Response to “Comment on a proposed method for finding barrier height distributions” [J. Chem. Phys. 103, 1235 (1995)]

John E. Straub and T. Keyes
Department of Chemistry, Boston University, Boston, Massachusetts 02215

D. Thirumalai
Department of Chemistry and Biochemistry, Institute for Physical Science and Technology, University of Maryland, College Park, Maryland 20742

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Several systems, such as proteins and glasses, are characterized by a complex potential energy surface, i.e., there are many minima that are separated by barriers of differing heights spanning the entire gamut of energy scales.[1–3] For these systems, it is meaningful to characterize the distribution of energy barriers, $g(E)$, which is notoriously very difficult to compute. In several papers, we have proposed and developed related methods for calculation of $g(E)$ from the temperature-dependent fraction $f_u(T)$ of unstable “instantaneous normal modes.” We have obtained $g(E)$ in peptides[4] and proteins[5] and the unit density Lennard-Jones liquid.[6] Our methods are necessarily approximate and rely on physically motivated simplifications. Probably the most important simplification is that the potential energy landscape is assumed to look the same from all the minima. This excludes the existence of “correlation” where the height of a barrier depends upon the depth of the connected minima. The assumption is clearly stated in our work. For example,[7] “We now invoke a major simplifying assumption, the equivalent minima model—the topology of the potential surface is identical when viewed from each minimum.” Again,[5] “We assume ... the potential energy as seen from the minimum of any basin will be identical to any other.”

In the accompanying Comment, Zwanzig[8] considers a one-dimensional potential energy function, $U(x)$, generated by successive placement of randomly chosen parabolas of alternating downward (barrier) and upward (minimum) curvature along the $U=0$ line; the minima have negative energy and the barriers positive energy. This model has a strong correlation. A minimum with negative energy E_α will have relative barrier energies E such that $E \geqslant |E_\alpha|$. *There is no possibility that a deep minimum will adjoin a low barrier.* Thus, the model is antithetical to the assumptions in our papers.

Zwanzig demonstrates that the Straub and Thirumalai (ST) integral equation theory,[4,5] starting from the exact $g(E)$, yields an incorrect T dependence of $f_u(T)$ at low T. For that example, the ST equation results in a linear T dependence while the exact result varies as $(1/T)\exp(-1/T)$. We consider this neither surprising nor a damaging criticism of our work, since Zwanzig’s model has strong correlation, explicitly excluded in our theories. It is therefore interesting and informative to repeat Zwanzig’s calculation for a one-dimensional potential with zero correlation.

We choose a one-dimensional rough potential of a form originally studied by Zwanzig:[9]

$$V(x)=x^2/2+\epsilon\cos(qx). \tag{1}$$

This potential consists of a quadratic “background” potential which varies slowly compared with the sinusoidal “roughness.” An effective Smoluchowski equation was proposed for coarse grained motion (on the length scale greater than $1/q$) which leads to the correct mean first passage time. At low temperatures, the effective diffusion constant is reduced from the original by an Arrhenius-like temperature factor $\exp(-2\beta\epsilon)$ since motion on a length scale greater than $1/q$ involves activated crossing of barriers of a height 2ϵ. For this to be true, it must be that the background (quadratic) potential be approximately constant over the coarse graining length scale $1/q$.

Using the integral equation of Straub and Thirumalai,[4,5] the fraction of unstable modes $f_u(T)$ and the distribution of intrinsic barrier heights $g(E)$ are related by[5]

$$f_u(T)=\int_0^\infty dE\; g(E)\bar{f}_u(T,E). \tag{2}$$

It is straightforward to calculate the fraction of unstable modes for this potential as a function of temperature. We use the original kernel $f_u(T,E)$ which was derived for a symmetric piecewise parabolic potential[4,5] with the result

$$f_u(T)=\int_0^\infty dE\; g(E)\,\frac{1}{1+e^{2\beta E/3}}\,. \tag{3}$$

Restricting ourselves to a region of x where the background potential varies slowly compared with the roughness potential, the intrinsic barrier height distribution for the potential [Eq. (1)] (as seen from any local minimum on the potential surface) is to a good approximation $g(E)=\delta(E-2\epsilon)$. The fraction of unstable modes for this model potential is simply

$$f_u(T)=\frac{1}{1+e^{4\beta\epsilon/3}}\,. \tag{4}$$

Note that the fraction of unstable modes for this model has a low temperature limiting behavior of $(1/T)\exp(-1/T)$. A comparison of the numerically computed $f_u(T)$ with that obtained from the ST integral equation is displayed in Fig. 1. The ST integral equation is successful because the potential in Eq. (1) satisfies the equivalent minima hypothesis and not because Eq. (1) can be fitted by a piecewise harmonic poten-

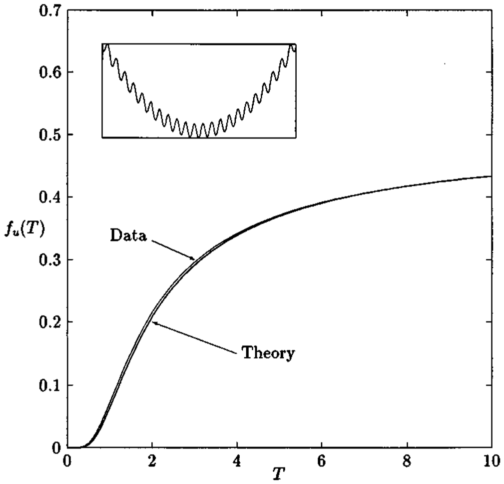

FIG. 1. The fraction of unstable modes as a function of temperature computed numerically and using the integral equation of Straub and Thirumalai for the one-dimensional rugged potential $V(x)=x^2/2+\epsilon\cos(qx)$ with $\epsilon=2$ and $q=10$ (shown by inset). The barrier height distribution is taken to be $g(E)=\delta(E-2\epsilon)$.

tial. In the example chosen by Zwanzig[8] the piecewise potential is *exactly* piecewise harmonic. Nevertheless, the ST integral equation is not satisfactory at low T because correlations in the potential violate the fundamental assumption of our theory.

The Comment of Zwanzig does serve to emphasize that our results for $g(E)$ are dependent on the validity of the "equivalent minima" hypothesis. It is of great interest to examine this hypothesis—and, more generally, to characterize the potential surface—in liquids and proteins. Correlations could be measured directly by computer simulation. Existing evidence favors low correlation. For both liquids and proteins, $f_u(T)\propto T$ at low T. For a system with nondelta function $g(E)$, Zwanzig's Comment shows that such behavior is inconsistent with strong correlation, while it is consistent with our theories. Our attitude has been, and is, that since $g(E)$ is such a crucial, and previously inaccessible, quantity, it makes sense to continue with approximate theories with clearly stated assumptions whose reliability can be examined.

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