Dynamics of myoglobin: Comparison of simulation results with neutron scattering spectra

JEREMY SMITH*, KRZYSZTOF KUCZERA†, AND MARTIN KARPLUS

Chemistry Department, Harvard University, 12 Oxford Street, Cambridge, MA 01238

Contributed by Martin Karplus, November 3, 1989

ABSTRACT **Molecular dynamics simulations are used to calculate the incoherent neutron scattering spectra of myoglobin between 80 K and 325 K and compared with experimental data. There is good agreement over the entire temperature range for the elastic, quasi-elastic, and inelastic components of the scattering. This provides support for the accuracy of the simulations of the internal motions that make the dominant contributions to the atomic displacements on a time scale of 0.3–100 ps (100–0.3 cm^{-1}). Analysis of the simulations shows that at low temperatures a harmonic description of the molecule is appropriate and that the molecule is trapped in localized regions of conformational space. At higher temperatures the scattering arises from a combination of vibrations within wells (substates) and transitions between them; the latter contribute to the quasi-elastic scattering.**

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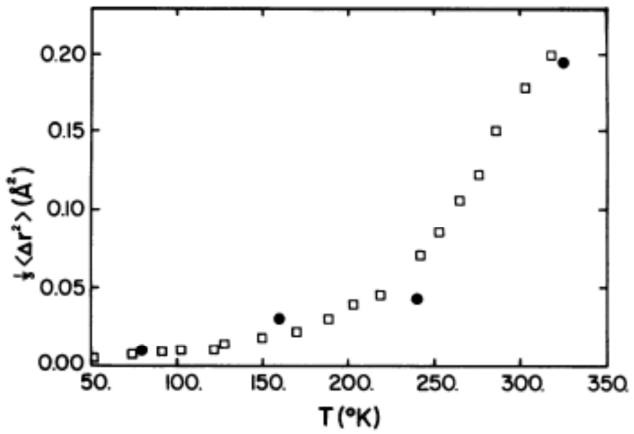

FIG. 1. Temperature dependence of the isotropically averaged mean squared displacements of myoglobin, $\frac{1}{3}\langle \Delta r^2 \rangle$, averaged over the exchangeable hydrogens. □, From the neutron experiment; ●, from molecular dynamics simulations.

Comment by Wolfgang Doster at bioneutron.de

The degree of agreement between simulation and experiment with respect to temperature dependent displacements and spectra is really remarkable. However one point remains obscure: It is never exposed, that this is a vacuum simulation of myoglobin. It is supposed to reproduce an effect, which is induced by hydration water. The authors simulate a dehydrated protein, which should not exhibit a dynamical transition. This discrepancy was swept under the carpet. Even in his review one year later in Qu. Rev. Biophys. (1991) Smith did not discuss this fact. By contrast the group of Bernie Brooks and Steinbach published at about the same time simulations of hydrated myoglobin with even better experimental agreement. The relevance of dynamic neutron scattering to biology was to test MD simulations and related force fields on a ps time scale. Around 1990 this was achieved by B. Brooks, R. Loncharich and Pete Steinbach.

Temperature Dependence of hydrated myoglobin, comparison of force field calculations with neutron scattering data by R. Loncharich and B. Brooks, J. Mol. Biol. (1990) 215, 439

This figures show simulated neutron scattering spectra versus T including the boson peak of hydrated myoglobin.

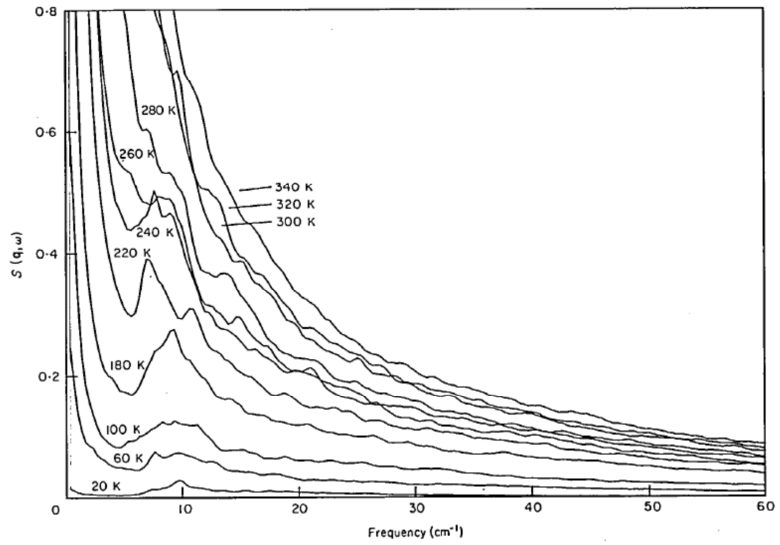

Figure 9. Incoherent scattering, $S(q, \omega)$, as a function of frequency (cm^{-1}). Spectra are calculated by numerical Fourier transform of $I(q, t)$.

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The effects of environment and hydration on protein dynamics: a simulation study of myoglobin

Peter J. Steinbach [a], Richard J. Loncharich [b] and Bernard R. Brooks [a]

[a] *Molecular Graphics and Simulation Laboratory, Division of Computer Research and Technology, National Institutes of Health, Bethesda, MD 20892, USA*

[b] *Supercomputer Applications and Molecular Design, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285-0403, USA*

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Three classes of molecular dynamics (MD) simulations of carboxy-myoglobin (MbCO) have been performed to investigate the environmental and temperature dependence of protein dynamics. The first class examines the effects of hydration. Simulations of MbCO were performed at 100 and 300 K with 0, 35, 100, 349, and 999 water molecules, and at 300 K with 3832 water molecules. The second class considers a cluster of three partially hydrated MbCO molecules (349 waters each) at 100, 180, 240, and 300 K. The third class of simulations, performed at 100 and 300 K, examines hydration by D_2O and also the effects of different vacuum models and long-range electrostatic cutoff methods. The simulations generally consist of 200 ps of heating and equilibration followed by 100 ps of dynamics used for analysis. Atomic fluctuation is compared to neutron scattering data to better determine the type of calculation needed to reproduce the low-temperature behavior of proteins. The simulations of hydrated myoglobin indicate that as the hydration increases: (i) agreement with the X-ray structure improves, (ii) the number of heavy-atom dihedral transitions decreases at both 100 and 300 K, and (iii) atomic fluctuations decrease at 100 K but increase at 300 K. The cluster and deuterated simulations exhibit atomic fluctuations at 100 K similar to, but slightly reduced from, those of a single hydrated myoglobin. Thus, our previous observation from MD simulations of low-temperature mean-square fluctuation three times larger than that observed experimentally does not appear to be due to the mass of the water model, nor the complete absence of intermolecular protein–protein contacts.

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Protein hydration elucidated by molecular dynamics simulation

(deviation from x-ray crystal structure/fluctuation/dihedral transitions/glass transition)

PETER J. STEINBACH AND BERNARD R. BROOKS*

Laboratory of Structural Biology, Division of Computer Research and Technology, National Institutes of Health, Bethesda, MD 20892

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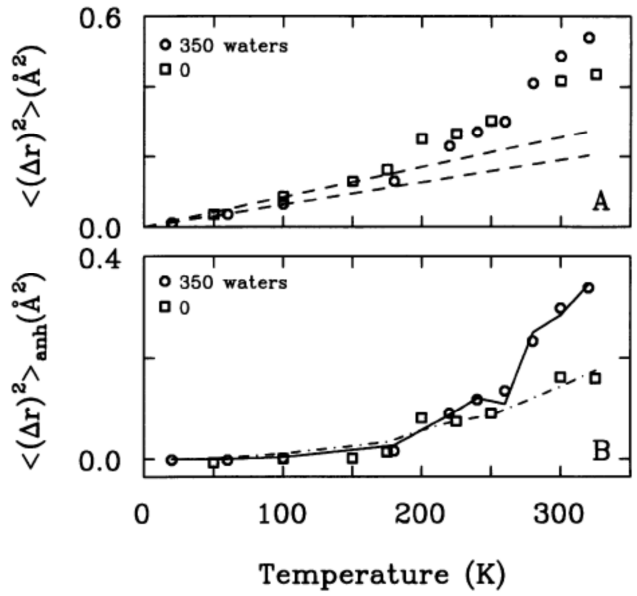

FIG. 3. (*A*) Mean-square fluctuation $\langle(\Delta r)^2\rangle$, averaged over all protein atoms for simulations of MbCO hydrated by 0 and by 350 water molecules (11). Harmonic fluctuation is extrapolated to high