

Helman *et al.* Respond: In the low-frequency (ω) limit, where the acoustic phonon density of states is given¹ by $\rho(\omega) \propto \omega^{d_{fr}-1}$ ($d_{fr} = 2d_f/d_w$, where d_f is the fractal dimension and d_w is the fractal dimension associated with a random walk restricted to the fractal), the weak cross-links (mainly hydrogen bonds) of the protein are important and may influence the effective values of both d_f and d_w as a result of finite-size effects. When cross links are present the fractal dimension should be deduced by counting the alpha carbons which, within successive radii R , are bridged either by the main chain or by cross links. Thus one expects that for a *finite* chain, as a function of the density of cross links (and assuming that the spatial structure of the protein backbone remains invariant), the effective value of d_f increases continuously from the chain fractal dimension² d_c (for zero density) up to the reentrant fractal dimension² d_r (for high density). However, the effective values of the fractal dimension d_c and d_r should be equal and coincide with the true fractal dimension d_f in the infinite-size limit. Also we expect that for a finite chain d_c approximates d_f better than d_r ($d_c \approx d_f$). On the other hand, it appears also quite plausible that for a *finite* chain as the density of cross links increases d_w makes a smooth crossover from $2d_c \approx 2d_f$ down to a value near to 2, while in the infinite-size limit we expect $d_w \approx 2$ for any nonzero density of cross links. Therefore for a nonzero concentration of cross links and for an *infinite* chain we expect $d_w \approx 2$ and $d_f \approx d_c$, which imply the experimentally observed relation $d_{fr} \approx d_c$. This corresponds to the case discussed in our paper.³ On the other hand, for a *finite* chain we expect the effective value of the fractal dimension to be larger than d_c and the effective value of d_w to be larger than 2, still giving the same value $d_{fr} \approx d_c$. This is the case discussed by Stapleton.²

Computer simulations could be used to study the dependence of d_f and d_w on the density of cross links and to assess the magnitude of the finite-size blurring. The experimental equivalent of such a study (chemical or thermal denaturation of the protein) is hard to perform, because the backbone naturally tends to modify its spatial structure simultaneously.

Like Stapleton,² although for different reasons,

Cates⁴ argues that the inclusion of short ("local" in his words) cross links (which obviously are the most relevant in the proteins) does not necessarily yield $d_w = 2$. As an example he refers to a work by Banavar, Harris, and Koplik⁵ who obtained $x \approx 0.46$ for $d = 2$ and 0.73 for $d = 3$; hence $d_w = d_f + \bar{z} = d_f + 2x \approx 2.92$ (or $d_{fr} = 2d_f/d_w \approx 1.37$) for $d = 2$ and $d_w \approx 3.46$ (or $d_{fr} \approx 1.15$) for $d = 3$. However, Havlin *et al.*⁶ have more recently obtained results which, as they point out, are *at variance* with those of Banavar, Harris, and Koplik⁵ for $d = 2$ (the discrepancy disappears for $d = 3$). Havlin *et al.*⁶ obtain for both $d = d_f = 1$ and $d = d_f = 2$, $d_w = 2$, thus supporting our model [note a misprint in their Table I: for $d = 1$ it should read $d_f = 1$, in accordance with their statement slightly below their Eq. (13)].

In summary, the fractal conception of a protein first introduced by Stapleton still seems to be adequate *if the cross links are taken into account*.

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