Helices in biomolecules

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Identical objects, regularly assembled, form a helix, which is the principal motif of nucleic acids, proteins, and viral capsids.

I. HELICES IN BIOLOGICAL MOLECULES

Double-stranded DNA is a double helix [1]. The principal secondary structures in proteins are α-helices [2] and β-sheets [3,4], which are sheets of helices. The fibrous protein α-keratin is a double α-helix; collagen is a triple helix. The cytoskeletal filaments—actin filaments, microtubules, and intermediate filaments—are helical assemblies of subunits. Helices occur in the capsids of viruses.

Helices are important and ubiquitous in biology because identical objects, regularly assembled, form a helix. This theorem—that a regular assembly of identical objects is a helix—has been known in the biological community since the work of Pauling [2–4] but is less familiar to physicists. Although it can be derived from the differential geometry of Lancret and de Saint Venant [5], I am unaware of a proof of it in the biological literature, where it often is illustrated by photographs of stacks of identical blocks, each rotated by a fixed angle about the vertical axis [6]. Because of its far-reaching implications for biology, a proof that is simple, direct, and self-contained should be useful. Such a proof is given in Sec. II. In Sec. III, some formulas about helices are derived. In Sec. IV, the theorem and these formulas are illustrated by and applied to nucleic acids, protein secondary structures, proteins, protein folding, and viral capsids. The theorem implies, in particular, that the β-strand [3,4], which is the second most common secondary structure in proteins, is a helix and that icosahedral viral capsids are made of helices. The paper ends with remarks about helices and evolution.

II. REGULARITY IMPLIES HELICITY

Suppose we have a collection of identical objects, which we label with the integers. Suppose each object has both a socket and a knob. Suppose that every knob can fit snugly into every socket and that, once seated, no further rotation of the knob in the socket is possible. We can set the knob of object 1 into the socket of object 2. Then we can put the knob of object 2 into the socket of object 3. Next, we can put the knob of object 3 into the socket of object 4. If we continue in this way, then the chain of objects will form a helix defined by the first 3 objects.

To see why, we fix our attention on a selected point, the same for all objects. We might choose the top of each socket.

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Let us call the selected point on the ith object $\mathbf{p}_i$. Let $\mathbf{a} = \mathbf{p}_2 - \mathbf{p}_1$, so $\mathbf{p}_2 = \mathbf{a} + \mathbf{p}_1$. The knob of each object protrudes from its object in a way that is arbitrary but the same for all our objects. So the vector $\mathbf{b} = \mathbf{p}_3 - \mathbf{p}_2$ has the same length as $\mathbf{a}$ and is related to it by a 3×3 rotation matrix R, $\mathbf{b} = R\mathbf{a}$. The rotation R includes any extra rotation of ϕ radians about the $\mathbf{b}$ axis that may occur in the rigid motion that attaches object 2 to object 1. So $\mathbf{p}_3 = \mathbf{b} + \mathbf{p}_2 = R\mathbf{a} + \mathbf{a} + \mathbf{p}_1$. What about $\mathbf{c} = \mathbf{p}_4 - \mathbf{p}_3$? Well, the lengths of all the vectors $\mathbf{p}_{i+1} - \mathbf{p}_i$ are the same, and they are all related by rotations. And since the objects are all identical, the vector $\mathbf{c}$ must be related to $\mathbf{b}$ by the rotation R in the rotated frame—that is, $\mathbf{c} = RRR^{-1}\mathbf{b} = R\mathbf{b}$. So $\mathbf{c} = R^2\mathbf{a}$, and thus the point $\mathbf{p}_4$ is given by $\mathbf{p}_4 = \mathbf{c} + \mathbf{p}_3 = R^2\mathbf{a} + R\mathbf{a} + \mathbf{a} + \mathbf{p}_1$. The general rule is

$$\mathbf{p}_{n+2} = \sum_{k=0}^{n} R^k \mathbf{a} + \mathbf{p}_1. \tag{1}$$

Every rotation matrix R has one real eigenvector $\hat{\mathbf{n}}$ with an eigenvalue of unity $R\hat{\mathbf{n}} = \hat{\mathbf{n}}$. The eigenvector $\hat{\mathbf{n}}$ is the axis of the rotation. The caret means that the axis $\hat{\mathbf{n}}$ is normalized, and we fix its sign by requiring that $\mathbf{a} \cdot \hat{\mathbf{n}} \geq 0$. (The other two eigenvectors $\mathbf{e}_{\pm}$ are complex with unimodular eigenvalues $R\mathbf{e}_{\pm} = e^{\pm i\theta}\mathbf{e}_{\pm}$ in which θ is the angle of the rotation R.)

Let us adopt a coordinate system in which the z axis is the axis of rotation $\hat{\mathbf{z}} = \hat{\mathbf{n}}$ and the vector $\mathbf{a}$ lies in the x-z plane $\mathbf{a} = a_x\hat{\mathbf{x}} + a_z\hat{\mathbf{z}}$. The rotation now is about the z axis, and so

$$R\mathbf{a} = R(a_x\hat{\mathbf{x}} + a_z\hat{\mathbf{z}}) = a_x(\cos\theta\hat{\mathbf{x}} + \sin\theta\hat{\mathbf{y}}) + a_z\hat{\mathbf{z}}, \tag{2}$$

in which we choose to have $-\pi < \theta \leq \pi$. If the product θa_z is positive, then the helix is right handed; if it is negative, then the helix is left handed. The kth power of R turns $\mathbf{a}$ into

$$R^k\mathbf{a} = R^k(a_x\hat{\mathbf{x}} + a_z\hat{\mathbf{z}}) = a_x(\cos k\theta\hat{\mathbf{x}} + \sin k\theta\hat{\mathbf{y}}) + a_z\hat{\mathbf{z}}. \tag{3}$$

So formula (1) for the point $\mathbf{p}_{n+2}$ gives

$$\mathbf{p}_{n+2} = (n+1)a_z\hat{\mathbf{z}} + \mathbf{p}_1 + a_x\sum_{k=0}^{n}(\cos k\theta\hat{\mathbf{x}} + \sin k\theta\hat{\mathbf{y}}). \tag{4}$$

Now by expressing $\sin k\theta$ and $\cos k\theta$ in terms of $\exp(i\theta)$ and by using the relation $(z-1)\sum_{k=0}^{n}z^k = z^{n+1} - 1$, one may derive the trigonometric identities

$$\sum_{k=0}^{n}\cos k\theta = \frac{1}{2}\left(\cos n\theta + \cot\frac{1}{2}\theta\sin n\theta + 1\right) \tag{5}$$

and

$$\sum_{k=0}^{n} \sin k\theta = \frac{1}{2}\left[\sin n\theta - \cot\frac{1}{2}\theta(\cos n\theta - 1)\right]. \quad (6)$$

By substituting these identities into Eq. (4), we find

$$\mathbf{p}_{n+2} = (n+1)a_z\hat{\mathbf{z}} + \mathbf{p}_1 + \frac{1}{2}a_x(\cos n\theta + \cot\frac{1}{2}\theta\sin n\theta + 1)\hat{\mathbf{x}}$$
$$+ \frac{1}{2}a_x[\sin n\theta - \cot\frac{1}{2}\theta(\cos n\theta - 1)]\hat{\mathbf{y}}. \quad (7)$$

If we call $\mathbf{v}$ the vector

$$\mathbf{v} = \frac{a_x}{2}\begin{pmatrix} 1 \\ -\cot\frac{1}{2}\theta \\ 0 \end{pmatrix}, \quad (8)$$

then we may write the general point $\mathbf{p}_{n+2}$ as

$$\mathbf{p}_{n+2} = R^n\mathbf{v} + na_z\hat{\mathbf{z}} + \mathbf{p}_1 + \mathbf{a} - \mathbf{v}, \quad (9)$$

which clearly is a helix.

A rotation R about a point $\mathbf{p_0}$ takes a point $\mathbf{p}$ into the point $\mathbf{p}'$ given by

$$\mathbf{p}' - \mathbf{p_0} = R(\mathbf{p} - \mathbf{p_0}). \quad (10)$$

By comparing this rule with our formula (9) for $\mathbf{p}_{n+2}$, we may infer that $\mathbf{v} = a_x\hat{\mathbf{x}} - \mathbf{r_0}$ in which $\mathbf{r_0}$ is the point where the axis $\hat{\mathbf{z}}$ crosses the x-y plane; equivalently,

$$\mathbf{r_0} = a_x\hat{\mathbf{x}} - \mathbf{v} = \frac{1}{2}a_x[\hat{\mathbf{x}} + \cot(\theta/2)\hat{\mathbf{y}}]. \quad (11)$$

Equation (9) for the point $\mathbf{p}_{n+2}$ now takes the form

$$\mathbf{p}_{n+2} - \mathbf{r_0} = R^n(a_x\hat{\mathbf{x}} - \mathbf{r_0}) + (n+1)a_z\hat{\mathbf{z}} + \mathbf{p}_1 \quad (12)$$

or more simply

$$\mathbf{p}_{n+2} - \mathbf{r_0} = R^n(\mathbf{a} - \mathbf{r_0}) + na_z\hat{\mathbf{z}} + \mathbf{p}_1 \quad (13)$$

since $R^n\hat{\mathbf{z}} = \hat{\mathbf{z}}$.

This helix rises by $\Delta z = a_z$ with each object and turns by the angle θ with each object, so its pitch is $p = (2\pi/\theta)\Delta z = 2\pi a_z/\theta$. Its axis is $\mathbf{r_0} + z\hat{\mathbf{z}}$ for all z.

The rotation matrix R is the product of a rotation $R(\mathbf{b}, \mathbf{a})$ that rotates the vector $\mathbf{a}$ into the vector $\mathbf{b}$ and a rotation $R(\phi\hat{\mathbf{b}})$ about the vector $\mathbf{b}$ by a dihedral angle ϕ:

$$R = R(\phi\hat{\mathbf{b}})R(\mathbf{b}, \mathbf{a}). \quad (14)$$

The first matrix $R(\mathbf{b}, \mathbf{a})$ is

$$R(\mathbf{b}, \mathbf{a}) = |\widehat{\mathbf{a}\times\mathbf{b}}\rangle\langle\widehat{\mathbf{a}\times\mathbf{b}}| + |\hat{\mathbf{b}}\rangle\langle\hat{\mathbf{a}}|$$
$$+ |\widehat{(\mathbf{a}\times\mathbf{b})\times\mathbf{b}}\rangle\langle\widehat{(\mathbf{a}\times\mathbf{b})\times\mathbf{a}}| \quad (15)$$

in Dirac notation with the carets meaning that all vectors are unit vectors. The second matrix $R(\phi\hat{\mathbf{b}})$ is [7]

$$R(\phi\hat{\mathbf{b}}) = e^{\phi\hat{\mathbf{b}}\cdot\vec{L}} = \cos\phi I + \hat{\mathbf{b}}\cdot\vec{L}\sin\phi + (1 - \cos\phi)\hat{\mathbf{b}}(\hat{\mathbf{b}})^{\mathsf{T}}, \quad (16)$$

in which the generators $(L_k)_{ij} = \epsilon_{ikj}$ satisfy $[L_i, L_j] = \epsilon_{ijk}L_k$ and T means transpose. In terms of indices, this formula for $R(\phi\hat{\mathbf{b}}) = e^{\phi\hat{\mathbf{b}}\cdot\vec{L}}$ is

$$R(\phi\hat{\mathbf{b}})_{ij} = \delta_{ij}\cos\phi - \sin\phi\epsilon_{ijk}\hat{\mathbf{b}}_k + (1 - \cos\phi)\hat{\mathbf{b}}_i\hat{\mathbf{b}}_j. \quad (17)$$

In these formulas, ϵ_{ijk} is totally antisymmetric with $\epsilon_{123} = 1$, and sums over k from 1 to 3 are understood.

III. PARAMETRIZING A HELIX

Suppose you are given a set of points that lie on a helix. How do you find the spacing Δz, the angle θ per step, the axis $\hat{\mathbf{n}}$, and a point $\mathbf{n}_0$ on the helix? A helix is defined by four points $\mathbf{p}_1, \mathbf{p}_2, \mathbf{p}_3, \mathbf{p}_4$. Let $\mathbf{a} = \mathbf{p}_2 - \mathbf{p}_1$, $\mathbf{b} = \mathbf{p}_3 - \mathbf{p}_2$, and $\mathbf{c} = \mathbf{p}_4 - \mathbf{p}_3$. If the axis of the helix points in the direction $\hat{\mathbf{n}}$ and $\mathbf{n}_0$ is any point on the axis, then the axis contains the points $\mathbf{n}_0 + z\hat{\mathbf{n}}$, where z is any real number.

The points $\mathbf{p}_i$ of the helix are evenly spaced by Δz in the $\hat{\mathbf{n}}$ direction. The spacing Δz is given by

$$\Delta z = \hat{\mathbf{n}}\cdot(\mathbf{p}_2 - \mathbf{p}_1) = \hat{\mathbf{n}}\cdot\mathbf{a}. \quad (18)$$

Because it is constant, the spacing Δz is also given by $\Delta z = \hat{\mathbf{n}}\cdot(\mathbf{p}_3 - \mathbf{p}_2) = \hat{\mathbf{n}}\cdot\mathbf{b}$ and by $\Delta z = \hat{\mathbf{n}}\cdot(\mathbf{p}_4 - \mathbf{p}_3) = \hat{\mathbf{n}}\cdot\mathbf{c}$. Thus the axis $\hat{\mathbf{n}}$ is orthogonal to $\mathbf{b} - \mathbf{a}$ and to $\mathbf{c} - \mathbf{b}$. So it must be parallel (or antiparallel) to the cross product $\mathbf{n}$ of these vectors,

$$\mathbf{n} = (\mathbf{b} - \mathbf{a})\times(\mathbf{c} - \mathbf{b}). \quad (19)$$

In terms of the length $\ell = |\mathbf{b} - \mathbf{a}| = |\mathbf{c} - \mathbf{b}|$ and the angle ϕ between the vectors $\mathbf{b} - \mathbf{a}$ and $\mathbf{c} - \mathbf{b}$, the vector $\mathbf{n}$ is of length $\ell^2\sin\phi$. The general direction of the helix is defined by the difference $\mathbf{p}_4 - \mathbf{p}_1 = \mathbf{a} + \mathbf{b} + \mathbf{c}$; so if σ is the sign of the dot product $(\mathbf{a} + \mathbf{b} + \mathbf{c})\cdot\mathbf{n}$, then the axis of the helix is the unit vector

$$\hat{\mathbf{n}} = \sigma\frac{(\mathbf{b} - \mathbf{a})\times(\mathbf{c} - \mathbf{b})}{\ell^2\sin\phi}. \quad (20)$$

The three other parameters of the helix are its radius ρ, its angle θ, and a point $\mathbf{n}_0$ on its axis. To find these, we note that for each of the four points $\mathbf{p}_i$,

$$[\hat{\mathbf{n}}\times(\mathbf{p}_i - \mathbf{n}_0)]^2 = \rho^2. \quad (21)$$

Subtracting this relation for $i=1$ from this relation for $i=2$ and recalling that $\mathbf{a} = p_2 - p_1$, we get an equation that is linear in $\mathbf{n}_0$:

$$2(\hat{\mathbf{n}}\times\mathbf{a})\cdot(\hat{\mathbf{n}}\times\mathbf{n}_0) = (\hat{\mathbf{n}}\times\mathbf{p}_2)^2 - (\hat{\mathbf{n}}\times\mathbf{p}_1)^2. \quad (22)$$

Similarly, subtracting Eq. (21) for $i=2$ from Eq. (21) for $i=3$ and recalling that $\mathbf{b} = \mathbf{p}_3 - \mathbf{p}_2$, we find

$$2(\hat{\mathbf{n}}\times\mathbf{b})\cdot(\hat{\mathbf{n}}\times\mathbf{n}_0) = (\hat{\mathbf{n}}\times\mathbf{p}_3)^2 - (\hat{\mathbf{n}}\times\mathbf{p}_2)^2. \quad (23)$$

An orthonormal basis is provided by the three vectors

$$\hat{\mathbf{e}}_1 = \frac{\mathbf{b} - \mathbf{a}}{|\mathbf{b} - \mathbf{a}|}, \quad \hat{\mathbf{e}}_2 = \hat{\mathbf{n}}\times\hat{\mathbf{e}}_1, \quad \hat{\mathbf{e}}_3 = \hat{\mathbf{n}}. \quad (24)$$

Subtracting Eq. (22) from Eq. (23), we get

$$2[\hat{\mathbf{n}}\times(\mathbf{b} - \mathbf{a})]\cdot(\hat{\mathbf{n}}\times\mathbf{n}_0) = (\hat{\mathbf{n}}\times\mathbf{p}_3)^2 - 2(\hat{\mathbf{n}}\times\mathbf{p}_2)^2$$
$$+ (\hat{\mathbf{n}}\times\mathbf{p}_1)^2 \quad (25)$$

or, using Eqs. (24),

$$2|\mathbf{b} - \mathbf{a}|(\hat{\mathbf{n}}\times\hat{\mathbf{e}}_1)\cdot(\hat{\mathbf{n}}\times\mathbf{n}_0) = (\hat{\mathbf{n}}\times\mathbf{p}_3)^2 - 2(\hat{\mathbf{n}}\times\mathbf{p}_2)^2$$
$$+ (\hat{\mathbf{n}}\times\mathbf{p}_1)^2. \quad (26)$$

So in terms of the definition

$$C_{321} = \frac{(\hat{\mathbf{n}} \times \mathbf{p}_3)^2 - 2(\hat{\mathbf{n}} \times \mathbf{p}_2)^2 + (\hat{\mathbf{n}} \times \mathbf{p}_1)^2}{2|\mathbf{b} - \mathbf{a}|}, \qquad (27)$$

we may use Eqs. (24) again to write Eq. (26) as

$$\hat{\mathbf{e}}_2 \cdot (\hat{\mathbf{n}} \times \mathbf{n}_0) = C_{321}. \qquad (28)$$

Since the unit vectors $\hat{\mathbf{e}}_i$ are complete and orthonormal, we may expand the axis point $\mathbf{n}_0$ as

$$\mathbf{n}_0 = \sum_{i=1}^{3} (\hat{\mathbf{e}}_i \cdot \mathbf{n}_0)\hat{\mathbf{e}}_i. \qquad (29)$$

Using Eqs. (24) and the relations $\hat{\mathbf{n}} \times \hat{\mathbf{e}}_2 = -\hat{\mathbf{e}}_1$ and $\hat{\mathbf{n}} \times \hat{\mathbf{e}}_3 = \mathbf{0}$, we have

$$\hat{\mathbf{n}} \times \mathbf{n}_0 = (\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0)\hat{\mathbf{e}}_2 - (\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0)\hat{\mathbf{e}}_1. \qquad (30)$$

So Eq. (28) now implies

$$\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0 = C_{321}. \qquad (31)$$

Expanding the vector $\mathbf{a}$ in terms of the basis $\{\hat{\mathbf{e}}_i\}$,

$$\mathbf{a} = \sum_{i=1}^{3} (\hat{\mathbf{e}}_i \cdot \mathbf{a})\hat{\mathbf{e}}_i, \qquad (32)$$

and using Eqs. (24), we find

$$\hat{\mathbf{n}} \times \mathbf{a} = (\hat{\mathbf{e}}_1 \cdot \mathbf{a})\hat{\mathbf{e}}_2 - (\hat{\mathbf{e}}_2 \cdot \mathbf{a})\hat{\mathbf{e}}_1. \qquad (33)$$

This relation and Eq. (30) imply

$$(\hat{\mathbf{n}} \times \mathbf{a}) \cdot (\hat{\mathbf{n}} \times \mathbf{n}_0) = (\hat{\mathbf{e}}_1 \cdot \mathbf{a})(\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0) + (\hat{\mathbf{e}}_2 \cdot \mathbf{a})(\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0). \qquad (34)$$

Using this expression and the notation

$$C_{21} = \tfrac{1}{2}[(\hat{\mathbf{n}} \times \mathbf{p}_2)^2 - (\hat{\mathbf{n}} \times \mathbf{p}_1)^2], \qquad (35)$$

we extract from Eq. (22) the result

$$(\hat{\mathbf{e}}_1 \cdot \mathbf{a})(\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0) + (\hat{\mathbf{e}}_2 \cdot \mathbf{a})(\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0) = C_{21} \qquad (36)$$

or, using Eq. (31),

$$\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0 = \frac{C_{21} - (\hat{\mathbf{e}}_1 \cdot \mathbf{a})C_{321}}{\hat{\mathbf{e}}_2 \cdot \mathbf{a}}. \qquad (37)$$

The inner product $\hat{\mathbf{e}}_3 \cdot \hat{\mathbf{n}}_0$ is arbitrary. So by substituting our formulas (31) for $\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0$ and (37) for $\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0$ into the expansion (29), we have a set of points $\mathbf{n}_0$ on the axis of the helix in terms of the free parameter $\hat{\mathbf{e}}_3 \cdot \hat{\mathbf{n}}_0$.

To find the radius ρ from Eq. (21), we use Eq. (30) for the cross product $\hat{\mathbf{n}} \times \mathbf{n}_0$:

$$\rho = \sqrt{[\hat{\mathbf{n}} \times \mathbf{p}_1 + (\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0)\hat{\mathbf{e}}_1 - (\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0)\hat{\mathbf{e}}_2]^2}, \qquad (38)$$

where the axis $\hat{\mathbf{n}}$ and the inner products $\hat{\mathbf{e}}_2 \cdot \mathbf{n}_0$ and $\hat{\mathbf{e}}_1 \cdot \mathbf{n}_0$ are given, respectively, by Eqs. (20), (31), and (37).

The cosine of the angle θ is

$$\cos\theta = \rho^{-2}[\hat{\mathbf{n}} \times (\mathbf{p}_1 - \mathbf{n}_0)] \cdot [\hat{\mathbf{n}} \times (\mathbf{p}_2 - \mathbf{n}_0)], \qquad (39)$$

and its sine is

$$\sin\theta = \rho^{-2}\hat{\mathbf{n}} \cdot [\hat{\mathbf{n}} \times (\mathbf{p}_1 - \mathbf{n}_0)] \times [\hat{\mathbf{n}} \times (\mathbf{p}_2 - \mathbf{n}_0)]. \qquad (40)$$

So the angle θ is the argument of the complex number $(\cos\theta, \sin\theta)$ in the interval $-\pi < \theta \leq \pi$, which is given by the second FORTRAN arctangent function atan2 as $\theta = \text{atan2}(\sin\theta, \cos\theta)$.

IV. EXAMPLES OF BIOHELICES

A. DNA

Although DNA is made out of nucleotides, its building block is the object dR-B-B$'$-dR in which dR is a deoxyribose sugar and B-B$'$ is a Crick-Watson base pair of adenine and thymine (A=T or T=A) or of cytosine and guanine (C≡G or G≡C). The four base pairs have nearly the same size, and so the four units dR-B-B$'$-dR are nearly identical. Phosphate groups glue these units into a regular chain. Each dR is linked by one phosphate group to the unit behind it and by another phosphate group to the unit ahead of it. This pattern of covalent bonds is nearly the same in all dR-B-B$'$-dR units. The result is a helix or a double helix [1] if one counts both chains of sugar-phosphate groups. For instance, the ideal B-DNA dodecamer d(CGCGAAT-TCGCG) at 1.4 Å resolution is a right-handed double helix with $a_z = \Delta z = 3.3$ Å, $\theta = 35.5°$, a diameter of 20 Å, and a pitch of 33.3 Å [8]. But other sequences of base pairs have θ as low as 26° or as high as 43°. When the relative humidity is below 75%, B-DNA turns into the A form, which is a right-handed helix with a pitch of 34 Å, but with $\theta = 26°$. The Z form, which can occur when the salt concentration is high, is a left-handed helix with $\theta = 18°$ and a pitch of 44 Å. The dodecamer d((AT)^6) forms coiled coils [9].

B. Secondary structures of proteins

Proteins are chains of amino acids. Except for proline, the 20 amino acids differ only in their side chains. The amino acids all have the same main chain N–C–C and are linked together N–C–C═N–C–C═N–C–C by peptide bonds, which resist rotations—the angle ω about the C═N bond usually is close to 180°. The dihedral angles ϕ and ψ describe rotations about the axes of the single bonds N–C and C–C. These angles are the principal degrees of freedom in proteins, but they are far from free. Ramachandran steric constraints force them to lie in three regions, more (proline) or less (glycine).

The α region lies near $\phi = -57°$, $\psi = -47°$, and $\omega = 180°$ [10]. A chain of amino acids with these dihedral angles is an α-helix [2]. By using Eqs. (18)–(40), one may show that the ideal α-helix is right handed and that it has 3.62 residues per turn, $\theta = 99.4°$, $a_z = \Delta z = 1.56$ Å, and a pitch of 5.64 Å. This geometry allows the carboxyl oxygen of the ith amino acid to flirt with the hydrogen of the main-chain nitrogen of the $i+4$th amino acid; the energy of the resulting N_{i+4}-H$\cdots$O=C$_i$ hydrogen bond is of the order of 0.3 eV.

The other two sterically allowed regions are side by side. The more important one, near $\phi = -139°$, $\psi = 135°$, and $\omega = -178°$ [11], generates helices that form hydrogen bonds between their main-chain amino and carboxyl groups when the helices are adjacent and antiparallel, forming an antiparallel β-sheet. Formulas (18)–(40) imply that the ideal antiparallel β-helix has 2.004 residues per turn, $a_z = \Delta z = 3.47$ Å, and a pitch of 6.95 Å. Although slightly left handed with $\theta = -179.7°$, it is nearly planar. Changes of ϕ, ψ, and ω by 1°

flip the angle θ across the cut at $\theta = \pi$; so antiparallel β-helices do not have definite helicity.

The other region, near $\phi = -119°$, $\psi = 113°$, and $\omega = 180°$ [12], generates helices that form hydrogen bonds between their main-chain amino and carboxyl groups when the helices are adjacent and parallel—a parallel β-sheet. The ideal parallel β-helix has 2.024 residues per turn, $a_z = \Delta z = 3.27$ Å, and a pitch of 6.62 Å. Although somewhat right handed with $\theta = 177.8°$, it is nearly planar. Changes of ϕ, ψ, and ω by 3 or 4° can flip the angle θ across the cut at $\theta = \pi$, and so parallel β-helices do not have definite helicity. In a parallel β-sheet, the distance along its main chain between an amino group and the carboxyl group to which it hydrogen-bonds is greater than in an antiparallel β-sheet (or an α-helix), and so proteins with parallel β-sheets fold slowly.

Students would get a more unified view of secondary structure in proteins and nucleic acids if authors of biochemistry textbooks called β-strands "β-helices."

C. Proteins

The main fibrous protein in hair, horn, and nails, α-keratin, is two α-helices wrapped around each other in a left-handed double helix. The key protein of the extracellular matrix holding cells in animal tissue, collagen, is three α-helices in a right-handed triple helix. Actin and tubulin form helical cytoskeletal filaments.

Globular and transmembrane proteins are α- and β-helices linked by loops and turns. They can be as dense as crystals; α-helices pack closely [13].

D. Remark about protein folding

Proline aside, any string of amino acids can fold into an α- or a β-helix. How does it decide? The solvent helps it decide. Proteins fold in salty water, a polar solvent. A protein in a polar solvent has a lower energy if the hydrophilic (charged or polar) side chains are on the outside and the hydrophobic ones are inside. Suppose two hydrophilic side chains are separated on the main chain by n hydrophobic ones. They will form a helix that cuts through the protein on a chord of length $n\Delta z$ with the two hydrophilic ones outside at its ends. But $\Delta z_\beta = 3.4$ Å for a β-helix is twice $\Delta z_\alpha = 1.6$ Å for an α-helix. So the choice between the two kinds of helices is decided in part by whether $n\Delta z_\alpha$ or $n\Delta z_\beta$ is closer to the thickness of the protein.

E. Viral capsids

The coats (or capsids) of filamentary viruses often are made of a single helix. For instance, the helical capsid of the tobacco mosaic virus consists of 2130 copies of a single protein [14].

The coats of icosahedral viruses [15] are made of nested helices in which $T = h^2 + hk + k^2 = 1, 3, 4, 7, \ldots$ protein molecules form an "asymmetric unit." Three of these asymmetric units form a triangular, primary helix of zero pitch. In turn, ten of these primary, triangular helices form two pentagonal, zero-pitch, secondary helices, and another ten of them form a secondary, beltlike, zero-pitch deca-helix. An icosahedron results when the two secondary pentagonal helices attach to opposite sides of the secondary belt of ten triangular helices. The capsid is made of $60T$ protein molecules.

F. Why all the helices?

Evolution, size, and geometry require them. Evolution forces economy. Cells use mass production to achieve economy, making many copies of identical or closely related objects. Cells are too small to have workers, so they use macromolecules. DNA polymerase makes DNA; RNA polymerase makes RNA; ribosomes make proteins; proteins fold automatically or via chaperones; protein complexes self-assemble. These processes assemble nearly identical objects in regular ways. Helices are ubiquitous because identical objects, regularly assembled, form helices.

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