DILUTE SOLUTION PROPERTIES OF GLYCOSAMINOGLYCANS AND PROTEOGLYCANS

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Like most biopolymers, the molecules of interest are linear covalent structures with "backbones" of simple repeating atomic sequences. The "unperturbed" dimensions can therefore be treated in terms of simple conformational models in solution; here "unperturbed" implies the absence of "long-range" intramolecular interactions between segments of the polymer. Such models also provide a good foundation for the study of structure in physiological environments.

The "equivalent-sphere" model of a polymer permits us to demonstrate experimentally that both polymer types of interest are essentially flexible coiling molecules. An important parameter of this model is the radius of gyration R_G, which is experimentally accessible in solution from light scattering data. When "non-perturbing" solvents or, less accurately, appropriate corrections for molecular expansion in "perturbing" solvents are available, unperturbed dimensions can be determined experimentally. The corrections require use of data on intermolecular interactions.

The classical method of calculation of unperturbed dimensions from local atomic structure of the repeating units which constitute the polymer "backbone" has been applied to hyaluronic acid (Cleland, 1971). Qualitatively, the glycosaminoglycans of ß-glycosidic structure are predicted to behave much like other ß-linked polysaccharides, such as cellulose.

The results of the calculation may be expressed in terms of the "worm-like" polymer model as a persistence length, which is a measure of chain "stiffness" representing the distance along the backbone contour over which the chain direction more or less "forgets" its original orientation. For DNA, for example, this distance is several hundred A, while for the glycosaminoglycans, the calculation estimates values between 10 and 100 A, depending on assumptions concerning the form of the interatomic interactions. The more probable values cluster around 50 ± 10 A.

A direct estimate of the persistence length of hyaluronic acid from small-angle x-ray scattering, which requires little or no correction for expansion, led to a value between 40 and 60 A(Cleland, 1977). An independent estimate from data for the limiting viscosity number (Laurent et al, 1960;Cleland and Wang, 1970), after correction for expansion, can be made from the recent theoretical treatment of a persistently curving cylinder (Yamakawa and Fujii, 1974) to provide a value of 40-45 A(Cleland, 1977). The

experimentally derived estimates are therefore in substantial agreement with those from the model. Available viscosity data for the other ß-glycosidic glycosaminoglycans (such as the chondroitin sulfates, CS; and keratan sulfate, KS) suugest that they have similar conformational properties to hyaluronic acid, as does the structurally related polymer, carboxymethyl cellulose.

A proteoglycan monomer has a graft copolymer structure (Mathews and Lozaityte, 1958) in which CS (mol wt ca 20,000) and KS (mol wt 8-10,000) chains are attached covalently to a polypeptide backbone. Proteoglycans from bovine nasal cartilage gave fractions ranging in mol wt from 0.8-2.5 x 10^6, in which the protein mol wt is roughly constant at about 120,000 and the KS mol wt at about 180,000 (ca 20 chains) (Kitchen and Cleland, unpublished). The total CS mol wt thus ranges from 0.5 to 2.2 x 10^6 (25 to 110 chains). The "perturbed" radius R_G in 4M guanidine hydrochloride varies in these fractions from about 350 to 500 A.

An estimate from the conformational calculations of Brant and Flory (1965) of the unperturbed dimensions of a random coiling polypeptide backbone of 1200 amino acids gives approximately R_G = 160 A, while addition of the small CS and KS side chains leads to the slightly higher value, 190 A, for a molecule of mol wt 2.5 x 10^6. The larger values observed experimentally are ascribable to expansion effects, either those associated with "long-range" interactions or those due to local stiffening, such as short-range interactions between backbone segments and side chains. Neither of these effects has yet a suitable theoretical treatment. An attempted extrapolation to eliminate side-chain effects from the data leads to R_G = 220 A for the protein-KS core, consistent with a reasonably expanded unperturbed value.

The conclusion is that glycosaminoglycan and proteoglycan dimensions and properties dependent on them are consistent with those expected from the conformational and equivalent-sphere models.

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