–like misfolding of healthy proteins resulting in TSE type diseases. Undoubtedly, speaking about detailed morphologies, metastable states and kinetics of conformational transitions, there is still a huge arena for study in copolymer solutions of semiflexible chains.

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The authors acknowledge interesting discussions with Professor A.Yu. Grosberg, Professor A.R. Khokhlov and Dr A.V. Gorelov.

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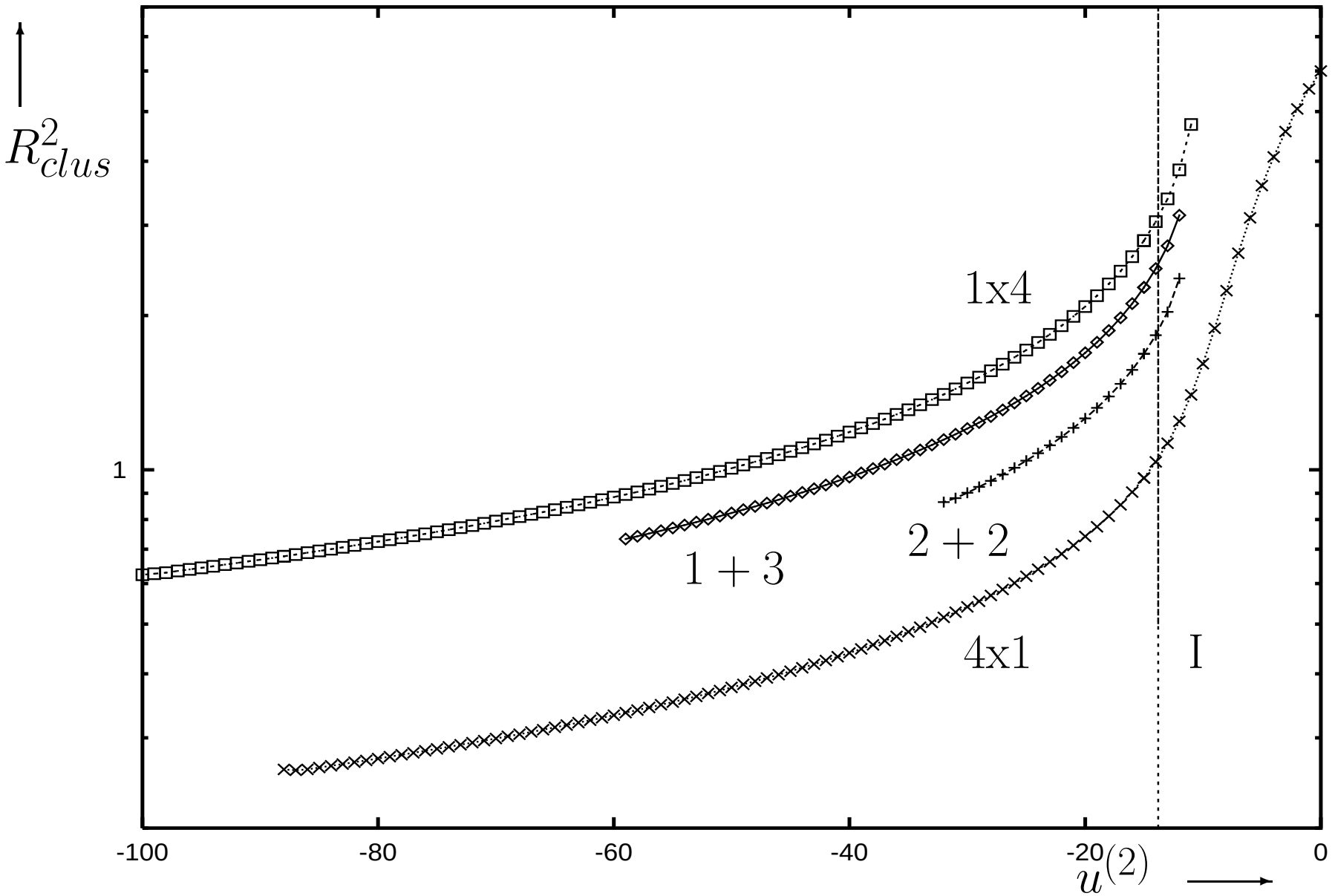

Fig. 1 Plot of the mean squared cluster size for different states. This data is obtained for open homopolymers with $N = 18$, $M = 4$, $L = 10$ and $u^{(3)} = 10$. We use the units of measurement in which $k_B T = 1$, $l = 1$ and $\zeta_b = 1$.

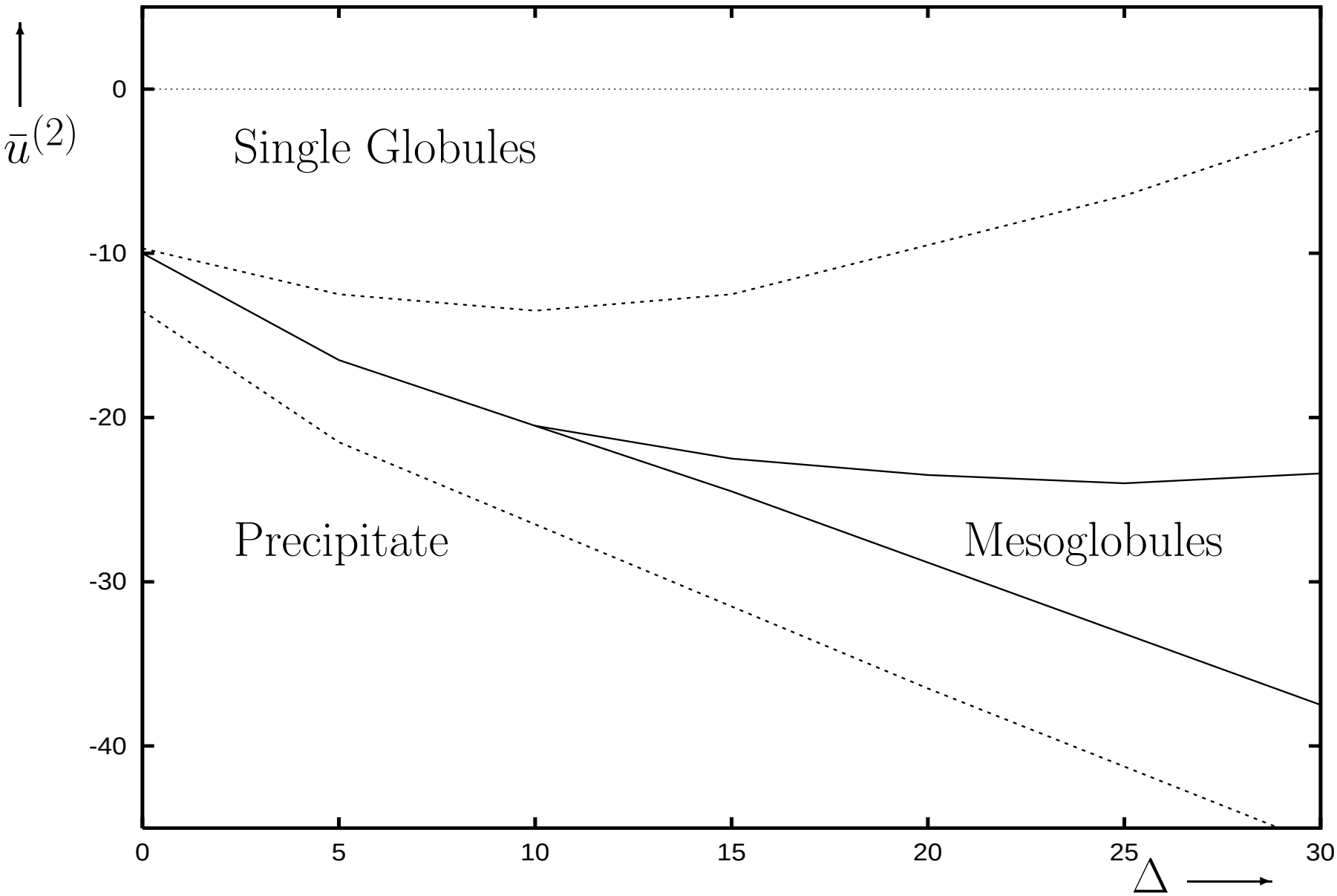

Fig. 2 Phase diagram for solutions of (ab) copolymers in variables of the amphiphilicity, Δ, and the mean second virial coefficient, $\bar{u}^{(2)}$, for polymers with $N = 18$, $M = 4$, $L = 5$ and $u^{(3)} = 10$. Only thermodynamically stable states are displayed.