At low pressure, the calculated sound velocity profiles match the experiment exceptionally well, and at high pressures, the results are close to the extrapolated experimental curves, despite the dramatic changes in the material that begin at 100 GPa (*7*). The agreement reinforces the conclusions of the diamond-cell (*3*) and shock-wave studies (*1*). Small differences between the latter two at the highest pressures arise from the uncertainty in fitting intermolecular interaction potentials to the experimental data. Indeed, the degree of molecular dissociation obtained from the analysis of the shock-wave data depends strongly on the form of the potentials. It must be admitted that the new calculations are also not without attendant approximations; in particular, the zero-point (quantum) motion of the protons is neglected, the electronic part is carried out within the local density approximation, and adiabatic corrections are approximate. In addition, all calculations were performed at 1000 K, whereas the temperature in Jupiter rises steeply with depth (reaching ~10,000 K at 300 GPa). Nevertheless, the emerging consensus—from diamond-cell experiments, shock-wave compression, and now theory—is highly encouraging, but signifying what?

One of the conclusions of all three studies is the need to revise either the interpretation of purported observations of the jovian free oscillations or existing interior models for the planet. The models predict a significantly larger characteristic free-oscillation frequency than indicated by the observations (*3*). One way to force agreement is to dissolve significantly more He (or other elements heavier than H) into the jovian mantle, but the amounts required would likely make the planet too dense. Recently, Lederer *et al.* (*11*) reported that at least some of the observations could be albedo features (relative variations in brightness of the planet's surface) rather than global oscillations: a portion of the frequency spectrum seems to be contaminated by variations in Jupiter's complex and highly turbulent atmosphere, which is coupled to the rapid rotation rate of the planet.

The implications of this new insight on dense hydrogen run deeper than this. Perhaps most compelling is that abrupt dissociation of hydrogen and the presence of distinct molecular and atomic (plasma) layers within the planet is probably overly simplistic. There is likely to be a transition zone between the two regions (perhaps loosely analogous to that in the mantle of the Earth) in which the molecular-atomic transition takes place, perhaps with no discrete boundary in Jupiter. At 150 to 400 GPa, the theoretical calculations predict evanescent stringlike structures that rapidly exchange protons and electrons at high temperatures (*2, 8*). In the language of chemical physics, this is a regime of intense reactive scattering. Moreover, electron transfer and dissociation at lower pressures imply that a portion of the planet's magnetic field may be generated at much shallower depths than previously thought. Nellis *et al.* (*1*) suggest that this also produces an unusual temperature profile at intermediate depths, which in turn controls the style of convection. Interestingly, an intermediate transition zone has also been proposed from analysis of observational data for the planet (*4*). How these changes in hydrogen are related to the complex phase diagram documented experimentally at lower temperatures is not yet fully established, but the calculated high-temperature charge-transfer processes likely parallel the charge-transfer states identified spectroscopically for the solid (*7*). With continued efforts to characterize dense hydrogen and hydrogen-helium (and more complex) mixtures, a chemical understanding of the interiors of the gas giants may emerge to complement that which is now developing for their atmospheres.

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Glycobiology: More Functions for Oligosaccharides

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Glycosylation is a major feature of the extracellular portion of CD2, a leukocyte antigen on T cells that mediates cellular adhesion. CD2 consists of two immunoglobulin G (IgG) superfamily domains, a V set (amino terminal) and a C2 set. The protein has three glycosylation sites—one in the adhesion domain that is characterized by the glycoforms [-$(GlcNAc)_2$-$(Man)_{5-8}$]. The nuclear magnetic resonance (NMR) solution structure of this adhesion domain, described on page 1273 of this issue (*1*), is the first example in which both the polypeptide and the attached oligosaccharide are defined.

The solution structure reveals that the core monosaccharides GlcNAc2 interact with the polypeptide, and as a result much of the remainder of the oligosaccharide is conformationally restricted. On the basis of the new structure and site-directed mutagenesis studies, the authors conclude that the glycan stabilizes an exposed cluster of five positive charges from surface lysines (Lys^{69}, Lys^{71}, Lys^{64}, and Lys^{55}, with Lys^{61} at the center), mainly through hydrogen bonds and van der Waals contacts (Fig. 1A). Elimination of the N-linked glycan leads to partial or complete unfolding and loss of counterreceptor (CD58) binding. The authors suggest that glycosylated Ig domains such as CD2 are not rigid protein scaffolds but have conformations that result from an interplay of dynamic interactions between the polypeptide and attached glycan. Interestingly, if the central Lys^{61} is replaced by glutamic acid (as in rat CD2), the negative charge allows the formation of a salt bridge with Lys^{69}, and rat CD2 is stable even without an attached oligosaccharide.

The concept that an oligosaccharide might have a structural role by susbstituting for one or more amino acids has been noted in the closely related structures of the variable domain of trypanosome variant surface glycoproteins (*2*). An α helix in one structure is replaced in another by the first three monosaccharides of an oligosaccharide, which bury the same core amino acids as the α helix.

The elegant biosynthetic glycan-processing pathway in the cell allows, in principle, the same oligosaccharide to be attached to quite different proteins without having to code the information into the DNA of the individual proteins. However, the orientation of the attached oligosac-

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charide with respect to the polypeptide may markedly affect the properties of the glycoproteins. For instance, in glycosylated bovine pancreatic ribonuclease (RNase) B, which contains a set of glycoforms [-$(GlcNAc)_2$-$(Man)_{5-9}$] similar to that of CD2, NMR studies have shown that there are no extensive interactions between the oligosaccharide and the protein, and that the dynamic motions of the oligosaccharide are independent of the protein. When the flexibility of the asparagine side chain is also taken into account, a large portion of the protein surface is "shielded" by the oligosaccharide (*3*) (Fig. 1B). This is probably why glycosylated RNase B is less active than the unglycosylated form in its interaction with double-stranded RNA (*4*). This comparison emphasizes one of the most important factors in understanding the roles of oligosaccharides attached to glycoproteins, that is, the same oligosaccharide on different proteins may have quite different properties, depending on the orientation with respect to its polypeptide.

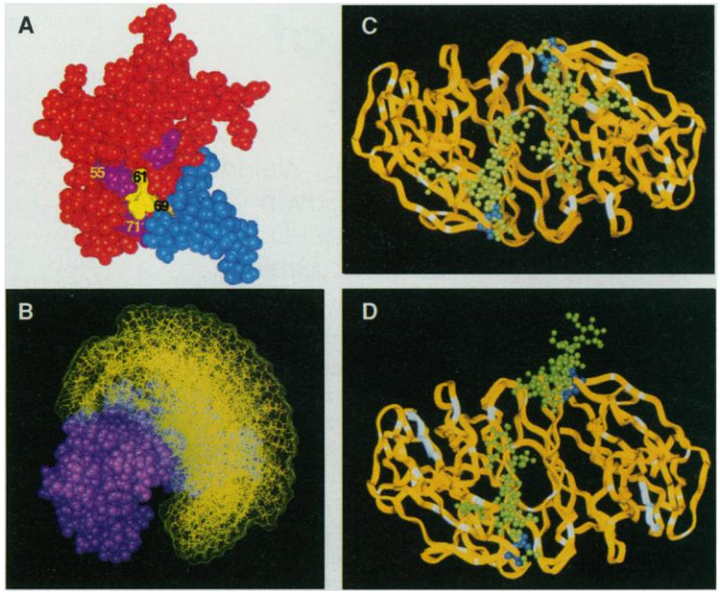

Fig. 1. (**A**) CD2. *N*-Glycan, blue; polypeptide, red; Lys^{61}, yellow; Lys^{69}, orange; Lys^{55} and Lys^{71}, purple (*1*). (**B**) Ribonuclease model showing dynamics of oligosaccharides (yellow) (*3*). (**C** and **D**) Immunoglobulin G Fc model (*5*, *7*). Oligosaccharides, green; Asn^{297} side chain, blue.

In the adhesion domain of CD2, the associated oligosaccharide set clearly has a structural role, and the close interaction with the protein probably means that it is not available for recognition by lectins. By contrast, the same oligosaccharides in orientations such as that on RNase B would be accessible to lectins, a property also affected by the number of copies of the oligosaccharides and their precise geometry of presentation.

Of course, different glycoforms of a protein may display quite different orientations of the oligosaccharides with respect to the protein, thus conferring different properties. A striking example is the structure of the Fc fragment of IgG. The conserved N-linked complex oligosaccharides at Asn^{297} on each heavy chain of the C_H2 domain occupy the interstitial space between the domains (Fig. 1C). Their presence stabilizes the hinge conformation of the Fc. The α(1–6) antenna of each oligosaccharide interacts with hydrophobic and polar residues on the domain surface. This interaction is particularly marked for the terminal galactose monosaccharide. There are also potential interactions with the domain surface and the terminal galactose on the α(1–3) antenna. The dynamic properties of the oligosaccharide are similar to those of the peptide, as is the case of CD2. However, loss of the two terminal galactoses, as in the Fc fragment from patients with rheumatoid arthritis, results in a loss of interaction between the domain surface and the oligosaccharide. This permits displacement and consequent exposure of the oligosaccharides, giving them the potential to be recognized by endogenous lectins (*5*) (Fig. 1D).

Protein glycosylation is influenced by three main factors (*6*): the overall protein conformation, the effect of local conformation, and the available repertoire of glycosylation-processing enzymes for the particular cell type. In general, the pattern of glycoforms is protein-specific, site-specific, and tissue- or cell-specific. The new results (*1*, *6*) demonstrate that the glycosylation of the full-length CD2 molecule (both domains) expressed in CHO cells shows site-specific glycosylation patterns. Is this also true for the natural glycoform set of CD2 from T cells? The technology is certainly available to sequence picomolar amounts. It may be that the interaction between the protein and the core of the oligosaccharide orients the oligomannose chain such that the accessibility of processing enzymes is restricted and that the site specificity is that of the oligomannose glycoforms.

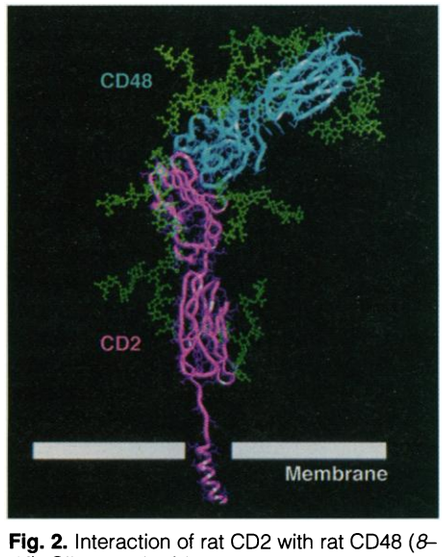

Fig. 2. Interaction of rat CD2 with rat CD48 (*8–10*). Oligosaccharides, green.

Many leukocyte antigens are heavily glycosylated. For instance, N-linked oligosaccharides contribute up to 50 percent of the mass of CD45, whereas O-linked sugars contribute up to 70 percent in mucin-like proteins such as CD43. The importance of defining glycosylation for a complete understanding of function is clearly apparent from a molecular model of the interaction of rat CD2 with its counterreceptor CD48, (Fig. 2), which highlights the dominant position of the oligosaccharides on the protein surfaces (one would expect this to be very similar for the human CD2-CD58 complex).

That one set of structures on different proteins can result in quite dramatic variations in properties of glycoproteins or that different glycoforms may have different properties emphasizes that there is no single unifying function for oligosaccharides. Clearly, a major function is to serve as recognition markers. However, they can also alter the intrinsic properties of proteins to which they are attached by altering the stability, protease resistance, or quaternary structure. Further, the large size of oligosaccharides may allow them to cover functionally important areas of proteins and to modulate the interactions of glycoproteins with other molecules. Finally, glycosylation is also highly sensitive to alterations in cellular function, and abnormal glycosylation is characteristic of a number of disease states, including rheumatoid arthritis and cancer, which may result in quite different functions for oligosaccharides.

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