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Influence of hydrodynamics on the dynamics of a homopolymer

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Abstract. We present an analytical approach of the dynamics of a polymer when it is quenched from a θ solvent into a good or bad solvent. The dynamics is studied by means of a Langevin equation, first in the absence of hydrodynamic effect, then taking into account the hydrodynamic interactions with the solvent. The variation of the radius of gyration is studied as a function of time. In both cases, for the first stage of collapse or swelling, the evolution is described by a power law with a characteristic time proportional to $N^{4/3}$ (N), where N is the number of monomers, without (with) hydrodynamic interactions. At larger times, scaling laws are derived for the diffusive relaxation time.

PACS. 75.10.Nr Spin-glass and other random models – 64.70.Pf Glass transitions – 71.55.Jv Disordered structures; amorphous and glassy solids

1 Introduction

The protein folding problem, and more precisely the dynamics of a protein as it collapses from a denatured state to its native state is still not well understood. At a simpler level, there are at present very few analytical models for the dynamics of the collapse of a homopolymer as it is put into bad solvent conditions.

Moreover, since one might expect the first stages of protein folding to be dominated by non-specific hydrophobic forces, this phenomenon should be quite similar to the collapse of a homopolymer chain.

Experimentation in this field is quite difficult [1]. However some promising results have been obtained by Hagen *et al.* [2]; based on optical techniques, these experiments can monitor protein folding up to the microsecond time-scale.

On the theoretical side, various models have been proposed and a lot of numerical work has been done.

According to de Gennes' theory [3], the process of collapse of a flexible coil leads to the formation of crumples on a minimal scale along the linear chain, which thickens and shortens under diffusion of the monomers, then forms new crumples of growing scale, until the final state of a compact globule is reached. In a refined model, Dawson *et al.* [4] consider a different two steps mechanism: first a fast formation of "pearls" along the chain, followed by a slower stage of compaction. This model has been revisited by Buguin *et al.* [5] who estimate the total time of collapse as $\tau_c = \frac{\eta a^3}{k_B\theta}\left(\frac{\theta}{|\Delta T|}\right)^4 N$ where η is the viscosity of the solvent, θ is the θ temperature, a is the monomer size and ΔT is the temperature quench. This time τ_c depends linearly on the molecular weight. For the case of proteins (see reference [2]), $N = 300$, which yields a collapse time of $\tau_c \sim$ a few ms.

Grosberg *et al.* [6] have included the role of self entanglement to de Gennes' model, and consider a two stage mechanism: first a collapse leading to a crumpled globule with characteristic time $\sim N^2$, and then a chain knotting driven by reptation with a longer characteristic time $\sim N^3$.

Monte-Carlo studies [7,8] and Langevin dynamics simulations [9] lead to diverging interpretations concerning the mechanisms of collapse.

In a series of articles, Timoshenko *et al.* [10] have developed an alternative theory based on a self-consistent method using Langevin equations that can be analyzed numerically; kinetics laws for the collapse of a homopolymer are obtained with or without hydrodynamics, at early and later stages. Another approach, concerning the collapse of a stiff chain can be found in [11].

In this article, we first recall the analytical technique already presented in [12] (Sect. 2). Then we apply it to the dynamics of the swelling or collapse of a homopolymer chain, first without (Sect. 3), then with hydrodynamic interactions (Sect. 4), and obtain in each case the behaviour of the radius of gyration as a function of time.

2 Summary of the method

We consider a homopolymer chain in a θ solvent – *i.e.* a Gaussian coil – consisting of N monomers, obeying the

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Langevin dynamics as the chain is quenched into good or bad solvent conditions (Eqs. (1, 2)).

Let's first neglect all hydrodynamic interactions, then the equations of motion for the system read:

$$\frac{\partial r}{\partial t} = -\Gamma_0 \frac{\partial H}{\partial r} + \eta(s,t) \tag{1}$$

$$H = \frac{k_B T}{2a_0^2}\int_0^N \left(\frac{\partial r}{\partial s}\right)^2 ds + k_B T V(r(s,t)) \tag{2}$$

where N is the total number of monomers, $r(s,t)$ is the position of monomer s in the chain, a_0 is the monomer length and $\Gamma_0 = \frac{D}{k_B T}$, D is the diffusion constant of a monomer in the solvent and $k_B T$ is the temperature. The intra-molecular as well as intermolecular interactions of the chain are contained in the potential $V(r(s,t))$. The thermal noise $\eta(s,t)$ is a Gaussian noise with zero mean and correlation given by:

$$\langle \eta(s,t)\eta(s,t')\rangle = 2D\delta(t-t').$$

The method consists in finding a virtual homopolymer chain which obeys a simpler Langevin equation, chosen so that its radius of gyration best approaches the radius of gyration of the real chain at each time t.

The virtual chain, defined by $r^{(v)}(s,t)$ is chosen to satisfy the Langevin equation:

$$\frac{\partial r^{(v)}}{\partial t} = -\Gamma_0 \frac{\partial H_v}{\partial r^{(v)}} + \eta(s,t) \tag{3}$$

$$H_v = \frac{k_B T}{2a^2(t)}\int_0^N \left(\frac{\partial r^{(v)}}{\partial s}\right)^2 ds \tag{4}$$

with the same friction coefficient and noise as the original equation, but with a much simplified Hamiltonian H_v. Indeed this Hamiltonian H_v represents a Gaussian chain, but with a time dependent Kuhn length $a(t)$.

Our method is a generalization of Edwards' Uniform Expansion Model [13] to dynamics, as has already been explained in [12]. This method works well for statics, and gives the Flory radius for a polymer in good solvent. The method is quite reliable, since it leads to the correct exponent to all orders of the expansion. We can assume that it will have the same degree of reliability in the case of dynamics, although we haven't tested it yet.

Let's define

$$\chi(s,t) = r(s,t) - r^{(v)}(s,t)$$
$$W = H - H_v.$$

Assuming that (3) is a good approximation to (1) , $\chi(s,t)$ and W can be regarded as small, and to first order in these quantities, the dynamical equations become:

$$\frac{\partial r^{(v)}}{\partial t} = \frac{D}{a^2(t)}\frac{\partial^2 r^{(v)}}{\partial s^2} + \eta(s,t) \tag{5}$$

$$\frac{\partial \chi}{\partial t} = \frac{D}{a^2(t)}\frac{\partial^2 \chi}{\partial s^2} + D\left(\frac{1}{a_0^2} - \frac{1}{a^2(t)}\right)\frac{\partial^2 r^{(v)}}{\partial s^2} + DF(r^{(v)}(s,t)) \tag{6}$$

where $F(r(s,t)) = -\frac{\partial V}{\partial r(s,t)}$ is the driving force for the swelling or collapse of the chain.

More precisely, in the following, for a chain in a good solvent, we will consider excluded volume interactions:

$$V(r(s,t)) = V_2(r(s,t)) = \frac{v}{2}\int_0^N ds \int_0^N ds' \delta(r(s,t) - r(s',t))$$

and for a chain in a bad solvent, we will take attractive two-body interactions and repulsive three-body interactions:

$$V(r(s,t)) = -V_2(r(s,t)) + V_3(r(s,t))$$

$$V(r(s,t)) = -\frac{v}{2}\int_0^N ds \int_0^N ds' \delta(r(s,t) - r(s',t)) + \frac{w}{6}\int_0^N ds \int_0^N ds' \int_0^N ds'' \delta(r(s,t) - r(s',t))\delta(r(s',t) - r(s'',t)),$$

where $v > 0$ and $w > 0$.

In this approximation, the radius of gyration of the chain becomes:

$$R_g^2(t) = \frac{1}{N}\int_0^N \langle r^2(s,t)\rangle ds \tag{7}$$

$$\simeq \frac{1}{N}\int_0^N \langle ((r^{(v)})^2(s,t) + 2r^{(v)}(s,t)\chi(s,t))\rangle ds. \tag{8}$$

The brackets denote the thermal average (that is an average over the Gaussian noise $\eta(s,t)$). Our approximation consists in choosing the parameter $a(t)$ in such a way that the first order in (8) vanishes:

$$\int_0^N \langle r^{(v)}(s,t)\chi(s,t)\rangle = 0$$

or in Fourier coordinates:

$$\sum_{n\neq 0} \langle \tilde{r}_n^{(v)}(t)\tilde{\chi}_n^*(t)\rangle = 0 \tag{9}$$

where the Fourier transform is given by:

$$\begin{cases} \tilde{r}_n(t) &= \frac{1}{N}\int_0^N e^{i\omega_n s} r(s,t) ds \\ r(s,t) = \sum_{n\neq 0} e^{-i\omega_n s}\tilde{r}_n(t). \end{cases}$$

We have used periodic boundary conditions, so that $\omega_n = \frac{2\pi n}{N}$. In addition, to get rid of the center of mass diffusion, we constrain the center of mass of the system to remain at fixed position, $\tilde{r}_0(t) = \tilde{r}_0^{(v)}(t) = \tilde{\chi}_0(t) = 0$.

Equations (5, 6) can easily be solved in Fourier space. We assume that at time $t = 0$, the chains are in a θ solvent, so that the initial condition $\{r(s,0)\}$ obeys Gaussian statistics. We choose the initial virtual chain to coincide with the real one, so that $r^{(v)}(s,0) = r(s,0)$ for any s. Denoting by $\overline{\cdots}$ the average over the initial conditions,

$$\frac{1}{a_0^2}-\frac{1}{a^2}=\frac{vN^3}{4\pi^2}\frac{\sum_{n\geq 1}\frac{1}{n^2}\int_0^1 du\int_0^t d\tau\frac{1-\cos 2\pi nu}{\alpha(\tau,u)^{1+\frac{d}{2}}}\left(a^2e^{-2A_n(t-\tau)}+(a_0^2-a^2)e^{-2A_nt}\right)}{\sum_{n\geq 1}\left(a^2\frac{1-e^{-2A_nt}}{2A_n}+(a_0^2-a^2)te^{-2A_nt}\right)} \tag{13}$$

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the correlation function of $r(s,0)$ (in Fourier space) is taken as:

$$\begin{aligned}\overline{\tilde{r}_n(0)}&=0\\ \overline{\tilde{r}_n(0)\tilde{r}_m^*(0)}&=\frac{a_0^2}{N\omega_n^2}\delta_{mn}.\end{aligned}$$

In Fourier space, the thermal noise is characterized by:

$$\begin{aligned}\langle\tilde{\eta}_n(t)\rangle&=0\\ \langle\tilde{\eta}_n(t)\tilde{\eta}_m^*(t')\rangle&=\frac{2D}{N}\delta_{nm}\delta(t-t').\end{aligned}$$

Replacing $\tilde{r}_n^{(v)}(t)$ and $\tilde{\chi}_n^*(t)$ by their expression in (9), and taking thermal and initial condition averages, we obtain an implicit equation for $a(t)$.

In order to take into account the hydrodynamic interactions with the solvent, one has to modify the Langevin equations in the following way [16]; equations (1, 3) have to be replaced by:

$$\frac{\partial r(s,t)}{\partial t}=\int_0^N ds'\mathbf{O}(r(s,t)-r(s',t))\times\left[-\frac{\partial H}{\partial r(s',t)}+\eta(s',t)\right] \tag{10}$$

$$\frac{\partial r^{(v)}(s,t)}{\partial t}=\int_0^N ds'\mathbf{O}(r^{(v)}(s,t)-r^{(v)}(s',t))\times\left[-\frac{\partial H_v}{\partial r^{(v)}(s',t)}+\eta(s',t)\right] \tag{11}$$

where $\mathbf{O}(r)$ is the Oseen tensor:

$$\mathbf{O}_{\alpha\beta}(r)=\frac{1}{8\pi\eta r}\left(\delta_{\alpha\beta}+\frac{r_\alpha r_\beta}{r^2}\right),$$

and η is the viscosity of the solvent.

3 Derivation of $\mathrm{R_g(t)}$ without hydrodynamic interactions

In this section, we neglect all hydrodynamic interactions and consider only two-body and three-body interactions between monomers.

Taking the Fourier transform of (5, 6), we obtain:

$$\frac{\partial\tilde{r}_n^{(v)}}{\partial t}=-\frac{D}{a^2(t)}\omega_n^2\tilde{r}_n^{(v)}+\tilde{\eta}_n$$

$$\frac{\partial\tilde{\chi}_n}{\partial t}=-\frac{D}{a^2(t)}\omega_n^2\tilde{\chi}_n-D\omega_n^2\left(\frac{1}{a_0^2}-\frac{1}{a^2(t)}\right)\tilde{r}_n^{(v)}+D\tilde{F}_n(r^{(v)}).$$

The solutions of these equations can be written in the form:

$$\tilde{r}_n^{(v)}(t)=\tilde{r}_n^{(v)}(0)e^{-D\omega_n^2f(t)}+\int_0^t d\tau e^{-D\omega_n^2(f(t)-f(\tau))}\tilde{\eta}_n(\tau)$$

$$\tilde{\chi}_n(t)=D\int_0^t d\tau e^{-D\omega_n^2(f(t)-f(\tau))}\times\left[\tilde{F}_n(r^{(v)}(\tau))-\omega_n^2\left(\frac{1}{a_0^2}-\frac{1}{a^2(\tau)}\right)\tilde{r}_n^{(v)}(\tau)\right]$$

where $f(t)=\int_0^t\frac{d\tau}{a^2(\tau)}$.

In the following, we will restrict our calculations to regions of time where $a(t)$ can be considered as a constant, and $f(t)=\frac{t}{a^2}$ in order to avoid too complicated expressions. This will be justified later, as we will study more specifically the two time regimes $t\ll\tau_l$ (short times), and $t\gg\tau_l$ (large times), where τ_l is some effective Rouse time defined implicitly by:

$$\frac{4\pi^2D}{N^2}\int_0^{\tau_l}\frac{d\tau}{a^2(\tau)}=1. \tag{12}$$

Performing the thermal average and the average over the initial conditions of (9) is equivalent to averaging with respect to $\tilde{r}_n^{(v)}(t)$ which is a Gaussian variable with zero mean and:

$$\langle\tilde{r}_n^{(v)}(t)\tilde{r}_m^{(v)*}(t')\rangle=\frac{\delta_{nm}}{N\omega_n^2}\left(a^2e^{-\frac{D\omega_n^2}{a^2}|t-t'|}+(a_0^2-a^2)e^{-\frac{D\omega_n^2}{a^2}(t+t')}\right)$$

and leads to an implicit equation for $a(t)$. Here and in the following, the brackets now stand for the average over $\tilde{r}_n^{(v)}(t)$.

In good solvent conditions, we don't have to take into account the three-body forces. We find the following implicit equation for a:

see equation (13) above

where $A_n=\frac{D\omega_n^2}{a^2}$, d is the dimensionality and

$$\alpha(\tau,u)=4\sum_{p\geq 1}\frac{1-\cos 2\pi pu}{N\omega_p^2}\left(a^2+(a_0^2-a^2)e^{-2A_p\tau}\right).$$

At short times $t\ll\tau_l$, the following approximation can be made:

$$\alpha(\tau,u)\simeq Na_0^2u(1-u).$$

The next step is to evaluate quantities of the form:

$$F(x)=\sum_{n\geq 1}\frac{1}{n^2}e^{-xn^2}\int_0^1\frac{1-\cos 2\pi nu}{[u(1-u)]^{1+\frac{d}{2}}}\,.$$

This function can be evaluated for small values of the parameter x (see Appendix A),

$$F(x)\simeq 2\sqrt{\pi}J_d x^{\frac{1}{2}-\frac{d}{4}}\text{ where }J_d=\int_0^\infty\frac{dy}{y^{\frac{d}{2}}}\int_0^y\frac{dz}{z^2}(1-e^{-\pi^2z^2}).$$

Then we can easily deduce from equation (13) the value of a in this regime, and express the radius of gyration as a function of time. In dimension $d=3$, we find

$$R_g^2(t)\sim(1+\left(\frac{t}{\tau_c}\right)^{\frac{3}{4}})\;R_g^2(0) \tag{14}$$

where the characteristic time τ_c is given by:

$$\tau_c=2^{-1/3}\,\left(\frac{3\pi^2}{32\;J_3}\right)^{\frac{4}{3}}\frac{a_0^2}{D}\left(\frac{a_0^3}{v}\right)^{\frac{4}{3}}N^{\frac{4}{3}}. \tag{15}$$

For large times $t\gg\tau_l$, the function α reduces to

$$\alpha(\tau,u)\simeq Na^2u(1-u),$$

and replacing into equation (13) gives the Flory radius of gyration at infinite times, and

$$R_g(t)\sim N^{\frac{3}{d+2}}a_0(1-e^{-\frac{t}{\tau_1}}), \tag{16}$$

with a relaxation time τ_1 given by:

$$\tau_1\sim N^{\frac{d+8}{d+2}}.$$

In particular in $d=3$, $\tau_1\sim N^{\frac{11}{5}}$.

In a bad solvent, at short times $t\ll\tau_l$, only the two-body attractive potential is relevant, so one has just to replace v by $-v$ in equation (13). Thus, in dimension $d=3$, the radius of gyration decreases as:

$$R_g^2(t)\sim(1-\left(\frac{t}{\tau_c}\right)^{\frac{3}{4}})\;R_g^2(0). \tag{17}$$

For large times $t\gg\tau_l$, the radius of gyration relaxes to that of a compact globule resulting from the balance between the two-body potential term already calculated (replacing v by $-v$) and the three-body potential term (see Appendix A), according to:

$$R_g(t)\sim(\frac{w}{v})^{\frac{1}{d}}N^{\frac{1}{d}}(1+e^{-\frac{t}{\tau_2}}), \tag{18}$$

where

$$\tau_2\sim\frac{1}{4\pi^2D}(\frac{w}{v})^{\frac{2}{d}}N^{1+\frac{2}{d}},$$

thus giving $\tau_2\sim N^{\frac{5}{3}}$ in dimension $d=3$.

4 Derivation of $R_g(t)$ with hydrodynamic interactions

If we take into account the hydrodynamics of the solvent surrounding the polymer, the dynamical equations include the Oseen tensor and are not exactly soluble any more. The system of equations that we consider in this section is:

$$\begin{aligned}\frac{\partial r(s,t)}{\partial t}&=\int_0^N ds'\langle\mathbf{O}(r(s,t)-r(s',t))\rangle\\&\quad\times\left[\frac{k_BT}{a_0^2}\frac{\partial^2 r}{\partial s'^2}+k_BTF(r(s',t))+\eta(s',t)\right]\end{aligned} \tag{19}$$

$$\begin{aligned}\frac{\partial r^{(v)}(s,t)}{\partial t}&=\int_0^N ds'\langle\mathbf{O}(r^{(v)}(s,t)-r^{(v)}(s',t))\rangle\\&\quad\times\left[\frac{k_BT}{a^2(t)}\frac{\partial^2 r^{(v)}}{\partial s'^2}+\eta(s',t)\right].\end{aligned} \tag{20}$$

This corresponds to the usual "preaveraging approximation", where $\mathbf{O}(r(s,t)-r(s',t))$ is replaced by its thermal average $\langle\mathbf{O}(r(s,t)-r(s',t))\rangle$. Fluctuations of this quantity are neglected, which has been shown to be valid for a Gaussian chain (Zimm regime) [16] and we assume that the same approximation can be made for a collapsed or a swollen chain. If we define $\nu(t)$ as the time-dependent exponent of the radius of gyration ($R_g(t)=a_0N^{\nu(t)}$), we have

$$\begin{aligned}\langle\mathbf{O}(r(s,t)-r(s',t))\rangle&=\frac{1}{6\pi\eta}\langle\frac{1}{|r(s,t)-r(s',t)|}\rangle\mathbf{I}\\&\simeq\frac{1}{6\pi\eta a_0}\frac{\mathbf{I}}{|s-s'|^{\nu(t)}}\,.\end{aligned}$$

where $\mathbf{I}$ is the identity tensor.

$a(t)$ and $\nu(t)$ are related *via* the relation

$$a(t)=a_0N^{\nu(t)-\frac{1}{2}}.$$

Let's define

$$h(s-s')=\frac{1}{|s-s'|^{\nu(t)}}$$

with

$$\begin{cases}h(s-s')=\sum_{k,k'}e^{-i\omega_k s}e^{i\omega_{k'}s'}\tilde{h}_{kk'}\\ \tilde{h}_{kk'}\qquad=\frac{1}{N^2}\int_0^N ds\int_0^N ds' e^{i\omega_k s}e^{-i\omega_{k'}s'}h(s-s').\end{cases}$$

If N is sufficiently large, which will be assumed here, $\tilde{h}_{kk'}$ is almost diagonal and, for $k,k'\geq 1$, reduces to

$$\tilde{h}_{kk'}=\tilde{h}_{-k,-k'}=\frac{2}{N}\omega_k^{\nu(t)-1}\delta_{kk'}\,.$$

$$\frac{1}{a_0^2} - \frac{1}{a^2} = \frac{vN^3}{4\pi^2} \frac{\sum_{n\geq 1} \frac{1}{n^2}\omega_n^{\nu-1} \int_0^1 du \int_0^t d\tau \frac{1-\cos 2\pi n u}{\alpha(\tau,u)^{1+\frac{d}{2}}} \left(a^2 e^{-2B_n(t-\tau)} + (a_0^2 - a^2)e^{-2B_n t}\right)}{\sum_{n\geq 1} \omega_n^{\nu-1} \left(a^2 \frac{1-e^{-2B_n t}}{2B_n} + (a_0^2-a^2) t e^{-2B_n t}\right)} \tag{23}$$

The dynamical equations for $\tilde{r}_n^{(v)}$ and $\tilde{\chi}_n$ are then:

$$\frac{\partial \tilde{r}_n^{(v)}}{\partial t} = \frac{N\tilde{h}_{nn}}{6\pi\eta a_0}\left[-\frac{k_B T}{a^2(t)}\omega_n^2 \tilde{r}_n^{(v)} + \tilde{\eta}_n\right] \tag{21}$$

$$\frac{\partial \tilde{\chi}_n}{\partial t} = \frac{N\tilde{h}_{nn}}{6\pi\eta a_0}\left[-\frac{k_B T}{a^2(t)}\omega_n^2 \tilde{\chi}_n - k_B T \omega_n^2 \times \left(\frac{1}{a_0^2} - \frac{1}{a^2(t)}\right)\tilde{r}_n^{(v)} + k_B T \tilde{F}_n(r^{(v)})\right] \tag{22}$$

and

$$\langle \tilde{\eta}_n(t)\tilde{\eta}_m^*(t')\rangle = \frac{2k_B T}{N}\frac{6\pi\eta a_0}{N\tilde{h}_{nn}}\delta_{nm}\delta(t-t').$$

The solutions of these equations are:

$$\begin{aligned}\tilde{r}_n^{(v)}(t) &= \tilde{r}_n^{(v)}(0)e^{-\frac{k_B T}{3\pi\eta a_0}g_n(t)} \\ &\quad + \frac{1}{3\pi\eta a_0}\int_0^t d\tau e^{-\frac{k_B T}{3\pi\eta a_0}(g_n(t)-g_n(\tau))}\omega_n^{\nu(\tau)-1}\tilde{\eta}_n(\tau) \\ \tilde{\chi}_n(t) &= \frac{k_B T}{3\pi\eta a_0}\int_0^t d\tau e^{-\frac{k_B T}{3\pi\eta a_0}(g_n(t)-g_n(\tau))}\omega_n^{\nu(\tau)-1} \\ &\quad \times \left[\tilde{F}_n(r^{(v)}(\tau)) - \omega_n^2\left(\frac{1}{a_0^2} - \frac{1}{a^2(\tau)}\right)\tilde{r}_n^{(v)}(\tau)\right]\end{aligned}$$

where $g_n(t) = \int_0^t d\tau \frac{\omega_n^{\nu(\tau)+1}}{a^2(\tau)}$. As in the previous section, we restrict the calculation at this stage to regions of time where $a(t)$ and $\nu(t)$ can be considered as constants and $g_n(t) = \frac{\omega_n^{\nu+1}t}{a^2}$.

The Gaussian variable $\tilde{r}_n^{(v)}(t)$ has zero mean and is now distributed according to

$$\langle \tilde{r}_n^{(v)}(t)\tilde{r}_m^{(v)*}(t')\rangle = \frac{\delta_{nm}}{N\omega_n^2}\left(a^2 e^{-\frac{k_B T}{3\pi\eta a_0}\frac{\omega_n^{\nu+1}}{a^2}|t-t'|} + (a_0^2-a^2)e^{-\frac{k_B T}{3\pi\eta a_0}\frac{\omega_n^{\nu+1}}{a^2}(t+t')}\right).$$

Performing the average of equation (9) according to this law leads again to an implicit equation for a; the results are the following.

In good solvent conditions, the implicit equation for a reads:

see equation (23) above

where $B_n = \frac{k_B T}{3\pi\eta a_0}\frac{\omega_n^{\nu+1}}{a^2}$, and

$$\alpha_h(\tau,u) = 4\sum_{p\geq 1}\frac{1-\cos 2\pi p u}{N\omega_p^2}\left(a^2 + (a_0^2-a^2)e^{-2B_p\tau}\right).$$

Let us now study more specifically the two regions of time $t \ll \tau_{l,h}$ (short times) and $t \gg \tau_{l,h}$ (large times) where $\tau_{l,h}$ is some effective Zimm time, defined by:

$$\frac{k_B T(2\pi)^{\frac{3}{2}}}{3\pi\eta a_0 N^{\frac{3}{2}}}\int_0^{\tau_{l,h}}\frac{d\tau}{a^2(\tau)} = 1. \tag{24}$$

At short times $t \ll \tau_{l,h}$, since $\alpha_h(\tau,u) \simeq N a_0^2 u(1-u)$, and ν can be taken equal to $\frac{1}{2}$ – this hypothesis is verified *a posteriori* – equation (9) can be solved by evaluating first the following function:

$$G(x) = \sum_{n\geq 1}\frac{1}{\sqrt{n}}\frac{1}{n^2}e^{-xn^{\frac{3}{2}}}\int_0^1 \frac{1-\cos 2\pi n u}{[u(1-u)]^{1+\frac{d}{2}}}.$$

This function is calculated for small values of the parameter x (see Appendix B),

$$G(x) \simeq \frac{2}{3}H_d x^{\frac{3-d}{3}}$$

$$\text{where } H_d = \int_0^\infty \frac{dy}{y^{\frac{d}{2}+1}}\int_0^\infty \frac{dz}{z^2}e^{-z}(1-\cos 2\pi y z^{\frac{2}{3}}).$$

From equation (23) the radius of gyration as a function of time in dimension $d = 3$ is found to be:

$$R_g^2(t) \sim (1 + \frac{t}{\tau_{c,h}})\ R_g^2(0) \tag{25}$$

where the characteristic time $\tau_{c,h}$ is given by:

$$\tau_{c,h} = \frac{3\pi^3}{\sqrt{2\pi}\ H_3}\frac{3\pi\eta a_0^3}{2k_B T}\frac{a_0^3}{v}N. \tag{26}$$

For large times $t \gg \tau_{l,h}$, the function α_h reduces again to $\alpha_h(\tau,u) \simeq N a^2 u(1-u)$ and

$$R_g(t) \sim N^{\frac{3}{d+2}}a_0(1-e^{-\frac{t}{\tau_1}}), \tag{27}$$

with a relaxation time $\tau_{1,h}$ given by:

$$\tau_{1,h} \sim \frac{\eta a_0^3}{k_B T}N^{\frac{9}{d+2}},$$

thus $\tau_{1,h} \sim N^{\frac{9}{5}}$ in $d = 3$.

In a bad solvent, at short times $t \ll \tau_{l,h}$, the dynamics of the collapse is the same as the dynamics of the swelling in a good solvent at short times, so one has just to replace v by $-v$ in equation (23). In dimension $d = 3$, the radius of gyration decreases as:

$$R_g^2(t) \sim (1 - \frac{t}{\tau_{c,h}})\ R_g^2(0). \tag{28}$$

$$\frac{1}{a_0^2}-\frac{1}{a^2}=\frac{v}{4\pi^2}\frac{N^{2-\frac{d}{2}}}{a_0^{2+d}}\frac{\sum_{n\geq 1}\frac{1}{n^2}\int_0^1 du\frac{1-\cos 2\pi nu}{(u(1-u))^{1+\frac{d}{2}}}\left(a^2\frac{1-e^{-2A_n t}}{2A_n}+(a_0^2-a^2)te^{-2A_n t}\right)}{\sum_{n\geq 1}\left(a^2\frac{1-e^{-2A_n t}}{2A_n}+(a_0^2-a^2)te^{-2A_n t}\right)}.$$

For large times $t \gg \tau_{l,h}$, the calculation of the radius of gyration is made by balancing the two-body potential term already calculated (replacing v by $-v$) and the three-body potential term (see Appendix B).

This leads to the result:

$$R_g(t) \sim (\frac{w}{v})^{\frac{1}{d}} N^{\frac{1}{d}}(1+e^{-\frac{t}{\tau_{2,h}}}), \tag{29}$$

where

$$\tau_{2,h} \sim \frac{\eta a_0^3}{k_B T} N^{\frac{3}{d}},$$

i.e. $\tau_{2,h} \sim N$ in dimension $d=3$.

5 Conclusion

Using a generalization of Edwards' Uniform Expansion Model, we have derived dynamic laws for the collapse or the swelling of a polymer; we have also been able to include hydrodynamic interactions with the solvent in the framework of the "preaveraging approximation". Our results give new insight in the problem of polymer collapse dynamics. Let us stress that the analytic calculations we made (at short times) are likely to give good results for the general forms of the laws, but maybe not for the precise values of the exponents. A comprehensive numerical study of the system has to be done in order to have a better physical understanding of our approximations; this is underway. Even more promising would be the confrontation with precise experimental data, but they are still lacking at the moment.

The first stage of the collapse is fast. If we assume that for proteins, the first stage of collapse is non-specific and driven by hydrophobic forces, then the characteristic time of this first stage will be the same as the one we find for a homopolymer. Note that this value is not the same with or without the hydrodynamic interactions. Numerically, we have taken $D \sim 10^{-5}\text{cm}^2/\text{s}$ for the diffusion constant of a single amino-acid in water, $\eta \sim 10^{-2}$ poise, $T = 300$ K. Due to the chain stiffness, a monomer unit in a protein consists approximately of 4 amino-acids [2]. Thus, for a chain of 300 amino-acids, $N = 75$, and we have taken $a_0 = 16$ Å and $v = 250$ Å^3. The integrals can be calculated explicitly; $J_3 = \frac{4}{3}\Gamma(\frac{1}{4})\pi^{\frac{3}{2}} \simeq 26.9$ and $H_3 \simeq 134.2$, and we find $\tau_c \simeq 10^{-7}$ s and $\tau_{c,h} \simeq 10^{-5}$ s. The expected time for the formation of α-helices in proteins is actually of the order of 10^{-7} s.

Note also that we have performed the Langevin simulation of equation (1) at short times, which gives a power law for $R_g(t)$ with an exponent $\simeq 0.65$, not too far from our prediction $(\frac{3}{4})$, and quite in agreement with the results of Kutznetsov *et al.* [10].

For longer times, we find that for the collapse, the relaxation time scales like $N^{\frac{5}{3}}$ without hydrodynamic interactions and like N with hydrodynamic interactions; these results are the same as those found by Kutznetsov *et al.* [10]. Numerically, these times are too short ($10^{-7}-10^{-6}$ s) compared to the experimental values of protein folding times, which range from 1 ms to 1 s. The homopolymer results can not be applied to proteins in this limit. For large times, our model doesn't take into account the topological constraints that give rise to the very slow rearrangements of the protein chain or even of a polymer chain in its compact phase. In this field it is interesting to stress the fact that no analytical theory of de Gennes' reptation model exists at present. In order to take into account the high energy barriers that separate metastable states in the later stages of the folding process, one would have to introduce a disorder-dependent Hamiltonian in the dynamical equations, as it has already been studied in [10]. However the validity of such variational schemes when disorder is present has still to be clarified.

Appendix A

We present here the detailed calculation for the dynamical behaviour of the radius of gyration at short times, in the case where hydrodynamic interactions can be neglected. We used the following identities ($\tilde{F}^*_{2,n}$ refers to the two-body force):

$$\sum_{n\neq 0}\int_0^t d\tau e^{-A_n(t-\tau)}\langle \tilde{r}_n^{(v)}(t)\tilde{F}^*_{2,n}(r^{(v)}(\tau))\rangle =$$

$$\frac{vN^2}{2\pi^2}\sum_{n\geq 1}\frac{1}{n^2}\int_0^1 du\int_0^t d\tau\frac{1-\cos 2\pi nu}{\alpha(\tau,u)^{1+\frac{d}{2}}}$$

$$\times\left(a^2 e^{-2A_n(t-\tau)}+(a_0^2-a^2)e^{-2A_n t}\right)$$

$$\sum_{n\neq 0}\omega_n^2\left(\frac{1}{a_0^2}-\frac{1}{a^2}\right)\int_0^t d\tau e^{-A_n(t-\tau)}\langle\tilde{r}_n^{(v)}(t)\tilde{r}_n^{(v)*}(\tau)\rangle =$$

$$\left(\frac{1}{a_0^2}-\frac{1}{a^2}\right)\frac{2}{N}\sum_{n\geq 1}\left(a^2\frac{1-e^{-2A_n t}}{2A_n}+(a_0^2-a^2)te^{-2A_n t}\right)$$

and in the limit of short times and in good solvent, equation (13) reads:

see equation above.

Let us now compute the function $F(x)$ for small values of x (in the previous equation, x takes the value $\frac{8\pi^2 Dt}{N^2 a^2}$).

$$F(x) = \sum_{n\geq 1} \frac{1}{n^2} e^{-xn^2} \int_0^1 \frac{1-\cos 2\pi n u}{[u(1-u)]^{1+\frac{d}{2}}}$$

$$F(x) = 2\sum_{n\geq 1} \frac{1}{n^2} e^{-xn^2} \sum_{p\geq 1} \frac{(-1)^{p+1}}{(2p)!} (2\pi n)^{2p}$$
$$\times \int_0^{\frac{1}{2}} \frac{u^{2p}}{[u(1-u)]^{1+\frac{d}{2}}} \cdot$$

The sum over n in the limit $x \to 0$ can be done using a Poisson transform, leading to:

$$\sum_{n\geq 1} e^{-xn^2} \simeq \frac{\sqrt{\pi}}{2} x^{-\frac{1}{2}}$$

$$\sum_{n\geq 1} e^{-xn^2} n^{2(p-1)} \simeq \frac{\sqrt{\pi}}{2} \frac{1.3\ldots(2p-3)}{2^{p-1}} \frac{\sqrt{x}}{x^p} \cdot$$

Replacing into the previous equation and after some algebra, one finally obtains the announced result:

$$F(x) \simeq 2\sqrt{\pi} x^{\frac{1}{2}-\frac{d}{4}} \int_0^{\frac{1}{2\sqrt{x}}} \frac{y\, dy}{[y(1-\sqrt{x}y)]^{1+\frac{d}{2}}} \int_0^y \frac{dz}{z^2}(1-e^{-\pi^2 z^2})$$
$$F(x) \simeq 2\sqrt{\pi} J_d x^{\frac{1}{2}-\frac{d}{4}},$$

where

$$J_d = \int_0^\infty \frac{dy}{y^{\frac{d}{2}}} \int_0^y \frac{dz}{z^2}(1-e^{-\pi^2 z^2}) \cdot$$

The expression of a can then be deduced from equation (13) as well as the radius of gyration. This goes as follows:

$$R_g^2(t) = \sum_{n\neq 0} \langle \tilde{r_n}^{(v)}(t) \tilde{r_n}^{(v)*}(t)\rangle$$
$$= \sum_{n\neq 0} \frac{1}{N\omega_n^2} \left(a^2 + (a_0^2 - a^2) e^{-\frac{2D\omega_n^2}{a^2} t}\right) \cdot$$

Thus,

$$\frac{d}{dt} R_g^2(t) = \frac{2D}{Na^2}(a^2 - a_0^2) \sum_{n\neq 0} e^{-\frac{2D\omega_n^2 t}{a^2}} \simeq \sqrt{\frac{D}{2\pi}} \frac{a^2 - a_0^2}{a} \frac{1}{\sqrt{t}} \cdot$$

The value of a in dimension $d = 3$ from (13) is

$$a^2 = a_0^2 \left(1 + \frac{2J_3}{3\pi^2} \frac{v}{a_0^3} \left(\frac{\sqrt{8\pi^2 D}}{a_0}\right)^{\frac{1}{2}} t^{\frac{1}{4}}\right).$$

Then, replacing the value of a and integrating over time gives the result (14) for the radius of gyration.

In a bad solvent, the short time analysis looks very much the same as before (one only needs to replace v by $-v$). For the long time behaviour however, the radius of gyration results from the balance between the two-body potential term (replacing v by $-v$) and the three-body potential term given by ($\tilde{F}_{3,n}^*$ refers to the three-body force):

$$\sum_{n\neq 0} \int_0^t e^{-A_n(t-\tau)} \langle \tilde{r}_n^{(v)}(t) \tilde{F}_{3,n}^*(r^{(v)}(\tau))\rangle =$$
$$\frac{wN^2}{3} \sum_{n\geq 1} \int_0^t d\tau e^{-A_n(t-\tau)} \langle \tilde{r}_n^{(v)}(t) \tilde{r}_n^{(v)*}(\tau)\rangle$$
$$\times \int_0^1 du \int_0^1 du' \int_0^1 du'' \frac{1}{[\Delta(\tau,u,u',u'')]^{\frac{d}{2}}}$$
$$\times \left[\frac{1-\cos 2\pi n(u-u')}{X(\tau,u,u')} + 2\frac{\cos 2\pi n(u-u') - \cos 2\pi n(u'-u'')}{Y(\tau,u,u',u'')}\right],$$

with

$$X(\tau,u,u') = 4\sum_{n\geq 1} \frac{1-\cos 2\pi n(u-u')}{N\omega_n^2} \left(a^2 + (a_0^2 - a^2) e^{-2A_n\tau}\right)$$
$$Y(\tau,u,u',u'') = 4\sum_{n\geq 1} (\cos 2\pi n(u-u') + \cos 2\pi n(u'-u'')$$
$$-\cos 2\pi n(u-u'') - 1) \frac{1}{N\omega_n^2} \left(a^2 + (a_0^2 - a^2) e^{-2A_n\tau}\right)$$
$$\Delta(\tau,u,u',u'') = 4X(\tau,u,u') X(\tau,u',u'') - Y^2(\tau,u,u',u'').$$

In the limit of large times, we find then that the radius of gyration relaxes to its Flory radius (in the collapsed state).

Appendix B

We derive now the expression of $R_g^2(t)$ at short times when hydrodynamic interactions are included in the model.

In good solvent conditions, the identities needed in the computation of (9) are:

$$\sum_{n\neq 0} \int_0^t d\tau e^{-B_n(t-\tau)} \omega_n^{\nu-1} \langle \tilde{r}_n^{(v)}(t) \tilde{F}_{2,n}^*(r^{(v)}(\tau))\rangle =$$
$$\frac{vN^2}{2\pi^2} \sum_{n\geq 1} \frac{1}{n^2} \omega_n^{\nu-1} \int_0^1 du \int_0^t d\tau \frac{1-\cos 2\pi n u}{\alpha_h(\tau,u)^{1+\frac{d}{2}}}$$
$$\times \left(a^2 e^{-2B_n(t-\tau)} + (a_0^2 - a^2) e^{-2B_n t}\right)$$

$$\sum_{n\neq 0} \omega_n^{\nu+1} \left(\frac{1}{a_0^2} - \frac{1}{a^2}\right) \int_0^t d\tau e^{-B_n(t-\tau)} \langle \tilde{r}_n^{(v)}(t) \tilde{r}_n^{(v)*}(\tau)\rangle =$$
$$\left(\frac{1}{a_0^2} - \frac{1}{a^2}\right) \frac{2}{N} \sum_{n\geq 1} \omega_n^{\nu-1} \left(a^2 \frac{1-e^{-2B_n t}}{2B_n} + (a_0^2 - a^2) t e^{-2B_n t}\right)$$

As in the previous section, equation (23) can be simplified in the limit of short times, giving

$$\frac{1}{a_0^2}-\frac{1}{a^2}=\frac{v}{4\pi^2}\frac{N^{2-\frac{d}{2}}}{a_0^{2+d}}$$
$$\times\frac{\sum_{n\geq 1}\frac{1}{n^2}\omega_n^{-\frac{1}{2}}\int_0^1 du\frac{1-\cos 2\pi nu}{(u(1-u))^{1+\frac{d}{2}}}\left(a^2\frac{1-e^{-2B_nt}}{2B_n}+(a_0^2-a^2)te^{-2B_nt}\right)}{\sum_{n\geq 1}\omega_n^{-\frac{1}{2}}\left(a^2\frac{1-e^{-2B_nt}}{2B_n}+(a_0^2-a^2)te^{-2B_nt}\right)}.$$

The useful function to compute is now $G(x)$, where

$$G(x)=\sum_{n\geq 1}\frac{1}{\sqrt{n}}\frac{1}{n^2}e^{-xn^{\frac{3}{2}}}\int_0^1\frac{1-\cos 2\pi nu}{[u(1-u)]^{1+\frac{d}{2}}}$$
$$G(x)=2\sum_{n\geq 1}\frac{1}{\sqrt{n}}\frac{1}{n^2}e^{-xn^{\frac{3}{2}}}\sum_{p\geq 1}\frac{(-1)^{p+1}}{(2p)!}(2\pi n)^{2p}$$
$$\times\int_0^{\frac{1}{2}}\frac{u^{2p}}{[u(1-u)]^{1+\frac{d}{2}}},$$

and the small parameter x takes the value $\frac{2k_BT}{3\pi\eta a_0}\left(\frac{2\pi}{N}\right)^{\frac{3}{2}}\frac{t}{a^2}$ in the above implicit equation for a.

The sum over n in the limit $x\to 0$ can be performed again:

$$\sum_{n\geq 1}\frac{1}{\sqrt{n}}e^{-xn^{\frac{3}{2}}}\simeq\frac{1}{3}\frac{1}{x^{\frac{1}{3}}}\Gamma\left(\frac{1}{3}\right)$$
$$\sum_{n\geq 1}\frac{1}{\sqrt{n}}e^{-xn^{\frac{3}{2}}}n^{2(p-1)}\simeq\frac{1}{3}\int_0^{\infty}dww^{\frac{4p}{3}-2}e^{-xw}$$
$$=\frac{1}{3}\frac{1}{x^{\frac{4p}{3}-1}}\Gamma\left(\frac{4p}{3}-1\right).$$

This gives the announced result for $G(x)$:

$$G(x)\simeq\frac{2}{3}x^{\frac{3-d}{3}}\int_0^{\frac{1}{2x^{\frac{2}{3}}}}\frac{dy}{(y(1-x^{\frac{2}{3}}y))^{1+\frac{d}{2}}}$$
$$\times\int_0^{\infty}\frac{dz}{z^2}e^{-z}(1-\cos 2\pi yz^{\frac{2}{3}})$$
$$G(x)\simeq\frac{2}{3}H_dx^{\frac{3-d}{3}},$$

where

$$H_d=\int_0^{\infty}\frac{dy}{y^{\frac{d}{2}+1}}\int_0^{\infty}\frac{dz}{z^2}e^{-z}(1-\cos 2\pi yz^{\frac{2}{3}}).$$

Following the same procedure as before, a and $R_g^2(t)$ can now be computed.

$$R_g^2(t)=\sum_{n\neq 0}\frac{1}{N\omega_n^2}\left(a^2+(a_0^2-a^2)e^{-2B_nt}\right),\ \text{and}$$
$$\frac{d}{dt}R_g^2(t)=(a^2-a_0^2)\frac{2k_BT}{3\pi\eta a_0^3}\frac{1}{\sqrt{2\pi N}}\sum_{n\neq 0}\frac{1}{\sqrt{n}}e^{-2B_nt}$$
$$\simeq\frac{1}{6\pi}\Gamma\left(\frac{1}{3}\right)\left(\frac{2k_BT}{3\pi\eta a_0^3}\right)^{\frac{2}{3}}\frac{a^2-a_0^2}{t^{\frac{1}{3}}}.$$

The value of a in dimension $d=3$ is from equation (23):

$$a^2=a_0^2\left(1+\frac{\sqrt{2\pi}}{4\pi^2}\frac{2H_3}{3\Gamma\left(\frac{1}{3}\right)}\frac{v}{a_0^3}\left(\frac{2k_BT}{3\pi\eta a_0^3}\right)^{\frac{2}{3}}t^{\frac{1}{3}}\right).$$

Replacing the value of a and integrating over time leads indeed to the result (25).

In a bad solvent, at short times $t\ll\tau_{l,h}$, the dynamics of the collapse is the same as before, replacing v by $-v$ in equation (23).

For large times $t\gg\tau_{l,h}$, there is a balance between the two-body potential term (replacing v by $-v$) and the three-body potential term given by:

$$\sum_{n\neq 0}\int_0^t d\tau e^{-B_n(t-\tau)}\omega_n^{\nu-1}\langle\tilde{r}_n^{(v)}(t)\tilde{F}_{3,n}^*(r^{(v)}(\tau))\rangle=$$
$$\frac{wN^2}{3}\sum_{n\geq 1}\int_0^t d\tau e^{-B_n(t-\tau)}\omega_n^{\nu-1}\langle\tilde{r}_n^{(v)}(t)\tilde{r}_n^{(v)*}(\tau)\rangle$$
$$\times\int_0^1 du\int_0^1 du'\int_0^1 du''\frac{1}{[\Delta_h(\tau,u,u',u'')]^{\frac{d}{2}}}$$
$$\times\left[\frac{1-\cos 2\pi n(u-u')}{X_h(\tau,u,u')}+2\frac{\cos 2\pi n(u-u')-\cos 2\pi n(u'-u'')}{Y_h(\tau,u,u',u'')}\right],$$

with

$$X_h(\tau,u,u')=4\sum_{n\geq 1}\frac{1-\cos 2\pi n(u-u')}{N\omega_n^2}$$
$$\times\left(a^2+(a_0^2-a^2)e^{-2B_n\tau}\right)$$
$$Y_h(\tau,u,u',u'')=4\sum_{n\geq 1}(\cos 2\pi n(u-u')+\cos 2\pi n(u'-u'')$$
$$-\cos 2\pi n(u-u'')-1)\frac{1}{N\omega_n^2}$$
$$\times\left(a^2+(a_0^2-a^2)e^{-2B_n\tau}\right)$$
$$\Delta_h(\tau,u,u',u'')=4X_h(\tau,u,u')X_h(\tau,u',u'')$$
$$-Y_h^2(\tau,u,u',u'').$$

This leads again to the announced result.

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