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Formation of microdomains in a quenched disordered heteropolymer

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Résumé. — Nous étudions par une méthode de répliques analogue à celle utilisée pour les verres de spin un large globule ou un fondu hétéropolymérique composés d'une chaîne désordonnée de monomères de deux types (A et B). Nous montrons qu'une séparation en microphase du troisième ordre se produit quand le système des maillons A et B étirés est thermodynamiquement incompatible. Une structure périodique de domaines riches en A et B se forme et la symétrie de cette phase dépend des fractions de monomères A et B. Quand cette fraction vaut 0,5, la structure lamellaire est favorisée.

Abstract. — A replica trick similar to that used in spin glass theory is implemented to study a structure of large heteropolymeric globule or a heteropolymeric melt with random quenched sequence of monomers of two types (A and B). It is shown that a microphase separation third order phase transition occurs when the system of torn A and B links becomes thermodynamically incompatible. A periodic structure of A- and B-rich domains is formed, and the symmetry of this phase depends on the fraction of A and B monomers. When this fraction is 0.5 the lamellar structure is favored.

1. Introduction.

Microphase separation is a well-known effect for polymeric systems. It has been investigated for block-copolymers composed of alternating long homopolymeric blocks poly-A-poly-B [1-3]. Formation of domain microstructure of different types — lamellar, hexagonal, etc. was shown in such systems both theoretically [1, 2] and experimentally [3].

Random copolymers composed of links of two types are very important for biological applications. The most remarkable feature of amino acid residues in proteins is their polarity. Water is a poor solvent for unpolar (hydrophobic) groups and a good solvent for polar (hydrophilic) groups. This causes segregation of unpolar groups from water in protein structures, and this segregation determines principal structural features of proteins such as globularity, formation of hydrophobic cores of protein domains, formation and stabilisation of amphiphilic α-helices and β-strands [4].

Such random heteropolymers were investigated in [5-7]. The behaviour in the vicinity of θ-point was investigated in [5, 6] and the size of a chain was determined there. Most important for protein application is the globular state of such heteropolymers; it was considered in [7], where it has been argued that the « two-letter » case of heteropolymer is the analog of Mattis
glass within the framework of spin-glass approach to the protein theory [8-11]. The « Mattis case » means complete recovering of the native state from the sequence of A and B links [7] as it is in the Hopfield model of associative memory with one remembered pattern [12]. In this paper we put forward another point of view that two letter encoded heteropolymer forms under definite conditions regular domain structure with regions enriched with A and B monomers. As regards recovering the native structure which is determined by definite chain fold, the « two-letter » code seems to be not sufficient, at least for large enough chains.

2. The model and mean field approximation.

Consider a heteropolymer of polymerisation index $N$ composed of links of two types positioned randomly along the chain. The sequence of links is described by a random process $\{\sigma(\tau)\}$ where $\sigma(\tau) = 1$ if the link $\tau$ is of type A and $\sigma(\tau) = -1$ if the link $\tau$ is of type B. The sequence $\{\sigma(\tau)\}$ may be interpreted as the primary structure of the chain.

Three types of two body interactions A-A, A-B, B-B are possible. It leads to general form of two-body interaction constant between arbitrarily chosen links $\tau$ and $\tau'$ [5-7]:

$$B(\tau, \tau') = B_0 + A(\sigma(\tau) + \sigma(\tau')) + \chi \sigma(\tau) \sigma(\tau').$$

(1)

Most non-trivial effects occur when $\chi \neq 0$. However, the last term in the r.s.p. of (1) was omitted in [5, 6], in contrast, we shall concentrate our attention on this term which leads to separation of A and B links; therefore we shall take $A = 0$ for simplicity. Moreover, we assume that A and B links appear in the sequence with equal probability.

The representation (1) was used in [7] to introduce order parameters:

$$\rho(r) = \int_0^N d\tau \delta(r(\tau) - r)$$

and

$$m(r) = \int_0^N d\tau \sigma(\tau) \delta(r(\tau) - r)$$

where $r(\tau)$ is the space position of the link with number $\tau$. These order parameters correspond to density of links of any type and the difference of densities of links of A type and B type, i.e. separation of links of different types. It can be seen easily that $\rho_A(r) = (\rho(r) + m(r))/2$ and $\rho_B(r) = (\rho(r) - m(r))/2$.

It is convenient now to express the partition function in terms of order parameters $\rho(r)$ and $m(r)$:

$$Z = \int D\rho(r) Dm(r) \exp\left(-\frac{F[\rho, m]}{T}\right)$$

(2)

here $F[\rho, m] = E[\rho, m] - TS[\rho, m]$, $T$ is the temperature. Further on, we shall take temperature to the unity and omit it from the equations. $E[\rho, m]$ is the « energy » corresponding to order parameters $\rho(r)$ and $m(r)$. $E[\rho, m]$ does not depend on sequence of links and it can be expressed through thermodynamic functions of a system of teared links [13]:

$$E[\rho, m] = F_0[\rho, m] - F_{id}[\rho, m]$$

where $F_0$ is the free energy of the system of teared monomers A and B and $F_{id}$ is the ideal gas contribution to the free energy:

$$F_{id}[\rho, m] = \int dr [\rho_A \ln (\rho_A/e) + \rho_B \ln (\rho_B/e)]$$

(3)
$E[p, m]$ can be obtained as Landau expansion:

$$E[m, \rho] = \frac{1}{2} B_0 \int \rho^2(r) \, d^3r + \frac{1}{6} C \int \rho^3(r) \, d^3r + \frac{1}{2} \int d^3r \{ \chi m^2(r) + c^2(\nabla m(r))^2 \} + \cdots$$  \hspace{1cm} (4)

Here $C$ is the three-body interaction constant which is assumed to be independent of link types; it describes steric repulsion. $c$ describes surface tension between $A$ and $B$ melts. Being interested in globular case we take $B_0$ to be negative and sufficiently large so that the globule is so dense that it is $A-B$ melt. The approximation of incompressibility can be applied which yields $\rho(r) = \text{const}$ inside the globule and $\rho(r) = 0$ outside it. We shall see later that in the vicinity of separation transition $\rho(r)$ is small. Therefore we may take:

$$E[m, \rho] = E_0 + \frac{1}{2} \int d^3r \{ \chi m^2(r) + c^2(\nabla m(r))^2 \} = E[m].$$  \hspace{1cm} (4a)

$S[m, \rho]$ is the entropy which corresponds to the number of chain passways which lead to given $m(r)$ and $\rho(r)$. It is given by:

$$S[\rho, m] = \ln \int D\tau \exp \left\{ - (1/2 a^2) \int_0^N (\partial r/\partial \tau)^2 \, d\tau \right\} \delta \left[ \rho(r) - \int_0^N d\tau \delta(r(\tau) - r) \right] \times$$

$$\times \delta \left[ m(r) - \int_0^N d\tau \sigma(\tau) \delta(r(\tau) - r) \right]$$  \hspace{1cm} (5)

here $a$ is the length of a chemical bond. The exponential term in the r.s.p of (5) describes elastic polymeric energy. Due to the entropic term the dependence on sequence of monomers arises. Calculation of the averaged free energy is done by the use of replica trick (see, e.g. [14]):

$$\langle F \rangle_{\text{av}} = - \langle \ln Z \rangle_{\text{av}} = - \lim_{n \to 0} [ (\langle Z^n \rangle_{\text{av}} - 1)/n ]$$  \hspace{1cm} (6)

where $\langle \rangle_{\text{av}}$ denotes averaging over all sequences of monomers. The independence of energy on the sequence of links makes it possible to yield $\langle Z^n \rangle_{\text{av}}$:

$$\langle Z^n \rangle_{\text{av}} = \left( \prod_{a=1}^\alpha [D\rho_a(r) \, Dm_a(r)] \exp \left\{ - \sum_a E[\rho_a, m_a] + S_{\text{eff}}[\rho_a, m_a] \right\} \right)_{\text{av}}$$  \hspace{1cm} (7)

where $\alpha$ is the replica index ($\alpha = 1, 2, \ldots, n$); $S_{\text{eff}}[\rho_a, m_a] = \ln \left( \exp \left\{ \sum_a S[\rho_a, m_a] \right\} \right)_{\text{av}}$ is the effective entropy which is determined by sets $\{m_a\}, \{\rho_a\}$.

Calculation of $S_{\text{eff}}$ can be done by the method introduced in [13] and applied in [10] within a framework of replica method. The direct way is to introduce external fields $\varphi_a(r)$ and $\vartheta_a(r)$ conjugated to $\rho_a(r)$ and $m_a(r)$. Consider a value:

$$Z_n[\varphi_a, \vartheta_a] = \left( \prod_{a=1}^\alpha D\varphi_a(\tau) \exp \left[ - (1/2 a^2) \sum_a \int_0^N (\partial \varphi_a / \partial \tau)^2 \, d\tau - \sum_a \int_0^N \varphi_a(\vartheta_a(\tau)) \, d\tau - \right.$$

$$- \sum_a \int_0^N \sigma(\tau) \vartheta_a(\vartheta_a(\tau)) \, d\tau \right)_{\text{av}}$$  \hspace{1cm} (8)
which has the meaning of partition function of $n$ identical chains in external field averaged over all realisations of $\sigma(\tau)$. The external field acting on a link $\tau$ is $\varphi_\alpha(r) + \sigma(\tau) \vartheta_\alpha(r)$. This partition function is easily expressed through macroscopic parameters $m(r)$ and $\rho(r)$:

$$Z_n[\varphi_\alpha, \vartheta_\alpha] = \int \prod_{\alpha=1}^n [D\rho_\alpha(r) Dm_\alpha(r)] \times$$

$$\times \exp \left\{ - \sum_\alpha \int_0^N \left[ \varphi_\alpha(r) \rho_\alpha(r) + \vartheta_\alpha(r) m_\alpha(r) \right] dr + S_{\text{eff}}[\rho_\alpha, m_\alpha] \right\}. \quad (9)$$

Macroscopic parameters $m_\alpha$ and $\rho_\alpha$ are low-fluctuating for globular chains [13] which makes it possible to substitute r.s.p. of (9) by the saddle-point value of the integrand:

$$\ln Z_n = - \sum_\alpha \int_0^N \left[ \varphi_\alpha(r) \rho_\alpha(r) + \vartheta_\alpha(r) m_\alpha(r) \right] dr + S_{\text{eff}}[\rho_\alpha, m_\alpha]. \quad (10)$$

Saddle point values of $m$ and $\rho$ are determined by equations:

$$\rho_\alpha(r) = - \delta \ln Z_n/\delta \varphi_\alpha(r) \quad m_\alpha(r) = - \delta \ln Z_n/\delta \vartheta_\alpha(r). \quad (11)$$

Therefore, it is sufficient to find the partition function in the external field (8) in order to determine the entropy $S_{\text{eff}}$.

Averaging in (8) is done easily when $\sigma(\tau)$ are statistically independent for different $\tau$. We assume for simplicity that monomers of each type appear with equal probability which is 1/2 in the case of A-B heteropolymer. In this case:

$$Z_n[\varphi_\alpha, \vartheta_\alpha] = \int \prod_{\alpha=1}^n Dr_\alpha(\tau) \exp \left\{ - \frac{1}{2} a^2 \sum_\alpha \int_0^N (\partial r_\alpha/\partial \tau)^2 d\tau - \sum_\alpha \int_0^N \varphi_\alpha(r_\alpha(\tau)) d\tau + \int_0^N d\tau \ln \left\{ \text{ch} \left( \sum_\alpha \vartheta_\alpha(r_\alpha(\tau)) \right) \right\}. \quad (12)$$

To find this value a ground state dominance approximation can be used which yields:

$$Z_n = \exp (-\lambda N) \quad (13)$$

where $\lambda$ is the smallest eigenvalue of the equation:

$$a^2 \Delta \psi + \lambda \psi = \left\{ \sum_\alpha \varphi_\alpha(r_\alpha) - \ln \left[ \text{ch} \left( \sum_\alpha \vartheta_\alpha(r_\alpha) \right) \right] \right\} \psi \quad (14)$$

and $\psi$ is the function of $n$ space vectors $\{r_1, r_2, \ldots, r_n\}$; $\Delta \equiv \sum_{\alpha=1}^n \partial^2/\partial r^2_\alpha$.

Our aim now is to obtain the expansion of entropy in powers of $m$ considering it to be small in the vicinity of transition point (see below). It can be done if we consider « interaction term » $\ln \left[ \text{ch} \left( \sum_\alpha \vartheta_\alpha(r_\alpha) \right) \right]$ in (14) as a perturbation. Expansion of $\lambda$ up to the second order of interaction yields:

$$\lambda = \sum_{\alpha=1}^n \bar{\varphi}_\alpha(k=0) - \sum_{\alpha=1}^n \sum_{k \neq 0} (a^2k^2)^{-1} \bar{\varphi}_\alpha(k) \bar{\varphi}_\alpha(-k) - \frac{1}{4} \sum_{\alpha \neq \beta} \sum_{k_1 \neq 0, k_2 \neq 0} [a^2(k_1^2 + k_2^2)]^{-1} \times \bar{\vartheta}_\alpha(k_1) \bar{\vartheta}_\alpha(-k_1) \bar{\vartheta}_\beta(k_2) \bar{\vartheta}_\beta(-k_2) \quad (15)$$
where \( \phi_\alpha (r) = \varphi_\alpha (r) - \frac{1}{2} \vartheta_\alpha^2 (r) \) and the standard Fourier transformation is used:

\[
\vartheta_\alpha (k) = V^{-1} \int d^3r \exp (ikr) \vartheta_\alpha (r) .
\]

Using (11), (12) and (15) we may express « external fields » \( \varphi \) and \( \rho \) through macroscopic parameters to the same order. The condition of incompressibility means that \( \tilde{\varphi}_\alpha (k) = 0 \) for \( k \neq 0 \) while for \( \tilde{\vartheta}_\alpha (k) \) we obtain:

\[
\tilde{\vartheta}_\alpha (k) = - \rho^{-1} m_\alpha (k) \left[ 1 + \rho^{-2} \sum_{k'=0} \sum_\beta \left[ a^2 (k^2 + k'^2) \right] m_\beta (k') m_\beta (-k') \right] . \tag{16}
\]

where ' means summation over all \( \beta \neq \alpha \). Substituting (16) to (15) and (10) we finally obtain:

\[
S_{\text{eff}} [\rho_\alpha, m_\alpha] = - V \left\{ \left( 2 \rho \right)^{-1} \sum_{\alpha = 1}^n \sum_{k \neq 0} m_\alpha (k) m_\alpha (-k) - \right. \\
\left. - (4 \rho^3)^{-1} \sum_{\alpha \neq \beta} \sum_{k_1, k_2 \neq 0} \left[ a^2 (k_1^2 + k_2^2) \right]^{-1} m_\alpha (k_1) m_\alpha (-k_1) m_\beta (k_2) m_\beta (-k_2) \right\} . \tag{17}
\]

This expression has a simple physical meaning. The first term in the r.s.p. of (17) corresponds to the entropy decrease of the phase separation in the mixture of teared A and B links, while the second term describes the chain effect and takes into account the quenched disorder in the distribution of A and B links on the sequence. This term corresponds to the replica interactions and changes sign when \( n < 1 \).

Combining equation (3) for the energy and equation (17) for the entropy we obtain for the free energy:

\[
F [m_\alpha] = V \left\{ \frac{1}{2} \sum_{\alpha = 1}^n \sum_{k \neq 0} \left( c^2 k^2 - b^2 \right) m_\alpha (k) m_\alpha (-k) - k_B T \left( 4 \rho^3 \right)^{-1} \sum_{\alpha \neq \beta} \sum_{k_1, k_2 \neq 0} \left[ a^2 (k_1^2 + k_2^2) \right]^{-1} m_\alpha (k_1) m_\alpha (-k_1) m_\beta (k_2) m_\beta (-k_2) \right\} . \tag{18}
\]

where \( b^2 = - \chi - \rho^{-1} \). It can be seen from (18) that a separation transition takes place when \( b^2 > 0 \) i.e. when \( \chi \rho < -1 \). This is the condition of separation in a system of teared links. When \( b^2 > 0 \) the free energy functional (18) can be rewritten in dimensionless variables:

\[
F [\mu_\alpha] = V \rho^3 a^2 b^6 c^{-2} \left\{ \frac{1}{2} \sum_{\alpha = 1}^n \sum_{q \neq 0} \left( q^2 - 1 \right) \mu_\alpha (q) \mu_\alpha (-q) - \right. \\
\left. - \frac{1}{4} \sum_{\beta \neq \alpha} \sum_{q_1, q_2 \neq 0} \left( q_1^2 + q_2^2 \right)^{-1} \mu_\alpha (q_1) \mu_\alpha (-q_1) \mu_\beta (q_2) \mu_\beta (-q_2) \right\} . \tag{18a}
\]

where \( \mu_\alpha = m_\alpha c (\rho^{-3} ab^{-2})^{-1} \). Some qualitative conclusions can be done right now. Taking dimensionless variables \( \mu \) and \( q \) of the order 1 we obtain the characteristic scale of microphase separation (MPS) \( R \sim k^{-1} \sim b^{-1} \) and amplitude \( m \sim b^2 \). The free energy per unit volume \( F/V \sim b^6 \). Therefore in the vicinity of transition \( (b \ll 1) \) we obtain large scale and weak MPS with continuous behaviour of the order parameter \( m \). This justifies the applied perturbation expansion for a determination of the lowest eigenvalue \( \lambda \) of the equation (14).
It should be noted that the functional (18a) is expressed through the following combinations of \( \mu_a(q) \):

\[
M_a(q) = \left( \sum_q \Delta(|q| - q) \mu_a(q) \mu_a(-q) \right)^{1/2}.
\]  

(19)

Where \( \Delta \) is Kronecker delta. \( M_a(q) \) is a function of scalar variable — the length \( q \) of the wave vector \( q \). The free energy functional (18a) is expressed very simply through \( M \):

\[
f[M_a] = \frac{1}{2} V \rho^3 a^2 b^6 c^{-2} \left\{ \sum_{\alpha = 1, q \neq 0} (q^2 - 1) M^2_\alpha(q) - \frac{1}{2} \sum_{\alpha \neq \beta, q_1, q_2 \neq 0} (q^2_1 + q^2_2)^{-1} M^2_\alpha(q_1) M^2_\beta(q_2) \right\}.
\]

(20)

Variation of this functional relative to \( M_a(q) \) yields:

\[
M_a(q) \left\{ (q^2 - 1) - \sum_\beta' \sum_{q_1 \neq 0} (q^2 + q^2_1)^{-1} M^2_\beta(q_1) \right\} = 0.
\]

(21)

One of the solutions of this equation is:

\[
M_a(q) = M_0 \Delta(q - q_0)
\]

(22)

where \( M_0 \) and \( q_0 \) are constants independent of replica indices. Substituting (22) into (20) and minimising it we finally obtain:

\[
q_0 = 1/\sqrt{3} \quad \text{and} \quad M_0 = 2/3.
\]

(23)

In order to investigate the stability of the obtained solution it is necessary to find the second variation of the free energy functional (20):

\[
\delta^2 f / \delta M_\alpha(q_1) \delta M_\beta(q_2) = \delta_{\alpha\beta} \Delta(q_1 - q_2) \left\{ (q^2_1 - 1) - \sum_\beta' \sum_{q_1 \neq 0} (q^2 + q^2_1)^{-1} M^2_\beta(q) \right\} + (\delta_{\alpha\beta} - 1) 2(q^2_1 + q^2_2)^{-1} M_\alpha(q_1) M_\beta(q_2).
\]

(24)

Substitution of the solution (22), (23) into (24) yields:

\[
\delta^2 f / \delta M_\alpha(q_1) M_\beta(q_2) = \delta_{\alpha\beta} \Delta(q_1 - q_2)(q^2_1 - q^2_0)(q^2_1 + q^2_0) + (\delta_{\alpha\beta} - 1) q^2_0 M^2_\alpha \Delta(q_1 - q_0) \Delta(q_2 - q_0).
\]

(25)

It is easy to see that all eigenvalues of the matrix (25) become positive when \( n \to 0 \). This means that the replica-symmetric solution (22, 23) is stable, i.e. it corresponds to the free energy minimum.

We come to the conclusion that any solution for the order parameter has the form:

\[
\mu_a(q) = \sum_{i = 1}^t A_i \Delta(q - q_i)
\]

(26)

where \( |q_i| = q_0 \) and \( \sum_{i = 1}^t A_i^2 = M^2_0 \). In order to find \( q_i \) and \( A_i \) it is necessary to take into account higher order terms in the expansion of free energy. Calculations analogous to those done in
[2] show that in our case when the concentrations of A and B-monomers are equal the minimal free energy is reached for \( f = 2 \), i.e. the solution is given by:

\[
\mu_\alpha (q) = \frac{1}{2} M_0 [\Delta (q - q^*) + \Delta (q + q^*)]
\]

where \( q^* \) is arbitrary vector having length \( q_0 \). Finally we obtain in the \( r \)-space:

\[
m_\alpha (r) = \frac{2}{3} b^2 a \rho^{3/2} c^{-1} \sin [(r \epsilon) bc^{-1}]
\]

where \( \epsilon \) is arbitrary unit vector. The result (28) is valid when \( q_0 a \ll 1 \) or \( abc^{-1} \ll 1 \). The structure (28) is of lamellar type. Free energy of the system is given by:

\[
\langle F \rangle_{av} = \frac{2}{27} V \rho^3 a^2 b^6 c^{-1}.
\]

3. Discussion.

We have shown the possibility of formation of domain structure in random copolymers. Very long macromolecules or polymeric melts will form a regular pattern of A- and B-rich domains. When the average numbers of A and B links are equal, the structure is of lamellar type while if these numbers are not equal, the structure is of micellar type. This is clear from qualitative considerations also. Indeed the quasionedimensional lamellar structure with equal volumes of A and B-rich blocks is natural for the case when the number of A and B monomers are equal.

The mathematical and physical reasons of the formation of periodic structures are quite unusual and differ from those in block copolymers. The stabilisation for large wave vectors \( k \), or for small sizes of domains is usual: it is due to the surface tension between A and B-rich domains. However, the stabilisation for small \( k \), or in other words, against large scale macroseparation is ensured by the fourth-order term in equation (18) which originates from polymeric entropy. It is very important that the fourth order term in equation (18) contains order parameters \( m_\alpha \) with different replica indices \( \alpha \) and \( \beta \), i.e. this term reflects the interactions between different replicas. It is well known [14] that this interaction is the mathematical reflection of quenched disorder. Therefore we come to the natural physical conclusion that the effect of quenched disorder prevents the system from macrophase separation.

It is worth mentioning that the described MPS transition is of the third order (free energy in Eq. (20) is proportional to \( (b^2)^3 \)). This is due to the fact that in the vicinity of the transition, the order parameter is characterised by two small parameters: the amplitude which is proportional to \( b^2 \) and the wave vector \( k \) which is proportional to \( b \).

All the above calculations and conclusions have been done within the framework of perturbation theory which assumes that the order parameters \( m_\alpha \) are small. This is confirmed by the final results which demonstrate the continuous behaviour of these order parameters. However, this consideration is unapplicable for the case when separation takes place on small scales, i.e. when \( k_0 a \gg 1 \) and the order parameters \( \rho \equiv m \) which is the case for complete exclusion of A-links from B-blocks and vice versa. Therefore, we cannot exclude the possibility that there exists another free energy minimum which corresponds to the described complete separation. Moreover, it is possible that the transition to this completely separated state may occur before the described continuous transition and in this case the MPS transition must be of the first order. We would like to emphasize only that these two possible transition scenarios are governed by different sets of parameters since for a high degree of segregation
the simple Landau-type expansion [3] fails and another phenomenological presentation of energy must be used; this presentation will contain other energetic parameters which describe interactions on microscopic scales.

It is interesting to compare MPS in statistical heteropolymers and in block-copolymers. The peculiar feature of MPS in block-copolymers is that there exists a definite large scale — the size of a block and this scale becomes the scale of a domain in mesophase. The MPS transition is of the first order and the size of domains coincides with this definite scale. It is very important that this size does not depend on the Flory parameter of separation $\chi$. In the case of random heteropolymers, there does not exist any predefined scale and the MPS transition is continuous (it is the third order phase transition!). It is remarkable that the regular lattice of domains appears in random heteropolymers and the size of domains strongly depends on the Flory parameter. The reason for the appearance of such a regular lattice is due to the fluctuational occurrence of A-rich and B-rich parts of the sequence which facilitates segregation on some definite scale.

It seems interesting to test these results either experimentally (using melts of random copolymers) or by numerical simulations.

References