# A fractal description of the vibrational dynamics of proteins: A beautifully complicated description?

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**The (Raman) spin-lattice relaxation rate $T_1^{-1}$ of a paramagnetic ion in proteins probes the vibrational dynamics of these systems. The cross-links between the various parts of the polypeptide chain play a crucial role in the dynamics. All theoretical attempts to explain the temperature dependence of $T_1$ as a consequence of the existence of short-range cross-links in the self-avoiding walk models of linear polymers have had, at best, very limited success. However, using a standard theoretical technique, Elber and Karplus computed $T_1$ for several proteins within the effective-medium approximation; the temperature dependence of $T_1$ was found to be in good agreement with the corresponding experimental observation.**

> 'Some of us should venture to embark on a synthesis of facts and theories, albeit with second-hand and incomplete knowledge of some of them, and at the risk of making fools of ourselves. So much for my apology.'
>
> –Erwin Schrödinger in *What is Life?*

PROTEINS are polymeric macromolecules with very large molecular mass. For example, a molecule of haemoglobin is much heavier than, say, a water molecule; the mass of a water molecule is only 18 daltons whereas that of a haemoglobin molecule is 64,650 daltons. A water molecule is approximately 4 Å in diameter whereas the size of a molecule of myoglobin (the muscle variety of haemoglobin) is 44 Å × 44 Å × 25 Å.

All proteins in living organisms are made up of only twenty different amino acids. When two amino acids combine to form a peptide bond, a molecule of water is removed so that the carbon atom of the carboxylic acid group on one amino acid is connected directly to the nitrogen atom of the amine group on the next amino acid. Typically, 100 to 500 amino acids link in this manner to form a polypeptide chain of amino-acid residues. The order of the amino acid residues along the polypeptide chain or chains of a protein is called the primary structure of the protein.

A polypeptide chain forms secondary structures, e.g. the so-called $\alpha$-helix or $\beta$-sheet, in appropriate environments. Hydrogen bonds, which are weak electrostatic chemical bonds, are important in the formation of secondary structure. Hydrogen bonds and disulphide bridges, which are covalent bonds, contribute to the tertiary structure of proteins, in which loops of the polypeptide chain are cross-linked. Hydrogen bonds are more relevant for the discussion in this review. A single hydrogen bond is very weak compared to the main-chain carbon–carbon single bond; it is these weak hydrogen bonds that are responsible for the extreme flexibility of the protein chains.

In this review I shall consider the vibrational dynamics of only two classes of proteins: (i) haem proteins (e.g. myoglobin), and (ii) iron–sulphur proteins (e.g. ferredoxin). Haemoglobin and myoglobin play crucial roles in the respiratory system of vertebrates; haemoglobin acts as the 'oxygen carrier' and myoglobin is the 'oxygen container'[1]. Ferredoxins are part of protein complexes that transfer electrons in photosynthesis.

## Theoretical physicist's model of a linear polymer

As stated earlier, proteins are polymers formed by the chemical bonding of amino acids. For simplicity, let us assume that all the monomers—the amino acids—are identical. If each monomer binds chemically with just two other monomers at its two ends, the resulting polymer is called a *linear polymer*. Strictly speaking, proteins are quasilinear polymers because of weak cross-links between various parts of the polypeptide chain.

If one is not interested in phenomena that take place at the length scales of individual monomers, a linear polymer in a $d$-dimensional space is usually described by a serpentine continuous curve $c(\varepsilon)$ parametrized by the contour variable $\varepsilon$ (Figure 1*a*). This is a continuum description. In the absence of intermonomer interaction the discretized version of this model would look like a random walk (RW) on a $d$-dimensional lattice where the orientation of each of the steps of the walk is an independent random variable. However, intermonomer interaction leads to an effective repulsive core around each monomer and, consequently, the chain cannot cross itself. This is called the *excluded-volume effect*[2]. In the corresponding discrete version the excluded-volume effect is taken into account by imposing the constraint that the random-walker cannot visit a lattice site more than once. Such walks are called *self-avoiding walks*

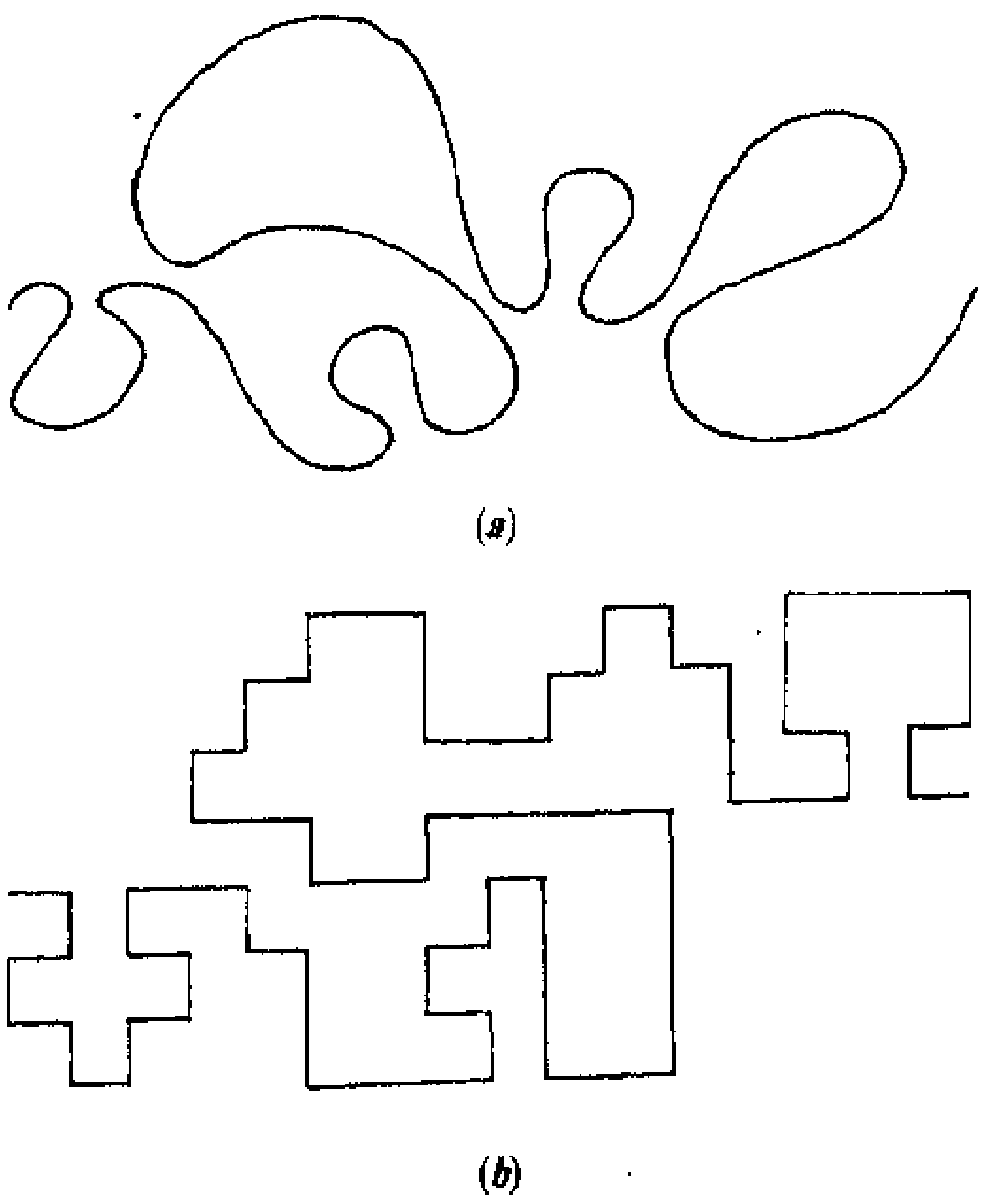

**Figure 1.** *a*, A continuum model of linear polymers. *b*, A discrete model of linear polymers (a self-avoiding walk).

(SAW) (Figure 1*b*). Thus SAW is a non-Markovian stochastic process whereas RW is Markovian.

The end-to-end distance $R$ of an $N$-step SAW depends on the configuration. Very simple arguments (the so-called Flory arguments) lead to the following relation between the mean-square end-to-end distance $\langle R^2 \rangle$ and the number of steps $N$:

$$\langle R^2 \rangle \sim N^{2\nu}, \qquad (1)$$

where

$$\nu = 3/(d+2) \text{ in } d \text{ dimension } (d \leq 4) \qquad (2)$$

in the Flory approximation. The Flory value (2) for $\nu$ is known to be exact in $d=1$ and $d=2$, and very close to the most precise numerical estimate in $d=3$.

Note that, for RW, $\nu = 1/2$ for all $d$. This implies that the repulsive self-avoiding constraint leads to 'swelling' of the chain compared to a chain without the self-avoiding constraint in all $d<4$. Physically, equations (1) and (2) describe a fundamental geometric property of a linear polymer, namely the asymptotic dependence of the mean-square end-to-end distance on the 'molecular weight' $N$.

## Fractal dimension and walk dimension

The relation (1) has been used quite extensively in literature over the last three decades. However, very recently, it has become fashionable to express relations (1) and (2) as

$$\langle R^2 \rangle \sim N^{2/d_f}, \qquad (3)$$

where

$$d_f = \nu^{-1}$$

is called the fractal dimension (see Mandelbrot[3] for an elementary introduction).

To briefly explain the concepts of fractals and fractal dimension: Consider a box containing apples, the total mass of the apples being $M$. Suppose the storage space in the box is increased by increasing the length of each edge from $L$ to $2L$. The box will now carry a mass $8M$ of apples, i.e.

$$M(2L) = 8M(L) = 2^3 M(L).$$

If the box is $d$-dimensional, then one would expect

$$M(\varepsilon L) = \varepsilon^d M(L).$$

Setting $\varepsilon = 1/L$, we have $M \sim L^d$. However, fractal objects are somewhat unconventional, because, for fractals,

$$M \sim L^{d_f}, \text{ where } d_f < d.$$

Usually, fractal dimensionality of a system without translational symmetry is a consequence of the dilation symmetry; a small part of the system, when magnified, looks similar to the original system. When observed through a 'microscope', if the system looks exactly identical to the original one, irrespective of the magnification factor, the system is called an exact fractal. On the other hand, if the original and the magnified systems look similar only on the average the system is called a statistical fractal.

In the light of the definition of fractal dimension, equation (3) can be interpreted physically as follows: On the average, there are $N$ monomers within a volume $R^{d_f}$, where $d_f < d$. In the Flory approximation,

$$d_f = (d+2)/3 \quad \text{for } d \leq 4. \qquad (4)$$

Model linear polymers are statistical fractals; large loops consist of smaller loops, and so on; there are loops on all length scales. However, so far as real linear polymers are concerned, there is an upper cutoff and a lower cutoff of length scales; the system is not a fractal outside these cutoffs.

Next, let us explore the relation between the mean-square end-to-end distance of a $t$-step RW on a fractal. Conventionally, this relation is expressed as

$$\langle R^2 \rangle \sim t^{2/d_w}, \qquad (5)$$

where $d_w$ is called the walk dimension. It is worth mentioning here that for RWs on Euclidean lattices $d_w = 2$ for all space dimensionalities $d$.

## ESR relaxation rate of iron in protein chains

Stapleton *et al.*[4] measured the (Raman) spin-lattice relaxation rate of iron in several proteins at low temperatures; the samples were in the form of frozen solutions. In the regimes of temperature relevant for these experiments, the relaxation rate $1/T_1$ was argued to be (see Appendix A)

$$(1/T_1) \sim T^n \quad \text{with } n = 3 + 2D, \tag{6}$$

provided the vibrational density of states (VDOS) of the proteins is given by

$$\Omega(w) \sim w^{D-1}. \tag{7}$$

It was observed that $n \simeq 6.3$ for haem proteins and $n \simeq 5.67$ for ferredoxin. These experimental data imply $D = 5/3$ for haem proteins and $D = 4/3$ for ferredoxin. Since, from (3) and (4), $d_f = 5/3$ and $4/3$ in $d = 3$ and 2 respectively for model linear polymers, it is tempting to identify $D$ as the fractal dimension $d_f$ of the proteins. In other words, the experimental data indicate that $(1/T_1) \sim T^{3+2d_f}$.

However, one may raise a serious objection against the identification of $D$ with $d_f$, because the secondary structure of proteins in frozen solution need not be represented by the simple SAW-like Flory model of linear polymers. Besides, the Flory expressions (3) and (4) are strictly valid for an isolated polymer chain. For a convincing identification, the fractal dimension of the sample proteins used in the ESR experiments must be measured by some other independent experimental technique. Such experiments have also been carried out. The coordinates of the α-carbons in the polypeptide chain can be obtained from the X-ray diffraction data. Therefore, the fractal dimension $d_f$ of a protein chain can be estimated using the definition (3). Following this method, Stapleton *et al.*[4] and Wagner *et al.*[5] demonstrated that $d_f \simeq 5/3$ for all the haem proteins they studied, this value is in excellent agreement with the corresponding Flory value in $d = 3$. Similarly, for ferredoxin, they observed that $d_f \simeq 1.37$, very close to the Flory value in $d = 2$. Does this observation imply that the cross-links are massless, so that the proteins are effectively linear polymers? Or, is the agreement between the experimental values of $d_f$ and the Flory values for linear polymers merely accidental? (See Stapleton[6] for a summary of the experimental results.)

Since frozen solutions of the proteins were used in the ESR experiment one would like to know the effect of the solvents on the observed results. Colvin and Stapleton[7] repeated the ESR experiment with several different solvent conditions and demonstrated that the number $n$ in relation (6) is weakly solvent-dependent.

## Theoretical interpretation of the experimental observation

The most general theoretical approach to protein dynamics, in principle, would be to construct the so-called dynamical matrix from the equations of motion of the monomers (or amino-acid residues) and, then, to compute the distribution of the eigenvalues of this matrix. Unfortunately, such direct calculation of $\Omega(w)$ is, in practice, difficult to carry out, because, unlike crystalline solids, proteins lack long-range order. Of course, some of the techniques developed to compute $\Omega(w)$ of other disordered systems can be used to compute $\Omega(w)$ of proteins. Nevertheless, it requires a lot of hard work to compute $\Omega(w)$ for just a single protein by such a direct, albeit approximate, method.

On the other hand, as shown in Appendix B, often the VDOS can be computed without diagonalizing the dynamical matrix. This approach has been used quite successfully to compute the VDOS of fractal objects. In this review I shall first discuss these indirect fractal-theoretic approaches in detail. Then, after pointing out the shortcomings of these approaches, I shall describe the approximate method followed in the direct approach for computing $\Omega(w)$.

### *A fractal description of the vibrational dynamics of proteins*

Motivated by the experimental work of Stapleton *et al.*[4] Alexander and Orbach[8] (AO) developed a simple, albeit indirect, formalism for calculating the $w$-dependence of $\Omega(w)$ utilizing the formal similarities between the phenomena of vibration and RW (see Appendix B). AO showed that (see Appendix C for details) the VDOS of fractals is given by

$$\Omega(w) \sim w^{d_s - 1}, \tag{8}$$

where

$$d_s = 2d_f/d_w \tag{9}$$

is called the spectral (or, fracton) dimension.

Let us now calculate $d_s$ of linear polymers following the arguments of AO. Suppose the random-walkers on a polymer chain can hop only to the nearest-neighbours *along the chain*. Then, if $N(t)$ is the number of monomers traversed in time $t$ and $R(t)$ is the end-to-end Euclidean distance of the walk,

$$N^2(t) \sim t, \tag{10}$$

and

$$N \sim R^{d_f}. \tag{11}$$

Equations (10) and (11) together imply

$$\langle R^2(t) \rangle \sim t^{1/d_f}. \tag{12}$$

Comparing equation (12) with the definition (5) of the walk dimension $d_w$, we get

$$d_w = 2d_f \tag{13}$$

for the AO model of diffusion on linear polymers. In the latter model, therefore,

$$d_s = 1 \neq d_f. \tag{14}$$

Thus, the AO model predicts

$$(1/T_1) \sim T^{3+2d_s}, \tag{15}$$

which does not agree with the corresponding experimental result (6) because $d_f \neq d_s$ in this model.

Alexander and Orbach[8] concluded that 'it is, in fact, hard to think of a situation where the vibration spectrum of a polymer would be adequately described by our free fracton model'. They conjectured that the solvent plays a dominant role.

### *Possible sources of error inadequacies in the fractal description of protein dynamics*

(i) The simple mechanism of diffusion only along the chain assumed by AO for calculating $d_w$ might be an oversimplified physical description of the diffusion equations that map onto the equations of vibration of the proteins under the transformation which led to equation (8).

(ii) The polymer–solvent interaction, which has been ignored in the theoretical analysis above, may play a crucial role, as indicated by experiments and as already conjectured by AO (see also Yang[9]). However, to my knowledge, so far no attempt has been made to take into account the protein–solvent interaction in order to explain the ESR data.

(iii) The approximations made in deriving expression (6) for $1/T_1$ may not be justifiable; in that case the fact that $D = d_f$ may be an accidental coincidence without any underlying physical reason.

### *Alternative mechanisms of diffusion on polymer chains; Calculation of $d_w$*

Helman *et al.*[10] suggested that the AO model of diffusion on polymer chains is too simple to account for the experimental observation. They generalized the AO model, taking into account the existence of cross-links. One way of incorporating cross-links in this model (note that since all the monomers are assumed to be identical in the SAW model of polymers this cross-linking procedure is not unique) is as follows: those sites on a SAW that are not nearest-neighbours along the SAW but are nearest-neighbours on the Euclidean lattice can be assumed to be connected by massless cross-links (Figure 2*a*). Note that, by construction, such cross-links are short-ranged. I shall refer to such short-range cross-links as 'bridges'. Diffusion on the polymer chains can now be modelled by RWs on SAWs. This phenomenon is somewhat similar to the phenomenon of RWs on other fractals (see Havlin and Ben-Avraham[11] for a review). Helman *et al.*[10] *conjectured* that if the density of such bridges is large enough, a random-walker would 'see' an effectively Euclidean lattice for which $d_w = 2$. Moreover, since the bridges are assumed to be effectively massless, $d_f$ remains unaffected by the existence of such cross-links, and hence one would expect $d_s = d_f$. If this scenario captured the essential physics of the problem, theory would have reconciled with experimental results. But, as we shall see, Nature chose to behave quite differently!

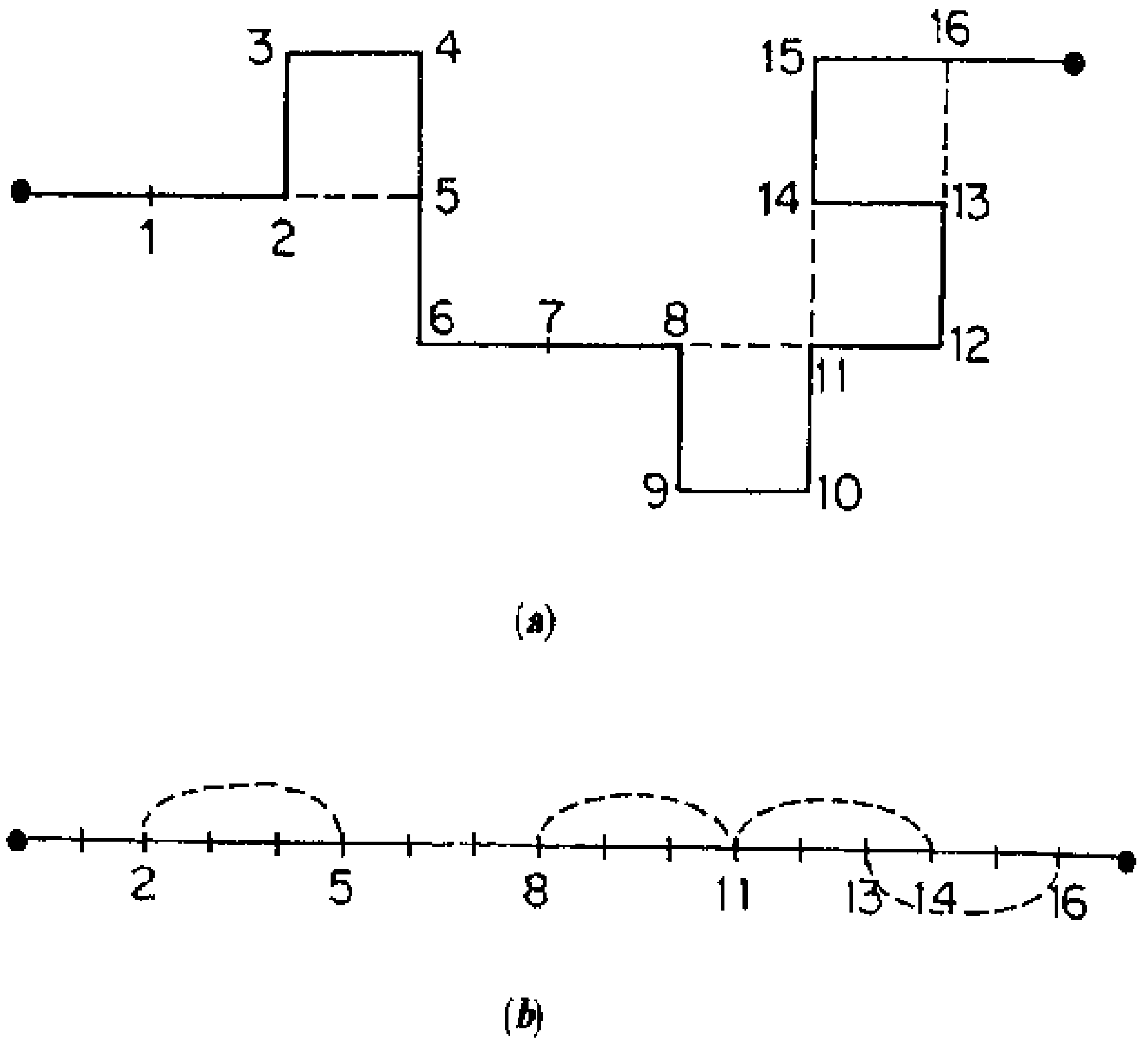

**Figure 2.** ***a***, A self-avoiding walk (solid line) with bridges (dashed lines). Random walk on the structure is like Levy flight in one dimension where the walker occasionally hops over a long distance. ***b***, A one-dimensional lattice (solid line) with occasional long-range hops (dashed lines).

In order to test the validity of the conjecture of Helman *et al.*[10] (the phenomenon of diffusion on SAWs with bridges), one must first appreciate the crucial differences between RW on SAWs with bridges and that without bridges. Consider a typical configuration of a segment of a polymer chain (Figure 2*a*). The sites labelled 2 and 5, for example, are not adjacent sites along the chain but are certainly nearest-neighbours on the square lattice in which the SAW has been embedded. The bond between the sites 2 and 5 constitutes a bridge. If hops of a random-walker across such bridges are not allowed the RW would be effectively one-dimensional, just as in the AO model. On the other hand, if hops of the random-walker across the bridges are also allowed this phenomenon would be somewhat similar to *Levy flights* in one-dimensional space (see Montroll and Schlesinger[12] for an introduction to Levy flights). The analogy between RWs on SAWs with local bridges and one-dimensional Levy flights becomes clear by stretching a SAW to a straight-line configuration (Figure 2*b*); hops across the bridges in Figure 2*a* correspond to long-range hops in Figure 2*b*. This analogy between the RWs on SAWs with bridges and Levy flights was first pointed out by Chowdhury and Chakrabarti[13]. Computer simulation (see Kremer and Binder[14] for the techniques of simulating SAWs) by two independent groups (Chowdhury and Chakrabarti[13], Yang *et al.*[15]) convincingly refuted the conjecture of Helman *et al.*[10] Moreover, despite some earlier claims[13] that the RWs on SAWs with bridges belong to a new universality class, more recent calculations[16–18] using longer chains strongly suggest that the latter belong to the same universality class as that without bridges, i.e. $d_w = 2d_f$. In other words, contrary to the conjecture of Helman *et al.*[10], inclusion of bridges in the AO model is inadequate to reconcile theory with experiment. Results of small-cell real-space renormalization[19,20], although not very reliable, seem to be consistent with the computer simulation data.

Bouchaud and Georges[21] made another attempt to rescue the fractal approach. They assumed that the model considered by, for example, Chowdhury and Chakrabarti[13] captures the essential physical aspects of the real protein systems but the theoretical treatments carried out by the latter authors were erroneous. The methodology followed by Bouchaud and Georges[21] is quite different from all the earlier ones. Suppose $P(l)$ is the probability of a loop of size $l$ joining two monomers across a bridge. We know (des Cloijeaux[22], Duplantier[23]) that for large $l$,

$$P(l) \sim l^{-\mu}, \quad (\mu = 43/16 \text{ and } 2.18 \text{ in } d = 2 \text{ and } 3 \text{ respectively}). \tag{16}$$

As a first approximation, let us suppose that on each monomer the walker can choose the size of his jump according to the probability distribution $P(l)$. Let $s$ be the length of the walk measured along the chain. Then,

$$s^2 \sim t^{d_s}, \quad \text{where } d_s = 2/(\mu - 1). \tag{17}$$

In the next approximation let us take into account the fact that the configuration of the polymer is *quenched*; on each monomer the lengths of the possible jumps are fixed for a given configuration of the chain. A diffusion law of the form $s^2 \sim t^{d_s}$ means that each bond is crossed $t/s$ times (i.e. $t^{1-d_s/2}$ times) and that $s$ different bonds (i.e. $t^{d_s/2}$ different bonds) are probed. Therefore, in the second approximation,

$$s \sim [t^{1-d_s/2}]^{\frac{1}{2}} \sum_{i=1}^{t^{d_s/2}} l_i \tag{18}$$

For $P(l) \sim l^{-\mu}$, we must have

$$s \sim (t^{1-d_s/2})^{1/2} \, (t^{d_s/2})^{1/(\mu-1)},$$

i.e.

$$s^2 \sim t^{1 - \frac{d_s}{2} + \frac{d_s}{(\mu-1)}}. \tag{19}$$

At this point we demand that the expressions (18) and (19) for $s$ must be consistent with each other. Imposing this self-consistency condition, we get

$$d_s = 2(\mu - 1)/(3\mu - 5). \tag{20}$$

Using the known values of $\mu$ in $d = 2$ and 3, we get $d_s = 1.19$ in $d = 2$ and $d_s = 1.69$ in $d = 3$ respectively[21]. Note that in this treatment $d_s$ has been expressed in terms of a new exponent $\mu$, which characterizes the loop statistics of linear polymers. Unfortunately, the quantity $P(l)$ used by these authors is somewhat different from the quantity calculated by des Cloijeaux[22] and hence the applicability of the value of $\mu$ computed by the latter authors to the work of Bouchaud and Georges remains questionable. Moreover, although the computed value of $d_s$ is in very good agreement with the experimentally observed value of $D$ for haem proteins the reason for lower $D$ for ferredoxin remains to be explained.

One may argue that better agreement with experimental data is expected if the range of the cross-links is longer than that of the bridges considered so far[24]. However, there is no unique prescription for inserting long-range cross-links in the SAW model.

Finally, it is worth mentioning that the models discussed in this section do not take into account the interaction of the polymer chains with the solvent.

Thus I conclude that at this point we are unable to find any satisfactory physical mechanism that could alter $d_w$ (and $d_s$) so as to reconcile theory with experiment without taking into account the effects of the solvent.

## Questionable validity of expression (6) for the relaxation rate

So far we have assumed that the experimental data can be described quite satisfactorily by the approximate expression (6) for $1/T_1$. Fitting the experimental data with this expression we obtained $D = d_f$ rather than the theoretically expected value $D = d_s$, thereby getting into a puzzling situation. Is it possible that the whole puzzle is an artefact of using an incorrect expression for $1/T_1$ (Liu[25])? Liu did not study the vibrational spectrum of polymers. He calculated the normal modes of vibration of an exact fractal, the Sierpinski gasket. He argued that, since the spin-lattice coupling matrix element is proportional to the local strain of the magnetic atom, $1/T_1$ should also be site-dependent. He pointed out that Stapleton *et al.*[4] derived expression (6) assuming the spin-lattice coupling matrix elements to be site-independent. For the Sierpinski gasket no simple power law dependence of the average $1/T_1$ on $T$ was observed over the entire temperature range. Liu conjectured that these results are consequences of the fact that the fractal system under consideration is not translationally invariant and, therefore, should be applicable also to the proteins. However, the vibrational properties of similar fractal structures need not be similar.

## 'Gentle warning on fractal fashions'

So far I have described attempts to infer the vibrational properties of proteins indirectly from the properties of RW on such structures by utilizing the formal similarities between those two problems, as explained in appendices B and C. But, as summarized in the preceding sections, all such indirect approaches of estimating the VDOS of proteins have failed.

Krumhansl[26] noted that 'Orbach and others have developed theories of vibrational spectra on fractals, proposing that anomalous vibrational-state densities occur in frequency regimes determined by the fractal structure'. But he warned that 'the inverse conclusion—anomalous vibrational spectra imply fractal structure—cannot generally be drawn on either experimental or theoretical grounds'. He drew attention to the well-known old results for many nonfractal systems to emphasize that such anomalous vibrational spectra can arise 'as a result of anisotropy and important noncentral forces'.

Subsequently, John Maddox[27] wrote: 'Fractal structures are understandably one of the captivating fashions of our times.... But fashions that are too pervasive can also be misleading, and require occasional correction.... J. A. Krumhansl, ..., in the gentlest manner, warns people against the tendency to look for fractal explanations everywhere'.

I have stated in an earlier section that there is considerable anisotropy in proteins; hydrogen bonds forming the cross-links are much weaker than the covalent bonds that form the primary structure. Moreover, there are important noncentral forces that give rise to the secondary structure[28]. The anomalous $T$-dependence of $T_1$ is not necessarily a 'geometrical effect' of the fractal structure of proteins; it could be a 'dynamical effect' of the anisotropy of the interactions.

## Direct computation of the VDOS of proteins

Elber and Karplus[29] computed the VDOS of several proteins from the dynamical matrix using the effective-medium approximation (EMA). In EMA one replaces the random system by an effective ordered medium such that the Green's function for the latter is equal to the configuration-averaged Green's function of the original system.

In the Elber–Karplus model each amino acid has the possibility of strong interactions with four neighbours; two of the neighbours are bonded to it along the chain whereas bonding with the two other neighbours occurs through its hydrogen-bonding groups (e.g. CO and NH). If all of these bonds could be formed by each of the amino acids the protein would behave as an effectively two-dimensional object ($d_f = 2$). However, in the proteins under consideration all the possible connectivity is not saturated; the lower connectivity leads to $d_f < 2$. Now one assumes that the protein may be described by an effectively two-dimensional network of bonds on the scale of acoustic wavelengths, which is the relevant length scale for the Raman ESR experiments. Within this EMA the distribution of the random variables is replaced by a single frequency-dependent variable. In the Elber–Karplus model the most convenient frequency-dependent variable is the so-called Dyson variable, $M_n^{-1} A_{n,n+1}(X_n - X_{n+1}) X_n^{-1}$, where the subscript labels either the rows or the columns. The variables $X_n$ are the Laplace transforms of the dihedral angles and the random variables $A_{n,n+1}$ are the force constant matrix elements.

Implementing this scheme numerically, Elber and Karplus[29] computed the VDOS for myoglobin and ferredoxin. Then inserting the DOS thus calculated, instead of the AO expression, in the expression for $1/T_1$, and integrating over $w$, they showed that, indeed, $1/T_1 \sim T^{3+2D}$, where $D = 1.6$ for myoglobin and $D = 1.4$ for ferredoxin, in good agreement with the corresponding experimental values.

## Conclusion

Let me now answer the question posed in the title of this paper. In general, the fractal-theoretic description is not complicated. In spite of allegations by a section of physicists that such descriptions are 'beautifully complicated' these approaches have been quite useful in explaining experimentally observed properties of several fractals. However, so far as the proteins are concerned, we must admit that fractal theories could not explain the experimental observations satisfactorily.

Why does the conjecture of Helman *et al.*[10] fail to explain the experimental data for proteins? The density of *long-range* cross-links in the secondary structure of the proteins is not as high as assumed by Helman *et al.* The fraction of hydrogen bonds involved in long-range cross-connection is only 14% in myoglobin and 60% in ferredoxin; the relatively lower value in myoglobin is a consequence of the formation of $\alpha$-helix[29]. Thus the failure of the conjecture of Helman *et al.*[10] is a consequence of the secondary structure (conformation) of the proteins in solution. If this is true, one would naturally expect that bridges would be absent in denaturated samples so that the experimental data should be consistent with the AO prediction, viz. $d_s = 1$. This, indeed, has been observed in recent experiments[30].

Chowdhury *et al.*[31] computed $d_w$ for SAWs with bridges, assuming different hopping probabilities along the chain and along the bridges. But it was observed that $d_w = 2d_f$ for all the finite ratios of these hopping probabilities. Using the definition of $d_s$ and the AO expression for $\Omega(w)$, one would get $D = 1$. Does this observation contradict the Elber–Karplus theory? Not at all, because the underlying physical pictures and methodology are quite different. So far as the model of Chowdhury *et al.*[31] is concerned, the result $d_w = 2d_f$ is correct. However, the failure of such models to explain the ESR data and the success of the Elber–Karplus model clearly demonstrate that the anomalous temperature-dependence of $T_1$ is a dynamical consequence of the distribution of the strength of the interaction between the amino-acid residues, rather than a geometrical effect.

There is another interesting and, perhaps, more challenging aspect of protein dynamics that we have not discussed in this work. Usually, the primary structure of proteins folds into a globular, three-dimensional form, called the native form. However, the conformations of the proteins are not static; these conformations transform spontaneously due to thermal fluctuations[32]. The dynamical effects of the conformational transformations of proteins[33] are very similar to some of the dynamical properties of a class of magnetic systems called spin glasses[34]. The physical reason for these similarities and the consequences will be explored in detail in a future publication.

## Appendix A

*Calculation of the (Raman) spin-lattice relaxation rate*

In the Raman process the spin relaxes by absorbing one quantum of lattice vibration and emitting another. The relaxation rate for the spin at the *i*th site is given by

$$(1/T_1) \sim \Sigma |M_i(w_n)|^2 |M_i(w_{n'}|^2 w_n w_{n'} f(w_n)[1-f(w_{n'})] \times \delta(w_{n'} - w_n + g\mu H), \qquad \text{(A.1)}$$

where

$$f(w) = [e^{\beta w} - 1]^{-1}.$$

Stapleton *et al.*[4] argued that, assuming $w_n = w_{n'}$, equation (1) can be approximated by

$$(1/T_1) \sim \int_0^{w_{\max}} \Omega^2(w) w^4 [e^{\beta w}/\{e^{\beta w} - 1\}^2]\, \mathrm{d}w \qquad \text{(A.2)}$$

where $w_{\max}$ is the upper cutoff of excitation energy. Further, let us assume for the time being that (see appendices B and C for the details)

$$\Omega(w) \sim w^{D-1},$$

where $D$ should be regarded as an adjustable parameter whose value is to be determined by fitting the experimental data with the corresponding theoretical expression. So, finally, in the low-temperature regime of interest, (A.2) reduces to the form

$$(1/T_1) \sim T^{3+2D} F_{3+2D}(\theta/T), \qquad \text{(A.3)}$$

where $F$ is a scaling function of its arguments, $T$ is the temperature, and $\theta = w_{\max}/k_B T$ is the Debye temperature. In the high-temperature limit we have

$$F_{3+2D}(\theta/T) \sim T^{-(2D-1)}, \qquad (T \gg \theta),$$

whereas in the low-temperature limit we have

$$F_{3+2D}(\theta/T) \to \text{constant}.$$

Thus, in the regime of temperature relevant for the Raman ESR experiment, the relaxation rate is given by

$$(1/T_1) \sim T^n \quad \text{where } n = 3 + 2D. \qquad \text{(A.4)}$$

## Appendix B

*Relation between the phenomena of vibration and random walk*

Consider the problem of RW on a one-dimensional lattice where the lattice sites are labelled by integers $n$. The corresponding Master equation is given by

$$\mathrm{d}P_n(t)/\mathrm{d}t = W_{n,n-1}(P_{n-1} - P_n) + W_{n,n+1}(P_{n+1} - P_n). \qquad \text{(B.1)}$$

where $P_n(t)$ is the probability that the particle (i.e. the random-walker) is at the site labelled $n$ at time $t$, and $W_{ij}$ is the rate of hopping from the $i$th site to one of its nearest-neighbours $j$. Let us assume that the transfer rates $W_{ij}$ are independent random variables, distributed according to a given probability distribution.

Next, let us consider the vibrational motion of a one-dimensional harmonic chain with unit masses and force constants $W_{i,j}$, the latter being assumed to be independent random variables. The equations of motion are

$$(\mathrm{d}^2 P_n/\mathrm{d}t^2) = W_{n,n-1}(P_{n-1} - P_n) + W_{n,n+1}(P_{n+1} - P_n), \qquad \text{(B.2)}$$

where $P_n$ denotes the displacement of the $n$th site. Note that equation (B.2) is formally very similar to (B.1) except for the fact that (B.1) involves the first derivative of $P_n(t)$ whereas (B.2) involves the second derivative. The initial condition for (B.1) is $P_n(t=0) = \delta_{n,0}$, whereas for (B.2) we need two initial conditions, viz. $P_n(t=0) = \delta_{n,0}$ and $(\mathrm{d}P_n/\mathrm{d}t)_{t=0} = 0$. The Laplace transform of equation (B.2) can be obtained by substituting $-w$ by $w^2$ in the Laplace-transformed (B.1).

It is quite straightforward to show that the 'density of states' for the RW problem, defined by (B.1), is given by (Alexander *et al.*[35])

$$\Omega(w') = -(1/\pi)\langle P_0(-w')\rangle.$$

In other words, the averaged autocorrelation

$$P_0(t) \sim \int_0^{\infty} \Omega(w') \mathrm{e}^{-w't}\, \mathrm{d}w', \qquad \text{(B.3)}$$

which, for discrete time steps $N$, is given by

$$P(0,N) \sim \int_0^{\infty} \Omega(w') \mathrm{e}^{-w'N}\, \mathrm{d}w'. \qquad \text{(B.4)}$$

Physically, $P(0,N)$ is the probability that the random-walker returns to the origin after $N$ steps if he was there initially. If $P(0,N)$ is known by some other independent method, then (B.4) can be used to compute $\Omega(w')$.

## Appendix C

*Density of vibrational modes of a fractal*

The probability $P(0,N)$ on a fractal is inversely proportional to the total volume $V(t)$ available on the fractal within the diffusion distance, i.e.

$$P(0,N) \sim 1/V(N), \qquad \text{(C.1)}$$

where

$$V(N) \sim \langle R^2(N)\rangle^{d_f/2} \qquad \text{(C.2)}$$

and

$$\langle R^2(N)\rangle \sim N^{2/d_w}. \qquad \text{(C.3)}$$

Therefore, on a fractal,

$$P(0,N) \sim N^{-(d_f/d_w)}. \qquad \text{(C.4)}$$

Using (C.4) and (B.4) we get

$$\Omega(w')\,\mathrm{d}w' \sim w'^x\, \mathrm{d}w', \qquad \text{(C.5)}$$

where

$$x = (d_f/d_w) - 1. \qquad \text{(C.6)}$$

In order to get the DOS for vibrational modes of the fractal we must replace $-w'$ by $w^2$. Thus we get (Alexander and Orbach[8])

$$\Omega(w)\,\mathrm{d}w \sim w^{2x}\,\mathrm{d}(w^2) \sim w^{2x+1}\,\mathrm{d}w,$$

i.e.

$$\Omega(w) \sim w^{d_s - 1}, \qquad \text{(C.7)}$$

where

$$d_s = 2d_f/d_w. \quad \text{(C.8)}$$

Since, for all $d$-dimensional Euclidean lattices, $d_w = 2$, $d_s = d_f = d$, and hence

$$\Omega(w) \sim w^{d-1},$$

a well-known result for $d$-dimensional harmonic lattices with isotropic interactions.

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