Glassy dynamics in DNA: Ruled by water of hydration?

A. P. Sokolov, H. Grimm, and R. Kahn

Citation: The Journal of Chemical Physics **110**, 7053 (1999); doi: 10.1063/1.478610
View online: https://doi.org/10.1063/1.478610
View Table of Contents: http://aip.scitation.org/toc/jcp/110/14
Published by the American Institute of Physics

Glassy dynamics in DNA: Ruled by water of hydration?

A. P. Sokolov
Department of Polymer Science, University of Akron, Akron, Ohio 44325-3909

H. Grimm
Institut für Festkörperforschung, Forschungszentrum Jülich, 52425 Jülich, Germany

R. Kahn
Laboratoire Leon Brillouin, C.E.Saclay, Bat. 563, F-91191 Gif sur Yvette, France

(Received 17 November 1998; accepted 13 January 1999)

Inelastic neutron scattering spectra of DNA-fibers are analyzed using ideas formulated recently in the field of the glass transition. The analysis reveals two temperatures, namely, $T\sim 180-200$ K and $T\sim 230$ K, at which the dynamics of DNA exhibits qualitative changes. The former is similar to the glass transition temperature, whereas the latter is similar to the crossover temperature recognized now as an important point for the dynamics of the glass transition. Exactly in this temperature range many other hydrated biopolymers show some dynamic transition and strong slowing down of their functions. The crossover temperature appears to be close to the crossover temperature of bulk water. A possible relation of the dynamic transition to functions of biomolecules and also to the dynamic transition in the hydration shell is discussed. © *1999 American Institute of Physics.* [S0021-9606(99)51514-6]

INTRODUCTION

One of the main characteristic of any system is its dynamic properties, i.e., the characteristic of atomic motion. Dynamic properties are especially important for biological molecules because the static structure, i.e., equilibrium positions of atoms, is a ''dead'' structure, ''life'' and functions are associated with molecular motions. It is evident that the dynamic properties of biomolecules strongly influence their functions. For example, blocking of conformational motion changes kinetics of chemical reactions drastically. Dynamics at the mesoscopic frequency scale $\sim 1-1000$ GHz usually reflects local conformational changes, i.e., jumps of atoms from one configuration to another, and collective vibrations.

Dynamics of biomolecules at this frequency range shows many similarities with dynamic spectra of glass forming liquids; there is a low-frequency vibrational mode, similar with the so-called boson peak in glasses; there is a fast anharmonic motion, similar with a fast picosecond relaxation in glasses.[1–4] Moreover, there were attempts to identify some kind of the glass transition temperature T_g, where one finds the onset of anharmonicity in the dynamics of biomolecules. One should note that even in conventional glasses T_g is an ill-defined quantity. Usually it is defined as a temperature where characteristic structural relaxation time τ_α is $\sim 10^2-10^3$ s. It appears also in many other properties of glasses, as a jump of specific heat, as an onset of anharmonicity in dynamic properties, in mean square displacements of atoms $\langle x^2\rangle$, etc. Similar behavior was also observed for different biomolecules. Already in the early eighties experiments on proteins using Mössbauer technique[5] demonstrated strong rise of $\langle x^2\rangle$ at temperatures above 170 K. Also inelastic and quasielastic neutron scattering measurements[1,6] demonstrated onset of strong increase of $\langle x^2\rangle$ at temperatures 180–200 K. This behavior was interpreted as some kind of T_g and, in particular, for myoglobin the analysis of $\langle x^2\rangle$ leads to estimate $T_g\approx 200$ K.[7] The glass transition like behavior has been observed also in macroscopic properties of proteins. For example, the thermal expansion coefficient and mechanical properties of amorphous protein films indicated the glass transition (strong change in the temperature dependence) at $T=150-170$ K.[8] Also a weak jump in the specific heat of proteins indicated some kind of T_g at 160–170 K.[9] Thus the value of T_g estimated for hydrated proteins scatters in the range 160–200 K. It depends on the system under investigation and method used for the estimate. Usually methods that are sensitive to high frequency dynamics (like Mössbauer or neutron scattering spectroscopy) may give higher estimate of T_g than analysis of macroscopic properties.

During the last decade, however, significant progress in understanding of the glass transition phenomenon was strongly stimulated by mode-coupling theory of the glass transition (MCT).[10] The theory analyses nonlinear feedback mechanism of relaxation in simple liquids and predicts an existence of another important temperature, some crossover temperature T_c, where dynamics of the liquid should show qualitative changes. Investigations which use neutron- and light-scattering techniques and also dielectric spectroscopy demonstrated that the scenario suggested by MCT for the high temperature range describes reasonably well, at least on a qualitative level, spectra of different ionic, van der Waals, hydrogen- and even covalent-bonded systems.[11–16] In all cases T_c was found to be significantly higher than T_g. It was also found that MCT predictions describes rather well dynamics of supercooled water and T_c was estimated at ~ 220 K.[17] The latter is close to the well-known temperature of water singularities.

All these results clearly demonstrate that the glass tran-

sition is not a monotonous process, some qualitative changes in the dynamics occur at temperatures considerably above the conventional glass transition temperature T_g. Up to now these new ideas from the field of the glass transition were applied to analysis of the dynamics of myoglobin,[1,2] only. A reasonable agreement between the MCT predictions and neutron scattering data have been obtained. Estimation of T_c gives a value ~200 K close to the temperature below which the myoglobin loses its biological function.[2]

It is the main goal of the present contribution to analyze whether or not a similar crossover temperature shows up also in dynamics and relaxation processes of other biomolecules. We applied the MCT ideas to the analysis of the dynamics of DNA, a molecule that differs strongly from proteins. Nevertheless, a reasonable agreement with the MCT scenario is found also in this case and the estimate of T_c gives a value ~230 K close to the crossover temperature of water. It is another goal of the paper to understand whether or not the crossover in dynamics of biomolecules is ultimately defined by T_c of water. Some speculations about this crossover in the dynamics of biomolecules and its possible influence on their functions are discussed.

EXPERIMENT

The inelastic neutron scattering spectroscopy is a suitable tool for measurements of atomic motion because it measures density fluctuations directly. Due to the extremely large incoherent neutron scattering cross section of hydrogen (~10 times larger than any other atom) neutron spectra of organic systems reflect mostly motions of H-atoms. However, it is believed that the motion of H-atoms at the low frequencies of interest here ($\leqslant$1 THz which is nearly 100 times lower than, e.g., stretching vibration of a C–H bond) follows collective vibrations of large molecular groups. We used neutron scattering data of oriented Li-DNA-fibers hydrated to 75% relative humidity with D_2O, and thus corresponding to the B-form of DNA with ~15 water molecules per base-pair. Details of the sample preparation and measurements can be found in Refs. 4,18. Most of the data have been obtained using neutrons with λ=5 Å and frequency resolution $\Delta\nu$ ~30 GHz.

The spectra summed over all scattering angles and scaled with the Bose temperature factor are presented in Fig. 1. Scattering intensity from D_2O is much weaker than the one from DNA (due to extremely high scattering of H-atoms in DNA). It means that the presented spectra reflect essentially the motion of the DNA-molecule. At low temperatures the spectra show an inelastic peak at ν~1 THz which corresponds to low-frequency vibrations of the DNA molecule. At higher frequencies all spectra fall well on a single curve which show harmonic behavior of the vibrations at this range. At lower frequencies, however, the increase of the quasielastic scattering intensity with temperature reflects strongly anharmonic motion of the molecule (some kind of conformational fluctuations). The inset in Fig. 1 presents the temperature dependence of the Bose-scaled integrated intensity at low frequencies. It seems to be rather constant below ~150 K and increases strongly with temperature above ~200 K. Interpolation of the data shows the onset of anharmonicity for motion of the DNA-molecule at $T \approx 180-200$ K. The onset of anharmonicity at this temperature range has been also found for other biomolecules, like myoglobin[1] and dismutase.[6]

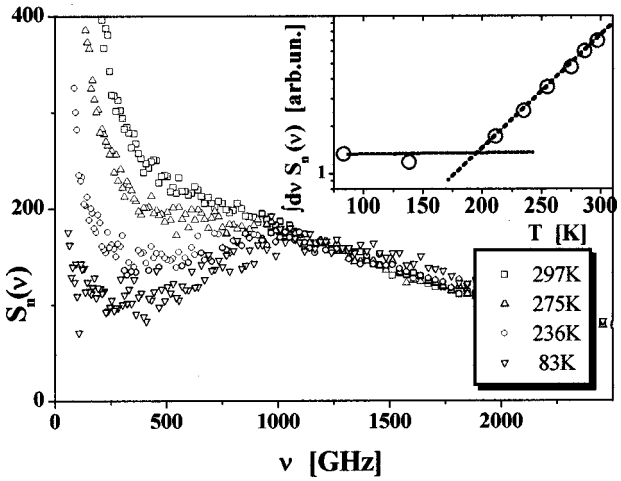

FIG. 1. Dynamic structure factor of DNA/D_2O at different temperatures measured with 5 Å neutrons. The spectra are rescaled by the temperature Bose factor, $n_B(\nu,T)=\{\exp(h\nu/kT)-1\}^{-1}$, to a common T=297 K; $S_n(\nu) = S(\nu)*n_B(\nu,297)/n_B(\nu,T)$. The inset shows temperature dependence of the rescaled intensity integrated in the frequency range 60–200 GHz.

For more detailed analysis of the anharmonic contribution we present the data as the susceptibility spectra $\chi''(\nu) = S(\nu)/n_B(\nu)$ (Fig. 2). In this representation relaxation processes are reflected as maxima in the spectra at $\nu \sim (2\pi\tau)^{-1}$ (τ is a relaxation time) and a separation between different processes would appear as a minimum. Indeed, the data presented in Fig. 2 demonstrate a minimum at frequencies below ~200 GHz which separates fast dynamics (dominates the spectrum at higher frequencies) and slow dynamics. In order to analyze the slow process in a broader frequency range we include in Fig. 3 the data obtained with higher resolution ($\Delta\nu$~7 GHz, using neutrons with λ=9 Å). Even at highest temperature, T=325 K, we were not able to resolve the slow process, i.e., the maximum is still inside of the resolution function (inset, Fig. 3). The thin solid line in Fig.

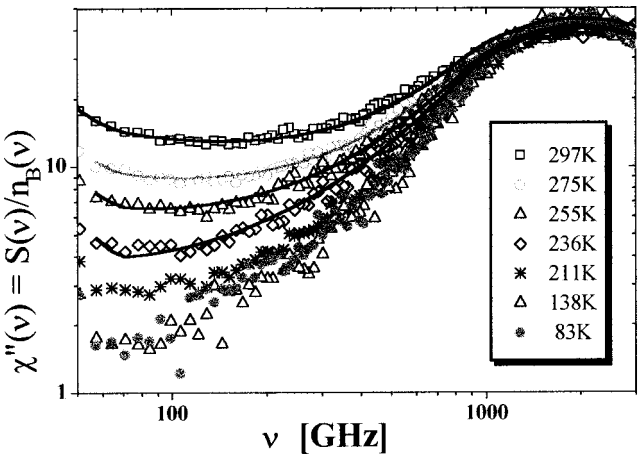

FIG. 2. The susceptibility spectra of DNA/D_2O at different temperatures (symbols) and their fit convoluted with the resolution function (lines).

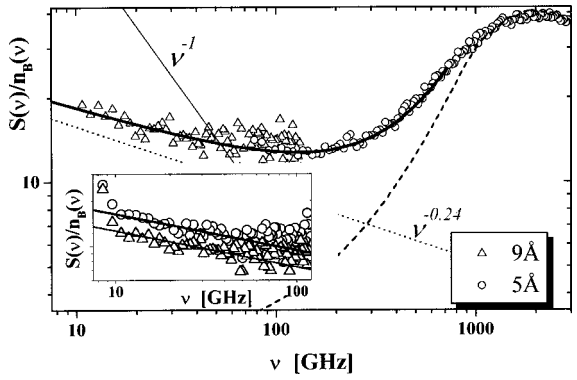

FIG. 3. The susceptibility spectrum of DNA/D_2O at $T=297$ K extended to lower frequency using the data measured with 9 Å neutrons. The thin solid line shows the slope expected for a single exponential decay process, the thick solid line shows the result of the fit, which is the sum of the slow process (the dotted line) and the fast process (the dashed line). The inset shows estimation of the exponent b from 9 Å neutron scattering data at $T=325$ K (○) and $T=297$ K (△). The lines show the slope with the exponent $b=0.24$.

3 demonstrates the slope of the spectrum $\chi''(\nu)\propto\nu^{-1}$ expected for a single exponential relaxation process. The experimentally observed spectrum shows much weaker decay, i.e., the slow process is strongly stretched. Approximating the low frequency end of the spectra by a power law, $\chi''(\nu)\propto\nu^{-b}$, we estimate the exponent $b\approx0.24\pm0.05$ (inset, Fig. 3). This result points out that the relaxation processes in DNA have either complicated behavior (hierarchy and/or strong coupling) or their relaxation times are broadly distributed. Extremely strong stretching is a characteristic feature of relaxation in polymeric systems, where molecular chains have many internal degrees of freedom. In this sense the DNA-molecule, as a biopolymer, is not exceptional.

It was shown[19] that relaxation processes in proteins measured in the time domain can be well approximated by the stretched exponential or Kohlrausch–Williams–Watts (KWW) decay function, $\phi(t)\propto\exp\{-(t/\tau_{\mathrm{KWW}})^{\beta}\}$, with stretching parameter $\beta=0.3$–0.5. It is interesting to note that the value of the stretching exponent, $b\approx0.24$, found here for the slow relaxation process in DNA, corresponds to the KWW stretching parameter $\beta\approx0.37$,[20] i.e., it is close to the value found for relaxation processes in proteins.

MCT SCENARIO AND THE DATA ANALYSIS

Now we turn to the analysis of the spectra in the way suggested by the mode coupling theory. MCT predicts that the relaxation in supercooled liquids occurs essentially in two steps; first on very short time scale (of the order of picosecond) the density–density correlation function $\Phi(t)=\langle\delta\rho(t)\,\delta\rho(0)\rangle/\langle\delta\rho(0)^2\rangle$ decays to a certain level, and then on a much longer time scale (from hundreds of picosecond to microsecond range, depending on temperature) a second, primary structural relaxation, the so-called α-relaxation, takes place and $\Phi(t)$ decays to the zero level.[10] As a result the susceptibility spectrum should show a minimum between these two processes. MCT predicts that the two processes are not simple exponential decays, they are stretched and have power-law spectral shapes, $\chi_S''(\nu)\propto\nu^{-b}$ for the high frequency tail of the slow process and $\chi_F''(\nu)\propto\nu^{a}$ for the low-frequency wing of the fast process. The latter, however, in real glass forming systems is usually modified due to vibrational contributions.[14] According to MCT's scenario at high temperatures the spectrum of the fast process as well as the amplitude and the shape of the slow process should be rather temperature independent, and the characteristic time of the slow process, τ_α, should show strong temperature variations, only. Thus, the susceptibility spectrum of the system at different temperatures can be described by a sum of the slow (can be approximated by a Cole–Davidson function) and the fast processes

$$\chi''(\nu,T)=\chi_S''(\nu)+\chi_F''(\nu)\approx I_S^{*}\,\mathrm{Im}[\{1+2\pi\nu\tau_\alpha(T)\}^{-b}]+\chi_F''(\nu) \qquad (1)$$

with the single temperature dependent parameter $\tau_\alpha(T)$. Here I_S is an amplitude of the slow process. MCT (in its idealized version) also predicts a critical temperature variation for τ_α,

$$\tau_\alpha(T)\propto(T-T_C)^{-\gamma}, \qquad (2)$$

where the exponent γ is directly related to the exponent b.[10] T_C is a crossover temperature where this MCT scenario should break down and below it the spectrum of the fast dynamics becomes temperature dependent.

We applied the suggested scenario for analysis of the presented spectra (Figs. 2 and 3). They indeed show the predicted minimum and the power law spectral shape for the high frequency tail of the slow process. As well as we could not resolve the slow process [i.e., we do not see the maximum in $\chi''(\nu,T)$] we simplified its spectral shape in Eq. (1) by a power law $\chi_S''(\nu)=\{\nu\tau_\alpha(T)\}^{-b}$ with $b=0.24$ and the single free parameter $\tau_\alpha(T)$. The latter, however, can be estimated in some arbitrary units only. So, for a complete description of the experimental spectra one should find the spectrum of the fast process $\chi_F''(\nu)$ which can be kept temperature independent [Eq. (1)]. According to MCT, the low-frequency tail of the fast process should have a power-law spectral shape, $\chi_F''(\nu)\propto\nu^{a}$. Relation between the exponents a and b gives value $a\approx0.18$ for $b=0.24$. It is not possible to identify this tail in the presented spectra because of strong vibrational contribution at high frequencies and the slow process contribution at low frequencies (Fig. 2). Due to that reason we approximated $\chi_F''(\nu)$ in the frequency range 50–800 GHz by second order polynomial with three free parameters. For their estimation we used an iterations procedure; first, we fitted the spectra at all temperatures in the frequency range 70–800 GHz using Eq. (1), then, we fixed parameters of the fast spectrum at their average values and repeated the fit using the only free parameter $\tau_\alpha(T)$; at the next step we fixed $\tau_\alpha(T)$ and repeated the fit with free parameters for the fast spectrum and then fixed them at their average values; after that we repeated the fit using the only free parameter $\tau_\alpha(T)$ and, etc. This iteration procedure rapidly converged in the high temperature region. However, we were not able to find any spectrum of $\chi_F''(\nu)$ which could be kept temperature independent below $T=236$ K. It means that the scenario works down to at least $T=236$ K, but breaks somewhere

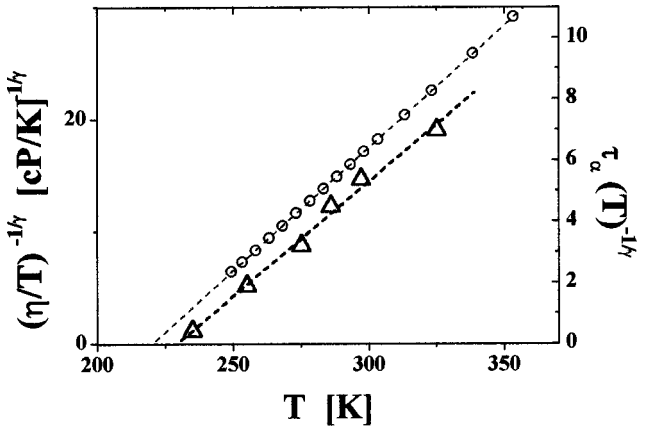

FIG. 4. Temperature dependence of the single fit parameter $\tau_\alpha(T)$ in the power $-1/\gamma$ (△), with γ=4.94. Temperature dependence of the viscosity time scale, (η/T), of water (○), here γ=2.05 (data from Ref. 17).

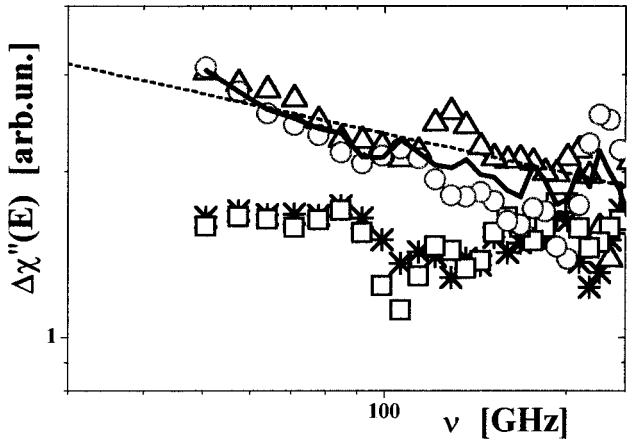

FIG. 5. Differences of the susceptibility spectra $\Delta\chi''(\nu)=\chi''(\nu,T_1)-\chi''(\nu,T_2)$: $T_1=275$ K and $T_2=255$ K (△); $T_1=255$ K and $T_2=236$ K (○); $T_1=297$ K and $T_2=236$ K (solid line, the intensity is scaled by a factor 0.25); $T_1=236$ K and $T_2=211$ K (□); $T_1=236$ K and $T_2=138$ K (*, the intensity is scaled by a factor 0.6). The dashed line shows $\Delta\chi''(\nu)\propto\nu^{-0.24}$.

above the next temperature point $T=211$ K. This gives an estimate of T_C in the range ~215–235 K. The resulting spectrum of the fast process, $\chi_F''(\nu)$, is shown in Fig. 3 (at $\nu>800$ GHz it was extended using smoothed spectrum measured at $T=138$ K). The final fit with the single free parameter $\tau_\alpha(T)$ describes reasonably well all spectra in the temperature range 325–236 K (Figs. 2 and 3).

An important point of the suggested scenario is a possibility to check the obtained temperature variation of $\tau_\alpha(T)$; it should follow the expected temperature variation [Eq. (2)] and the so obtained value of T_C should agree with the above estimate. The exponent γ can be directly calculated from the value of the exponent b via the transcendent equation,[10] which gives $\gamma\approx4.94$ for $b=0.24$. Indeed, $\tau_\alpha(T)^{-1/\gamma}$ varies rather linear with temperature and results in an estimate of $T_C\approx230$ K (Fig. 4) in a good agreement with the analysis of the spectral shape.

The experimental spectra (Fig. 2) show, however, nothing specific or critical in the temperature range around $T=230$ K; the temperature variation of the spectra seems to be monotonous. This situation is similar to that observed for glass forming systems and is the main objection against the MCT's scenario. The latter predicts qualitative changes for the temperature variation of the spectra at T_c. In order to test that prediction without any model assumption we analyzed differences between the susceptibility spectra, $\Delta\chi''(\nu)$, measured above and below 236 K. The analysis (Fig. 5), indeed, shows a qualitative change of the differential spectral shape around 230 K: $\Delta\chi''(\nu)$ has the same shape in the temperature range 297–236 K, which differs qualitatively from $\Delta\chi''(\nu)$ in the range 236–138 K. Moreover, the shape of $\Delta\chi''(\nu)$ at high temperatures is similar to the shape of the high frequency wing of the slow process, $\Delta\chi''(\nu)\propto\nu^{-0.24}$ (Fig. 5). The latter agrees, at least qualitatively, with the MCT's scenario that the main variation of the susceptibility spectrum at high temperatures is a shift of the slow process, whereas below T_c also the spectrum of the fast dynamics shows significant variations. This analysis clearly demonstrates that there are two temperature ranges, above and below ~230 K, where dynamics show different temperature variations.

DISCUSSION

Very often neutron and light scattering spectra of biomolecules are described by a sum of a few Lorentzians. Parameters of these Lorentzians depend on the resolution function of the spectrometer, etc.[22] Many authors try to ascribe every Lorentzian to some specific motion of the biomolecule. However, the presented here results clearly demonstrate stretched relaxation spectra in a broad frequency range. These spectra can not be described just by a sum of a few Lorentzians; one should assume either a broad distribution of relaxation processes or nonexponential relaxation.

One particular description of the nonexponential relaxation in liquids is suggested by the mode-coupling theory. As it is shown above the scenario suggested by MCT describes reasonably well the spectrum of DNA and its temperature variations. This fact by itself is rather surprising because MCT was developed originally for simple liquids. However, the suggested scenario at least on a qualitative level was found to be a good approximation for spectra of different glass forming liquids[11–15] and also describes well the spectra of supercooled water.[17] The presented results together with the results published previously for myoglobin[1] show that the dynamics of these complicated biomolecules can be also described using basic physical ideas.

The presented analysis shows an existence of two characteristic temperatures for the dynamics of DNA. (i) Onset of anharmonicity which clearly happens somewhere below 210 K (Fig. 2), most probably around $T\sim180-200$ K (inset Fig. 1). This onset of anharmonicity is usually interpreted for the glass forming systems as a sign of T_g and is consistent with estimates of T_g for proteins.[6–9,21] (ii) Some dynamic transition at $T\sim230$ K which we ascribe to the MCT's crossover temperature T_c. The presented analysis (Figs. 2–5) clearly demonstrates that the crossover in dynamics appears at temperatures significantly higher than the onset of anharmonicity. We want to stress that the dynamic transition just in the temperature range between 180 K and 230 K has been ob-

served using different experimental techniques for variety of biological macromolecules.[3,6–9,21,22] Based on our results one can speculate that this is the transition range between T_g and T_c and it appears to be similar for many biomolecules. The crossover temperature obtained for DNA is also close to the characteristic temperature below which functions of biomolecules slow down significantly. For example, it was found that crystalline ribonuclease A loses function just below 220 K,[23] a function of bacteriorhodopsin slows down significantly around 200 K,[24] and efficiency of the photoinduced electron transfer drops down below ~230 K.[5]

According to modern ideas the dynamics of the glass forming liquids below T_C is controlled by the potential energy landscape which does not play an important role at higher temperatures.[25–27] It means that below T_C the system is trapped in some local minimums of the potential and cannot reach all points of the phase space within a reasonably short time (some nonergodic states develop at short times). This localization in phase space blocks chemical reactions, diffusion, and other processes which require a few different states. In the case of biomolecules this scenario explains why their functions slow down significantly just below this temperature range. For example, it is known that the binding process of CO to myoglobin or hemoglobin requires a few different states. Below T_c the system cannot easily reach all of them. As a result some concurrent processes, which have negligible influence at higher temperatures, can become important below T_c and finally disable the function of the molecule.

The estimated crossover temperature appears to be very close to the critical temperature of water (see, Fig. 4) which leads us to speculate about the role of hydration in critical dynamics and functions of biomolecules. That is, the hydration shell has critical behavior in the dynamics at $T \approx 210-230$ K and the motion of biomolecules is coupled to the surrounding water. As a result the hydration shell hinders the motion of macromolecules and suppresses their functions. This suggestion agrees with the analysis of dynamics of hydration water in protein,[28] where it was found that below 230 K all the diffusion motions of water molecules appear to be frozen. Also a comparison of dry and hydrated bacteriorhodopsin demonstrated that only the hydrated sample shows a strong change in the dynamics at $T \approx 230$ K.[3] Thus we expect that a decrease of the level of hydration should suppress the dynamic transition observed in DNA at $T \approx 230$ K. These speculations also agree with the recent experiments on chemical reaction kinetics in myoglobin and hemoglobin in different water/glycerol and trehalose solutions.[29–31] Results of these investigations showed that the viscosity of the solvent plays a major role in the slowing down of the chemical reaction kinetics and properties of the proteins play a secondary role, only.

In that sense it is interesting to speculate that T_c, where the first temporary limitation of the phase space happens, can be important for suppression of the functions. For most of the biological molecules this temporary delay is enough to hinder the biochemical processes. Thus it would be important to find a way of controlled shift of the crossover temperature. It can serve for preservation of the biomolecules in different conditions, the problem that is now important in pharmaceutical industry. One of the ways is already actively discussed in the literature and is under different tests in laboratories; ''putting proteins under glass.''[30–32] It was demonstrated that one could suppress the biochemical reactions already at room temperature putting the proteins in sugar surroundings. It would be important to continue investigations along this line in order to check an influence of the hydration level and other solvents including sugars on critical dynamics of biomolecules, whether or not T_C can be shifted in that way and whether or not the process of biomolecule stabilization can be understand in the framework of these physical ideas.

ACKNOWLEDGMENTS

The authors are thankful to D. Richter, G. Büldt, and J. Fitter for helpful discussions.

[1] W. Doster, S. Cusack, and W. Petry, Nature (London) **337**, 754 (1989).
[2] W. Doster, S. Cusack, and W. Petry, Phys. Rev. Lett. **65**, 1080 (1990).
[3] M. Ferrand, A. J. Dianoux, W. Petry, and G. Zaccai, Proc. Natl. Acad. Sci. USA **90**, 9668 (1993).
[4] H. Grimm and A. Rupprecht, *Inelastic Neutron Scattering Studies of Oriented DNA, Nonlinear Excitations in Biomolecules*, edited by M. Peyrard (Springer, Berlin, 1994), p. 101.
[5] F. Parak, E. N. Frolov, A. A. Kononenko, R. L. Mössbauer, V. I. Goldanskii, and A. B. Rubin, FEBS Lett. **117**, 368 (1980).
[6] C. Andreani, A. Filabozzi, F. Menzinger, A. Desideri, A. Deriu, and D. D. Cola, Biophys. J. **68**, 2519 (1995).
[7] F. Parak and H. Frauenfelder, Physica A **201**, 332 (1993).
[8] V. N. Morozov and S. G. Gevorkian, Biopolymers **24**, 1785 (1985).
[9] J. L. Green, J. Fan, and C. A. Angell, J. Phys. Chem. **98**, 13780 (1994).
[10] W. Götze and L. Sjögren, Rep. Prog. Phys. **55**, 241 (1992).
[11] W. Knaak, F. Mezei, and B. Farago, Europhys. Lett. **7**, 529 (1988).
[12] G. Li, W. M. Du, X. K. Chen, H. Z. Cummins, and N. J. Tao, Phys. Rev. A **45**, 3867 (1992).
[13] P. Lunkenheimer, A. Pimenov, M. Dressel, Yu. G. Goncharov, R. Böhmer, and A. Loidl, Phys. Rev. Lett. **77**, 318 (1996).
[14] A. P. Sokolov, W. Steffen, and E. Rössler, Phys. Rev. E **52**, 5105 (1995).
[15] A. Brodin, L. Börjesson, D. Engberg, L. M. Torell, and A. P. Sokolov, Phys. Rev. B **53**, 11511 (1996).
[16] A. P. Sokolov, Science **273**, 1675 (1996); Endeavour **21**, 109 (1997).
[17] A. P. Sokolov, J. Hurst, and D. Quitmann, Phys. Rev. B **51**, 12865 (1995).
[18] H. Grimm and A. Rupprecht, Physica B **234–236**, 183 (1997).
[19] G. U. Nienhaus, J. D. Müller, B. H. McMahon, and H. Frauenfelder, Phys. D **107**, 297 (1997).
[20] C. P. Lindsey and G. D. Patterson, J. Chem. Phys. **73**, 3348 (1980).
[21] I. E. T. Iben, D. Braunstein, W. Doster, H. Frauenfelder, M. K. Hong, J. B. Jonson, S. Luck, P. Ormos, A. Schulte, P. J. Steinbach, A. H. Xie, and R. D. Young, Phys. Rev. Lett. **62**, 1916 (1989).
[22] J. Fitter, R. E. Lechner, and N. A. Dencher, Biophys. J. **73**, 2126 (1997).
[23] B. F. Rasmussen, A. M. Stock, D. Ringe, and G. A. Petsko, Nature (London) **357**, 423 (1992).
[24] T. Iwasa, F. Tokunaga, and T. Yoshizawa, Biophys. Struct. Mech. **6**, 253 (1980).
[25] C. A. Angell, in *Complex Behavior of Glassy Systems*, edited by M. Rubi (Springer, Berlin, 1997), p. 1.
[26] G. Diezemann, H. Sillescu, G. Hinze, and R. Böhmer, Phys. Rev. E **57**, 4398 (1998).
[27] M. Schulz, Phys. Rev. B **57**, 11319 (1998).
[28] M.-C. Bellissent-Funel, J. Texeira, K. F. Bradely, and S. H. Chen, J. Phys. I **2**, 995 (1992).
[29] A. Ansari, C. M. Jones, E. R. Henry, J. Hofrichter, and W. A. Eaton, Science **256**, 1796 (1992).
[30] S. J. Hagen, J. Hofrichter, and W. A. Eaton, Science **269**, 959 (1995); J. Phys. Chem. **100**, 12008 (1996).
[31] D. S. Gottfried, E. S. Peterson, A. G. Sheikh, J. Wang, M. Yang, and J. M. Friedman, J. Phys. Chem. **100**, 12034 (1996).
[32] K. C. Fox, Science **267**, 1922 (1995).