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KINETICS
OF ROTATIONAL-DEFORMATIONAL EXCITATIONS
IN GLOBULAR MACROMOLECULES

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It is now widely appreciated that biological macromolecules possess a rich spectrum of internal motions with characteristic times encompassing some 15 orders of magnitude. One of the frontiers today in molecular biology is the study of low-frequency internal motion in macromolecules and the relevant biological functions. Consequently, it is important to reveal the origin of this kind of internal motion and to build the corresponding physical models. A good discussion of these models is given, e.g., in[1]. The models (the elastic global model, the harmonic model and the quasi-continuity model) are based on a reasonable conception that the origin of the low-frequency internal motion is due to the existence of a series of weak bonds and a large number of atoms distributed around these bonds. The calculated wave numbers for some biological molecules within these simple models are close to their corresponding observed values [1]. That is, the adopted physical models reflect quite well the real origin of the low-frequency motion in biological macromolecules. Possibly, complicated but unessential factors that were neglected during the approximate treatment are either cancelled out by each other or reach an internal mutual equilibrium in a much shorter time in comparison with the period of the low-frequency motion.

Another phenomenological model of the low-frequency collective motions in biological macromolecules has been proposed in our previous papers [2,3]. The model is called to take effectively into account acoustic thermal vibrations of the particles constituting the macromolecule and the displacements and turns of the molecular groups and fragments. It is assumed that these motions lead to small changes (vibrations) of the globule surface with respect to its equilibrium form. To describe such (in the most simple case quadrupole) deformations of the globule, it is convenient to use a set of five collective variables: three Euler angles $\vec{\theta}=(\theta_1,\theta_2,\theta_3)$ giving the orientation of the molecule-fixed axes with respect to the laboratory frame and two parameters β and γ ($0\leq\beta<\infty$, $0\leq\gamma\leq\pi/3$) characterizing the form of the macromolecule in its own coordinate system. Such

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dynamical variables have been successfully applied modelling excited states of atomic nuclei [4].The starting Lagrangian and dissipative function of the macromolecule in solution are formally the same as for a viscous liquid drop under surface tension in other viscous fluid. It must be noted that the used parameters of the elasticity (C) and the dissipation (Z) are phenomenological, effective and they have to be considered as being caused by quite distinct mechanisms than those in a homogeneous liquid. At the present time, there is no microscopic theory that allows one to calculate these parameters. If the deformed macromolecule is modelled by a homogeneous liquid drop with a large viscosity η and surface tension σ in a liquid with the viscosity coefficient η', we have $Z=5R_0^3(\eta+8\eta'/3)$ and $C=4\sigma R_0^2$ with R_0 being the equilibrium radius of the drop [5]. The probability density of the transition of the macromolecule from the initial state ($\beta(0)$, $\gamma(0),\vec{\theta}(0)$) to the final state ($\beta,\gamma,\vec{\theta}$) during the time t, $W(\beta,\gamma,\vec{\theta};\beta(0),\gamma(0),\vec{\theta}(0);t)$ is the solution of the Einstein-Smoluchowski kinetic equation. This equation that describes the Brownian motion of deformable particles in diffusion approximation has been obtained in[5]. It can be written in the following form:

$$\frac{\partial W}{\partial t} = \frac{C}{Z}(5+\beta\partial/\partial\beta)W + [D_\beta\beta^{-4}\frac{\partial}{\partial\beta}\beta^4\frac{\partial}{\partial\beta} + D_\gamma\frac{1}{\sin3\gamma}\frac{\partial}{\partial\gamma}\sin3\gamma\frac{\partial}{\partial\gamma}$$

$$- \sum_{\sigma=1}^{3} D_\sigma^r L_\sigma^2] W. \tag{1}$$

Here, L_σ are the projections of the quantum-mechanical angular momentum onto the molecule-fixed axes ($\hbar=1$), $D_\beta=k_BT/Z$ and $D_\gamma=k_BT/Z\beta^2$ are the diffusion coefficients in the space of the internal parameters. The principal diffusion coefficients in the space of rotations, $D_\sigma=k_BT/4Z\beta^2\sin^2(\gamma-2\pi\sigma/3)$, are also determined by the dissipation of the deformable particle.

The initial condition and the volume element in our 5-dimensional space are as follows:

$$W(0) = \delta(\beta-\beta(0))\delta(\gamma-\gamma(0))\delta(\vec{\theta}-\vec{\theta}(0))/\beta^4\sin3\gamma, \tag{2}$$

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$$d^5\alpha = \beta^4 \sin 3\gamma d\beta d\gamma \sin\theta_2 d\theta_1 d\theta_2 d\theta_3. \tag{3}$$

The stationary solution of eq.(1) is the Boltzmann distribution

$$W_{\infty\sim} \exp(-c\beta^2/2k_BT). \tag{4}$$

In the present paper, we obtain the solution of the kinetic equation (1) and use it to construct the autocorrelation Van Hove function which is necessary in the interpretation of spectroscopic experiments. It is well known that the internal motion of macromolecules has a considerable influence on their heat motion in solutions. In its turn, this affects the spectroscopic and relaxation experimental data in the time and frequency domains, with which the model predictions can be confronted. The experimental techniques that are perspective to be used in such measurements are, e.g., the inelastic neutron scattering [6], light scattering[7] or the Moessbauer absorption and Rayleigh scattering spectroscopy[8]. The spectrum of the elastic incoherent Rayleigh scattering of Moessbauer radiation [9] is determined by the autocorrelation Van Hove function $F(\vec{k},t)$

$$g(\omega) = \frac{\Gamma}{4\hbar} \int_{-\infty}^{\infty} dt \, \exp(-i\omega t - \frac{\Gamma|t|}{2\hbar}) F(\vec{k},t),$$

$$F(\vec{k},t) = (1/N) \sum_{j=1}^{N} \langle \exp i k \vec{X}_j(t) \, \exp(-i k \vec{X}_j(0)) \rangle, \tag{5}$$

where ω is the difference between the frequency of gamma-quanta and the resonance frequency, $k=(4\pi/\lambda)\sin(\theta/2)$ is the momentum transfer at the scattering, θ is the scattering angle, Γ is the natural line width and $X_j(t)$ is the position of the jth atom (scatterer). The angular brackets denote the statistical averaging. Note that the spectra of the light or slow neutron scattering are given by analogous expressions with $\Gamma=0$. The information obtained from the scattering data is, in fact, averaged over the whole macromolecule and does not depend on the positions of separate Moessbauer marks.

The motion of an atom can be divided into the sum of the motion of the center of mass of the Brownian particle and the independent displacements $\vec{r}_j(t)$ together with the surroundings. The translational motion will be described in the diffusion approximation. The detailed mobility analysis of the deformed drop in a liquid [10] showed that at small Reynolds numbers the resistance force during the motion of the drop is the same as for a liquid sphere, that is, the translational diffusion coefficient is a scalar

$$D = \frac{k_B T}{6\pi R_0 \eta'} \frac{\eta + \eta'}{\eta + 2\eta'/3} . \tag{6}$$

The mean square angle of the particle rotation during the characteristic time $\tau_0 \sim R_0^3 \eta/\sigma R_0^2$ is given by the estimation $<\phi^2>^{1/2} \sim D_{rot}\tau_0$ ($D_{rot} \sim k_B T/R_0^3 \eta'$ is the rotational diffusion coefficient) and is always small. Really, $D_{rot}\tau_0 \sim (\eta/\eta')k_B T/\sigma R_0^2 < 10^{-1}$ if $R_0 \sim 10\text{Å}$ and $\eta \sim 80\eta'$. We express the displacement of the atom in the center-of-mass system $\vec{r}_j(t) - \vec{r}_j(0)$ during the time t into the small contributions from the rotations and small changes of the distance r_{0j} from the center of mass. That is, omitting the index j, we write $\vec{r}(t) - \vec{r}(0) = \vec{n}(t)r(t) - \vec{n}(0)r(0)$, where $\vec{n}(t)$ is the unit vector of the direction to the atom. Then, $r(t) = r_0(1 + \Sigma\alpha_\nu(t)Y_{2\nu}(\theta,\phi))$ considering the displacement $r(t) - r_0$ to be modulated by the factor in brackets that follows from the expansion in spherical harmonics within the used quadrupole approximation. Using also $\vec{n}(t) - \vec{n}(0) \approx \vec{\phi}(t) \times \vec{n}(0)$, where $\vec{\phi}$ is the angle of rotation of the vector $\vec{n}$ (from some initial $\vec{\phi}(0)$ to $\vec{\phi}(0) + \vec{\phi}$), we obtain

$$\vec{r}(t) - \vec{r}(0) \approx r_0\vec{\phi}(t) \times \vec{n}(0) + r_0\zeta_0\vec{n}(0)[\beta(t) - \beta(0)],$$

$$\zeta_0 = \sqrt{5/16\pi}[(3\cos^2\theta_0' - 1)\cos\gamma + \sqrt{3}\sin^2\theta_0'\cos2\phi_0'\sin\gamma]. \tag{7}$$

We have retained in (7) only the terms of the first order of small quantities. The molecule-fixed axes are directed along the principal axes of the ellipsoid (macromolecule). The angles θ_0' and ϕ_0' give the orientation of the vector $\vec{n}(0)$ in the rotating coordinate system.

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Using all we have said above the Van Hove function reads

$$F(\vec{k},t) \approx e^{-k^2 Dt} \, N^{-1} \sum_{j=1}^{N} <\exp[i\vec{\gamma}\vec{\phi}(t) + i\zeta(\beta(t)-\beta(0)]>. \qquad (8)$$

Here, the vector $\vec{\gamma}$ and the scalar ζ have been introduced as functions of the initial Euler angles $\theta_1, \theta_2, \theta_3$,

$$\gamma_1 = kr_0(\sin\theta_0'\sin\phi_0'\cos\theta_2 - \cos\theta_0'\sin\theta_2\cos\theta_3),$$

$$\gamma_2 = kr_0(\cos\theta_0'\sin\theta_2\sin\theta_3 - \sin\theta_0'\cos\phi_0'\cos\theta_2),$$

$$\gamma_3 = kr_0\sin\theta_0'\sin\theta_2\cos(\phi_0'+\theta_3),$$

$$\zeta = \zeta_0 kr_0[\sin\theta_0'\sin\theta_2\sin(\phi_0'+\theta_3)+\cos\theta_0'\cos\theta_2]. \qquad (9)$$

The vector $\vec{k}$ is assumed to lie along the axis z of the laboratory frame; the angles $\theta_1, \theta_2, \theta_3$ determine its orientation in the system connected with the macromolecule.

   The angles of rotations are small quantities. This can be used to write approximately the operator L_σ from (1) in the form[11] $L_\sigma \approx -i\partial/\partial\phi_\sigma$, that is, equation (1) becomes much simpler. In the initial condition (2) the delta-function depending on the Euler angles becomes simply $\delta(\vec{\phi})$ and the volume element (3) is $d\vec{\phi}$. In the small rotation approximation the angular brackets in (8) mean the averaging, that is to be carried out according to the rule

$$<B> = \int d^5\alpha(0)W_\infty(\beta_0) \int \beta^4 d\beta \sin3\gamma d\gamma d\vec{\phi} \; W(\beta,\gamma,\vec{\phi};\beta_0,\gamma_0,t)B, \qquad (10)$$

$$\beta_0 = \beta(0), \; \gamma_0 = \gamma(0).$$

The limits of integration over $\vec{\phi}$ are here extended to infinity [11].

   Now, we can construct the Green function of our simplified problem determining the probability of the transition during the time t from the initial state $\{\beta_0, \gamma_0, \vec{\phi}(0)\}$ to the final state $\{\beta, \gamma, \vec{\phi}(0)+\vec{\phi}\}$. It can be done using the proper functions obtained by the separation of variables[4]. The Van Hove function (8) is expressed through the auxiliary function

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$$w(t) = \int \exp(i\vec{\gamma}\vec{\phi})W d\vec{\phi} \qquad (11)$$

that can be written in the form

$$w(t) = \sum_l \Gamma_l(\gamma)\Gamma_l(\gamma_0)w(\beta,\beta_0,t,s_l), \qquad (12)$$

where the Green function of the "deformational vibrations" is determined through the series of the Laguerre polynomials

$$w(\beta,\beta_0,t,s) = 2(\kappa/2)^{5/2}e^{-y}(yy_0)^{s-1} \qquad (13)$$

$$\times\sum_{n=0} \frac{n!}{(n+2s-1/2)!} L_n^{2s-1/2}(y) L_n^{2s-1/2}(y_0)\exp[-2\kappa\tau(n+s-1)].$$

Here, the dimensionless time $\tau=tk_BT/Z$ and the elasticity constant $\kappa=C/k_BT$ have been introduced; $y=\kappa\beta^2/2$ and $s_l=(1/4)(1+3\sqrt{1+4\varepsilon_l})$ depends on the separation parameters ε_l. The equation for determining $\Gamma_l(\gamma)$ reads

$$\left(\frac{1}{\sin 3\gamma} \frac{\partial}{\partial\gamma} \sin 3\gamma \frac{\partial}{\partial\gamma} - \sum_{\sigma=1}^{3} \frac{\gamma_\sigma^2}{4\sin^2(\gamma-2\pi\sigma/3)} + 9\varepsilon_l\right)\Gamma_l = 0, \qquad (14)$$

with the vector components γ_σ from (9). We failed to find the proper functions and values of this equation in the general case. Formally, the problem coincides with that of the quantum-mechanical motion of a particle on the sphere with the potential

$$u(\gamma) = \sum_{\sigma=1}^{3} \frac{\gamma_\sigma^2}{4\sin^2(\gamma-2\pi\sigma/3)} .$$

Averaging this potential over all possible orientations given by the Euler angles $\vec{\theta}(0)$ and over the positions of scatterers inside the Brownian particle, we have

$$\bar{u}(\gamma) = 9a^2\sin^{-2}3\gamma, \qquad a=kR_0\sqrt{10}/6. \qquad (15)$$

The proper functions of eq.(14) in the region $[0,\pi/3]$ with the potential (15) and the zero boundary conditions are the Legendre polynomials[12] $P_{a+1}^{-a}(\cos 3\gamma)$ and the proper values are

$\varepsilon_1 = (a+1)(a+1+1)$, $1=0,1,2,\ldots$.

To obtain the scattering spectrum according to (10) with the help of (12), the averaging over the equilibrium Euler angle distribution must be done and the result has to be summed over all scatterers. The sum can be approximately replaced by the volume integration. It is difficult to carry out these calculations in an explicit form. That is why, we construct the exact result depending on γ_σ^2 and ζ^2 from (9) <u>in</u> the form of the Taylor expansion near the values γ_σ^2 and ζ^2 and limit ourselves to the first expansion term[11]. The result for the function (8) is rather complex. The averaging over the γ-vibrations gives the following expression:

$$F(k,t) \approx e^{-k^2Dt} \sum_{1,n} |A_1|^2 T^{s_1-1+n} (1-T)^{5/2} \frac{1}{n!} \frac{\Gamma^2(n+s_1+3/2)}{\Gamma(n+2s_1+1/2)} |B_{ns_1}|^2,$$

(16)

where $T = \exp(-2\kappa\tau)$, $A_1 = \int \sin 3\gamma \, \Gamma_1(\gamma) d\gamma$, (17)

$$B_{ns} = \pi^{-1/2} \Gamma(s+n+2) 2^{3(s+n+3/2)} \Psi(-s-n-3/2, 1/2, -\lambda^2(1-T)/4),$$ (18)

and $\lambda^2 = 2\overline{\zeta^2}/\kappa = 2(kR_0)^2/20\pi\kappa$, with Ψ being the degenerate hypergeometric function.

More significant simplifications of the result are possible only after some additional approximations. So, in the problems of the scattering and absorption of Moessbauer gamma-quanta the condition $kR_0 \gg 1$ can be used. In the experiments of the quasi-elastic light scattering from the statistical coils of various polymers [13,14] the dependence of the first cumulant on kR_g is studied in the intermediate region $kR_g \sim 1$ and in the limit $kR_g \gg 1$ (R_g is the hydrodynamic radius of the macromolecule). Theoretical estimations of the cumulant Ω_1 for chain molecules with the inclusion of hydrodynamic interactions show the following interesting and considerable peculiarity: Ω_1 does not depend on the size of the chain or its segments and $\Omega_1 \sim k_B T k^3/\eta$.

Let us study the asymptotics of the autocorrelation function in our case under the condition $kR_0 \gg 1$. In this case $\varepsilon_1 \approx a^2$ and does not depend on the summation index 1. Then,

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the summation over all l and the integration over the initial and final states in γ lead to the unity factor. Using the asymptotics for the function Ψ[12] at large s that is true evenly in the neighbourhood of T=1, one finds

$$|\Psi|^2 \sim \exp\left(- \frac{\lambda^2(1-T)}{4} - [s\lambda^2(1-T)]^{1/2}\right). \qquad (19)$$

This expression does not contain the summation index n. Then the sum in (16) can be easily found to give

$$F(k,t) \approx e^{-\kappa^2 Dt}\ T^s \exp\left[\frac{1}{2}(1-T)(s-\lambda^2/2) - [s\lambda^2(1-T)]^{1/2}\right]. \qquad (20)$$

In this note we will not dwell on the analysis of the Fourier transform of $F(k,t)$ that determines the spectrum of the scattering from the system of noninteracting globules. Let us find the effective width of this spectrum, Ω_1. It is defined as follows:

$$\frac{1}{\Omega_1} = \int_0^\infty dt\ F(k,t). \qquad (21)$$

This is equivalent to the approximation of the true spectrum by a single Lorentzian of the width Ω_1. Taking into account again the condition s>>1, we have

$$\frac{1}{\Omega_1} \simeq \frac{\tau_0}{2\kappa s\lambda^2} \int_0^\infty dx\ \exp(-\sqrt{x} - xp), \qquad (22)$$

$$p=1/4s+1/2\lambda^2+\tau_0 k^2 D/2s\lambda^2, \qquad \tau_0 = Z/k_B T.$$

So,

$$\Omega_1 \simeq \frac{\kappa s\lambda^2}{\tau_0}\left(\sum_{n=0}^\infty \frac{\Gamma(2n+2)}{\Gamma(n+1)}\ (-p)^n \right)^{-1}, \qquad (23)$$

with the major term

$$\Omega_1 \simeq \kappa s\lambda^2/\tau_0 \sim k_B Tk^3/\eta. \qquad (24)$$

Thus, the effective width of the spectrum is proportional to the cube of the momentum transfer at the scattering and to the ratio of the temperature and viscosity. It contains no more parameters of the problem and does not

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depend on the characteristic sizes of the globule R_0 and $l^* = \sqrt{k_B T/\sigma}$ (_ the mean square amplitude of the deviation from the equilibrium radius). The result agrees with experimental observations and coincides with model calculations for chain macromolecules with the necessary inclusion of the hydrodynamic interaction. The obtained results significantly supplement our previous works [2,3].

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