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The Shape of Myosin Subfragment-1. An Equivalent Oblate Ellipsoid Model Based on Hydrodynamic Properties†

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ABSTRACT: The molecular weights of the two heads of myosin subfragment-1, S-1(A1) and S-1(A2), based on sedimentation equilibrium are 120 000 and 110 000. Hydrodynamically, the two heads are indistinguishable, with intrinsic viscosity, $[\eta]$, of 0.064-0.065 dL/g and sedimentation coefficient, $s^0_{20,w}$, of 5.8 S. Together with the rotational correlation time taken from the literature (235 ns), all three hydrodynamic properties can be better fitted with an equivalent oblate ellipsoid of revolution than a prolate model. The width of the equatorial axis of the ellipsoid is about 135 Å (the axial ratio is about 6). Probably, the S-1(A1) and S-1(A2) molecules have a half-doughnutlike or a flattened pearlike shape rather than an elongated one.

The cross-section of striated muscle fibers shows that the thick filaments of myosin are arranged in a hexagonal lattice and each filament is surrounded by six thin filaments of actin (Huxley, 1969). The two heads of myosin known as subfragment-1 constitute the cross-bridges linking the heavy and thin filaments; the heads are believed to be functionally different and are termed as S-1(A1) and S-1(A2) (Weeds and Taylor, 1975), but the shape of the molecules remains to be solved.

Recently, the methods of preparation for muscle proteins and their enzymatically digested fragments have been much modified. In this work we determine the molecular weights and hydrodynamic properties of myosin S-1(A1) and S-1(A2) rather than those of their mixture. Traditionally, globular proteins are approximated by the prolate ellipsoids of revolution, although sperm whale myoglobin, the first protein whose structure was solved by x-ray diffraction methods, has dimensions of 44 × 44 × 24 Å^3 (quoted by Dickerson and Geis, 1969), which is equivalent to an oblate model having an axial ratio of about two. We will show that the myosin subfragment-1 molecule hydrodynamically fits an oblate model better than a prolate one.

Experimental Section

Preparation of Proteins. Myosin from the back muscle of rabbit was prepared as mentioned previously (Wu and Yang, 1976), but without the purification step on a DEAE-Sephadex column.[1] The protein in 50% glycerol, 20 mM Tris-HCl, 0.5 M KCl, and 0.5 mM dithioerythritol (pH 6.8) was stored at −40 °C. The stock solution was diluted with 10 vol of cold water before use and centrifuged; the precipitate was redissolved in an appropriate buffer.

Myosin subfragment-1 (S-1) was obtained by digesting myosin filaments with α-chymotrypsin (Weeds and Taylor, 1975), and the two myosin heads, S-1(A1) and S-1(A2), were separated on two columns: a DEAE-cellulose (Whatman DE 52) column for S-1(A1) and impure S-1(A2), followed by rechromatographing the latter fraction on a CM-cellulose (Bio-Rad Cellex CM) column to obtain S-1(A2). Both purified fractions were concentrated on an Amicon filter XM 50 and dialyzed against 0.1 M NaCl, 20 mM sodium phosphate buffer, 1 mM EDTA, and 0.5 mM dithioerythritol (pH 7.0). Sodium azide (1 mM) was added to prevent bacterial growth.

Disc gel electrophoresis in a nondissociating buffer was done on 5% polyacrylamide gels without sample gel and stacking gel (Davis, 1964). Sodium dodecyl sulfate gel electrophoresis was carried out on 10% gel with 50 mM sodium phosphate buffer (pH 7.0) (Weber and Osborn, 1969).

Methods. Viscosities were measured in a suspension-type Ubbelohde capillary viscometer (specially made by our glassblower). The solvent flow time were about 2100 s at 5 °C and 1200 s at 25 °C. The data were treated according to the equation:

$$(t - t_0)/t_0C = [\eta]_{uncorr} + k'[\eta]_{uncorr}^2C$$

where t and t_0 are the flow times of the solution and solvent, C is the protein concentration, and k' is a constant. Because myosin S-1 has low intrinsic viscosities, we used long solvent flow time to improve the precision of the data. Even for the most dilute solutions used, $(t - t_0)$ was at least more than 35 s. The protein concentrations based on the micro-Kjeldahl method, assuming a 16% nitrogen content, ranged from 0.5 to 1.3%. The intrinsic viscosity is further corrected for the density difference between solution and solvent by (Tanford, 1955):

$$[\eta] = [\eta]_{uncorr} + (1 - \bar{v}\rho)/100$$

where $\bar{v}$ is the partial specific volume of the protein and ρ the solvent density. The density correction amounts to about +0.003 dL/g.

Sedimentation velocity at 5 and 25 °C and sedimentation equilibrium at 5 °C were studied with a Spinco Model E analytical ultracentrifuge. The schlieren patterns showed a single,

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[1] Abbreviations used are: DEAE, diethylaminoethyl; Tris, tris(hydroxymethyl)aminomethane; EDTA, ethylenediaminetetraacetic acid; EPR, electron paramagnetic resonance.

symmetrical peak. The second moment positions were used for calculating sedimentation coefficient, s, although the peak position method would yield the same s^0 value (extrapolated to zero concentration) within experimental errors. The concentrations ranged from 0.3 to 1.3%. The meniscus depletion method with Rayleigh interference optics (Yphantis, 1964) was used for determining the molecular weight of the fractions at two concentrations (0.25 and 0.50 mg/mL). The partial specific volume, $\bar{v}$, of myosin S-1 based on amino acid composition (Lowey et al., 1969) was calculated as 0.74 mL/g and assumed to be the same for the two heads.

Method of Analysis

For an ellipsoid of revolution we define b as the equatorial semiaxis and a the semiaxis of revolution. The axial ratio is $p = a/b$ for a prolate and $q = b/a$ for an oblate model; the volume in both cases is $V = 4\pi ab^2/3$. An equivalent ellipsoid of revolution, which has the same hydrodynamic properties as the real, rigid macromolecule, contains two parameters, the p or q, and V_e, the effective volume, of the particle, noting that V_e does not necessarily equal V (Sadron, 1942; Scheraga and Mandelkern, 1953). Any single hydrodynamic property, such as intrinsic viscosity ($[\eta]$), sedimentation coefficient (s^0), diffusion coefficient (D^0), or rotary diffusion coefficient (θ^0), cannot determine the axial ratio of the particle without knowing V_e. But it is possible to estimate the length, L, of a prolate ellipsoid (Yang, 1961a,b) or the width, W, of an oblate ellipsoid with reasonable accuracy, since:

$$L\ (\text{Å}) \equiv 2a = 6.82([\eta]M_r)^{1/3}(p^2/\nu)^{1/3} \quad (1)$$

$$L\ (\text{Å}) = 1.76 \times 10^{-17}[M_r(1 - \bar{v}\rho)/\eta_0 s^0](Fp^{2/3}) \quad (2a)$$

$$= 1.46 \times 10^{-9}(T/\eta_0 D^0)(Fp^{2/3}) \quad (2b)$$

and

$$L\ (\text{Å}) = 353(T/\eta_0\theta^0)^{1/3}(Jp^2)^{1/3} \quad (3)$$

Likewise, it can be shown that:

$$W\ (\text{Å}) \equiv 2b = 6.82([\eta]M_r)^{1/3}(q/\nu)^{1/3} \quad (4)$$

$$W\ (\text{Å}) = 1.76 \times 10^{-17}[M_r(1 - \bar{v}\rho)/\eta_0 s^0](Fq^{1/3}) \quad (5a)$$

$$= 1.46 \times 10^{-9}(T/\eta_0 D^0)(Fq^{1/3}) \quad (5b)$$

and

$$W\ (\text{Å}) = 353(T/\eta_0\theta^0)^{1/3}(Jq)^{1/3} \quad (6)$$

Here M_r is the molecular weight, ν the viscosity increment, $1/F$ the translational frictional ratio (f/f_0), $1/J$ the rotary frictional ratio (ζ/ζ_0), η_0 the solvent viscosity in poise, and T the absolute temperature. The six shape factors, $(p^2/\nu)^{1/3}$, etc., in eq 1 to 6 are rather insensitive toward the axial ratio p or q, especially when the latter is large. Because myosin S-1 has a small axial ratio, we adopt a modified approach by presetting several axial ratios and calculating the lengths and widths of the two kinds of ellipsoids according to eq 1 to 6. The choice of oblate vs. a prolate model is based on the consistency of the calculated widths or lengths from three hydrodynamic properties, $[\eta]$, s^0, and θ^0. Once L or W is determined, we automatically fix the dimension of the equatorial axis.

Equations 1 to 6 do not include the V_e term, which, however, is needed to narrow the range of axial ratio allowed. At present this is still a difficult problem. The next best approach is a compromise between the Oncley treatment and the theoretically sound concept of equivalent hydrodynamic ellipsoid (see Yang, 1961b). Two assumptions are introduced: (a) the specific volume, v_{sp}, of the macromolecule is replaced by $\bar{v}$, which is a measurable quantity, and (b) V_e equals the sum of $\bar{v}$ and the volume occupied by the water of hydration, w, in grams per gram, multiplied by the weight per molecule:

$$V_e \simeq M_r(\bar{v} + w/\rho)/N_A \quad (7)$$

Here N_A is the Avogadro number. Equation 7 is of course only an approximation; it has been a controversial subject for more than two decades. Recognizing the assumptions involved, we use eq 7 to limit the range of p or q with some reservations. After both a and b are chosen, we calculate w in eq 7. The cutoff of p and q is arbitrarily set at $w = 0$ (anhydrous) and 1 (for a recent review on water of hydration for proteins, see Kuntz and Kauzmann, 1974).

For an ellipsoid with three semiaxes, a, b, and c, its radius of gyration is given as:

$$R_g^2 = (a^2 + b^2 + c^2)/5 \quad (8)$$

which reduces to:

$$R_g^2 = (a^2 + 2b^2)/5 \quad (9)$$

for an ellipsoid of revolution. The low-angle x-ray scattering or neutron scattering method measures the radius of gyration; these techniques do not distinguish water of hydration from free water; that is, w can be regarded as zero. Equation 9 in turn leads to:

$$a^3 - 5R_g^2 a + \frac{3M_r v_{sp}}{2\pi N_A} = 0 \quad (10)$$

which gives three sets of solutions of a and b; two sets correspond to a prolate and an oblate model, respectively (the third set gives a negative a and is discarded). Again eq 10 has the problem of determining the specific volume, v_{sp}, of the macromolecule unless we assume $v_{sp} \simeq \bar{v}$.

Results

The fraction S-1(A1) of myosin that first emerges from a DEAE-cellulose column sometimes appears as a split peak (peak I in Figure 1A). However, gel electrophoresis of peak I in either a dissociating or a nondissociating buffer could not detect this heterogeneity. With a nondissociating buffer S-1(A1) appears as a single band (Figure 2). In dodecyl sulfate solution the protein dissociates into a heavy chain of M_r = 92 000 and a light chain of M_r = 24 000. Another thin band of M_r = 70 000 is probably a degraded product of the heavy chain. Peak II in Figure 1A is mostly S-1(A2) that is contaminated with S-1(A1); this fraction is rechromatographed on a CM-cellulose column after dialysis against 50 mM Tris-HCl (pH 7.5). Myosin S-1(A2) emerges first as peak II_a (Figure 1B) at the void volume (peak II_b in this case is a mixture of S-1(A1) and S-1(A2)). Gel electrophoresis of peak II_a in a nondissociating buffer shows a single band slightly tainted with S-1(A1) (Figure 2). In the presence of dodecyl sulfate, the electrophoretic pattern is similar to that of S-1(A1), except the light chain now has an M_r of 16 000. Thus, electrophoretic results suggest that S-1(A1) has a M_r of about 120 000 and S-1(A2) 110 000.

For data of high-speed sedimentation equilibrium at 5 °C plots of log C in terms of fringe displacement vs. the square of radius (from the center of rotation) gave straight lines for both myosin S-1(A1) and S-1(A2). These results suggest that the samples were essentially homogeneous. The weight-average molecular weights of S-1(A1) and S-1(A2) were calculated to be 120 000 and 110 000, respectively. Since the protein concentrations used in these experiments were low (0.025 and 0.05%) and approached infinite dilution near the cell top, the

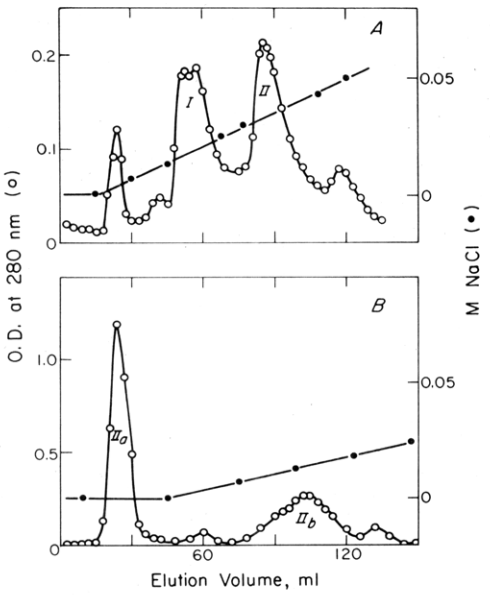

FIGURE 1: Chromotography of myosin S-1 on a DEAE-cellulose column, 1.5 × 30 cm (A), and on a CM-cellulose column, 1.6 × 24 cm (B). Seven milliliters of S-1 at 5 mg/mL was loaded on the column and eluted with 50 mM Tris-HCl (pH 7.5) and a linear gradient of NaCl to 0.1 M. For preparative purposes, a 2.5 × 50 cm column was used. See text for details.

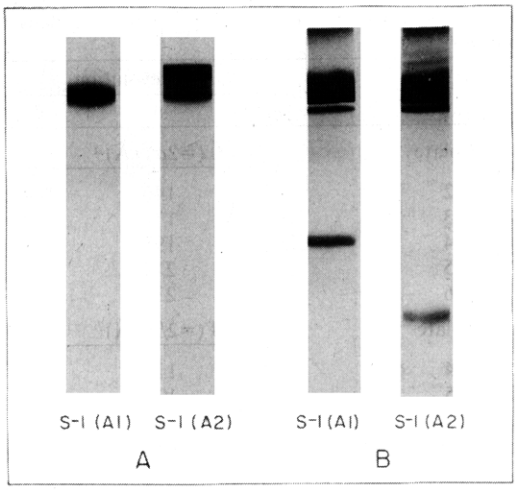

FIGURE 2: Gel electrophoresis of pooled fractions of myosin S-1(A1) from a DEAE-cellulose column (peak I in Figure 1A) and S-1(A2) from a CM-cellulose column (peak II_a in Figure 1B). A and B in nondissociating buffer and in sodium dodecyl sulfate containing system, respectively.

molecular weights were found to be concentration independent. The reciprocal of the sedimentation coefficients, $1/s_{20,w}$, varied linearly with the concentrations (in percent) used, with a slope of 0.020 and 0.018 for S-1(A1) and S-1(A2), respectively, where s was expressed in Svedberg units. The (uncorrected) reduced viscosity, $(t - t_0)/t_0C$, virtually showed no dependence on the concentrations used ($k' \simeq 0$). The data at 5 and 25 °C fell on the same line for both $[\eta]$ and $s^0_{20,w}$. Both myosin S-1(A1) and S-1(A2) have the same $[\eta]$ and s^0 within experimental error.

Table I summarizes the physical properties of myosin S-1(A1) and S-1(A2) together with some literature values of subfragment-1 without separation of the two heads. Because S-1(A1) and S-1(A2) are hydrodynamically indistinguishable, Table II only lists the results of the calculated length and width for S-1(A1) according to eq 1–6. (Three figures are listed for the calculated axes of revolution because of small differences at various axial ratios, in particular, of the oblate model.) The results for S-1(A2) will only be off by 1–3% due to the difference in molecular weights between the two heads. Comparison of the upper and lower halves of the results in Table II indicates that the three hydrodynamic properties, $[\eta]$, s^0, and θ^0, are consistent with each other for an equivalent oblate ellipsoid of revolution. We find that an axial ratio of about six for the oblate model would give a water of hydration of about 0.4 g/g. Of course this does not completely rule out $q = 5$ or 7; any attempt to determine the axial ratio to the first decimal would take the mathematical model too literally. Furthermore, the assumptions introduced in eq 7 should cause some uncertainty in the reported axial ratios, regardless of the model chosen.

For an oblate ellipsoid of revolution, solution of eq 10 (assuming $v_{sp} \simeq \bar{v}$) leads to $2b = 100$ and 110 Å if the radius of gyration, R_g, is taken as 32 and 35 Å, respectively (Table I). The corresponding $2a$ is about 28 and 23 Å, respectively. For a prolate model, similar calculations give $2a = 127$ or 144 Å and $2b = 46$ or 43 Å for $R_g = 32$ or 35 Å. Here again these results should be viewed with caution because of some uncertainty in v_{sp}. The length or width based on R_g is shorter than

TABLE I: Physical Properties of Myosin Subfragment-1.

Properties	Subfragments S-1(A1)	Subfragments S-1(A2)	S-1 (lit.)
M_r	120 000[a]	110 000[a]	115 000[a]
$[\eta]$, dL/g	0.064	0.065	0.064[a]
$s^0_{20,w}$, S	5.8	5.8	5.8[a]
$\bar{v}$, mL/g	(0.74)[b]	(0.74)[b]	0.728[a]
$D^0_{20,w}$, cm^2/s	(4.6×10^{-7})[c]	(5.0×10^{-7})[c]	4.33×10^{-7} [d]
θ^0, 1/s			7.1×10^5 [e] (4 °C)
R_g, Å			32[f]
			35[g]

[a] Lowey et al. (1969) for S-1; our single preparation showed M_r = 116 000 and 107 000. [b] Based on amino acid composition of myosin S-1. [c] Calculated from the Svedberg equation: $D^0 = s^0RT/M(1 - \bar{v}\rho)$. [d] Jones and Perry (1966). [e] Calculated from the average rotational correlation time, Φ, as reported by Mendelson et al. (1973), assuming $\Phi = 1/(6\theta^0)$. [f] Kretzschmar et al. (1976). [g] Worcester et al., manuscript to be published.

that based on hydrodynamic measurements, but a layer of water shell around the protein molecule could add several angstroms. Actually, there is no a priori reason that hydrodynamic and scattering results must agree with each other (see Discussion).

Discussion

The heterogeneity of the two myosin heads (S-1) may not be confined to the (A1) and (A2) light chains even with improved enzymatic digestion of myosin. But hydrodynamic properties are not sensitive enough to detect any difference in shape of S-1(A1) and S-1(A2), as evidenced by the identical results listed in Table I. Our $[\eta]$ and s^0 values appear to coincide with early results of myosin S-1 by Lowey et al. (1969). For viscosity measurements these authors used viscometers having a solvent flow time of about 400 s at 20 °C; the concentrations of S-1 ranged from 0.24 to 0.85% as read from their Figure 6 (cf. our methods in the Experimental Section).

The rotary diffusion coefficient, θ^0, was obtained from the relation: $\Phi = 1/(6\theta^0)$, where Φ is the rotational correlation time based on the results of nanosecond fluorescence depolarization (assuming no concentration dependence in dilute solutions; for

TABLE II: The Length or Width of Myosin Subfragment-1 (A1) Based on Hydrodynamic Properties for an Equivalent Ellipsoid of Revolution.

Axial ratio	Axis of revolution			Equatorial axis			Water of hydration[c]		
	$[\eta]$	s^0	θ	$[\eta]$	s^0	θ	$[\eta]$	s^0	θ
Prolate	L (=2a) (Å)[a]			2b (Å)			w (g/g)		
2	148	140	143	74	70	72	1.46	1.13	1.25
3	179	174	162	60	58	54	0.99	0.85	0.54
4	201	198	173	50	50	43	0.64	0.58	0.14
5	216	217	181	43	43	36	0.36	0.47	Neg
6	228	234		38	39		0.15	0.23	
Oblate	W(=2b) (Å)[b]			2a (Å)			w (g/g)		
4	132	127	131	33	32	34	0.82	0.65	0.90
5	136	130	134	27	26	27	0.63	0.46	0.60
6	138	132	135	23	22	23	0.45	0.30	0.40
7	140	134	136	20	19	19	0.32	0.19	0.24
8	141	135	137	18	17	17	0.21	0.10	0.08

[a] Based on eq 1, 2a, and 3. [b] Based on eq 4, 5a, and 6. [c] Based on eq 7 (see text for the assumptions involved).

TABLE III: Shape Factors for the Calculation of Width of an Oblate Ellipsoid of Revolution.[a]

Axial ratio, q	Viscosity $(q/\nu)^{1/3}$	Translational diff coeff $(Fq^{1/3})$	Rotary diff coeff $(Jq)^{1/3}$
1	0.737	1.000	1.000
2	0.889	1.209	1.209
3	0.956	1.305	1.270
4	0.995	1.363	1.295
5	1.020	1.397	1.307
6	1.038	1.423	1.314
7		1.443	
8	1.061	1.456	1.321
9		1.469	
10	1.075	1.478	1.324
12	1.085	1.492	1.326
15	1.095		1.328
16		1.512	
20	1.106	1.523	1.329
25	1.112	1.533	1.329
30	1.116	1.538	1.330
40	1.122	1.546	1.330
50	1.126	1.551	1.330
60	1.129	1.555	1.330
80	1.132	1.558	1.331
100	1.132	1.561	1.331

[a] For shape factors of a prolate ellipsoid of revolution, see Yang (1961b).

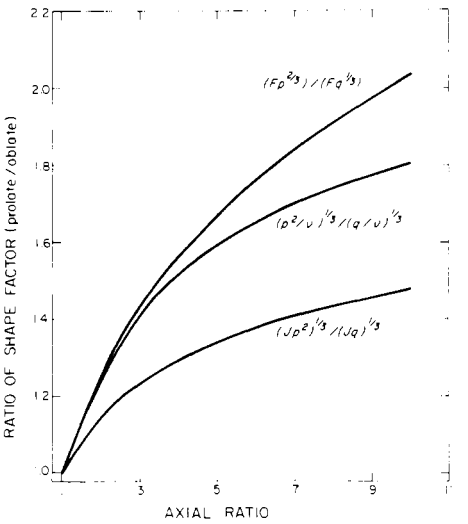

FIGURE 3: Ratio of the shape factors for a prolate to an oblate ellipsoid of revolution at different axial ratios.

the determination of θ^0, see Yang, 1958). Such calculations of course involve some assumptions about the rotational motion. Mendelson et al. (1973) reported an average Φ of 235 ns for myosin S-1 at 4 °C. The fluorescent conjugate is believed to be rigidly buried inside a hydrophobic domain; otherwise, any intramolecular freedom would lower the Φ value, which cannot be attributed to the protein–dye molecule as a whole. Using the electric birefringence method, Kobayasi and Totsuka (1975) found a relaxation time of 250 ns at room temperature. By saturation transfer EPR spectroscopy, Thomas et al. (1975) observed a rotational correlation time of about 185 ns presumably at 20 °C; this is equivalent to 305 ns at 4 °C, which is much larger than that reported by Mendelson et al. (1973). We have no explanation for this large discrepancy.

All hydrodynamic properties of a macromolecule should be consistent with a chosen mathematical model. A more sophisticated technique does not necessarily provide more reliable information than a simple tool such as viscometry. The equivalent ellipsoid under a translational motion (s^0 and D^0) could also differ from that under a rotational motion ($[\eta]$ and θ^0) to some extent. But this possibility is not applicable here, since $[\eta]$ and s^0 give similar results.

The shape factors, $(p^2/\nu)^{1/3}$, etc., in eq 1 to 6 not only depend on the chosen model, a prolate vs. an oblate, but also vary differently with the axial ratio among the three hydrodynamic properties of the same model (see Table III). These very differences help to decide on an appropriate model that hydrodynamically resembles the real particles. It seems surprising that the calculated dimensions based on $[\eta]$ and s^0 are close to each other, regardless of the mathematical model chosen. Figure 3 shows that at any axial ratio, conversion of the shape factor from a prolate to an oblate model or vice versa is most drastic for sedimentation or diffusion coefficients. The corresponding changes for the shape factor of $[\eta]$ are close to those of s^0 and D^0. In contrast, the changes in shape factors are gradual for rotary diffusion coefficients. Thus, a prolate model converted from an oblate one of the same volume would give much larger lengths based on $[\eta]$ and s^0 rather than on θ^0.

According to eq 1 and 4 the errors in L or W are only one-third of those in the product ($[\eta]M_r$). On the other hand, the errors in s^0 or D^0 (eq 2 and 5) are equivalent to those of the calculated dimensions. Any error in rotary diffusion coefficient (or rotational correlation time) is again reduced to about one-third of that in the calculated L or W (eq 3 and 6). The rotational correlation time as determined by Thomas et al. (1975) is 30% higher than that by Mendelson et al. (1973); this would increase the length or width in Table II by about 9%. In that case the three hydrodynamic properties would be consistent with a prolate model having an axial ratio of 3 with a water of hydration of about 1 g/g. For an oblate model the increased width would be inconsistent with that based on $[\eta]$ and s^0.

Combining any two quantities of $[\eta]$, s^0, and θ^0 to eliminate V_e leads to three functions (β, δ, and μ) that only depend on axial ratios of either the prolate or the oblate model (Scheraga and Mandelkern, 1953; Scheraga, 1961). But these functions are rather insensitive to the variations in axial ratios, and any error in experimental quantities can lead to quite different conclusions. With the $[\eta]$ and s^0 values in Table I, myosin S-1(A1) has a β value of 2.23×10^6, which would correspond to a prolate model with $p = 5$ and rule out the oblate model (the β value only varies from 2.12×10^6 for a sphere to 2.15×10^6 for an oblate with $q = 300$). But if the β value is reduced by 4%, the resultant β value can be either an oblate with $q = 6$ to 15 or a prolate with $p = 2$. Combining $[\eta]$ with θ^0, a δ value of 2.15 corresponds to a prolate with a p between 1 and 2 or an oblate with a q of 4 to 5. Similar calculations of the μ function from s^0 and θ^0 give a μ value of 1.12, which suggests an oblate with a q of 9 or a prolate with a p of 2. The unavoidable experimental errors make the use of these functions very uncertain.

The radius of gyration, R_g, of a particle depends on the actual distribution of mass. It is not surprising that an equivalent hydrodynamic ellipsoid may not have the same R_g as the real molecule. Nor should a hydrodynamic ellipsoid be identical with a thermodynamic one. Furthermore, different models can happen to have the same R_g. As an illustration we consider a flattened pearlike model for myosin S-1 which can be approximated by a right cone or, more appropriately, a truncated right cone. For a right cone it can be shown that:

$$h^2 + 2d^2 = 80R_g^2/3 \qquad (11)$$

where h is the height and d the diameter. Combining eq 11 with the volume of the cone (again assuming $v_{sp} \simeq \bar{v}$):

$$\pi hd^2/12 = M_r v_{sp}/N_A \simeq M_r\bar{v}/N_A \qquad (12)$$

leads to $d = 113$ Å and $h = 43$ Å for $R_g = 32$ Å or $d = 125$ Å and $h = 35$ Å for $R_g = 35$ Å for a flattened cone. These diameters of unhydrated particles are somewhat smaller than the $2b$ of an oblate ellipsoid of revolution in Table II. (Equations 11 and 12 also give another set of solutions for an elongated right cone.) By removing a small right cone having a height $^1/_{10}$th that of the original cone, the volume and mass of the truncated right cone would only be reduced by 0.1% and the corresponding R_g would hardly be affected. Such a truncated right cone will have a top diameter of 11 or 13 Å for the two experimental R_g values.

An early electron micrograph by shadowing technique showed two globular heads of myosin S-1 (Lowey et al., 1969). The negative staining electron micrograph indicates an elongated, banana-like particle for S-1, which wraps around the thin actin filament (Moore et al., 1970). Suffice it to say, experimental interpretations of electron microscopic results are by no means straightforward. Whether the real molecule of myosin S-1 in its dried state may appear as a bent banana or even a flattened pear remains to be solved. Hydrodynamically, the current experimental data indicate that the myosin S-1 molecules, be they half-doughnutlike or flattened pearlike, in solution can be better approximated by an equivalent oblate ellipsoid of revolution than a prolate model. There is also a certain risk by presuming that the shape of a protein molecule remains unaltered at all when the molecule is dried. Carefully interpreted, the hydrodynamic properties of a protein can provide information concerning its shape in solution, which in turn is related to its biological function.

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