

## Preaveraged Hydrodynamic Interaction Revisited via Boundary Element Computations

Sergio R. Aragon\* and David K. Hahn

*Department of Chemistry and Biochemistry, San Francisco State University,  
1600 Holloway Avenue, San Francisco, California 94132-4163*

Received June 20, 2005

**Abstract:** The effect of preaveraging the Oseen tensor to yield a scalar approximation is examined for transport problems of rigid objects with stick boundary conditions using new very high accuracy computational codes. Nearly exact computations are compared to analytical results and preaveraged results for spheroids and, similarly, for a set of three globular proteins. In agreement with previous work, we find that the error in translational diffusion is less than 1%. However, in the case of rotational diffusion and intrinsic viscosity, the error is sensitively dependent on shape. In the case of the axial component of the rotational diffusion, the error is about –34% independent of shape, but for the perpendicular component, the error starts at –30% (sphere) and decreases as the axial ratio increases and then yields a similar but positive error. For the intrinsic viscosity, the errors are around 10% near spherical and decrease toward the needle or disk shape. For the globular proteins, the errors are similar to those found for the ellipsoids near the spherical shape. The calculations show that preaveraging is acceptable only for translational diffusion of rigid objects.

### I. Introduction

It is well-known that the hydrodynamic interaction between two spheres is a series expansion whose first term is the Oseen<sup>1</sup> tensor, and to second order in the distance between the spheres, the interaction can be variationally represented by the Rotne–Prager<sup>2</sup> tensor. The tensorial nature of the hydrodynamic interaction, HI, requires more extensive computations when doing bead modeling dynamics of polymers and often the interaction is orientationally averaged to save computation time,<sup>3</sup> but this may not always be justified. When such orientational averaging is performed, the Oseen tensor becomes proportional to the Green function for electrostatic problems. Several authors have taken advantage of this and have developed extensive formulas that connect, in an approximate manner, the transport properties of rigid bodies with electrostatic properties of these bodies. In particular, the capacitance of an arbitrarily shaped conductor has been related to the translational diffusion coefficient,<sup>4</sup> while the polarizability has been related to the intrinsic viscosity<sup>5</sup> and the normal component of the polarizability has been related to the rotational diffusion coefficient of the body.<sup>6</sup> Zhou<sup>6</sup> has further developed these formulas

and has applied them to the computation of the transport properties of proteins by the use of a boundary element method. As we show below, such computations can be very inaccurate, requiring the use of empirical correction factors to gain agreement with experiment.

Studies based on interacting bead hydrodynamics by Garcia de la Torre and co-workers<sup>7</sup> have shown that the translational diffusion coefficient is not sensitive to the tensorial part of the HI tensors so that the preaveraged approximation is expected to work well. On the other hand, accurate enough hydrodynamic computations of rigid body transport have not been available until recently in order to quantitatively determine the error in this approximation, in particular for the rotational diffusion and intrinsic viscosity. In this work, we perform hydrodynamic computations of high accuracy to address this issue, restricted to stick boundary conditions.

### II. Theory

In a recent paper, Aragon<sup>8</sup> has described a very accurate implementation of the method introduced by Youngren and Acrivos<sup>9</sup> for the boundary element method of solution of

the exact integral equation formulation of the resistance problem. This integral equation has also been used by Allison<sup>10,11</sup> to study the electrophoretic mobility of proteins and DNA. For stick boundary conditions, the equation yields the velocity field at the surface of a body moving in a solvent which is quiescent at infinity. The unknown quantities are the surface stresses (force/area),  $\mathbf{f}(\mathbf{x})$ . The equation is

$$\mathbf{v}(\mathbf{y}) = \int_{sp} \ddot{\mathbf{T}}(\mathbf{x}, \mathbf{y}) \cdot \mathbf{f}(\mathbf{x}) dS_x \quad (1)$$

This is the exact solution to the Stokes equation of hydrodynamics under stick boundary conditions, and it applies to the case of small Reynold's number flow. The kernel of the equation is the Oseen tensor given by

$$\ddot{\mathbf{T}}(\mathbf{x}, \mathbf{y}) = \frac{1}{8\pi\eta|\mathbf{x} - \mathbf{y}|} \left[ \ddot{\mathbf{I}} + \frac{(\mathbf{x} - \mathbf{y})(\mathbf{x} - \mathbf{y})}{|\mathbf{x} - \mathbf{y}|^2} \right] \quad (2)$$

The integral eq 1 is solved numerically by replacing the surface with a collection of  $N$  triangles that smoothly tile the molecular surface. Then we can write

$$\mathbf{S} = \sum_{j=1}^N \Delta_j \quad (3)$$

We place the coordinate  $\mathbf{x}_j$  at the center of the small triangle  $\Delta_j$  and take the surface stress force  $\mathbf{f}(\mathbf{x})$  to be a constant over the entire patch area. This is the basic approximation: it is clear that it will become a better and better approximation as the triangle is made small. Thus, an extrapolation to zero size triangle leads to a very precise value for the transport properties. With this approximation, eq 1 becomes a set of  $3N$  equations for  $3N$  unknowns  $\mathbf{f}(\mathbf{x})$

$$\mathbf{v}(\mathbf{y}_k) = \sum_{j=1}^N \ddot{\mathbf{G}}_{kj} \cdot \mathbf{f}_j \quad (4)$$

The centerpiece of this set of equations is a set of  $N$  completely known  $3 \times 3$  matrices of coefficients that contain all geometric information, the integrals of the Oseen tensor over a surface patch

$$\ddot{\mathbf{G}}_{kj} = \int_{\Delta_j} \ddot{\mathbf{T}}(\mathbf{x}, \mathbf{y}_k) dS_x \quad (5)$$

The set of  $3N$  equations can be written all at once

$$\begin{bmatrix} \mathbf{v}_1 \\ \vdots \\ \mathbf{v}_N \end{bmatrix}_{3N \times 1} = \begin{bmatrix} \ddot{\mathbf{G}}_{11} & \ddots & \ddots & \ddot{\mathbf{G}}_{1N} \\ \vdots & \ddots & \ddots & \vdots \\ \ddot{\mathbf{G}}_{N1} & \ddots & \ddots & \ddot{\mathbf{G}}_{NN} \end{bmatrix}_{3N \times 3N} \begin{bmatrix} \mathbf{f}_1 \\ \vdots \\ \mathbf{f}_N \end{bmatrix}_{3N \times 1} \quad (6)$$

from which the unknown surface stress forces can be readily obtained by matrix inversion of the  $3N \times 3N$  super matrix  $\ddot{\mathbf{G}}$

$$[\mathbf{f}]_{3N \times 1} = [\ddot{\mathbf{G}}]_{3N \times 3N}^{-1} [\mathbf{v}]_{3N \times 1} \quad (7)$$

The total force and torque on the body can be computed from the surface stress forces, and these are directly related to the friction tensors ( $\ddot{\mathbf{K}}$ ) of the body

$$\mathbf{F} = \sum_{j=1}^N \mathbf{f}_j(\mathbf{x}) \Delta_j = -\ddot{\mathbf{K}}_{tt} \cdot \mathbf{v}_p - \ddot{\mathbf{K}}_{tr} \cdot \omega_p \quad (8)$$

$$\mathbf{T} = \sum_{j=1}^N \mathbf{x}_p \times \mathbf{f}_j(\mathbf{x}) \Delta_j = -\ddot{\mathbf{K}}_{rt} \cdot \mathbf{v}_p - \ddot{\mathbf{K}}_{rr} \cdot \omega_p \quad (9)$$

The particle can be assumed to have specific translation velocity  $\mathbf{v}_p$  and angular velocity  $\omega_p$  (for example  $\omega_p = 0$  and  $\mathbf{v}_p = (v_x, 0, 0)$ ) to solve the above equations. Thus, 6 calculations suffice to determine all components of the friction tensors. The friction tensors form part of a larger  $6 \times 6$  tensor that contains information about the pure translational friction ( $tt$ ), the pure rotational friction ( $rr$ ), and the coupling that may exist between these ( $rt$  and  $tr$ ). There are actually only 3 independent friction tensors because the  $\ddot{\mathbf{K}}_{tr}$  tensor is the transpose of the  $\ddot{\mathbf{K}}_{rt}$  tensor. The diffusion tensors are finally obtained from the friction tensors by an easy  $3 \times 3$  matrix inversion

$$\ddot{\mathbf{D}}_{tt} = kT[\ddot{\mathbf{K}}_{tt} - \ddot{\mathbf{K}}_{tr} \cdot \ddot{\mathbf{K}}_{rr}^{-1} \cdot \ddot{\mathbf{K}}_{rt}]^{-1} \quad (10)$$

$$\ddot{\mathbf{D}}_{rr} = kT[\ddot{\mathbf{K}}_{rr} - \ddot{\mathbf{K}}_{tr} \cdot \ddot{\mathbf{K}}_{tt}^{-1} \cdot \ddot{\mathbf{K}}_{rt}]^{-1} \quad (11)$$

In the final step, the tensors are transformed to the "Center of Diffusion". The details of the procedure, the regularization method, the extrapolation to an infinite number of patches, and the Fortran program, BEST, that accomplished this are described in Aragon.<sup>8</sup>

If one preaverages the HI, then the effective quantity that appears in eq 1 is simply

$$T(\mathbf{x}, \mathbf{y}) = \frac{1}{6\pi\eta|\mathbf{x} - \mathbf{y}|} \quad (12)$$

Thus, if one turns off the tensor pieces in the BEST computation (the dyadic following the unit matrix in eq 2), for translation and rotation, one must simply multiply the computed quantity by  $4/3$ . On the other hand, the intrinsic viscosity is proportional to moments of the surface stress forces, and the scaling factor for this case is the inverse,  $3/4$ . This is done automatically in the BEST program.

A comment on why the preaveraging approximation is expected to be a good approximation is in order. Hubbard and Douglas<sup>4</sup> have made the argument that the rotational dynamic motions of the Brownian particle can be considered to perform an operation of angular averaging on the surface stress forces  $\mathbf{f}$ . From this they have derived the existence of a spherically symmetric stress potential which describes the average flow field around the body and a corresponding relation between the friction coefficient and the electrostatic capacitance. From this relation they proceed to show that preaveraging the hydrodynamic tensor yields estimates that are only a few percent off from known analytical results for a variety of shapes. A crucial factor that allows this to work is that the friction force is a simple integral over the surface stresses over the body. When one considers the intrinsic viscosity or rotational diffusion, on the other hand, two important differences arise. In rotational diffusion, one is interested in the total torque on the body, and now it is a higher moment of the surface stress force that needs to be

**Table 1.** Translational Diffusion Coefficients of Ellipsoids of Revolution ( $1/\text{\AA}$ )

$p, 1/p$	prolate and sphere				oblate			
	exact	BEST	PAV	% err.	exact	BEST	PAV	% err
1	1.3333	1.3333	1.3312	-0.16				
4	0.7104	0.7104	0.7091	-0.19	0.45378	0.45384	0.45282	-0.23
8	0.4651	0.4652	0.4643	-0.19	0.24282	0.24283	0.24228	-0.22
30	0.1821	0.1820	0.1816	-0.22	0.068369	0.068406	0.068031	-0.55

**Table 2.** Rotational Diffusion Coefficients of Ellipsoids of Revolution ( $1/\text{\AA}^3$ )

$1/p$	prolate and sphere							
	$D_r^\perp$				$D_r^\parallel$			
	exact	BEST	PAV	% err	exact	BEST	PAV	% err
1	1.0000	1.0002	0.661	-34				
4	$7.362 \times 10^{-2}$	$7.363 \times 10^{-2}$	$6.452 \times 10^{-2}$	-12	$3.467 \times 10^{-1}$	$3.467 \times 10^{-1}$	$2.281 \times 10^{-1}$	-34
8	$1.330 \times 10^{-2}$	$1.330 \times 10^{-2}$	$1.339 \times 10^{-2}$	0.65	$1.822 \times 10^{-1}$	$1.822 \times 10^{-1}$	$1.1995 \times 10^{-1}$	-34
30	$3.993 \times 10^{-4}$	$3.993 \times 10^{-4}$	$4.595 \times 10^{-4}$	15	$4.983 \times 10^{-2}$	$4.956 \times 10^{-2}$	$3.452 \times 10^{-2}$	-30

$p$	oblate							
	$D_r^\perp$				$D_r^\parallel$			
	exact	BEST	PAV	% err	exact	BEST	PAV	% err
4	$3.391 \times 10^{-2}$	$3.393 \times 10^{-2}$	$3.040 \times 10^{-2}$	-10	$2.778 \times 10^{-2}$	$2.777 \times 10^{-2}$	$1.840 \times 10^{-2}$	-34
8	$4.502 \times 10^{-3}$	$4.505 \times 10^{-3}$	$4.771 \times 10^{-3}$	5.9	$3.964 \times 10^{-3}$	$3.962 \times 10^{-3}$	$2.624 \times 10^{-3}$	-34
30	$8.712 \times 10^{-5}$	$8.721 \times 10^{-5}$	$10.83 \times 10^{-5}$	24	$8.370 \times 10^{-5}$	$8.372 \times 10^{-5}$	$5.529 \times 10^{-5}$	-34

integrated over the surface of the body ( $\mathbf{r} \times \mathbf{f}$ ); while in the intrinsic viscosity, even more complex higher moments arise. In addition, for rotational diffusion, there are no other dynamics that can serve as the heuristic physical averaging process, and the components of the friction tensor can be quite different for different rotational motions. In the case of translational friction, all the components of the friction tensor are very similar, even when the shape is very anisotropic. A representation by an angular average is therefore expected to work. Furthermore, for the computation of the intrinsic viscosity, we do assume that the rotational Brownian motion does provide an orientational average; however, the more complex moments of the surface stress that enter into the computation provide significant differences between a computation that averages the hydrodynamic interactions at the outset and one that adds the average effect of the higher moments. This, however, probably explains the fact, as shown below, that the error of preaveraging in the intrinsic viscosity is smaller than that for rotational diffusion.

### III. Results and Discussion

To investigate the error in preaveraged approximation, we performed computations on ellipsoids of revolution for which analytical formulas exist<sup>12</sup> and for a set of three proteins using our program BEST. We discuss the ellipsoid results first.

**A. Ellipsoids.** Table 1 shows the values obtained for the average translational diffusion coefficient ( $1/3 \text{ Tr } D_t$ ) as a function of axial ratio for both prolate and oblate ellipsoids with three methods: the analytic formulas, the accurate BE solution, and the approximate preaveraged solution. Note that the values in Tables 1 and 2 are given in internal BEST units,

$1/A$  and  $1/A^3$ , respectively, and that a factor of  $kT/(8\pi\eta)$  has been taken out for convenience.

The analytic formula for the translational diffusion  $\mathbf{D}[p]$  is a function of the axial ratio  $p = b/a$ , where  $a$  is the semiaxis of revolution. Omitting the factor of  $kT/(8\pi\eta)$ , we have

$$\mathbf{D}_t[p] = 4G[p]/3a \quad (13)$$

where

$$G[p] = \text{Log} \left[ \frac{1 + \sqrt{1 - p^2}}{p} \right] / \sqrt{1 - p^2}, \quad \text{for prolate ellipsoids, } p < 1 \quad (14)$$

$$G[p] = \text{ArcTan}[\sqrt{p^2 - 1}] / \sqrt{p^2 - 1}, \quad \text{for oblate ellipsoids, } p > 1 \quad (15)$$

Table 1 shows three computations, including the percent error of the preaveraged approximation (PAV) compared to the analytical formulas. The table demonstrates that the full HI done in BEST is indeed very accurate and that the error in the preaveraged approximation is insignificant. As noted by Douglas and Garbozcsi,<sup>5</sup> for the case of the ellipsoids, the PAV approximation actually yields the exact value. The small discrepancy we observe arises as a small systematic error due to curvature in the extrapolation of the properties to an infinite number of triangles. The full HI computation (BEST) is extremely linear, providing better accuracy. As previously observed in the literature, there is no harm in preaveraging the Oseen tensor for translational diffusion of rigid bodies. In Aragon,<sup>8</sup> it is shown that the full translational

**Table 3.** Viscosity Factors of Ellipsoids of Revolution

$p, 1/p$	prolate and sphere				oblate			
	exact	BEST	PAV	% err	exact	BEST	PAV	% err
1	2.5000	2.4997	2.2611	-9.5				
4	4.6633	4.6626	4.4153	-5.3	4.0593	4.0578	3.7524	-7.5
8	10.103	10.099	9.8616	-2.4	6.7002	6.6985	6.2520	-6.7
30	74.505	74.515	74.751	0.32	21.585	21.564	20.464	-5.1

diffusion tensor is computed in exact agreement with the analytic formulas by BEST.

In Table 2, we show the data similarly arranged for the two eigenvalues of the rotational diffusion tensor. In experiments, the end-over-end rotation (or perpendicular component) is the quantity that is typically observable. The analytic formulas are

$$Drr_{||} = \frac{1}{a^3 p^2} \frac{3(1 - p^2 G[p])}{2(1 - p^2)} \quad (16)$$

$$Drr_{\perp} = \frac{1}{a^3} \frac{3(G[p](2 - p^2) - 1)}{2(1 - p^4)} \quad (17)$$

Table 2 shows once more that the full HI case done in BEST is very accurate and that the error of the preaveraged approximation is quite large, on the order of 30% for either shape in the case of the axial rotation (parallel component), independent of the axial ratio. The error in the perpendicular component is extremely sensitive to the axial ratio. The preaveraged approximation underestimates the tensor by around 30% at small axial ratios and overestimates by a similar amount for an increasing axial ratio. The error is zero for a specific axial ratio dependent on the shape. Preaveraging the Oseen tensor is not appropriate for rotational diffusion. Significant empirical corrections are required in this case, as seen in the work of Zhou.<sup>6</sup>

In Table 3, we show the data for the dimensionless viscosity factor,  $\Sigma$ , of ellipsoids compared to the formula of Simha,<sup>13</sup> assuming negligible orientation of the ellipsoid in the flow field. The intrinsic viscosity is proportional to the viscosity factor, and it can be written in terms of the particle density:  $[\eta] = \Sigma/\rho$ . The Simha formula is

$$\Sigma = \frac{2(1 - p^2)^2}{15p^2} \left( \frac{3(1 - 2p^2 + p^2 G[p])}{(1 + (p^2 - 2)G[p])(3p^2 G[p] - 2p^2 - 1)} + \frac{3p^2 G[p](5p^2 + 8) - 41p^2 + 2}{(G[p](p^2 + 2) - 3)(3p^4 G[p] - 5p^2 + 2)} \right) \quad (18)$$

Note that the formula given by Richards<sup>18</sup> is incorrect.

Table 3 shows that the intrinsic viscosity is again accurately computed with the full tensor, while the preaveraged approximation makes errors of up to 10%, with significant dependence on axial ratio. The preaveraging yields no error for a prolate ellipsoid of axial ratio near 30, but the error will increase again beyond that. The axial ratio for which this happens in the oblate case is larger. Since the intrinsic viscosity is sensitive only to shape and not size, such errors can lead to a misrepresentation of the shape of the object

**Table 4.** Polyhedron Transport Properties

solid	$X_t^a$		$X_r^a$		$\xi$	
	BEST	PAV	BEST	PAV	BEST	PAV
tetrahedron	0.8229	0.8502	0.4778	0.3940	4.210	3.798
cube	0.922	0.937	0.751	0.544	3.10	2.75
octahedron	0.9318	0.9456	0.7726	0.5583	3.016	2.679
dodecahedron	0.9733	0.9791	0.9137	0.6236	2.691	2.397
icosahedron	0.9808	0.9846	0.9356	0.6344	2.636	2.358

<sup>a</sup>  $X_q = D_q/D_q^0$ , where  $D_q^0$  is the diffusion coefficient of a same-volume sphere. "t" represents translation, "r" represents rotation, and  $\xi$  is the viscosity factor.

that could be deduced from these values. In the case of large axial ratios, when the values are used to interpret data on a homologous series with fixed molecular thickness, the shape dependence will yield an overestimate of the molecular length. The errors noted here are comparable to those quoted by Douglas and Garboczi.<sup>5</sup>

**B. Polyhedra.** Polyhedra can be used to study the dependence of the error on account of the presence of sharp corners in a body.<sup>14</sup> Are the errors in the preaveraged translational friction coefficient significant, in particular, for a tetrahedral shape? To test whether the preaveraged approximation has significant errors dependent on shape, we have computed the viscosity factor, the translational, and the rotational friction coefficients for the entire series of Platonic solids. The data are shown in Table 4.

The data show that there is a shape dependent effect for the translational friction,  $X_t$ , but it is small. The largest error does indeed occur for the object that has the sharpest corners, the tetrahedron, but even there it is only 3.3%. The error tends to disappear as the surface tends toward a smooth shape and is less than 1% for the last two members of the series.

The rotational friction coefficient has large errors that range from 21% for the tetrahedron to 47% for the icosahedron. There is significant shape dependence, with the shapes closest to spherical having the largest error, and the size of the errors is comparable to what we find for ellipsoids of revolution. The viscosity factor is uniformly underestimated by 11% with no significant shape dependence.

**C. Proteins.** To evaluate the effect of the preaveraged HI for irregular shapes, we discuss data obtained for a set of three globular proteins, lysozyme, myoglobin, and human serum albumin (input crystal structures obtained from the Brookhaven database). Figure 1 shows a typical triangulation of the hydrated surface of myoglobin. In Table 4 we show the equivalent data discussed above for the ellipsoids. In this case, we report the average of the rotational diffusion tensor to compare against the accurate computations of BEST. In addition, we have used a water hydration thickness of 1.1 Å



**Table 5.** Hydrodynamic Properties of Proteins<sup>a</sup>

protein	$D_t (10^{-7} \text{cm}^2/\text{s})$				$D_r (10^7/\text{s})$				$[\eta] (\text{cm}^3/\text{g})$			
	exp	BEST	PAV	% err	exp	BEST	PAV	% err	exp	BEST	PAV	% err
lysozyme	10.9	11.0	11.1	0.91	2.04	2.09	1.49	-29	3.00	3.22	2.90	-9.9
myoglobin	10.2	10.4	10.3	-0.96	1.46	1.67	1.20	-28	3.25	3.37	2.99	-11
albumin	6.15	6.17	6.23	0.97	0.357	0.349	0.260	-26	3.9	3.92	3.58	-8.7

<sup>a</sup> Lysozyme (2CDS, hen); myoglobin (1MBO, sperm whale); albumin (1AO6, human serum).

**Table 6.** Protein Translation Friction Coefficients ( $10^{-11} \text{kg/s}$ )<sup>a</sup>

protein	PDB	$f_d$	$f_s$	BEST	PAV	$f_k$
ferredoxin	1FCA		2.62	2.66	2.63	2.63
ribonuclease S	2RNS	3.79	3.80	3.67	3.63	3.62
lysozyme	2CDS	3.61	3.71	3.68	3.64	3.59
trypsin	1TPO	4.18	4.36	4.25	4.21	4.18
subtilisin BPN'	1SBT	4.48	4.48	4.48	4.43	4.38
carboxypeptidase A	1M4L		4.91	4.86	4.80	4.68
thermolysin	2TLX		4.57	4.97	4.92	4.77
deoxyhemoglobin	2HHB		6.06	6.05	5.99	5.91

<sup>a</sup>  $f_d$  = experimental friction coefficient by diffusion.  $f_s$  = experimental friction coefficient by sedimentation.  $f_k$  = Kirkwood formula.

as determined in an extensive study of protein transport presented elsewhere.<sup>15,16</sup>

It is clear that the same picture emerges. The preaveraged approximation is quite good for translational diffusion, but it is poor for rotation (28% error) and the intrinsic viscosity (10% error). The BEST computations also agree quite well with experiment.<sup>15,16</sup>

A further comparison with a set of proteins that includes those previously computed by Teller<sup>17</sup> and co-workers (their Table 2) is shown in Table 6. In this case, only the translational friction coefficient is shown in order to compare with their computations.

We see again that for this entire set of proteins, the accurate BEST results and the preaveraged results differ by at most 1%. Preaveraging is quite accurate for irregular shapes. The comparison between BEST and the Kirkwood formula shows errors that range from 1.1% to 4.2%. Teller<sup>17</sup> et al. claimed that the discrepancy in the Kirkwood formula

for translational friction for typical proteins was as large as 7%. However, our accurate computations show that the actual error of the Kirkwood formula is somewhat smaller. Our computations also show that the Kirkwood formula is not equivalent to preaveraging, as is well-known. The BEST values agree with experiment to within experimental error.<sup>15</sup>

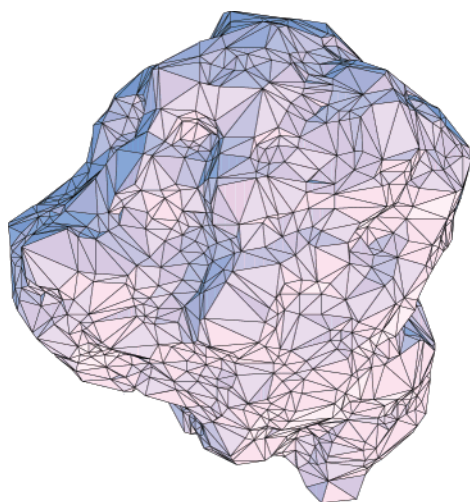
## IV. Conclusions

For the accurate computation of transport properties of rigid bodies, the hydrodynamic interaction should not be preaveraged except for the case of translational diffusion. For translational diffusion, the typical error in the preaveraging approximation is 1%, except for shapes with sharp corners, such as a tetrahedron, where the error rises moderately to about 3%. The errors are quite large for the rotational diffusion tensor, approaching 30%, and significant for the intrinsic viscosity, around 10%. The errors are shape dependent but take their typical magnitudes in the important case of globular proteins.

**Acknowledgment.** This research was supported through a grant from the National Institutes of Health, MBRS SCORE Program – Grant #S06 GM52588 to S.A. Helpful comments from Prof. J. M. Schurr are gratefully acknowledged.

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**Figure 1.** Triangulation of the hydrated surface of myoglobin.

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CT050158F