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Description of Irregularity in Biological Structures

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Abstract

A systematic theoretical analysis is made of the kinds of structural irregularity which occur in biological systems. The theoretical problems investigated were: (1) the precise meaning of the term 'paracrystal' when applied to biological systems such as tropomyosin tactoids, collagen fibrils, keratin and the myelin sheath of nerve; (2) the relationship between the paracrystal and liquid-theory descriptions of disorder which have recently been applied to the structure of collagen fibrils; (3) how structural irregularity affects the diffraction patterns (X-ray, neutron and electron) which are commonly used to investigate the structure of these systems experimentally. The conclusions are: (1) paracrystalline disorder of the first kind refers to a spatially disordered crystal but for biological systems it would generally be impracticable to distinguish this from thermal disorder; (2) paracrystalline disorder of the second kind provides a conceptually clumsy method for describing liquid-like systems; (3) paracrystal models are not strictly valid for finite systems; (4) modern liquid theory, as applied, for example, to the structure of the collagen fibrils, provides an elegant and economical alternative to paracrystal theory for disorder of the second kind; (5) the presence of peaks in diffraction patterns from biological systems does not necessarily imply that the system has very much regularity, *i.e.* it is not evidence for the existence of a lattice.

1. Introduction

Biological systems are not usually perfect crystals – the arrangements of their constituent molecules are generally less ordered. Such disordered systems are commonly referred to as 'paracrystals'. This term has been used, for example, to describe tactoids of tropomyosin (O'Brien, Gillis & Couch, 1975; Stewart & McLachlan, 1976). Often in such cases no quantitative description of the disorder is intended and in consequence the only structural information conveyed is that the system is not a perfect crystal.

Hosemann & Bagchi (1962) defined two kinds of paracrystalline disorder. Disorder of the first kind applies to systems with some degree of long-range order, *i.e.* truly disordered crystals. Systems in which there is no long-range order are said to exhibit disorder of the second kind. Hosemann (1973) has indicated that the purpose of the paracrystal theory of such systems is to enable the structure of liquid-like states to be described. Hosemann (1951) applied his paracrystal theory to the interpretation of X-ray diffraction patterns from α- and β-keratin and from collagen. More recently the stacking of lipid bilayers in the myelin sheaths of nerves has been described as paracrystalline with disorder of the second kind (Blaurock & Nelander, 1976; Nelander & Blaurock, 1978; Hybl, 1976, 1977). Collagen fibrils have recently been described as paracrystals by Hosemann, Dreissig & Nemetschek (1974).

Disorder of the second kind is equivalent to the Prins (1931) theory of the liquid state; modern theories are based on Mayer's theory of dense gases (Salpetre, 1958) and have recently been applied to the structure of collagen fibrils. In these fibrils there are two distinct sorts of disorder possible: a lateral irregularity (Woodhead-Galloway & Machin, 1976*a*) and an irregularity involving the axial relationships between the rod-like molecules (Cox, Grant & Horne, 1967; Woodhead-Galloway & Young, 1978). Equatorial X-ray diffraction patterns from elastoidin spicules (fish fin-ray collagen fibrils) can be satisfactorily accounted for by a modern liquid-theory description of the lateral irregularity (Woodhead-Galloway *et al.*, 1978). These results have led to a liquid-crystal model for the collagen fibril (Hukins & Woodhead-Galloway, 1977,

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1978; Hukins, 1978) which in many respects resembles the paracrystal model of Hosemann, Dreissig & Nemetschek (1974). (It should be noted that other kinds of models exist – for a review see Miller, 1976.)

Our purpose is to consider systematically the various kinds of structural irregularity which can occur in biological systems. In consequence we achieve a clearer understanding of the term 'paracrystal' and are able to relate it to the liquid theory description of disorder. We also consider the effect of these kinds of irregularity on the diffraction patterns (X-ray, neutron or electron) which are used to study the structures of such systems experimentally. Note that disorder may be considered in one dimension as in, for example, the stacking of lipid bilayers in myelin. Thus our arguments can be developed in one dimension and still apply to a real biological system. Structural irregularity can equally well be considered in two dimensions, as in the distribution of visual pigment in the retina (Blasie & Worthington, 1969) or in three dimensions – the arguments are essentially the same and some of the results readily generalized.

2. Definitions and notation

Consider a one-dimensional array of N identical entities which we term 'atoms' but which might equally well be molecules, crystallites, microfibrils or lipid bilayers. Let x_n denote the instantaneous position of the nth atom. Then the structure may be described by a correlation function defined by

$$P(x) = \left\langle \sum_{n,m} \delta(x + x_n - x_m) \right\rangle,$$

where the sum is over all N atoms. Throughout this paper brackets $\langle\ \rangle$ denote an average over all relevant states and δ is the Dirac delta function. This equation may be written in the form

$$P(x) = N\left[\delta(x) + (1/N)\left\langle \sum_{n\neq m} \delta(x + x_n - x_m) \right\rangle\right]. \quad (1)$$

In order to relate the structure $P(x)$ to its diffraction pattern we calculate its Fourier transform

$$S(q) = \int P(x) \exp(-iqx)\, dx$$

$$= N\left\{1 + (1/N)\left\langle \sum_{n\neq m} \exp[-iq(x_n - x_m)] \right\rangle\right\}. \quad (2)$$

If $f(q)$ is the Fourier transform of an atom, the intensity distribution of the diffraction pattern is given by

$$I(q) = f^2(q)S(q). \quad (3)$$

For many purposes it may be more informative to consider the form of $S(q)$, which describes interference effects, than $I(q)$, which depends also on the structure of the scattering atoms in a particular system. Note that q is related to θ, the Bragg angle, by

$$q = (4\pi/\lambda) \sin\theta,$$

where λ is the wavelength of the waves used in the diffraction experiment.

3. Thermal disorder of a regular lattice

The case discussed here is familiar in X-ray crystallography. We consider it in order to develop our arguments in later sections. Note that we consider atoms as independent oscillators – this is the familiar model which was used by Einstein to derive his expression for the specific heat of a crystal (see, for example, Guggenheim, 1959).

We denote atomic positions by

$$x_n = nd + u_n,$$

where d is the distance between equi-spaced lattice points and u_n is the time-dependent displacement of the nth atom from its lattice point. From (2),

$$S(q) = N\left\{1 + (1/N)\left\langle \sum_{n\neq m} \exp[-iq(nd + u_n - md - u_m)] \right\rangle\right\}$$

$$= N\left\{1 + (1/N) \sum_{n\neq m} \exp[-iq(n-m)d] \times \langle \exp(-iqu_n) \exp(iqu_m) \rangle\right\}$$

$$= N\left\{1 + (1/N) \sum_{n\neq m} \exp[-iq(n-m)d] \times \langle \exp(-iqu_n) \rangle \langle \exp(-iqu_m) \rangle\right\},$$

the last equality arises because the oscillators are independent. We now use the Born (1942) theorem which states that

$$\langle \exp(-qu_n) \rangle = \exp[-(q^2/2)\langle u_n^2 \rangle] \quad (4)$$

(see Appendix, Note 1) and define the root-mean-square displacement, μ, by

$$\mu^2 = \langle u_n^2 \rangle,$$

which is independent of n, to obtain

$$S(q) = N\left\{1 + \exp(-2W)(1/N) \sum_{n\neq m} \exp[-iq(n-m)d]\right\},$$

$$W = q^2 \mu^2/2. \quad (5)$$

Now, $\exp(-2W)$ is the Debye–Waller factor which appears in X-ray crystallography. As W tends to 0 this

factor tends to 1 and the stationary lattice result is recovered, *i.e.*

$$S_{\text{lattice}}(q) = N\left\{1 + (1/N)\sum_{n\neq m}\exp[-iq(n-m)d]\right\}. \quad (6)$$

From (5) and (6), we obtain for a thermally disordered lattice

$$S(q) = \exp(-2W)S_{\text{lattice}}(q) + N[1 - \exp(-2W)]. \quad (7)$$

The first term in (7) indicates that the interference function S_{lattice}, which is non-zero only at the so-called 'reciprocal-lattice points' will diminish with increasing q; the second indicates that diffuse intensity will appear between the reciprocal-lattice points.

4. Static disorder of the first kind

Our equation (7) has the same form as equation (2) of Blaurock & Nelander (1976). Their equation describes interference effects expected from a lattice which is slightly perturbed in that atoms have static displacements from equi-spaced lattice points. The two equations are identical if the distribution of static displacements is Gaussian and there is no correlation between the displacements from different sites. In this case $2W$ is identified as $q^2\zeta^2$ where ζ^2 is the mean-square static displacement of the atoms from the lattice sites.

5. Simultaneous disorder of the first kind and thermal disorder

We now consider the more realistic case where the system with disorder of the first kind is simultaneously subject to thermal disorder and define the following: x_n^0 = site about which nth atom vibrates = $nd + V_n$ (not a perfect lattice); x_n = instantaneous position of the nth atom; $x_n - x_n^0 = \varepsilon_n$ = thermal displacement of the nth atom; $x_{n+1}^0 - x_n^0 = d + \Delta_n$ = separation between sites about which atoms are vibrating. Thus, V_n is the displacement of the nth atom from its lattice site in the absence of thermal motion and

$$\Delta_n = V_{n+1} - V_n.$$

From (2),

$$S(q) = N\left\{1 + (1/N)\left\langle\sum_{n\neq m}\exp[-iq(x_n - x_m)]\right\rangle\right\}$$

$$= N\left\{1 + (1/N)\left\langle\sum_{n\neq m}\exp[-iq(x_n^0 - x_m^0 + \varepsilon_n - \varepsilon_m)]\right\rangle\right\}$$

$$= N\{1 + (1/N)\sum\exp[-iq(n-m)d]\times\langle\exp[-iq(V_n - V_m + \varepsilon_n - \varepsilon_m)]\rangle\}$$

$$= N\{1 + (1/N)\sum\exp[-iq(n-m)d]\times\langle\exp[-iq(V_n - V_m)]\rangle\times\langle\exp[-iq(\varepsilon_n - \varepsilon_m)]\rangle\}.$$

Now, if ζ^2 is the mean-square static displacement, then

$$\langle\exp[-iq(V_n - V_m)]\rangle = \exp(-q^2\zeta^2),$$

and if the Einstein model of independent oscillators of § 3 is adopted, then

$$\langle\exp[-iq(\varepsilon_n - \varepsilon_m)]\rangle = \exp(-q^2\mu^2),$$

where μ^2 is the mean-square thermal displacement.

Thus, $S(q)$ has the same form as in (7) except that now

$$2W = q^2(\mu^2 + \zeta^2).$$

Unless diffraction experiments can be performed at different temperatures there is no way of distinguishing thermal from static disorder. In biological systems this causes a real problem because low temperatures would lead to freezing of water in the structure and consequent perturbation; high temperatures would lead to denaturation.

In fact, the Einstein model is not the best model for thermal disorder. A better approximation is provided by the theory of Born & von Karman (1912) when

$$\langle\exp[-iq(\varepsilon_n - \varepsilon_{n-m})]\rangle_n = \exp(-q^2\rho_m^2).$$

Here, ρ is defined in Note 2 of the Appendix and the subscript n implies an average over all sites specified by values of n. Using this theory, together with the model for static disorder based on the Einstein model (*i.e.* paracrystalline disorder of the first kind), leads to

$$S(q) = N\left\{1 + (1/N)\sum_{n\neq m}\exp[-iq(n-m)d]\times\exp[-q^2(\zeta^2 + \rho_{n-m}^2)]\right\}$$

$$= N\left\{1 + \sum_{n\neq 0}\exp(-iqnd)\times\exp[-q^2(\zeta^2 + \rho_n^2)]\right\}.$$

Fourier transformation of this expression for $S(q)$ yields a description of the structure in terms of $P(x)$. The result is

$$P(x) = N\left\{\delta(x) + \sum_{n\neq 0}(1/2\pi)[\pi/(\zeta^2 + \rho_n^2)]^{1/2}\times\exp[-(x - nd)^2/4(\zeta^2 + \rho_n^2)]\right\}.$$

Since ρ_n increases as n increases, the function $P(x)$ consists of a series of peaks which broaden as x increases. Thus the system is increasingly disordered with increasing x.

6. Simultaneous disorder of the second kind and thermal disorder

We now repeat the analysis of the previous section except that we now consider the static disorder to be of the second kind. As before, we obtain from (2)

$$\begin{aligned} S(q) &= N\Big\{1 + (1/N)\Big\langle \sum_{n\neq m} \exp[-iq(x_n^0 - x_m^0 + \varepsilon_n \\ &\quad - \varepsilon_m)]\Big\rangle\Big\} \\ &= N\Big\{1 + (1/N) \sum_{n\neq m} \langle \exp[-iq(x_n^0 - x_m^0)] \rangle \\ &\quad \times \langle \exp[-iq(\varepsilon_n - \varepsilon_m)] \rangle\Big\}. \end{aligned} \tag{8}$$

According to the Born–von Karman theory,

$$\langle \exp[-iq(\varepsilon_n - \varepsilon_m)] \rangle = \exp(-q^2 \rho_{n-m}^2). \tag{9}$$

After some manipulation (see Appendix, Note 3) (8) and (9) yield

$$\begin{aligned} S(q) = N + \sum_{n>0} &\{\exp(-iqd)G(q) \exp(-q^2 \rho_1^2) + \text{CC} \\ &+ \exp(-2iqd)G^2(q) \exp(-q^2 \rho_2^2) + \text{CC} \\ &+ \exp(-3iqd)G^3(q) \exp(-q^2 \rho_3^2) + \text{CC} \\ &+ \ldots\}, \end{aligned} \tag{10}$$

where CC denotes the complex conjugate of the preceding term and

$$G(q) = \langle \exp(-iq\Delta_n) \rangle.$$

In the Einstein approximation all the ρ_n are identical. Fourier transformation of $S(q)$ then yields the description of the structure of the system

$$\begin{aligned} P(x) &= N\Big\{\delta(x) + \frac{1}{2\pi} \int dq \exp(iqx) \sum_{n\neq 0} \exp[-q^2(\rho_n^2 \\ &\quad + n\alpha^2/4)] \exp(-iqnd)\Big\} \\ &= N\Big(\delta(x) + \frac{1}{2\pi} \sum_{n\neq 0} \Big[\frac{\pi}{(n\alpha^2/4) + \rho_n^2}\Big]^{1/2} \\ &\quad \times \exp\Big\{\frac{-(x - nd)^2}{4[(n\alpha^2/4) + \rho_n^2]}\Big\}\Big). \end{aligned} \tag{11}$$

7. Validity of paracrystal theories

Strictly, the theory for disorder of the first kind, as exemplified by equation (2) in Blaurock & Nelander (1976), is only valid when N tends to infinity. [For further details of their treatment see our equation (13).] Our equation (5) which expresses the result of thermal disorder is valid whatever the value of N. It has been presumed that this is also true when the disorder is not thermal but a static distribution of the atomic positions about the lattice points. However, it is only in the limit N tends to infinity that the full character of this static distribution will be revealed. It is not clear whether in practice the Blaurock & Nelander value ($N = 10$) was sufficiently close to infinity for the purposes of their investigation. The adequacy of such an approximation is better investigated by simulation than by analysis.

The same problem arises for disorder of the second kind where again the analysis is only valid as N tends to infinity. It is worth demonstrating this point for the case where $N = 2$. Then, from (1) and (2),

$$\begin{aligned} P(x) &= 2[\delta(x) + (1/2)\delta(x - x_1 + x_0) \\ &\quad + (1/2)\delta(x - x_0 + x_1)], \\ S(q) &= 2\{1 + (1/2) \exp[-iq(x_1 - x_0)] \\ &\quad + (1/2) \exp[-iq(x_0 - x_1)]\} \\ &= 2[1 + \cos q(x_1 - x_0)]. \end{aligned} \tag{12}$$

However, the formulation of Blaurock & Nelander would give, in the absence of thermal disorder,

$$\begin{aligned} P(x) &= 2[\delta(x) + (1/2)g(x - d) + (1/2)g(x + d)], \\ S(q) &= 2[1 + G(q) \cos qd], \end{aligned} \tag{13}$$

where $g(x)$ is the inverse Fourier transform of $G(q)$.

Comparison of (12) and (13) shows that the latter contains a spurious probability distribution that has no place in a *static* model; X-rays see the *actual* positions of atoms. Thus, the equation used by Blaurock & Nelander in their analysis of X-ray diffraction from myelin has no real status if N is small.

8. Dense gas approach to disorder

The dense gas approach as formulated here recognizes that, even in the absence of long-range order, there is order of a statistical kind (short-range order) because every atom excludes the others from the space which it occupies itself. If this exclusion is the source of short-range order then an expression for $S(q)$ can be derived. Thus modern theories are conceptually much simpler than the paracrystal theory for disorder of the second kind.

Equation (2) can be rewritten in the form

$$S(q) = N\{1 + (N/V) \int [g(x) - 1] \exp(-iqx)\, dx\},$$

where V is the volume occupied by the assembly. The distribution function $g(x)$ is defined so that (N/V) $g(x) \times \mathrm{d}x$ is the probability of finding an atom between distances x and $x + \mathrm{d}x$ from an origin which is an arbitrarily chosen atom centre and then $(N/V)g(x)$ is a probability density. [In two and three dimensions $g(x)$ is the 'radial distribution function'.] The total correlation function is defined by

$$h(x) = g(x) - 1,$$

so that

$$S(q) = N[1 + (N/V) \int h(x) \exp(-iqx)\, \mathrm{d}x].$$

Following Ornstein & Zernicke (1914), it is customary to argue that the total correlation between two atoms arises from: (i) the direct influence of one atom on the other – described by the direct correlation function $C(x)$ and (ii) an indirect influence *via* a third atom. Thus,

$$h(x) = C(x) + (N/V) \int h(x')C(x - x')\, \mathrm{d}x'.$$

We can now use the properties of $C(x)$ to calculate $h(x)$ and hence $S(q)$. It has been repeatedly proved (*e.g.* Woodhead-Galloway, Gaskell & March, 1968) that asymptotically (*i.e.* for large x)

$$C(x) = -\varphi(x)/kT,$$

where k is Boltzmann's constant, T the absolute temperature and $\varphi(x)$ the intermolecular potential function. In our formulation

$$\varphi(x) = \begin{cases} \infty & x < d \\ 0 & x \geq d \end{cases},$$

where d is the length of an 'atom'. Hence,

$$C(x) = \begin{cases} 0 & x \geq d \\ h(x) = -1 & x < d. \end{cases}$$

and

Experimental results from a variety of liquids indicate that, except when q tends to 0, the simple potential function used here is perfectly adequate (*e.g.* Enderby, 1972). Note that $\varphi(x)$ defined here is the one-dimensional case of the 'hard sphere' model which is often used to predict 'allowed' conformations of biological macromolecules.

This formulation (Lebowitz & Percus, 1966) of short-range order is exact and has an explicit solution in one dimension (Thiele, 1963; Wertheim, 1963). Then,

$$S(q) = [1 + (A/\xi^2) \sin^2(\xi/2) + (B/\xi) \sin(\xi)]^{-1}, \qquad \xi = qd, \tag{14}$$

where

$$A = 4\eta^2/(1 - \eta)^2,$$

$$B = 2\eta/(1 - \eta)$$

and the packing fraction η is defined by

$$\eta = Nd/V, \tag{15}$$

which represents the fraction of space occupied by atoms.

Fig. 1 shows $S(q)$ plotted against ξ for $\eta = 0{\cdot}9$. Note that even for a system which possesses only short-range order $S(q)$, and hence $I(q)$, exhibits a series of peaks. These peaks decrease in height and increase in width with increasing q. The dependence of $S(q)$ on η can also be calculated in two (Woodhead-Galloway & Machin, 1976*b*) and three (Thiele, 1963; Wertheim, 1963) dimensions.

9. Diffraction from disordered systems

We have seen that for an infinite array of equispaced atoms (*i.e.* a crystal) $S(q)$ is an infinite array of delta functions (the reciprocal lattice). The introduction of disorder into this ideal system affects $S(q)$ in several ways. As a result the following effects can be observed in the diffraction pattern, $I(q)$: continuous diffuse scatter appears between the peaks which may themselves become less intense, broader and even displaced.

It is clear from (7), and from the discussion of § 5, that thermal disorder or static disorder of the first kind has two effects in q space. Diffuse intensity given by $[1 - \exp(-2W)]$ appears and increases as q increases. Also the peaks become less intense as q increases – their amplitude decays as $\exp(-2W)$. Neither the

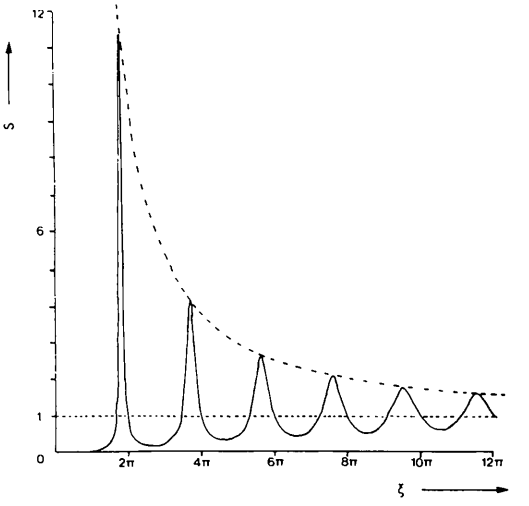

Fig. 1. $S(q)$ for a dense gas with a packing fraction, η, defined in (15), of 0·9 plotted against ξ as defined in (14). The dotted envelope of the peaks falls off approximately as $1/\xi$.

positions nor the widths of the peaks are affected. If N, the number of atoms, is infinite then the peaks have no finite width; finite peak width is the consequence of the finite size of a real array.

If the system has no long-range order the diffraction pattern departs more radically from the ideal case. For q increasing, the peaks not only become less intense but they also become broader and their positions may be displaced from those expected of an ordered array as shown in Fig. 2. Fig. 3 shows a computed example of such a diffraction pattern – the peaks are not well resolved and it seems pointless to separate the pattern into continuous diffuse scatter with even degraded lattice peaks superposed upon it. In any case, such a separation would be technically very difficult – even for highly crystalline fibres; the estimation of peak intensities above diffuse background is not trivial (Langridge *et al.*, 1960). For the dense-gas model described in § 8 the shape of $S(q)$ depends only on the packing fraction η. Fig. 4 shows how the first peak position varies as η increases from 0 to 1.

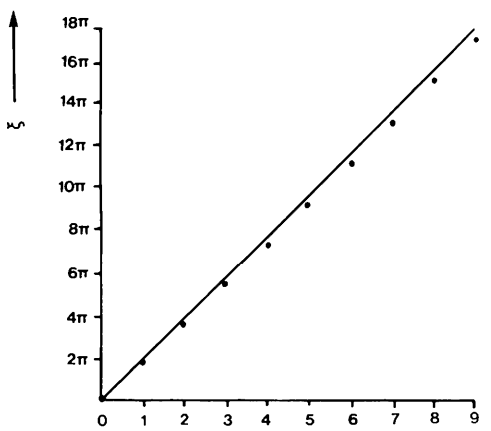

Fig. 2. Comparison of peak positions in $S(q)$ for a dense gas and a crystal. The continuous line joins the ξ values, defined in (14), predicted by a crystal model which has a repeat distance a; each peak may be specified by the value of an integer h. Dots represent the positions of corresponding peaks calculated for a dense gas in which atoms have length a and the packing fraction, η, defined in (15), has a value of 0·9. Asymptotically the position of the hth peak is at $\xi = \pi(4h - 1)/2$.

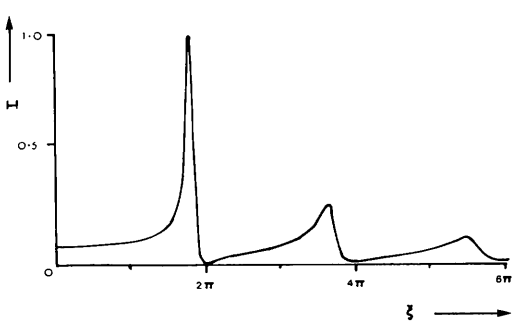

Fig. 3. $I(q)$ computed for a stack of lipid bilayers, using the theory of a dense gas, plotted against ξ as defined in (14). $S(q)$ was taken from Fig. 1 and $f(q)$, of (3), was $n \sin(qd)/qd$ where n is related to the number of electrons in a bilayer.

10. Conclusions

Because our analysis may use some unfamiliar concepts and notation we conclude by summarizing the more important results. Throughout this section we use the term 'atom' in the general sense of § 2.

(1) Paracrystal disorder of the first kind refers to a spatially disordered crystal. The mineral phase in bone may well provide an example (Wheeler & Lewis, 1977). In practice, spatial disorder and thermal vibrations are unlikely to be distinguished for biological systems because the distinction requires experiments to be performed over a range of temperatures. Strictly speaking this spatial disorder is probably only defined analytically for an effectively infinite array of atoms and not for finite structures.

(2) Paracrystal disorder of the second kind refers to a system with no long-range order. Thus the system has no underlying lattice, in the usual crystallographic sense. Equation (11) shows that for a real system this theory leads to an extremely complicated description of its structure. Practical application of the paracrystal theory with disorder of the second kind is very difficult because of the need to define distribution functions and to assign values to the many parameters involved. Strictly speaking this analytical description also only applies to an infinite array of atoms and not to a finite structure.

(3) Modern theories of dense gases provide a conceptually simple model for systems with no long-range order. The theory is probably valid for finite systems and its application is straightforward. Both peaks and diffuse scatter arise naturally from a single

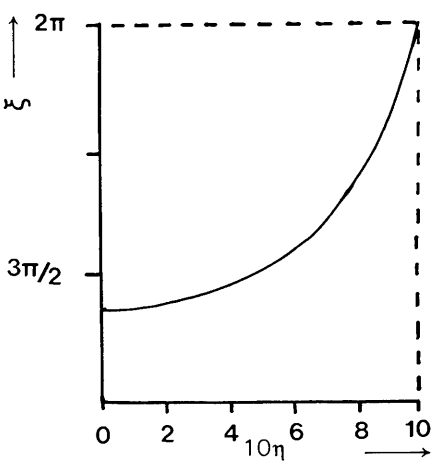

Fig. 4. Dependence of the first peak position in $S(q)$ for a dense gas as a function of the packing fraction, η, defined in (15). Peak positions are specified by ξ, as defined in (14).

expression for $S(q)$. Note that although we have described this approach as a 'liquid' theory we do not imply that atoms diffuse as in a liquid. We simply mean that their arrangement has only the short-range order characteristic of liquids. Notice that in practice $S(q)$ is defined very largely by one parameter, the packing fraction.

(4) The appearance of peaks in $I(q)$, the diffraction pattern from a biological system, does not necessarily imply that the system has any underlying lattice. An example of a system computed using (14) (a stack of lipid bilayers) in which peaks appear, even in the absence of long-range order, is provided by Fig. 3.

Thus, biological systems may often be less ordered than conventional descriptions might imply. There is *a priori* no good reason to suppose that the arrangement of molecules in a biological system is likely to possess long-range order, *i.e.* to be crystalline. Indeed, Williams (1977) has written that 'the staggering feature of all biological chemistry is organization without simple order'.

APPENDIX
Mathematical notes

Note 1

If u_n is normally distributed, *i.e.* according to

$$g(u_n) = (1/\pi^{1/2}\alpha)\exp(-u_n^2/\alpha^2),$$

then (4) is exact. It is easy to check this to the order of the leading terms by expansion and comparison.

$$\langle u_n^2\rangle = \int_{-\infty}^{\infty} u_n^2 g(u_n)\,du_n$$
$$= (\alpha^2/\pi^{1/2})\int_{-\infty}^{\infty} x^2\exp(-x^2)\,dx$$
$$= \alpha^2/2.$$

Thus,

$$\exp[-(q^2/2)\langle u_n^2\rangle] \simeq 1 - q^2\alpha^2/4,$$

whereas

$$\langle\exp(-iqu_n)\rangle \simeq \langle 1 - iqu_n - q^2u_n^2/2\ldots\rangle$$
$$\simeq 1 - (q^2/2\alpha\pi^{1/2})\int_{-\infty}^{\infty}\exp(-u_n^2/\alpha^2)u_n^2\,du_n$$

(since $\langle iqu_n\rangle = 0$)

$$\simeq 1 - (q^2\alpha^2/2\pi^{1/2})\int_{-\infty}^{\infty} x^2\exp(-x^2)\,dx$$
$$= 1 - q^2\alpha^2/4.$$

Note 2

$$\rho_n^2 = \frac{d}{2M}\int_0^{\pi/d}\frac{dq}{2\pi}\frac{\hbar}{\omega_q}\coth(h\omega_q/2kT)[1-\cos(qnd)].$$

Here, the symbols not defined in the main paper are: ω_q, the phonon frequency as a function of wave number; M, the atomic mass; h, Planck's constant; T, absolute temperature; $\hbar = h/2\pi$. In the Einstein model, ω_q is independent of q and ρ_n^2 tends to μ^2 independently of n. However, more generally, ρ_n tends to a maximum value of ρ as n increases.

Note 3

Here we derive (10) from (8) using (9). From (8) and (9) we obtain

$$S(q) = N + \Big\langle \sum_{n>0}\{\exp[-iq(x^0_{n+1} - x^0_n)]\exp(-q^2\rho_1^2)$$
$$+ \text{CC} + \exp[-iq(x^0_{n+2} - x^0_n)]\exp(-q^2\rho_2^2)$$
$$+ \text{CC} + \exp[-iq(x^0_{n+3} - x^0_n)]\exp(-q^2\rho_3^2)$$
$$+ \text{CC} + \ldots\}\Big\rangle$$

$$= N + \Big\langle \sum_{n>0}\{\exp[-iq(x^0_{n+1} - x^0_n)]\exp(-q^2\rho_1^2)$$
$$+ \text{CC} + \exp[-iq(x^0_{n+2} - x^0_{n+1})]$$
$$\times \exp[-iq(x^0_{n+1} - x^0_n)]$$
$$\times \exp(-q^2\rho_2^2) + \text{CC} + \ldots\}\Big\rangle$$

$$= N + \sum_{n>0}\{\exp(-iqd)\langle\exp(-iq\Delta_n)\rangle$$
$$\times \exp(-q^2\rho_1^2) + \text{CC} + \exp(-2iqd)$$
$$\times \langle\exp(-iq\Delta_{n+1})\exp(-iq\Delta_n)\rangle$$
$$\times \exp(-q^2\rho_2^2) + \text{CC} + \ldots\}$$

$$= N + \sum_{n>0}\{\exp(-iqd)G(q)\exp(-q^2\rho_1^2) + \text{CC}$$
$$+ \exp(-2iqd)G^2(q)\exp(-q^2\rho_2^2) + \text{CC}$$
$$+ \ldots\},$$

which is the required result where CC is the complex conjugate of the preceding term.

The approximations made above are that, for example,

$$\langle\exp(-iq\Delta_{n+2})\exp(-iq\Delta_{n+1})\exp(-iq\Delta_n)\rangle$$
$$= \langle\exp(-iq\Delta_{n+2})\rangle\langle\exp(-iq\Delta_{n+1})\rangle\langle\exp(-iq\Delta_n)\rangle$$

and

$$\langle\exp(-iq\Delta_{n+2})\rangle = \langle\exp(-iq\Delta_{n+1})\rangle$$
$$= \langle\exp(-iq\Delta_n)\rangle = G(q).$$

In making separations like this it is assumed that successive atoms are laid down without reference to the pre-existing structure except that there is a statistical

distribution function $g(\Delta)$, which might, for example, be Gaussian when

$$g(\Delta) = (\pi\alpha^2)^{-1/2} \exp(-\Delta^2/\alpha^2).$$

As N tends to infinity all possible configurations will be assumed during the aggregation process. The general term in the series of (10) is

$$G^n(q) \exp(-q^2 \rho_n^2) \cos(qnd),$$

which approximates to

$$\exp\{-q^2[(n\alpha^2/4) + \rho_n^2]\} \cos(qnd)$$

if $g(\Delta)$ is Gaussian. Note that d is only defined for disorder of the second kind (as in § 5) if

$$\langle \Delta_n \rangle = 0.$$

This condition is essentially a description of a disordered model of the kind we are investigating, *i.e.* one in which all possible 'atomic' configurations are assumed.

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The Electron-Density Distribution in Silicon

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Abstract

The electron-density distribution in crystalline silicon was refined with a three-parameter density model which was originally designed by Brill. The same data sets were used as by other authors [Price, Maslen & Mair (PMM) (1978). *Acta Cryst.* A**34**, 183–193; Hansen & Coppens (1978). *Acta Cryst.* A**34**, 909–921] in refining their multipole models. The data sets are (1) the 15 Mo $K\alpha$ room-temperature data of Aldred & Hart

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