

Glyco-Forum section

Letter to the Glyco-Forum

Controversial iduronate ring conformation in dermatan sulphate

V.S.R.Rao, P.V.Balaji and P.K.Qasba¹

Laboratory of Mathematical Biology, National Cancer Institute, National Institutes of Health, Bldg Park 5, Room 410, 12420 Parklawn Drive, MSC 8105, Bethesda, MD 20892-8105, USA

¹To whom correspondence should be addressed

Glycosaminoglycans are linear polymers of alternating acidic (β -D-glucuronic acid or α -L-iduronic acid; just β -D-galactose in keratan sulphate) and basic (2-amino-2-deoxy- β -D-galactosamine or 2-amino-2-deoxy- β -D-glucosamine) monosaccharides. The repeating disaccharide unit is often *N*-acetylated or *N*-sulphated and/or *O*-sulphated (except in hyaluronic acid). Glycosaminoglycans constitute the carbohydrate part of proteoglycans which have been shown to take part in a wide range of biological functions. For example, they are involved in forming the extracellular matrix with collagen to bind to growth factors with a high degree of specificity and regulate the growth factor activity, and are also shown to have anti-coagulant, antilipaemic, antiangiogenic and antitumour activities (Casu, 1985; Casu *et al.*, 1988; Hardingham and Bayliss, 1989; Hardingham and Fosang, 1992). Hence an understanding of the structure and conformation of glycosaminoglycans is of the utmost importance to understand their biological functions.

Although a great deal of information is available about the chemical structure of glycosaminoglycans, the conformation of some of them, particularly dermatan sulphate which consists of alternating *N*-acetyl- β -D-galactosamine (β -D-GalNAc) and α -L-iduronic acid (α -L-IdUA) residues, has been the subject of much debate. While the conformation of β -D-GalNAc is well established (4C_1) (Takai *et al.*, 1972; Virudachalam and Rao, 1976), there are conflicting views about the conformation of α -L-IdUA. Such an uncertainty about the conformation of α -L-IdUA has led to controversy about the chain conformation of dermatan sulphate. Mitra *et al.* (1983) considered a 4C_1 conformation for α -L-IdUA in order to satisfy the repeat distance of the helical chain derived from X-ray diffraction studies. However, Ragazzi *et al.* (1990) found that all the three ring conformations, 4C_1 , 2S_0 and 1C_4 (Figure 1), are compatible with the unit axial rise observed by Mitra *et al.* (1983). Based on the X-ray diffraction and ${}^{13}C$ NMR studies, Winter *et al.* (1986) showed that α -L-IdUA in dermatan sulphate assumes very similar conformations both in solid state and solution with trans-diaxial orientation of hydroxyl groups as in the 1C_4 conformation. Rees *et al.* (1985) suggested that α -L-IdUA assumes predominantly a 1C_4 conformation based on low coupling constant values and circular dichroism studies. They also suggested that a small fraction of the 4C_1 conformation is in equilibrium with the predominant 1C_4 conformation to

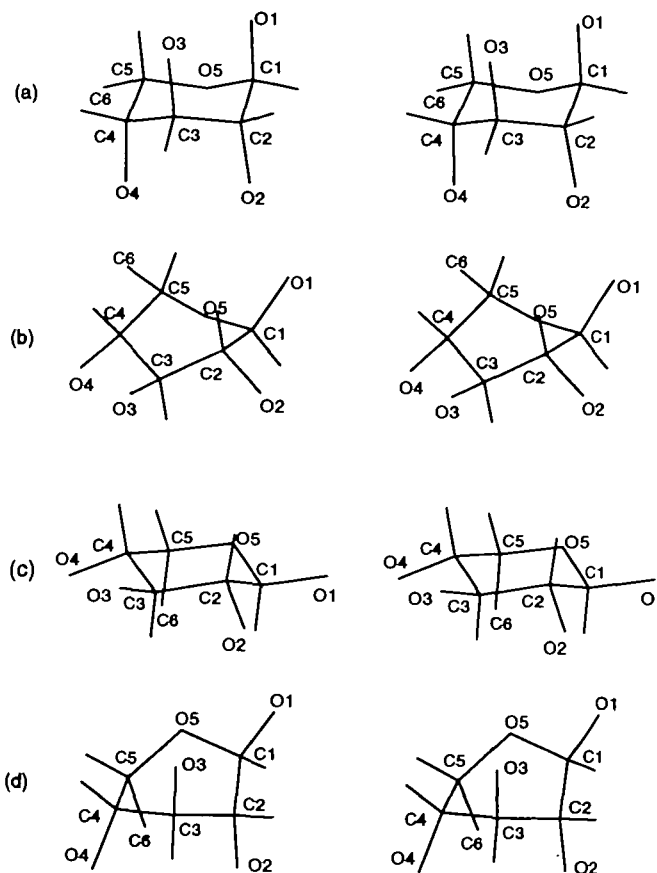


Fig. 1. Stereo diagram showing the possible conformations for the pyranose ring in α -L-iduronate. (a) 1C_4 ; (b) 2S_0 (also referred to as 3S_3); (c) 4C_1 ; (d) 0S_2 (also referred to as 3S_5).

explain the periodate oxidation studies. However, such an equilibrium cannot explain the higher value for ${}^3J_{H_2,H_3}$ compared to ${}^3J_{H_3,H_4}$ (Gatti *et al.*, 1979; Table I). On the other hand, Casu *et al.* (1986) suggested that the 2S_0 skew boat conformation also explains the susceptibility of the α -L-IdUA to periodate oxidation. Recently, Venkataraman *et al.* (1994) reported that the 1C_4 conformation of α -L-IdUA does not provide the required repeat length and suggested yet another conformation, 0S_2 (0T_2) (Figure 1d), as a likely candidate for α -L-IdUA in dermatan sulphate. However, the ${}^3J_{H_2,H_3}$ and ${}^3J_{H_3,H_4}$ values calculated by these authors for α -L-IdUA in either the 4C_1 or 1C_4 conformations are approximately equal, in contrast to the experimental values where ${}^3J_{H_2,H_3}$ is much higher than ${}^3J_{H_3,H_4}$ (Table I). The ${}^3J_{H,H}$ values calculated for 0S_2 conformation are also quite different and have least agreement with the experimental values. Moreover, this conformation is least favoured energetically among the four conformations that have been considered by the earlier workers. Although the calculated ${}^3J_{H,H}$ values of α -L-IdUA in 2S_0 conformation show similar

Table I. Calculated vicinal coupling constants (Hz) for α -L-iduronate

	$J_{H1,H2}$	$J_{H2,H3}$	$J_{H3,H4}$	$J_{H4,H5}$	Reference
4C_1	7.7	10.1	9.9	4.9	Forster & Mulloy, 1993
	7.9	9.9	9.7	4.5	Venkataraman <i>et al.</i> , 1994
1C_4	2.1	2.8	3.0	0.4	Forster & Mulloy, 1993
	3.1	4.5	4.5	0.0	Venkataraman <i>et al.</i> , 1994
2S_0	5.8	9.5	6.1	3.6	Forster & Mulloy, 1993
	5.1	9.4	5.4	4.3	Venkataraman <i>et al.</i> , 1994
0S_2	1.0	4.5	0.9	8.6	Venkataraman <i>et al.</i> , 1994
Distorted ${}^1C_4^a$					
1	2.1	4.6	1.7	1.8	
2	3.2	4.6	2.8	1.8	
3	2.1	4.7	1.9	2.1	
4	2.4	4.2	3.4	0.7	
Dermatan ^b sulphate	3.0	6.0	3.5	3.3	Gatti <i>et al.</i> , 1979

^aCalculated using Haasnoot's equation [equation (8), Haasnoot *et al.* (1980). Electronegativity values were taken from Huggins (1953)].

^bExperimental values.

trends in the variation of ${}^3J_{H,H}$ values, i.e. ${}^3J_{H2,H3} > {}^3J_{H3,H4} \approx {}^3J_{H1,H2} \approx {}^3J_{H4,H5}$, these values are high compared to the experimental values (Table I). Recently, Forster and Mulloy (1993) fitted the NMR data of α -L-IdUA in GlcNAc-IdUA-GlcNAcOMe with relative fractions of chair and twist boat conformations, but it is unlikely that in solution iduronic acid residues exist in chair \leftrightarrow twist boat conformational equilibrium as the 2S_0 conformation has at least 4 kcal/mol higher energy than the 1C_4 conformation (Forster and Mulloy, 1993). In all these studies, equations found in Haasnoot *et al.* (1980) were used to calculate the ${}^3J_{H,H}$ values for various saccharide geometries. These were compared with the experimental ${}^3J_{H,H}$ values to arrive at a pyranose ring conformation without testing the validity of this equation for pyranosides. The calculated ${}^3J_{H,H}$ values reported for α -L-IdUA by different authors for the same conformation also differ significantly (Table I).

Using Haasnoot's equation [equation (8) in Haasnoot *et al.* (1980)], we have calculated the ${}^3J_{H,H}$ values for a number of saccharide derivatives whose NMR data are available and compared these with the experimental values (Figure 2, Table II). Generally, a high value (7–11 Hz) is expected for the coupling constant when the coupling protons are in axial-axial orientations, whereas a low value of 1–5 Hz is expected when they are in axial-equatorial or equatorial-equatorial orientations. Although there is a general agreement between the calculated and experimental coupling constants, the observed values, however, cannot be reproduced in quite a few cases by Haasnoot's equation. However, these differences in $J_{H,H}$ values may not signify substantial differences in the ring conformations since a small change in the geometry (bond angle and bond length) may have large effects on the $J_{H,H}$ values (Karplus, 1963). Thus, Haasnoot's equation does not predict 'accurate values' for the torsion angles and hence the deviations in the pyranose ring geometry. However, this equation is useful for predicting qualitatively the orientational effects of electronegative atom/groups on the J values. For example, for the various galactopyranosides, the calculated ${}^3J_{H4,H5}$ values differ from the experimental values by as much as 2 Hz (Table II) and, for α -D-xylopyranosides, the calculated ${}^3J_{H4a,H5e}$ value (4.37 Hz) is low compared to the experimental value (5.7 Hz). In both these cases, i.e. β -D-galactose (H4,H5) and α -D-xylose (H4,H5e), the coupling protons are in *gauche* orientation,

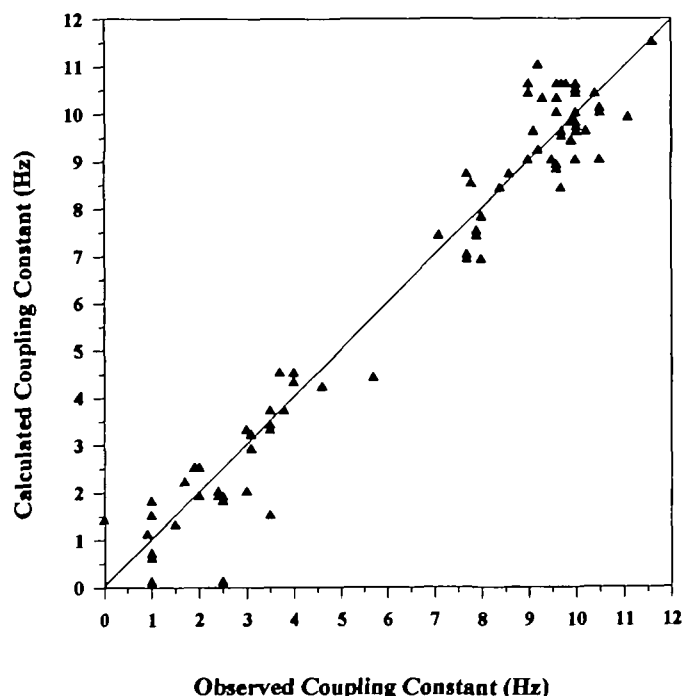


Fig. 2. Plot of observed versus calculated coupling constants. The values and the saccharide names are listed in Table II. Calculation of the coupling constants is described in the legend to Table I. Oligosaccharide structures were built using the Biopolymer module of Biosym's InsightII package, energy minimized using CVFF force field ($\epsilon = 4r$) and conjugate gradient minimization algorithm until the maximum gradient was <0.001 kcal/mol/Å.

but the electronegative atoms (O4, O5) are in *gauche* (β -D-galactose) and *trans* (α -D-xylose) orientations (Figure 2). Such a difference in the orientation of the electronegative atoms with respect to the coupling protons will have opposing effects on the J values: in β -D-galactose, it will have a decreasing effect (trans-coplanar effect) (Abraham and Gatti, 1969) and in α -D-xylose it will have an increasing effect. In the case of α -D-glucose and α -D-mannose, even though the electronegative atoms are similarly oriented with respect to the coupling protons (Figure 2), the J values are different due to the axial 2-OH in mannose which affects the H1-C1-C2-H2 torsion angle (Rao, 1974).

In the case of α -L-IdUA (1C_4), the relative orientations of the coupling protons with respect to the electronegative atoms at C5 \rightarrow C4, C4 \rightarrow C3/C3 \rightarrow C2 and C2 \rightarrow C1 are similar to that in β -D-galactose (C5 \rightarrow C4), α -D-xylose (C5 \rightarrow C4) and α -D-mannose (C2 \rightarrow C1), respectively (Figure 2). In view of this, one expects coupling constants values of ~ 1.7 (${}^3J_{H1,H2}$), 5.5 (${}^3J_{H2,H3}$, ${}^3J_{H3,H4}$) and 0.9–1.6 (${}^3J_{H4,H5}$). Although these expected values differ significantly from the observed values, they are nevertheless closer to these values than to the calculated values for 2S_0 or 0S_2 conformations (Table I). In *in vacuo* molecular dynamics studies, it was found that the disaccharide D-GalNAc1,4 α -L-IdUA occasionally accesses a conformation in which the α -L-IdUA ring deformed slightly from its 1C_4 geometry, resulting in a slight increase in the O3-GalNAc to O1-IdUA distance. In these conformations, the calculated coupling constants not only show the trends where ${}^3J_{H2,H3} > {}^3J_{H3,H4} \approx {}^3J_{H4,H5} \approx {}^3J_{H1,H2}$, but are also close to the experimental values (Table I).

Based on the above, it is suggested that in solution α -L-IdUA in dermatan sulphate exists predominantly in a 'slightly distorted' 1C_4 conformation. However, a small fraction of these residues

Table II. Observed and calculated^c vicinal coupling constants (Hz) for some monosaccharides and their derivatives

# ^a	³ J _{H1,H2}	³ J _{H2,H3}	³ J _{H3,H4}	³ J _{H4,H5}
	Exp/Calc	Exp/Calc	Exp/Calc	Exp/Calc
1	8.0/7.8	10.0/10.0	2.5/1.8	1.0/0.1
2	3.5/3.7	10.5/10.0	2.5/1.8	2.5/0.1
3	1.0/0.7	3.0/2.0	3.5/3.4	1.0/1.5
4	1.0/0.6	2.5/1.9	9.7/9.5	9.0/10.6
5	1.0/0.6	2.0/1.9	10.0/9.7	10.0/10.6
6	2.0/2.5	2.0/1.9	10.0/9.6	10.0/10.6
7	1.0/0.6	2.4/2.0	10.0/9.8	10.0/10.6
8	1.9/2.5	2.4/1.9	10.2/9.6	9.8/10.6
9	7.7/7.0	8.6/8.7	9.1/9.6	9.7/10.6
10	7.7/6.9	7.7/8.7	9.7/9.6	9.7/10.6
11	4.0/4.3	9.6/8.9	9.6/10.3	9.6/10.6
12	3.7/4.5	10.5/9.0	3.5/3.3	1.0/1.5
13	4.0/4.5	10.0/9.0	3.0/3.3	3.5/1.5
14	8.0/6.9	9.6/8.8	3.5/3.3	0.0/1.4
15	3.5/3.3	9.3/10.3	9.2/11.0	11.1/9.9
				5.7/4.4 ^b
16	3.8/3.7	10.0/10.4	9.5/9.0	9.0/10.4
17	1.7/2.2	NA	NA	NA
18	1.0/1.8	NA	NA	NA
19	7.1/7.4	NA	NA	NA
20	7.9/7.5	9.2/9.2	NA	NA
	7.9/7.4	9.9/9.4	NA	<0.9/1.1
	8.4/8.4	NA	3.1/3.2	NA
21	9.7/8.4	10.4/10.4	9.0/9.0	10.0/10.5
	7.8/8.5	9.9/9.8	3.1/2.9	1.5/1.3
	NA	NA	11.6/11.5	10.5/10.0
			4.6/4.2 ^d	

^aSaccharide name: (1) 4-Deoxy-4-fluoro-1,2,3,6-tetra-*O*-acetyl-β-D-galactopyranose. (2) 4-Deoxy-4-fluoro-2,3,6-tri-*O*-acetyl-α-methyl-D-galactopyranoside. (3) 2-Deoxy-2-fluoro-3,4,6-tri-*O*-acetyl-β-D-trifluoromethyl-D-talopyranoside. (4) 2-Deoxy-2-fluoro-3,4,6-tri-*O*-acetyl-β-trifluoromethyl-D-mannopyranoside. (5) 2-Deoxy-2-fluoro-1,4,6-tri-*O*-acetyl-3-*O*-methyl-β-D-mannopyranose. (6) 2-Deoxy-2-fluoro-1,4,6-tri-*O*-acetyl-3-*O*-methyl-α-D-mannopyranose. (7) 2-Deoxy-2-fluoro-1,3,4,6-tetra-*O*-acetyl-β-D-mannopyranose. (8) 2-Deoxy-2-fluoro-1,3,4,6-tetra-*O*-acetyl-α-D-mannopyranose. (9) 2-Deoxy-2-fluoro-3,4,6-tri-*O*-acetyl-β-phenyl-D-glucopyranoside. (10) 2-Deoxy-2-fluoro-4,6-*O*-diacetyl-3-*O*-benzyl-β-methyl-D-glucopyranoside. (11) 2-Deoxy-2-fluoro-1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose. (12) 2-Deoxy-2-fluoro-3,4,6-tri-*O*-acetyl-α-trifluoromethyl-D-galactopyranoside. (13) 2-Deoxy-2-fluoro-1,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose. (14) 2-Deoxy-2-fluoro-1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose. (15) 2,3,4-tri-*O*-acetyl-α-methyl-D-xylopyranoside. (16) α-D-glucose. (17) α-D-mannose. (18) β-D-mannose. (19) β-D-galactose. (20) β-D-GalpNAc-(1,4)-β-D-Galp-(1,4)-D-Glc. (21) α-D-Neup5Ac-(2,3)-β-D-Galp-(1,4)-β-D-GlcNAc-(1,4)-Asn [³J_{H5,H6} in Neup5Ac = 10.5 (expt.)/10.1 (calc.)]. Data for saccharides: #1 to #14 are from Csuk and Glaenger (1988) for #15 from Durette and Horton (1971), for #16 from Koch and Perlin (1970), for #17 to #19 from Lemieux and Stevens (1966), for #20 from Dorland *et al.* (1986) and for #21 from Breg *et al.* (1989).

^b³J_{H4,H5}

^cSee legend to Table I.

^dJ_{H3,H4}

NA, not applicable.

may exist in ⁴C₁ conformation in solution as this conformation has only 1.4 kcal/mol higher energy than the ¹C₄ conformation and this explains the results of periodate oxidation studies as suggested by Rees *et al.* (1985). There is also evidence that in the crystalline state, the ¹C₄ conformation for the α-L-IdUA is consistent with the observed X-ray fibre repeat value (Ragazzi *et al.*, 1990; R.Chandrasekharan, personal communication). The recent proposal that α-L-IdUA is in a ⁰S₂ conformation (Venkataraman *et al.*, 1994) is less likely as it satisfies neither the NMR data nor energy criteria. It should be recalled that this skew conformation was proposed

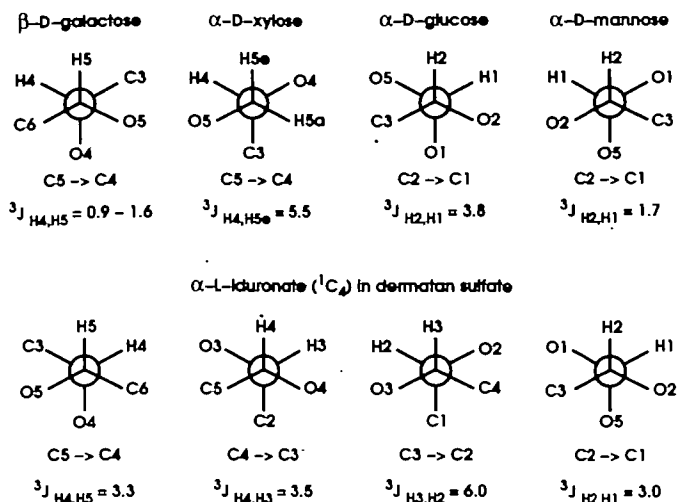


Fig. 3. Newman projections along C-C bonds in some of the monosaccharides. The name of the saccharide, bond along which projections are drawn and the coupling constant values are also shown. Coupling constants were taken from Breg *et al.* (1989), Dorland *et al.* (1986) and Vliegthart *et al.* (1983) (for β-D-galactose), Durette and Horton (1971) (for α-D-xylose; data obtained for the tetra-acetate derivative), Koch and Perlin (1970) (for α-D-glucose), Lemieux and Stevens (1966) (for α-D-mannose) and Gatti *et al.* (1979) (for α-L-iduronate).

based on the assumption that the ¹C₄ conformation cannot satisfy the fibre repeat value reported by the X-ray diffraction studies.

Acknowledgements

The authors thank Prof. R.Chandrasekaran, Purdue University, for providing the n and h values for dermatan sulphate.

References

- Abraham, R.J. and Gatti, G. (1969) Rotational isomerism. Part VII. Effect of substituents on vicinal coupling constants in XCH₂CH₂Y fragments. *J. Chem. Soc. B*, 961-968.
- Breg, J., Kroon-Batenburg, L.M.J., Strecker, G., Montreuil, J. and Vliegthart, J.F.G. (1989) Conformational analysis of the sialyl α(2→3/6) N-acetylglucosamine structural element occurring in glycoproteins by 2-dimensional NOE ¹H-NMR spectroscopy in combination with energy calculations by hard-sphere exo-anomeric and molecular mechanics force-field with hydrogen-bonding potential. *Eur. J. Biochem.*, **178**, 727-739.
- Casu, B. (1985) Structure and biological function of heparin. *Adv. Carbohydr. Chem. Biochem.*, **43**, 51-134.
- Casu, B., Choay, J., Ferro, D.R., Gatti, G., Jacquinet, J.C., Petitou, M., Provasoli, A., Ragazzi, M., Sinay, P. and Torri, G. (1986) Controversial glycosaminoglycan conformations. *Nature*, **332**, 215-216.
- Casu, B., Petitou, M., Provasoli, M. and Sinay, P. (1988) Conformational flexibility: A new concept for explaining binding and biological properties of iduronic acid-containing glycosaminoglycans. *Trends Biochem. Sci.*, **13**, 221-225.
- Csuk, R. and Glaenger, B.I. (1988) N.M.R. spectroscopy of fluorinated monosaccharides. *Adv. Carbohydr. Chem. Biochem.*, **46**, 73-195.
- Dorland, L., van Halbeek, H., Vliegthart, J.F.G., Schauer, R. and Wiegandt, H. (1986) A 500-MHz ¹H-NMR study of oligosaccharides derived from gangliosides by ozonolysis-alkaline fragmentation. *Carbohydr. Res.*, **151**, 233-245.
- Durette, P.L. and Horton, D. (1971) Conformational studies on pyranoid sugar derivatives by N.M.R. spectroscopy. Correlation of observed proton-proton coupling constants with the generalised Karplus equation. *Org. Magn. Res.*, **3**, 417-427.

- Forster, M.J. and Mulloy, B. (1993) Molecular dynamics study of iduronate ring conformation. *Biopolymers*, **33**, 575–588.
- Gatti, G., Casu, B., Torri, G. and Vercellotti, J.R. (1979) Resolution-enhanced ¹H-n.m.r. spectra of dermatan sulphate and chondroitin sulphates: conformation of the uronic acid residues. *Carbohydr. Res.*, **68**, C3–C7.
- Haasnoot, C.A.G., De Leeuw, F.A.A.M. and Altona, C. (1980) The relationship between proton–proton NMR coupling constants and substituent electro-negativities I. *Tetrahedron*, **36**, 2783–2792.
- Hardingham, T.E. and Bayliss, M.T. (1990) Proteoglycans of articular cartilage changes in aging and in joint disease. *Semin. Arth. Rheum.*, **Suppl. 1**, 12–33.
- Hardingham, T.E. and Fosang, A.J. (1992) Proteoglycans: Many forms and many functions. *FASEB J.*, **6**, 861–870.
- Huggins, M.L. (1953) Bond energies and polarities. *J. Am. Chem. Soc.*, **75**, 4123–4126.
- Karplus, M. (1963) Vicinal proton coupling in nuclear magnetic resonance. *J. Am. Chem. Soc.*, **85**, 2870–2871.
- Koch, H.J. and Perlin, A.S. (1970) Synthesis and ¹³C-NMR spectrum of D-glucose-3d. Bond polarisation differences between the anomers of D-glucose. *Carbohydr. Res.*, **15**, 403–410.
- Lemieux, R.U. and Stevens, J.D. (1966) The magnetic resonance spectra and tautomeric equilibria of aldoses in deuterium oxide. *Can. J. Chem.*, **44**, 249–262.
- Mitra, A.K., Arnott, S., Atkins, E.D.T. and Isaac, D.H. (1983) Hyaluronic acid: molecular conformation and interactions in the tetragonal form of the potassium salt containing extended chains. *J. Mol. Biol.*, **169**, 873–901.
- Ragazzi, M., Provasoli, A. and Ferro, D.R. (1990) Molecular mechanics and the structure of iduronate containing carbohydrates. In French, A.D. and Brady, J.W. (eds), *Computer Modelling of Carbohydrate Molecules*. American Chemical Society, Washington DC, Vol. 430, pp. 332–344.
- Rao, V.S.R. (1974) Conformation of pyranose ring in mono-, di-, and polysaccharides by nuclear magnetic resonance. *J. Ind. Inst. Sci.*, **56**, 253–281.
- Rees, D.A., Morris, E.R., Stoddart, J.F. and Stevens, E.S. (1985) Controversial glycosaminoglycan conformations. *Nature*, **317**, 480.
- Takai, M., Watanabe, S., Ashida, T. and Kakudo, M. (1972) β-D-galactosamine hydrochloride. *Acta Crystallogr.*, **B28**, 2370.
- Venkataraman, G., Sasisekharan, V., Cooney, C.L., Langer, R. and Sasisekharan, R. (1994) A stereochemical approach to pyranose ring flexibility: Its implications for the conformation of dermatan sulphate. *Proc. Natl Acad. Sci. USA*, **91**, 6171–6175.
- Virudachalam, R. and Rao, V.S.R. (1976) Theoretical investigation on 2-acetamido-2-deoxy aldohexopyranoses conformation and anomeric effect. *Carbohydr. Res.*, **51**, 135.
- Vliegenthart, J.F.G., Dorland, L. and van Halbeek, H. (1983) High-resolution, ¹H-nuclear magnetic resonance spectroscopy as a tool in the structural analysis of carbohydrates related to glycoproteins. *Adv. Carbohydr. Chem. Biochem.*, **41**, 209–374.
- Winter, W.T., Taylor, E.S., Stevens, E.S., Morris, E.R. and Rees, D.A. (1986) Solid-state ¹³C NMR and X-ray diffraction of dermatan sulfate. *Biochem. Biophys. Res. Commun.*, **137**, 87–93.

Meeting Announcements

Eurocarb VIII

Seville
July 2–7, 1995

Information:
Prof. Manuel Gomez-Guillen
Departamento de Quimica Organica,
Facultad de Correos 553,
41071 Sevilla,
Spain
Fax: +34 54 624952

Biochemical Society Glycobiology Group Colloquia

Manchester
July 18–19, 1995

Two day meeting on 'Mucins'; information from

Dr J. Sheehan,
Department of Biochemistry,
University of Manchester.

Dublin (University College)
September 13, 1995

One day meeting on 'Carbohydrate Recognition Proteins'; information from

Dr M. Taylor,
Glycobiology Institute,
Department of Biochemistry,
University of Oxford.

36th International Conference on the Biochemistry of Lipids (ICBL)

Washington, DC
August 9–11, 1995

The 36th International Conference on the Biochemistry of Lipids (ICBL) will be held in Washington, DC on August 9–11, 1995, on the campus of Georgetown University. The theme of the conference is 'Lipids as modulators of molecular events'. The Conference Lecture will be given by Michael S. Brown. The sessions are (i) Lipid-Protein Interaction, (ii) Glycosphingolipids and Cell Signalling, and (iii) Newer Approaches in the Treatment of Cardiovascular and Glycolipid Disorders.

Presentations include:

Prenylation, lipid-protein interaction

John Glomset

Protein farnesylation and biological activity

Jay Gibbs

Myristoylation of proteins and biological activity

Alan Aderem

The essential role of phosphoinositides in membrane and protein trafficking

Scott Emr

ICBL Distinguished Scientist Lecture

Lipids as modulators of molecular events

Michael S. Brown

Role of sphingoglycolipids in signal transduction

Subroto Chatterjee

Sphingolipid derived products: role in signal transduction and cell regulation

Yusuf Hannun

Gangliosides and sphingolipids as modulators of transmembrane signalling

Sen-Itiroh Hakomori

Regulation of oncogenes by glycosphingolipids

Yoshita Nagai

Biosynthesis of Le X in colon cancer

Subash Basu

CHD: Lessons from alcohol research

Bill Lands

Gene therapy for hyperlipoproteinemia, FH

Jayanta Chowdhury

Mechanism based toxicity of zaragozic acids—potent inhibitors of squalene synthase

James Bergstrom

Non-instrumental measurements of serum lipids

P.Singh/K.Strahs

Enzyme replacement and genetic therapy for lipid storage disorders

Roscoe Brady

Role of glycolipids and carbohydrates in cell adhesion: therapeutic approaches for anti-inflammatory drugs

B.Rao

Cerezyme: a recombinant glucocerebrosidase for Gaucher's Disease

Francis S.Furbish

For information contact:

Ms Hattie Johnson, Georgetown University, Office of Continuing Professional Education, 2233 Wisconsin Avenue, NW, Suite #333, Washington, DC 20007-2197, USA

Telephone: (202) 687-8735, Toll-free: (800) 382-3613.

Fax: (202) 687-3019.

XIIIth International Symposium on Glycoconjugates

Seattle, Washington, USA

August 20–26, 1995

The poster session is of central importance. All posters will be on display during the entire symposium period, and it is hoped special poster discussion times will be set aside in the evenings. Based on past experiences, 'hot new findings' will often be found in the posters rather than the plenary lectures or symposium talks.

A total of 32 minisymposia (topic sessions) have been defined. Each session will be organized and chaired by two leading scientists in the specific field; names of most of the organizers are shown below. The deadline for submission of abstracts will be March 1, 1995. The final programme, abstract submission form, and registration form will be included with the third circular, which will be mailed in January 1995. Chairpersons of each topic session will select minisymposium speakers from the submitted abstracts. All abstracts will be published in a special issue of the *Glycoconjugate Journal*.

GLYCO XIII will focus on functional roles of glycoconjugates, in addition to advances in biosynthesis, degradation, and the molecular–genetic basis of these processes. Glycobiology of plants, yeasts, moulds, and bacteria will be covered in view of the remarkable progress in this area. In glycopathology sessions, in addition to covering the functional role of glycosylation in cancer progression, inflammatory, and infectious processes, we will focus on aberrant glycosylation correlated with autoimmune disorders, parasitosis, AIDS progression, and other diseases. Because of the rapid expansion of glycobiology and glycopathology, and the diversity of new research trends, GLYCO XIII will include a greater number of topic sessions (~32) than ever before.

Mini-symposium sessions

Conformational structures of glycoconjugates
 Glycosylation affecting protein structure and function
 Glycomimetics that modify glycosylation
 Carbohydrate–protein interactions
 Dolichol-linked pathways
 Plant glycobiology
 Golgi enzyme targeting
 New methods of glycoconjugate analysis
 Carbohydrate-dependent cell adhesion I and II
 Plant and animal lectins
 Biology of proteoglycans
 Glycosaminoglycan synthesis and molecular–genetic basis
 Glycobiology of yeasts, moulds and bacteria
 Glycosylation regulation through glycosyltransferase genes
 Synthesis and molecular–genetic basis of developmentally regulated carbohydrate epitopes
 Functional role of O-linked glycans with mucin-type domains
 Molecular–genetic basis of sphingolipidosis and other neuronal diseases
 Sialic acid, sialidase, and polysialic acid
 Synthesis and degradation of glycosphingolipids
 Glycobiology of immunocytes and immune responses
 Molecular genetics of histo-blood groups and diseases
 Transmembrane signalling control by glycosphingolipids and sphingolipids I, II
 Organization and trafficking of glycosphingolipids in membranes
 Glycosphingolipid interactions and receptor function
 Gangliosides in neurobiology
 Role of glycoconjugates in bacterial and viral infections
 Glycopathology of parasites
 Glycosylation and cancer
 Aberrant glycosylation causing or closely associated with disease processes (autoimmune, AIDS, etc.)

Session chairs and organizers

M.Aebi	S.C.Basu
R.R.Brentani	D.R.Bundle
S.Chatterjee	E.A.Davidson
J.W.Dennis	R.A.Dwek
A.D.Elbein	M.E.Etzler
T.Feizi	M.Fukuda
C.G.Gahmberg	M.C.Glick
I.J.Goldstein	S.Handa
V.Hascall	C.G.Hellerqvist
R.L.Hill	O.Hindsgaul
C.Hirschberg	R.C.Hughes
A.Kobata	R.N.Kolesnick
S.Kornfeld	J.Kośczielak

R.A.Laine	R.Ledeen
Y.C.Lee	U.Lindahl
B.Lindberg	C.Lingwood
J.B.Lowe	D.M.Marcus
J.S.O'Brien	T.Ogawa
T.Osawa	J.C.Paulson
H.Rahmann	P.W.Robbins
H.Schachter	R.Schauer
R.L.Schnaar	N.Sharon
S.Spiegel	A.Surolia
S.Suzuki	Y.Suzuki
F.A.Troy	N.Taniguchi
B.Tuomanen	A.Varki
J.F.G.Vliegthart	W.M.Watkins
T.Yamagata	W.W.Young
R.K.Yu	

Plenary lectures to date

J.Baenziger, Glycosylation affecting protein structure function; K.Bock, Glycopeptides as oligosaccharide scaffolds and mimetics; K.Drickamer, Carbohydrate-protein interaction; R.Gilmore, Dolichol-linked pathways; P.Albersheim, Carbohydrates as plant cell elicitors; G.Warren, Mechanism of Golgi enzyme targeting; M.M.Burger, Sponge cell recognition based on specific glycan-to-glycan interaction; M.Bernfield, Syndecan and related cell-surface proteoglycans; N.L.Shaper, Transcriptional control of glycosyltransferase gene expression; J.Marsh, Transgenic approach for testing glycosylation function; G.W.Hart, O-linked GlcNAc controlling nuclear and cytoplasmic function; P.R.Crocker, Sialoadhesin and its gene expression; Y.Inoue, KDN glycans: Their occurrence, structure, biosynthesis, and possible function; K.Sandhoff, Synthesis and degradation of glycosphingolipids and function of metabolites; G.Tettamanti, Metabolic fate and functional implications of exogenous glycosphingolipids; F.Wieland, Organization and trafficking of glycosphingolipids in membranes; K.-A.Karlsson, Cell surface glycoconjugates as attachment sites in the adhesion of microbes to animal tissues; T.Kinoshita, Genetic defect in PI-glycan synthesis causes paroxysmal nocturnal haemoglobinuria; V.Nussenzweig, Liver proteoglycan homing receptors for malaria parasites; R.A.Reisfeld, Anti-cancer therapy based on tumour-associated ganglioside antigens; N.Radin, Effects of ceramide analogues on sphingoglycolipid metabolism and cell growth; Y.Nagai, Ganglioside as a signalling molecule in neural function; A.M.Lefter, Selectins, oligosaccharides and sphingolipid derivatives in reperfusion injury.

Organizing committee

S.Hakomori, Chairman
B.Bendiak
K.Handa
E.Holmes
Y.Igarashi
S.Leverly
E.Nudelman
A.Singhal
M.Stroud
T.Toyokuni
T.White
S.Iron, Secretary

For further information, please contact:

Convention Services Northwest
1809 7th Avenue, Suite 1414
Seattle, WA 98101, USA
Telephone: (206) 292-9198; Fax: (206) 292-0559

Cellucon—International Cellulose Conference

Stresa—Lake Maggiore
September 10–16, 1995

Information:

Dr B.Focher
Stazione Sperim. Carta Cellulosa,
Piazza Leonardo da Vinci,
20133 Milan,
Italy
Fax: +39 2 2365039

Carbohydrate-Mediated Cell-Cell Interactions in Inflammation and Metastasis

Paris

October 8–12, 1995

Application deadline: 28 April.

Information:

INSERM
Conferences Philippe Laudat
101, rue de Tolbiac,
75654 Paris Cedex 13,
France
Tel.: +33 (1) 44.23.60.89/87
Fax: +33 (1) 44.23.60.89
E-mail: laudat@tolbiac.inserm.fr

Third International Glycobiology Symposium: Current Analytical Methods

San Diego, California, USA

November 29, 1995–December 2, 1995

Scientific Organizing Committee

Chair: R.Reid Townsend, University of California, San Francisco, USA

Members: Jacques Baenziger, Washington University, St Louis, USA; Steven A.Carr, SmithKline Pharmaceuticals, King of Prussia, USA; Harald Conradt, Gesellschaft für Biotechnologische Forschung, mbH, FRG; William Hancock, Hewlett Packard Corporation, Palo Alto, USA; Vincent Hascall, Cleveland Clinic Foundation, Cleveland, USA; Arland Hotchkiss, Jr, US Department of Agriculture, Philadelphia, USA; Adrianna Manzi, University of California, San Diego, USA; Milos Novotny, Indiana University, Bloomington, USA; Stanley Prusiner, University of California, San Francisco, USA; Harry Schachter, University of Toronto, Toronto, Canada; Sandro Sonnino, University of Milan, Milan, Italy; Michael Spellman, Genentech, South San Francisco, USA; Robert Trimble, Department of Health, Albany, New York,

USA; Herman van Halbeek, University of Georgia, Athens, USA; André Verbert, Université des Sciences et Technologies de Lille, France.

For further information contact:
Conference Manager, Paddy Batchelder
Tel: 510-426-9601;
Fax: 510-484-3024.

Satellite Meeting of the XVIII ICS 'Conformational Studies of Carbohydrates'

Garda Lake
July 16–19, 1996

Information:
Dr Massimo Ragazzi
Istituto Chimica Macromolecole CNR,
via E. Bassini 15C,
20133 Milan,
Italy

XVIII International Carbohydrate Symposium

Milan, Italy
July 21–26, 1996

Information: Dr Annamaria Naggi, Executive Secretary, XVIII International Carbohydrate Symposium, Istituto di Chimica e Biochimica 'G. Ronzoni', via G. Colombo 81, 20133 Milan, Italy.
Fax: 39 (2) 70633007.

Erratum

Regulation of N-linked glycosylation. Neuronal cell-specific expression of a 5' extended transcript from the gene encoding N-acetylglucosaminyltransferase I

by Jing Yang, Mantu Bhaumik, Yun Liu and
Pamela Stanley

Glycobiology, 4, 703–712, 1994.

During the reproduction process, several of the major bands in Figure 2 of the paper became difficult to discern. An earlier photograph of the same blot is presented below.

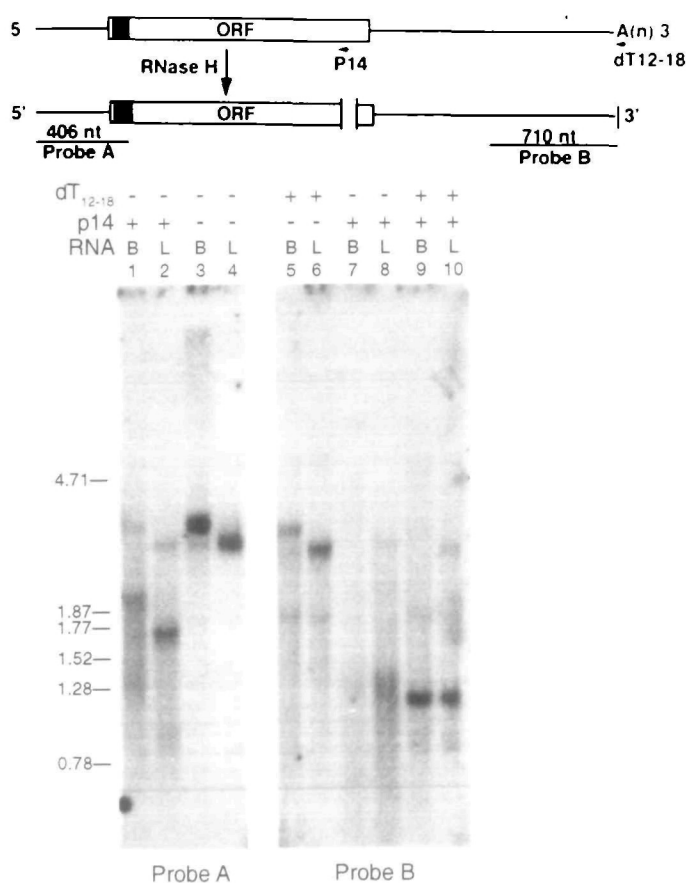


Fig. 2. Molecular basis of the difference between the ~2.9kb and ~3.3kb *Mgat-1* RNAs. Total RNAs (~15µg) from mouse brain (B) and liver (L) were hybridized to P14 and/or to dT₁₂₋₁₈. Following digestion with RNase H, the samples were electrophoresed in a 1.2% glyoxal-agarose gel, transferred and hybridized to probe A or probe B at 65°C overnight. The blots were finally washed in 2 × SSPE and 0.4% SDS at 65°C for 30 min.