

MODELLING THE CONFORMATION OF MUCUS GLYCOPROTEINS IN SOLUTION

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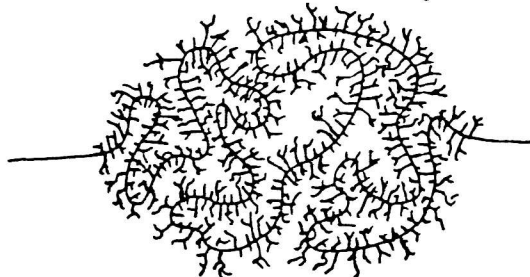
In our earlier communication(1) a greatly expanded spheroidal model for the gross conformation of mucus glycoproteins in solution was described. This model was based on hydrodynamic evidence from a variety of glycoproteins and further hydrodynamic and electron microscopic data from a cystic fibrosis bronchial glycoprotein (CF PHI) and a lower molecular weight ovarian cyst glycoprotein. We now develop this model to see if we can establish some general principles for the assembly of mucus glycoproteins from a fundamental subunit, consistent with the principal biological role of mucus to immobilize water and form a space filling protective layer.

The accepted primary structure of a mucus glycoprotein consists of a polypeptide chain surrounded by serine and threonine linked oligosaccharides of chain length ranging from 3 to 30 units (2). Evidence based on the susceptibility of mucus glycoproteins to pronase attack suggest the presence of unglycosylated free protein regions at the ends of the glycopolypeptide chain (3) and that the central glycosylated region is highly coiled (1) consistent with the high proportion of proline in the peptide moiety. The resulting coiled domain (Fig.1) would have considerable flexibility and an enormous capacity to entrain solvent in which it is suspended. This structure is thought to form the fundamental subunit of MW $\sim 600,000$ from which the higher molecular weight mucins are built: thiol reduction of large molecular weight glycoproteins ('mucins') produces molecules of comparable M. Wt. to the 600,000 'subunit'.

On this model therefore the cystic fibrotic glycoprotein CF PHI of MW $\sim 2.1 \times 10^6$ would be thought to consist largely of 3-4 of such covalently linked subunits. Electron microscopy of unidirectionally metal shadowed material appears to confirm this model: the largest proportion of the molecular forms existed as 'trimers' (plate 1 of ref 1; see esp 1b). Because of the difficulties in determining the MW's. of the 'low profile areas' the association observed could possibly be a non-covalent aggregation, the cross-linking being within the low profile areas .

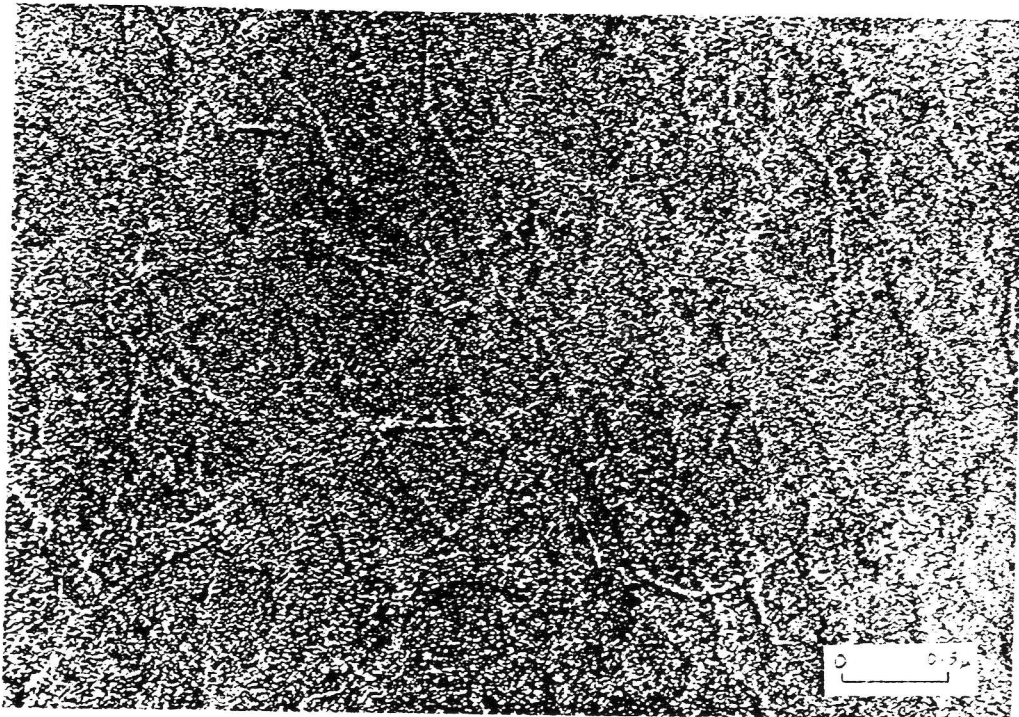
At higher concentrations further images from electron microscopy (Fig.2) on CF PHI reveal extensive molecular overlap: this is to be expected from the high tendency of mucins to gel (4).

Fig. 1. Hypothetical main subunit (after Pigman (2)). The continuous line represents the polypeptide and the attached chains the oligosaccharides. Not to scale.



Our thesis requires further testing by the examination using electron microscopy of a wider variety of mucins, prepared under both reducing and non-reducing conditions. The development of methods which preserve the 3 dimensional order of the normally highly solvated mucins without subjecting them to concentrated glycerol may be of great value (5).

Fig. 2. Electron micrograph of unidirectional platinum shadowed CF PHI after air drying a 0.1 mg/ml solution in distilled water onto freshly cleaved mica.



References

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