MODELLING BIOLOGICAL MACROMOLECULES IN SOLUTION: THE GENERAL TRI-AXIAL ELLIPSOID

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Appendix III Illustration of use of the Π function (equation 57) by application to data for hemoglobin

The Π function obtained in section 1.7. can be applied to molecular covolume and viscosity data available for hemoglobin. The molecular covolume, U, is related to the 2nd virial coefficient, B employed in osmometry by $U = 2BM_r^2$. Baghurst et al (1975), using a molecular weight of 64,500 found the value of the product BM_r to be 4.8 ml/gm. Using instead the exact value for the molecular weight found by sequence analysis to be 64,793, this product becomes 4.78 ml/gm; this gives the ratio U/M_r to be 9.56 ml/gm. From the plot of reduced specific viscosity against concentration (Figure 51) an intrinsic viscosity of 2.99 ml/gm has been determined by a least squares fit to the new universal equation for transport coefficients at all solute concentrations (see section 1.7.1. and Appendix IV). The value of Π is calculated to be 3.20, corresponding to a spherical particle (Figure 24). This is consistent with the findings of x-ray crystallography (Perutz et al, 1960). The value of ν for a spherical particle is the Einstein value of 2.5. By back substitution into equation (8) and using a value for M_r of 64,793 one obtains a value for V_e of 1.286×10^{-19} cm^3. This corresponds to a Stokes radius of 31.3 Å, in excellent agreement with the result of 32.3 Å calculated by Alpert & Banks (1976) from the diffusion coefficient determined by laser correlation spectroscopy and agrees exactly with the result of 31.3 Å calculated by Laurent & Killander (1964) from the diffusion coefficient determined by gel filtration, both groups assuming a hard sphere model. The Stokes radius can also be found directly from the molecular covolume and molecular weight assuming a hard sphere model: Baghurst et al (1975)

determined a value of 31.3 Å, again in exact agreement. The corresponding radius of the sphere calculated from the crystallographic dimensions of 64 x 55 x 50 Å of Perutz et al (1960) is 28.0 Å, indicating hemoglobin to be swollen in solution by approximately 40% (v/v).

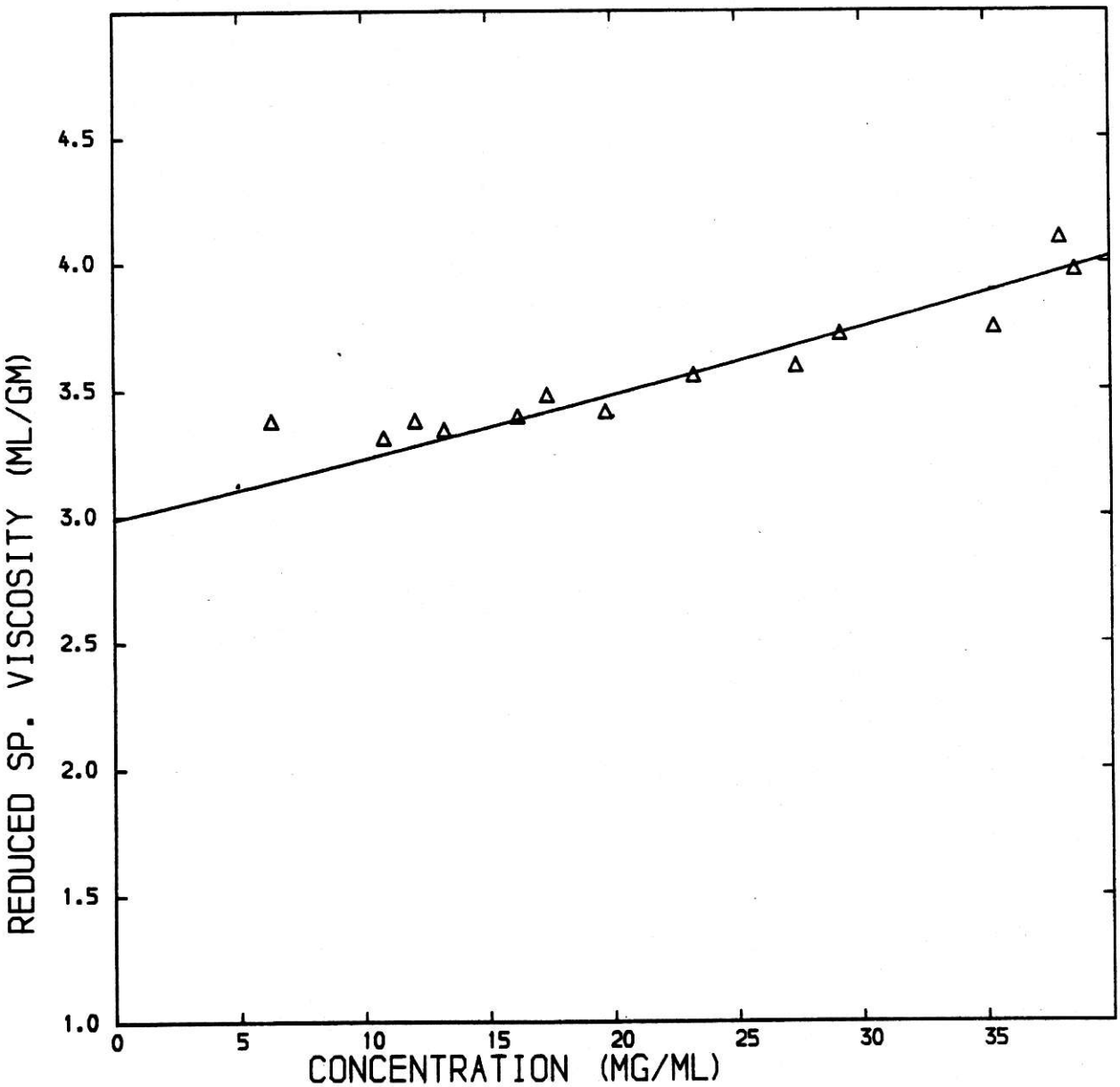
If one uses standard errors of ±.03 (≡ 1%) and ± .096 (≡ 1%) in U/M_r respectively, the calculated standard error (Paradine & Rivett, 1960) in Π is ± .045. The maximum error corresponds to an axial ratio of 1.8 for a prolate model but as high as 6.8 for an oblate model, indicating the difficulty in applying Π to macromolecules that are oblatoid.

Figure 51.

Plot of reduced specific viscosity versus concentration for human oxy - hemoglobin (0.1M KCl, buffer pH = 6.0).

The curve fitted is that due to a weighted least squares fit to the new universal equation for the concentration dependence of transport coefficients (equation 60). The weighting factor used was (1/concentration).

$[\eta] = 2.99$ ml/gm, $k_\eta = 7.8$ ml/gm.


REDUCED SP. VISCOSITY (ML/GM)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0
5
10
15
20
25
30
35
CONCENTRATION (MG/ML)

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